

A large, stylized, semi-transparent 'R' logo is positioned in the upper right quadrant of the cover. It consists of a solid circle on the left and a vertical bar on the right, with a curved line connecting them to form the letter 'R'.

MODERN RHEUMATOLOGY

Volume 29 Supplement 2019

ABSTRACT SUPPLEMENT

The 63rd Annual Scientific Meeting of
the Japan College of Rheumatology

April 15-17, 2019
Kyoto

Japan College of Rheumatology

JAPAN COLLEGE OF RHEUMATOLOGY ABSTRACT SUPPLEMENT

CONTENTS

ABSTRACTS

Presidential Lecture	S2
Presidential Symposium	S2
Special Symposium	S3
Symposium	S5
Educational Lecture	S32
Meet the Expert	S38
Luncheon Seminar	S45
Evening Seminar	S58
Annual Course Lecture Luncheon Seminar	S67
Workshop	S67
International Concurrent Workshop	S173
Poster Session	S211
English Poster Session	S393
AUTHORS' INDEX	S403

Presidential Lecture

PL

Talk about the future

Hisashi Yamanaka

Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: None

The 63rd Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology will be held at Kyoto from April 15th to 17th, 2019. And, two weeks after this meeting, Heisei era will be terminated. During the 30 years of Heisei era, rheumatology has made a tremendous progress. MTX was approved in 1999, the first biologics was approved in 2003, and the management of rheumatoid arthritis (RA) has been remarkably changed. IORRA cohort study conducted in Institute of Rheumatology, Tokyo Women's Medical University from 2000, has continuously recorded the changes of the patient's outcome in these years. Remission, once was a dream in Heisei 1st, however, has become reality in 55% of patients in Heisei 30th. Indeed, a dream has become a reality. Over the last 15 years, we have discussed the methodology how to achieve remission (Toward Remission). However, nowadays when the remission rate become over 50%, we should discuss how to optimize the treatment strategy in patients who has achieved remission (Beyond Remission). These include the reduction/discontinuation of drugs, pharmacoeconomical issues and others. However, along with the EBM centered medicine, we may have weighted toward the feasible, short term outcomes. Now, it is quite important to verify the long-term outcome of patients, since all clinical practitioner wishes the patients who have unfortunately suffered from chronic illness can spend a happy life. Furthermore, we have come to a point to consider the essential questions, how can we cure RA or how can we prevent the onset of RA. These are dreams now, however, someday dream will become reality, just as the speech of Martin Luther King, Jr., as 'I have a dream'. However, dream is a dream, reality cannot be achieved without the effort to have steps to the reality. First, we need to have dream, then to have steps toward the reality. As the president of JCR 219, I would like to take the opportunity of the Presidential Speech to emphasize the importance of the long-term outcome of patients, and the necessity to have dreams.

Presidential Symposium

PS-1

Future rheumatology – evolution, revolution and disruption

Gerd R Burmester^{1,2}

¹Department of Rheumatology and Clinical Immunology, Charite University Hospital, Berlin, Germany, ²Free University and Humboldt University of Berlin, Germany

Conflict of interest: None

Medicine as one of the most important disciplines for the welfare of the human being is currently at the brink of major disruptive changes. Examples include automated reading and evaluation of CT and MRI images in radiology, detection of skin tumors via smartphones in dermatology, automated evaluation of the retina, e.g. in diabetes or macular degeneration in ophthalmology and investigation of the gene expression profile for the planning of optimal chemotherapy in pathology. Rheumatology is one of the most successful disciplines in medicine, especially with regard to integrating novel diagnostic and therapeutic tools, which has dramatically changed the course of especially inflammatory rheumatic diseases. Nevertheless, also in rheumatology many changes can be envisioned. These include the dramatic new developments in systems biology with new technologies based on "big data" for complex biological systems that we encounter particularly in the multifactorial rheumatic diseases. These address the high volume of data composed of clinical data, "omics", sensors/wearables, speed of data generation and processing, variety (history, imaging, lab data, insurance data, omics, social media), veracity and value (utilizing the data to the interest of the patient). Novel approaches will allow insights into disease mechanisms and may lead to new diagnostic and therapeutic tools. The combination of clinical signs, novel biomarkers and imaging techniques will make diagnosis much easier, and telemedicine approaches will allow access to specialists around the world addressing also rare diseases. This lecture will cover some of these items and hopefully raise enthusiasm for the new developments in our exciting discipline.

PS-2

Rheumatoid Arthritis and the Mucosal Origins Hypothesis: Implications for Pathogenesis and Prevention

Michael V Holers¹, Yuko Okamoto¹, Kristine A Kuhn¹, Meagan Chriswell¹, Nickie Seto², Mariana J Kaplan², Ashley Visser¹, Marie Feser¹, Laura K Moss¹, Jennifer Seifert¹, Kristen J Polinski³, Jill M Norris³, Kristen M Demoruelle¹, Kevin D Deane¹

¹University of Colorado School of Medicine, Denver, USA, ²Systemic Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH, Bethesda, USA, ³Colorado School of Public Health, Department of Epidemiology, Aurora, USA

Conflict of interest: Yes

Individuals at high risk for the future development of seropositive rheumatoid arthritis (RA) can be identified by first-degree relative status to an RA proband or the presence in the serum of highly informative and predictive patterns of RA-related autoantibodies, including anti-citrullinated protein antibodies (ACPA) and/or at least two rheumatoid factor (RF) isotypes. Prior studies using HRCT imaging of the lungs have shown that a subset of serum RA-related autoantibody positive at-risk individuals exhibit small airways disease. Recent studies in at-risk individuals have demonstrated the presence of pulmonary mucosal inflammatory processes associated with local sputum ACPA production, as measured by cyclic citrullinated peptide 3 (CCP3) immunoreactivity. Sputum anti-CCP3 positivity was also associated with sputum hyper-cellularity as well as increased neutrophil extracellular traps (NETs). In further analyses, the proportion of sputum neutrophils undergoing NETosis containing citrullinated-histone H3 (cit-H3) was significantly higher in at-risk subjects. In addition, sputum ACPA and DNA-cit-H3 levels significantly correlated with local levels of key pro-inflammatory cytokines. Other mucosal sites in at-risk individuals, including the cervico-vaginal, periodontal and gut mucosa, also exhibited autoantibody production, inflammation and/or evidence of dysbiosis. With regard to environmental exposures, there was an apparent protective relationship of high levels of omega-3 intake on ACPA and RF positivity. A murine model has been developed

that demonstrates several features relevant to human disease pathogenesis. Finally, CCP3+ at-risk individuals are being enrolled in the StopRA prevention trial, which compares hydroxychloroquine to placebo on the development of biomarkers and classified RA. In sum, it is likely that future treatment of RA will include prevention and novel therapeutics targeting immune processes that are unique to the pre-clinical period of disease.

PS-3

How can we make discoveries in medicine? I learned from my experience

Naoyuki Kamatani
Gout Foundation of Japan

Conflict of interest: Yes

It is an important strategy to conduct medical research in accordance with consensus of the current academic society. However, it is equally important to aim for discoveries far away from it. I mainly conducted research following the latter strategy, so I will explain the method that can be recommended in such a case. The important thing is “to find a similar structure in different layers and discover a missing element in one layer”. The element that appears to be missing in one layer is often not actually absent, but is only difficult to recognize. Discovering it leads to big discoveries, and discerning its presence leads to good predictions. In 2015, I proposed a “six-layer structure” consisting of life, species, groups, families, individuals, and cells as a framework to make discoveries in medicine and biology. Each is a collection of elements with that layer’s name, and the previous layer is a set of subsequent layers. We reported MTAP deficiency of human cancer cells, the first reported result of a mutation of a tumor suppressor gene. That was based on the fact that genetic enzyme deficiency present in the individual layer and the species layer was missing in the cell layer. The first proposal for personalized treatment of cancer (for MTAP-deficient cancer) was based on the fact that antibiotics take advantage of the genetic difference between humans and bacteria in the species layer. Thus, we may be able to take advantage of the genetic difference between normal and malignant cells in the cell layer. A similar rationale was used in the development of cladribine, a drug for lymphocytic leukemia, and febusostat, a drug for gout. Now I am developing a new drug ATP enhancer whose idea originated from a similar rationale that the importance of energy (ATP) is, unlike things (compounds) and information (gene), not sufficiently recognized in the cell layer despite the fact that the importance of the three items are well recognized in the society (population layer).

Special Symposium

SS1-1

From “The Lady of the Lamp” to “The Lady of the Stamp” – Nightingale’s life from the viewpoint of the “gender equality” era –

Okiko Miyake^{1,2}

¹Baika Women’s University, Japan, ²International Institute for Children’s Literature, Osaka, Japan

Conflict of interest: None

As female role models, Florence Nightingale, Marie Curie and Helen Keller have enjoyed popularity beyond the times. Unfortunately, no such role models can be found in Japanese history, so I will consider Nightingale, who contributed to medical development, as a case for “gender equality”. Nightingale (1820-1910) worked with 38 nurses during the Crimean War. This lasted for about 2 years in the mid-30s, but has brought her international fame. She published “Notes on Nursing” at the age of 39 and established the Nightingale Nursing School the following year. However, she became ill after that and spent most of her time in bed until she passed away at the age of 90. Biographies aimed at children described Nightingale as something of a “saint”; however her work after becoming ill differs from her earlier work. Based on her experience, she recorded details descriptions of the hospitals and the life conditions of soldiers. Using these descriptions and statistical analyses, she gave an overview of the situation at the front lines. She proposed strategies for improving hygiene in military settings and hospitals. As such, she became a relentless “social reformer”. After her death, numerous biographies have been published based on the remaining records and about 12,000 letters. Mary Seacole (1805-1881), a Creole woman, was active during the same era as Nightingale. During the Crimean War, she opened the British Hotel near the frontline, where she served meals and provided folk remedies. These achievements have been largely ignored, but they are starting to be reevaluated now. I would like to investigate Nightingale as the pragmatist, from “saint” to “reformer”, while also considering Seacole’s contributions. [References] Sir Edward Cook: The Life of Florence Nightingale, 1913 Lytton Strachey “Florence Nightingale” Eminent Victorians, 1918 Cecil Woodham-Smith: Florence Nightingale, 1820-1920, 1950 Mary Seacole: Wonderful Adventures of Mrs Seacole in Many Lands, 1857

SS2-1

Systemic autoimmune response to modified proteins as a biomarker – ACPA and more

Gerd R Burmester^{1,2}

¹Department of Rheumatology and Clinical Immunology, Charite University Hospital, Berlin, Germany, ²Free University and Humboldt University of Berlin, Germany

Conflict of interest: None

One of the most important serological discoveries in the field of rheumatology in recent years has been the characterization of autoantigens in RA that contain the amino acid citrulline. The starting point for this discovery was the identification of the target antigen of the anti-keratin antibodies (AKA) first described in 1979, which have a high specificity for RA. The target antigen is fillagrin, a protein specifically expressed in keratin-producing epithelial cells with structure-forming functions. Since fillagrin is only expressed in epithelial cells and neither in the joint nor in other organs, this finding could not initially be interpreted pathogenically. Subsequent studies showed that only the citrullinated forms of fillagrine were recognized by the AKA. Citrullination of proteins takes place enzymatically by deimination of arginine to citrulline and represents a posttranslational modification, which causes a change in the charge state of the protein. This leads to changes in the three-dimensional structure of the proteins and the associated antigenic properties. Citrullination plays an important physiological and biochemical role in the regulation of cell differentiation and programmed cell death (apoptosis). Due to the difficulties in isolating the pure fillagrine, only the relevant citrullinated epitopes were used to develop a test using synthetic peptides as antigens, which were given a ring structure by an intramolecular disulfide bridge binding, giving the citrulline epitope a prominent position. With these cyclic citrullinated peptides (CCP) as antigens in the assay routinely

used today, an improvement in specificity to 96 to 98% could be achieved with approximately the same sensitivity. In the meantime, several studies have shown that anti-CCP antibodies not only have a high specificity but also a high predictive value for an erosive course of the disease and thus have a prognostic value. Other citrullinated antigens are fibrin and fibrinogen. Close cross-reactivity between fillagrin and citrullinated fibrin has been confirmed by investigations with citrullinated peptide derivatives of both proteins. Some publications have described a high diagnostic specificity and sensitivity for the detection of anti-citrullinated fibrinogen antibodies in RA patients. Using ELISA, a sensitivity of about 75% with a specificity of 98% for RA was achieved. Thus, the diagnostic properties of this antigen in rheumatoid arthritis are comparable to the CCP antigen. In addition, citrullinated fibrinogen offers comparable sensitivity and specificity to CCP in early rheumatoid arthritis. Both markers have been described as good predictors of radiological disease progression. Furthermore, a close association with the occurrence of positive anti-CCP antibodies in patients with rheumatoid arthritis was confirmed. An interesting citrullinated autoantigen is the citrullinated form of α -enolase, an enzyme that plays a role in glycolysis. The citrullinated α -enolase was found together with other citrullinated antigens in synovial tissue in patients with rheumatoid arthritis. In addition, citrullinated vimentin was described as a relevant autoantigen, interestingly with expression in synovial tissue. Citrullinated vimentin is presumably the target antigen of the already known anti-Sa antibodies with a high specificity. Direct evidence that ACPA contribute to experimental inflammation is provided by showing that antibodies specific to citrullinated fibrinogen enhance arthritis in a mouse model. Moreover, the presence of anti-CCP antibodies and not RF was found to be correlated with the shared epitope (SE) containing HLA-DRB1 alleles. Interestingly, local production of ACPA in the synovium is inferred from 1.4-fold higher titer in synovial fluid versus serum. Recently, it was demonstrated that through a combination of intracellular protein citrullination in the osteoclast as well as autocrine production of interleukin 8 (IL-8), ACPA can enhance osteoclastogenesis in human monocytes in vitro. Furthermore, in an IL-8 dependent manner, ACPA induced both bone loss and pain in mice. Another major post-translational modification of proteins in RA is carbamylation, where preferentially lysine residues are converted to homocitrulline in a chemical reaction mediated by isocyanate that interacts with the ϵ -amino group of lysine forming a new class of autoantigens with the induction of anti-Carb antibodies. In humans, isocyanate is formed by the decomposition of urea into ammonia and cyanate, which is consequently transformed to its reactive form, isocyanate. Thus, hyperuremia, which associates with chronic kidney failure, promotes the formation of isocyanate. In addition to hyperuremia, smoking also leads to isocyanate formation, and thus thiocyanate, a metabolite of cyanide that is present in cigarette smoke, represents another precursor for isocyanate. In fact, smoking has been identified as a prominent environmental risk factor for RA. During inflammation, myeloperoxidase is released from neutrophils and utilizes H₂O₂ to oxidize thiocyanate to cyanate that subsequently promotes protein carbamylation at sites of inflammation. In addition to RF and ACPA, anti-CarP antibodies precede the onset of RA, and their presence is an independent risk factor in arthralgia patients for the development of RA. Moreover, anti-CarP antibodies are associated with disease development - thus, the sensitivity for these antibodies in pre-symptomatic individuals is 13.9% and increased to 42.2% in established RA. This lecture will address the utility of antibodies against modified proteins, particularly in rheumatoid arthritis, in the expanding universe of the "auto-immunome."

SS2-2

Imaging in diagnosis and monitoring of rheumatic and musculoskeletal diseases

Annamaria Iagnocco

Università Degli Studi di Torino, Italy

Conflict of interest: Yes

Imaging techniques are crucial tools in the diagnosis and monitoring of RMDs. X-Ray is the reference standard in many cases, particularly for structural damage assessment, but Doppler ultrasound (DUS) and MRI are increasingly utilized for both inflammatory and structural lesions evaluations. Recently, interesting results have also been obtained with the use of new modalities and hybrid techniques in specific RMDs. In RA, DUS or MRI are used to improve the diagnosis and monitor disease ac-

tivity. The periodic evaluation of joint damage by x-Ray is still the gold standard, however MRI and DUS are more responsive to change and should be used to monitor inflammation and structural progression. In patients with cervical involvement, X-Ray and MRI are performed for detecting and monitoring functional instability. In axial SPA, x-Ray is recommended as the first imaging method to diagnose sacroiliitis. MRI is performed if the diagnosis cannot be made radiographically and for assessing and monitoring inflammatory activity. For axial structural damage follow-up, x-Ray is still the reference method. When peripheral SPA is suspected, US or MRI are used to detect peripheral enthesitis but also for assessing arthritis, tenosynovitis and bursitis. In terms of monitoring of peripheral involvement, US and MRI are performed for disease activity, while x-Ray is used for structural damage progression. In OA, imaging is not required to make the diagnosis in typical disease presentation. However, in atypical cases, imaging is useful to confirm or make alternative diagnosis. Routine imaging in OA follow-up is not recommended, but it is used if symptoms rapidly change and disease unexpectedly progresses. If imaging is needed, x-Ray should be used as the first tool. However, soft tissues assessment is recommended by US and MRI while more useful information on bone involvement is given by CT and MRI.

SS2-3

Treatment strategy for pre-RA and early RA

Johannes W Bijlsma

University Medical Center Utrecht, The Netherlands

Conflict of interest: Yes

The lecture will discuss two areas: prevention of RA and treatment of (very) early RA. In both areas we will focus on two main questions: A: Can we **prevent** RA Question one: are we presently able to reliable diagnose pre-RA Question two: if so, are we able to intervene in order to prevent RA becoming active B: Can we **treat** early RA effectively ? Question one: are we presently able to reliable diagnose early RA Question two: if so, are we able to effectively treat early RA Up to date evidence will be discussed. The main message will be that prevention is a good area for continued research, but not yet for clinical practice; on the other hand, early diagnosis and effective treatment should be clinical practice anno 2019. This message is in line with the EULAR campaign: Don't delay, connect today.

Symposium

S1-1

Optimal rheumatic care through a multidisciplinary approach -From the physicians' point of view-

Hideko Nakahara

Division of Allergy, Rheumatology and Connective Tissue Diseases, Department of Internal Medicine, NTT West Osaka Hospital

Conflict of interest: None

The prevalence of therapeutic agents such as biologics has significantly broadened treatment options, allowing the implementation of T2T strategies with the goal of achieving remission. However, remission may not always be attained or sustained due to complications or a host of other reasons. Prevention and early detection of infection and maintaining adherence to treatment are crucial for implementing the appropriate treatment. Psychological and social support and physical care are another important factor in the treatment plan. In the past, rheumatic care focused primarily on providing medical treatment and dealing with symptoms; however, in recent years, the approach to treatment has taken on a broader scope. Patients must be considered not only as "patients" with a disease, but also as "people" who live their lives with the burden of an illness. Remission should be considered not only from the point of view of relieving symptoms, but also making sure that patients are able to live fulfilling lives. The overarching principles of EULAR recommendations for patient education are: "patient education is designed to support and enable people to manage their life and optimize their health and well-being" and "communication and shared decision making between people and healthcare professionals are essential". Doctors alone are not able to provide such supports, making interdisciplinary cooperation crucial for providing effective treatment. As such, sharing information is vital for enabling multidisciplinary cooperation. According to the updated T2T recommendations, "the involvement of the patient in making decisions and the type of information provided should be recorded, along with the treatment target" and "the agreed and documented target should be visible in the patient records to every health professionals involved in the monitoring". In this presentation, I would like to consider how we as health professionals can provide the best possible care to our patients.

S1-2

The best therapy for rheumatoid arthritis (RA) patients: A pharmacist's view

Keiko Funahashi

Clinical Research, Matsubara Mayflower Hospital

Conflict of interest: None

The importance of team medical care is being recognized, and within each field, specialist pharmacists monitor side effects, avoid serious events and are expected to recommend prescriptions for best results. Team medical care is usually talked from an in-hospital perspective, but it is necessary to include drug dispensary pharmacists because most RA patients are managed by the outpatient department in use of self-injection or oral medicine. Adherence is of prime importance. Poor adherence causes lack of efficacy, and further medication by staff unaware of adherence issues and thus has a socio-economic effect as well. The pharmacist often must involve family or caregiver to reveal the causes of the poor adherence. Secondly, it is important to manage side effects. Monitoring the occurrence and severity is important, but just as important are team communication and patient education. For example, herpes zoster, which is induced by tsDMARDs, cause sequelae if treatment is delayed. It is necessary to confirm side effects at each examination, but also inform patients how to contact us on a holiday. Half of all RA patients aren't examined by a rheumatic specialist. The pharmacist has to consult with the doctor, if there is a question about usage of drugs and suggest a change of drug to improve adherence. In addition, in the face of an aging society, the issues of polypharmacy, renal function decline, cognitive decline and frailty need to be addressed. It is important for the pharmacist to investigate the problem that is not clear on at the hospital side. The generalist pharmacist has knowledge of not only the anti-rheumatic drug but also other drugs. The aging RA patient has many problems, but pharmacists can offer a multi-faceted approach to drug use in team medical care.

S1-3

Physical therapy in the era of biological DMARDs ~Preventing sarcopenia~

Shinichiro Fujita¹, Ryoza Harada², Kazuhiko Ezawa³, Koji Takasugi³, Misuzu Fujimori³, Kie Inoue¹, Wataru Yamamoto⁴, Keiichiro Nishida⁵

¹Department of Rehabilitation, Kurashiki Sweet Hospital, Kurashiki, Japan, ²Department of Orthopedics, Rheumatic Disease Center, Kurashiki Sweet Hospital, Kurashiki, Japan, ³Department of Internal Medicine, Rheumatic Disease Center, Kurashiki Sweet Hospital, Kurashiki, Japan, ⁴Department of Health Information Management, Kurashiki Sweet Hospital, Kurashiki, Japan, ⁵Department of Orthopedics, Okayama University Hospital, Okayama, Japan

Conflict of interest: None

Pharmacotherapy, surgical therapy, rehabilitation and care has been the basis of therapy for patients with rheumatoid arthritis. Exercise therapy, occupational therapy, patient education have been recommended for the treatment of the rheumatoid arthritis by the guidelines, Japan College of Rheumatology. Advanced drug treatment in recent years has improved the control of disease activity, and has been easier to achieve clinical remission. Likewise, advanced surgical techniques makes it easier to achieve structural remission, and has been improving physical function in patients with rheumatoid arthritis. In such situations, rehabilitation has been also changing to achieve functional remission. In recent years, the concept of senile syndrome such as flail, locomotive syndrome, sarcopenia etc. has been proposed for elderly people. In patients with rheumatoid arthritis, skeletal muscle mass decreases with low activity and inflammatory decomposing protein. Since patients with high disease activity have low skeletal muscle mass, they have been required to improve drug therapy. Decreasing skeletal muscle mass increases the risk of falling fractures. Life prognosis of patients with rheumatoid arthritis has improved and, flail and sarcopenia should be considered in rehabilitation treatment to the elderly patient with rheumatoid arthritis. Patients with rheumatoid arthritis often have joint deformity, decreased body function, decreased skeletal muscle mass, and decreased muscle strength, and are likely to become sarcopenia. Rehabilitation improve the physical function and activity of daily living of patients with rheumatoid arthritis and reduce the risk of falling fractures. As a part of treatment, we measure the muscle mass of patients. When the muscle mass value is low, we practice appropriate exercise for the patient and support nutritional status of the patient. By such treatment, we are trying to prevent sarcopenia and improve the physical function of the patient with rheumatoid arthritis.

S1-4

Social security system for recovery of the patients with rheumatoid arthritis, "From now on"

Noriko Mawatari^{1,2}

¹Kanazawa City Regional Comprehensive Support Center Kamiaraya, ²School of Regional Development Studies, College of Human and Social Sciences, Kanazawa University

Conflict of interest: None

The advancement of medicine drastically changed the course of treatment of rheumatoid arthritis. Nowadays specialists can diagnose and intervene rheumatism at an early stage and prevent joint destruction and deformity. Multidisciplinary team approach brought long term improvement of quality of life of the patients. However, current social welfare system has not been adequately updated to address the current needs of the patients. I would like to present the overview of transition of treatment after the year of 1983, the history of patients' support group, and the changes of social security system and welfare policies and the relationship among them, based on literature review. I then will raise political subject from social worker's perspective, especially on the need to improve medical service coverage.

S1-5

Psychological support to person with Rheumatoid Arthritis

Takuro Motonaga¹, Mika Mori², Mayuko Mabuchi³, Yoshie Sakai⁴

¹Teikyo University, Japan, ²Jikei University School of Medicine, Japan, ³Tokyo University of Agriculture and Technology, Japan, ⁴Atomi Univer-

sity, Japan

Conflict of interest: None

Various types of psychological supports are implemented to person with Rheumatoid Arthritis (RA). Psychiatrists might treat the person with comorbid psychiatric disorders. Clinical psychologists might approach when the person want to receive psychotherapy. But Various health professionals including medical doctors and nurses already implement various types of psychological supports through their professional intervention to the disease. We developed multidisciplinary educational programs for nurse concerning psychological support on this view point. The program focuses on nurses' practices that may have good effect for their mental health. The program also considers how to implement psychological support on very busy practice environments. The psychological supports have a goal to enhance their QOL. The supports also have a goal to higher quality of medical treatments of RA in medical facilities. Clear and high goal setting, for example 'Treat to Target, needs good relationship between person and medical staffs, which may be provided through patients' participations. Psychological supports become more important when medical staffs will implement 'Treat to Target.' We would like to share these ideas among medical doctors and other health professionals including nurses, Psychological support is an important concept when various health professionals collaborate each other on the treatment of RA.

S1-6

Knowledge and Skills to Support People Living with Chronic Illness

Yuriko Kuroe

Gifu College of Nursing, Japan

Conflict of interest: None

No one can avoid the eternal themes of birth, aging, sickness, and death even if our situations change dramatically, We all face the prospect of getting sick, and any illness can become chronic, so anyone living in modern society has the possibility of living with chronic illness. In this situation, we must continue over the course of our lives to manage our illnesses with various measures 24 hours a day, 365 days a day, not resting even for a day. At times, life with illness seems lacking in color, quarrels arise within the family, we get irritated at a body that does not move as it is supposed to and anxious about how to control it properly. Not knowing who to consult at such times may also affect us. Who will listen to my worries when things are going badly? Who will consider my situation holistically including my daily life and specific medical treatment methods? Where are these people? M.L. Jaquinta and colleagues reported the following in their report about lived experience of people living with RA: Grieving while growing, Persuading self and others of RA's authenticity, Cultivating resilience, Confronting negative feeling, Navigating the healthcare system, masterminding new lifeway. When supporting people with chronic illness, we must know, for example, what living with rheumatoid arthritis is like and approach it with the diverse outlooks held by the people living those lives. This is because chronic illness exhibits various aspects as time goes by, and these aspects change dynamically. It is important to know the characteristics of this chronicity and fully provide the necessary support in each transition phase. I would like everyone to think about supporting people living with chronic illness. 1. Knowledge to support people living with chronic illness: rheumatoid arthritis 2. Skills to support people living with chronic illness: Speaking about and listening to life stories.

S2-1

Sonoanatomy make it possible to improve the comprehension of musculoskeletal disease of connective tissue disease

Kenta Misaki

Department of Rheumatology, Kita-Harima Medical Center

Conflict of interest: Yes

There is a traditional dictum from famous general (Shogun): 'Fill up the outer moat first' means that it is necessary a roundabout approach to achieve the aim. We Rheumatologist have been also faced the challeng-

ing of combating to refractory connective tissue disease (CTD) as well as invulnerable castle. Biologics (Bio) was approved under our medical insurance in 2003. Additionally many useful examination tools or makers have been applied in clinical setting. Thanks to those, it is possible for Rheumatologist to rival intractable CTD more directly, and to proceed the dairy medical practice in a favorable environment. However it seem that there are some trends to capture the tower keep first for the purpose of achievement: for example meaningless abuse of Bio, exhaustive measurement of specific antibody and overconfidence of radiographic imaging procedures. Systematic assessment based on physical examination is crucial to make a diagnosis and manage the disease activity in particular for seronegative cases. I used to be a Rheumatologist mentioned above just after junior resident, especially about musculoskeletal anatomy, to have left the assessment to Orthopedics because I believed the knowledge of anatomy is for surgeons until my study abroad for musculoskeletal ultrasound (MSKUS) to Spain. The fact that Rheumatologists in Europe have a detailed knowledge about anatomy as well as Orthopedics revealed the importance of filling up the outer moat. As MSKUS based on anatomy is called sonoanatomy, sonoanatomy make it possible to make an unexpected diagnosis, have the conference for minute part surgery in Europe. In this symposium, I am going to introduce the educational system of sonoanatomy in EULAR and the utility of MSKUS for our dairy medical practice with actual cases. Additionally, I want to emphasize that Sonoanatomy never fail to improve our comprehension of CTD and assessment to differential diagnosis.

S2-2

Does the musculoskeletal ultrasound examination improve the physical examination skill?

Michihiro Ogasawara

Department of Internal Medicine and Rheumatology, Juntendo University Faculty of Medicine, Tokyo, Japan

Conflict of interest: None

The physical examination technique is a basic technique used for diagnosis and disease evaluation in musculoskeletal diseases typified by rheumatoid arthritis. Diagnosis, treatment strategy and outcome could be differ depending on the judgment result, so its technical capability and the judgment result must be more accurate and highly reproducibil. In the evaluation of synovitis of rheumatoid arthritis, presence or absence and degree of joint tenderness and swelling, and these numbers are regarded as useful activity judgment findings. The causes of joint pain are roughly classified into inflammatory, degenerative and psychogenic, but since either can cause tenderness, it is difficult to distinguish the three from the tenderness. However, as an advantage of tenderness judgment, it is possible to identify an anatomical lesion site by searching for a tender portion by using the pain awareness as a guide. On the other hand, swelling joint includes synovial fluid accumulation and synovial thickening. Synovial fluid accumulation is not seen in psychogenic joint pain, but since it is recognized in both degenerative as well as inflamed joint pain, discriminatory ability in differential diagnosis of the two is insufficient. Therefore, in order to judge whether it is inflammatory or not by clinical examination, it is important to not only detect the presence or absence of joint swelling, but also to detect the presence or absence of specific synovial thickening due to inflammatory arthritis. However, in fact, the sensation of synovial thickening is difficult to distinguish from soft tissues such as subcutaneous fat, compared to the sensation of synovial fluid which is more easily judged, so it is often difficult to make judgments. On the other hand, the sensation of hotness and redness of the joint suggests the presence of synovitis with high sensitivity if it is in the acute phase, but the sensitivity decreases after the acute phase, and the detectability of synovitis becomes insufficient. Therefore, in some cases / joints that are difficult to judge synovitis, in order to more accurately judge synovitis, it is necessary to make correct judgment and judgment correction of clinical assessment using musculoskeletal ultrasound examination. We reported in the past that autofeedback of ultrasound image after physical examination will improve the examination technique. In order to utilize the musculoskeletal ultrasound as a learning tool for improving the physical examination and to contribute widely to the examination procedure improvement, it is considered that future identification and dissemination activities of higher utilization methods with higher relevance are needed.

S2-3

Is Musculoskeletal Ultrasound Necessary for Monitoring in Patients with Rheumatoid Arthritis?

Shin-ya Kawashiri^{1,2}, Yushiro Endo², Atsushi Kawakami²

¹Department of Community Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ²Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: Yes

Musculoskeletal ultrasound (MSUS) is excellent in the detection of synovitis in patients with rheumatoid arthritis (RA) and the synovitis score, especially the power Doppler (PD) score by MSUS well reflects the clinical disease activity. We have used MSUS for therapeutic monitoring from 10 years ago. In many patients, clinical disease activity and MSUS synovitis score fluctuate in parallel, but deviations of each score are observed in some patients. It is also known that residual synovitis is detected by MSUS at a constant frequency in patients achieving clinical remission. In addition, residual synovitis is a risk of joint destruction and relapse. Therefore, accurate evaluation of disease activity using MSUS seems to be important for improving patient's prognosis. However, in the ARCTIC trial ¹⁾ and the TaSER trial ²⁾ conducted in Europe, additional value in strengthening treatment according to disease activity by periodic PD evaluation compared with clinical evaluation was not demonstrated. In the first place, there are still many issues in monitoring, such as patients requiring monitoring, scoring system (assessment joint/ assessment lesion), assessment timing (periodic or necessary), assessment frequency and so on. We have been promoting the cohort study for patients who introduced molecular targeted therapeutic drugs (bDMARDs and tsDMARDs) in collaboration with multi-center of hospitals in Kyushu region from 2013 ³⁾. In this study, we have evaluated disease activity every 3 months by MSUS, and have analyzed associations between MSUS score, clinical disease activity, radiographic change, and serum biomarkers. In this symposium, we will outline the usefulness of monitoring by MSUS in patients with RA based on the results of our cohort study and latest evidence. References; 1) BMJ 2016; 354: i4205, 2) Ann Rheum Dis 2016;75:1043, 3) Arthritis Care Res (Hoboken). 2018 Feb 26. doi: 10.1002/acr.23551.

S2-4

Ultrasonographic pathological findings and treatment strategies in patients with psoriatic arthritis

Tadashi Okano¹, Kentaro Inui¹, Koji Mandai¹, Yutaro Yamada¹, Setsuko Takeda², Yuko Yoshida², Emi Yamashita², Asami Fujii², Yuko Sugioka³, Tatsuya Koike^{3,4}, Hiroaki Nakamura¹

¹Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan, ²Central Clinical Laboratory, Osaka City University Hospital, Osaka, Japan, ³Center for Senile Degenerative Disorders (CSDD), Osaka City University Graduate School of Medicine, Osaka, Japan, ⁴Shirahama Foundation for Health and Welfare, Wakayama, Japan

Conflict of interest: None

CASPAR classification is usually used for the diagnosis of psoriatic arthritis (PsA), but it is defined that there are inflammatory conditions such as arthritis/enthesitis/spondylitis as the premise. However, it is sometimes difficult only by clinical examination to distinguish whether joint symptoms are due to inflammation or degenerative change. The usefulness of ultrasonography (US) in the diagnosis of PsA has been reported, especially in early diagnosis and differential diagnosis with other rheumatic disease. Moreover, by using US, physicians can detect subclinical inflammation even in patients without obvious swelling or positive inflammatory findings. There are some specific findings to make differential diagnosis with rheumatoid arthritis (RA). In RA, intra-articular synovitis is the main pathology, whereas intra-articular synovitis occurs secondary to tendon and ligament enthesitis in PsA. Reflecting this mechanism, in peripheral joint of PsA, US inflammatory findings with Doppler signals are often found not only in the intra-articular synovium but also in the tendon enthesis or subcutaneous tissue. In addition, inflammation around the flexor tendon and extensor tendon is also found in patients with PsA. In extensor tendon, inflammation may be observed

around the tendon at the MCP joint level and slightly proximal to the metacarpal head. It is called PTI (peritenon extensor tendon inflammation) pattern. Furthermore, inflammatory findings of large entesis such as enthesitis of the extensor carpi radialis brevis tendon to the humeral lateral epicondyle and enthesitis of the Achilles tendon to the calcaneus are the most important findings in US examination for PsA. US has huge utility comparing with traditional methods for diagnosis such as clinical examination, laboratory test and conventional radiography. In this presentation, we demonstrate the pathological specific findings and treatment strategy of PsA with typical US images.

S2-5

Present practice and future prospects of joint ultrasonography by sonographers

Mutsumi Nishida^{1,2}, Hitoshi Shibuya¹, Takanori Teshima²

¹Diagnostic Center for Sonography, Hokkaido University Hospital, ²Division of Laboratory and Transfusion Medicine, Hokkaido University Hospital

Conflict of interest: Yes

[Objectives] Early detection of synovitis is critical for arthritis clinic. Ultrasonography (US) is capable to detect early rheumatoid synovitis. The aim of this study was to report present practice and future prospective of joint US by sonographers. [Methods] Questionnaire survey was done for medical practitioners according to the following items; 1. Professions, 2. Scale of facilities, 3. Presence or absence of performing joint US, 4. The number of joint US per month, 5. Professions performing US, 6. Available or not available of performing US in the future, 7. Interest for joint US, 8. Problems [Results] Response rate was 8.9% (82/926), 1. Clinical technologists / Radiographers 91.5 / 7.3%, 2. Medical centers / Clinic / Hospitals (<200) / Hospitals (≥200 / Others 14.6 / 14.6 / 13.4 / 28 / 40.2 / 3.7%, 3. Joint US Presence / Absence / Do not know 45.1 / 52.4 / 2.4%, 4. The number of joint US; <50 exams / ≥50 exams 95/5%, 5. Sonographers / Physicians / Sonographers and Physicians 48.6/24.3/27%, 6. Available / Not available / Do not know 9.1/41.9/50%, 7. Interesting / Not interesting / Do not know 52.3/11.4/ 36.4%, 8. Problems; No trainers/ No knowledge of disease / Poor understanding of anatomy and scanning methods/ No order of US / No certified system for joint US sonographers / Time consuming / Others 46 / 43 / 31 / 25 / 8 / 8 / 4. [Discussion and Results] The ratio of facilities performing joint US were nearly half of them, the number of US was <50/month. Half of US were performed by sonographers, and physicians, and sonographers showed nearly 30%, and physicians performed the rest of them. Even not available US in the present, more than half of sonographers interested in joint US. Once problems are solved, sonographers can perform joint US in the near future. Establishing training and certification systems for sonographers and make the exam time shorten are needed to be solved.

S2-6

Development of the guidelines for clinical management using musculoskeletal ultrasound

Kei Ikeda

Department of Allergy and Clinical Immunology, Chiba University Hospital

Conflict of interest: None

Japan College of Rheumatology-Committee for the Standardization of Musculoskeletal Ultrasonography (JCR-CoSMUS) has published the guidelines of musculoskeletal ultrasound scanning for rheumatoid arthritis (RA) in 2011 and the guidelines of interpreting musculoskeletal ultrasound images for RA in 2014. However, for the further spread and advance of this technique, a larger number of technicians/technologists need to perform musculoskeletal ultrasound as they do in the other areas such as cardiac and abdominal ultrasound in Japan. For this purpose, a simple core set that can be easily learned and performed in daily practice needs to be developed. This core set should focus on the synovial Doppler signal, which is shown to be reproducible, and should be comprised of a small number of joints with simple anatomical structure, in which synovitis frequently occurs in RA. Moreover, strategies based on this ultrasound core-set need to be established, which rheumatologists can uti-

lize in the diagnosis and the treatment guide. Therefore, the Japan Agency for Medical Research and Development (AMED) project “Optimization and standardization of ultrasound-based management of rheumatoid arthritis”, together with JCR-CoSMUS, is now developing the guidelines for the management of RA using musculoskeletal ultrasound in order for the technicians/technologists to be more deeply involved in this technique. In this presentation, the current progress will be reported.

S3-1

Treatment strategies of the rheumatoid foot based on its pathological condition

Takumi Matsumoto

Department of Orthopaedic Surgery, Faculty of Medicine, The University of Tokyo

Conflict of interest: None

Improvement in rheumatoid arthritis (RA) control due to the development of powerful disease-modifying anti-rheumatic drugs has led to a decreased involvement and surgery of the large joints. This shifting allows both the patients and physicians to focus on the foot, which have been prone to be put aside behind other priorities. Appropriate control of the disease activity and improvement of bone fragility in RA patients enable the surgeons to adopt the joint-preserving surgeries nowadays, which was generally not applicable before the era of biologic agents. In other words, we are facing an era of being able to apply a variety of techniques, which has been accumulated through the experience in treating foot and ankle of other pathologies than RA, to RA foot. Stereotypical strategy such as resection arthroplasty for forefoot deformity and tibiotalocalcaneal fusion for hindfoot deformity, which were the gold standards in a couple of decades ago, has become a thing of past. On the other hand, a wide variety of involved sites and deformities make surgeons feel it difficult to select an appropriate treatment plan for individual cases. Other difficult point that makes it difficult to comprehend RA foot is that the progression of RA foot deformity is affected by both factors including disease activity and mechanical load. In addition to the knowledge about the pros and cons of each surgical technique, understanding the pattern of destruction and its future prospect is essential to construct an appropriate strategy for RA foot. This lecture will give an outline about the patterns of destruction in RA foot and their characteristics, and will provide a treatment strategy based on estimated prognosis of each pattern. Especially, this lecture will highlight the destructive pattern starting from mid-foot joints as a pattern worth heeding because this pattern generally progresses to flat foot in just a couple of years since its involvement without any marked symptom.

S3-2

Total assessment and management of loading alignment against rheumatoid foot deformity

Makoto Hirao¹, Kosuke Ebina¹, Hideki Tsuboi², Takaaki Noguchi³, Shigeyoshi Tsuji³, Yasuo Kunugiza⁴, Koichiro Takahi⁵, Hideki Yoshikawa¹, Jun Hashimoto³

¹Department of Orthopedics, Osaka University Graduate School of Medicine, ²Orthopaedics/Rheumatology, Osaka Rosai Hospital, ³Orthopaedics/Rheumatology, National Hospital Organization, Osaka Minami Medical Center, ⁴Department of Orthopaedics, JCHO Hoshigaoka Medical Center, ⁵Orthopaedics/Rheumatology, National Hospital Organization, Toneyama Hospital

Conflict of interest: None

Patients with rheumatoid arthritis (RA) often suffer from destructive changes of the ankle joint and valgus hindfoot simultaneously. It is plausible to understand that correction even in hindfoot could also improve the displacement of weight-bearing line passing the ankle joint. Thus, first, we selected hindfoot correction to preserve the ankle joint mobility, and then ankle pain has been observed. Before performing the total ankle arthroplasty (TAA), such concept to correct the hindfoot firstly is very important. We had also experienced the cases that hallux valgus (HV) deformity was improved after hindfoot realignment. On the other hand, there were cases with the progression of valgus hindfoot showing the recurrence of HV deformity after forefoot surgery. Varus hindfoot is also

troublesome to cause the recurrence of lesser toe MTP joint subluxation after metatarsal shortening offset osteotomy. So valgus correction and midfoot osteotomy are also necessary to obtain the plantigrade position. Taken together, correcting of the displacement of the loading axis not only between the hip joint and hindfoot, but also between hindfoot and forefoot is very important against comprehensive RA foot deformity.

S3-3

Combination with EF-Fix for distal tibial fracture of Rheumatoid arthritis

Takeshi Kashiwagura¹, Moto Kobayashi², Natsuo Konishi², Masakazu Urayama², Hiroki Ito², Takayuki Tani², Tsutomu Sakuraba², Toshiaki Aizawa², Hidekazu Abe², Norio Suzuki², Keiji Kamo², Hiroshi Aonuma², Yusuke Sugimura², Tetsuya Kawano², Yosuke Iwamoto², Yoshiaki Kimura¹, Manabu Akagawa¹, Ikuko Wakabayashi³, Koji Nozaka⁴, Naohisa Miyakoshi⁴, Yoichi Shimada⁴

¹Department of Orthopedic Surgery, Akita City Hospital, ²AORA (Akita Orthopedic Group on RA), ³Department of Rehabilitation Medicine, Akita City Hospital, ⁴Department of Orthopedic Surgery, Akita University Graduate School of Medicine

Conflict of interest: None

Along with advances in drug therapy, the prognosis of patients with rheumatoid arthritis (RA) is also prolonged. In RA, besides having bone fragility in the disease itself, it further exacerbates with aging, so the ADL improves, the risk of injury to fractures increases. Fractures around the ankle often occur, and in RA cases it becomes more complicated. We experienced a case in which Ilizarov external fixation was used for a distal tibial fracture of an elderly RA patient. There are 3 cases, all cases are females. Surgery by external fixation was chosen due to small distal bone fragment, during biologic administration, complications and internal antithrombotic drugs, and having bone fragility. In two cases, the MATILDA method was used, in one case closed restoration using Olive wire was performed, and it was fixed using Ilizarov external fixation. After the operation patients walked according to the pain, leaving bed on average 3.3 days, parallel bar walking 5.3 days, discharge from 70.7 days. Bone fusion was obtained in all cases. In the case of RA, it has bone fragility, strong fixation is necessary, there is symmetrical joint disorder, there is a concern of contralateral joint disorder at one side therapy release. Because of many mergers of obstacles, it can be cited that it is difficult to adjust the load using crutches. By preliminary combined loading at the early stage, functional deterioration can be minimized. In many cases, ADL declines with trauma as a trigger, and it is useful to aim for early exit from the bed to prevent further exacerbation in cases already having dysfunction like RA. External fixation surgery is entering a super aged society, it becomes a powerful option of injury of lower limb in RA.

S3-4

Therapeutic strategy of joint preservation for ankle in RA: Distraction arthroplasty

Tomoyuki Nakasa, Yasunari Ikuta, Yusuke Tsuyuguchi, Yuki Ota, Munekazu Kanemitsu, Nobuo Adachi
Department of Orthopaedic Surgery, Hiroshima University Hospital

Conflict of interest: None

The treatment for the rheumatoid arthritis (RA) has been significantly developed. However, surgery for the damaged joint is still performed to improve the activities of daily living. Although joint preservation surgery for the fore foot deformity in RA has been widely recognized, arthrodesis or total ankle replacement still plays an important role in the ankle joint of RA. For osteoarthritis (OA) of ankle, various surgical treatments are chosen depending on age, activity and stage. Arthrodesis and total ankle arthroplasty are usually performed for the end stage of OA. Especially, arthrodesis is often performed for highly active cases, but there are many problems as it may interfere with daily living due to limitation of range of motion. Distraction arthroplasty (DA) is the method to enlarge joint space by external fixator with articulation and combined with arthroscopic microfracture. This technique has been performed for the end stage of OA ankle, but we performed DA for RA patients who denied to be performed arthrodesis. [Case 1] A 34-year old female who was treated by

methotrexate, etanercept for 5 years. Her left ankle pain increased and joint space of ankle was disappeared. DA was performed, and her symptom was significantly improved. [Case 2] A 39-year old female who was treated by methotrexate for 5 years. She had severe left ankle pain, so she was recommended to have ankle arthrodesis. She denied to have arthrodesis, so DA was performed. Her symptom was significantly improved and joint space enlarged. Also range of motion improved. Even for RA patients, DA was able to obtain good results in the short term. DA may be a one surgical option in order to preserve the ankle joint in RA.

S3-5

Reconstructive surgery using total talar prosthesis for end-stage hindfoot arthropathy in patients with ankle osteoarthritis and rheumatoid arthritis

Ryota Hara^{1,2}, Hiroaki Kurokawa², Akira Taniguchi², Yasuhito Tanaka^{1,2}

¹The Center for Rheumatic Diseases, Nara Medical University, ²Department of Orthopaedic Surgery, Nara Medical University

Conflict of interest: None

The talus does not have the origin and insertion of the muscles and is responsible for the center of the dorsi-planar flexion of talocrural joint and varus-valgus motion of talocalcaneal joint due to the passive movement. Through such anatomical characteristics, replacement of artificial implant on the talus is reasonable and we developed an artificial talus designed as a custom made implant using alumina ceramic excellent in affinity at the joint surface in 1999. Since 2005, we have used third-generation implant replaced the whole talus with a total talar prosthesis and the clinical results were generally good in patients with osteonecrosis of the talus. In cases of failed TAA with subsidence of talus component, we have often used total talar prosthesis in combination with tibial component (combined TAA). Arthrodesis and exchanged TAA are indicated as revision surgery of TAA in many cases, but the former have some problems of immobility, pseudarthrosis and leg length shortening due to bone defect, and the latter of low survival rate. Combined TAA is an ideal surgical procedure to solve these problems and good clinical results have been obtained. In recent years, we have indicated combined TAA as a primary surgery for end-stage arthropathy of AOA and RA with collapsed talus and good clinical results have been obtained for a short term. Careful consideration of indication can lead primary combined TAA to one of the options for hindfoot reconstruction surgeries for AOA and RA. As for the indication of combined TAA in the primary surgery at the present time, age and alignment need to satisfy the indication criteria of TNK ankle in addition to talar collapsing. We consider that it is desirable that cartilage of the articular surface preserves to some extent on the side of the calcaneus and the navicular. In the future, we need to study the limits of indication to cases of preoperative calcaneofibular ligament dysfunction and malalignment of hindfoot.

S3-6

Experience of and future prospects for a new ankle prosthesis

Koichiro Yano¹, Haruki Tobimatsu¹, Yu Sakuma¹, Koei Oh¹, Katsunori Ikari¹, Ken Okazaki²

¹Department of Orthopedic Surgery, Institute of Rheumatology, Tokyo Women's Medical University, ²Department of Orthopedic Surgery, Tokyo Women's Medical University

Conflict of interest: Yes

For the first time in 15 years, a new ankle prosthesis, the Trabecular metal ankle system® (TM ankle, Zimmer-Biomet), was released in Japan in August 2018. The two prostheses which had been used in Japan require an anterior approach while the TM ankle prosthesis is based on a new concept using a lateral approach with lateral malleolus cutting. An anterior approach occasionally causes delayed wound healing and wound dehiscence after surgery because of pressure on the wound from the anterior tibial muscle tendon and extensor hallucis longus muscle tendon. Deep infection from wound complications is a substantial problem of the anterior approach. The biggest advantage of a lateral approach is that such a subsequent wound complication does not occur. In addition, the amount of bone cutting can be minimized by performing a semicircular osteotomy according to the shape of the talocrural joint. Moreover, implanting

the prosthesis on solid cancellous bone may improve the long-term outcomes. Furthermore, improvement of long-term outcomes is expected because the bone contact area of the prosthesis is made with trabecular metal, which has reported good outcomes from the studies of hip and knee prosthesis. Correct osteotomy is possible because surgeons can visualize the anatomical rotational center of the talocrural joint using a rigid alignment stand device. However, there are some disadvantages. Many pins are needed to fix the lower leg on the alignment stand device. In addition, a lateral malleolus osteotomy is needed to expose the talocrural joint. As a result, surgical invasions are bigger and operation time is longer than those with anterior approach. Although an improvement of long-term outcome is expected in theory, it currently remains unclear because the TM ankle prosthesis was only recently released globally. Since August 2018, we have performed 11 total ankle replacements using the TM ankle prosthesis. We will discuss their outcomes and future prospects for the TM ankle prosthesis in this session.

S4-1

Central Nervous System Lupus

John G Hanly

Dalhousie University, Halifax, Nova Scotia, Canada

Conflict of interest: None

Systemic lupus erythematosus (SLE) has the potential to cause autoimmune mediated inflammation and dysfunction in all organ systems including the nervous system. Case definitions for 19 neuropsychiatric (NP) syndromes, compiled by the American College of Rheumatology (ACR), is the most widely adopted classification of neuropsychiatric SLE (NPSLE). In the assessment of individual patients and events, attribution rules are needed to determine whether a NP event is due to SLE or a competing co-morbidity or both. Overall, approximately 35% of NP events are attributed to SLE but this varies between 0% and 100% for individual manifestations. Regardless of attribution, NP events are associated with a significant negative impact on health related quality of life, even when other factors such as global SLE disease activity, cumulative organ damage and medications are taken into account. Ischemic and inflammatory mechanisms are key components of the immunopathogenesis of NPSLE. Microangiopathy, intravascular thrombosis, increased permeability of the blood-brain barrier and autoantibody mediated production of pro-inflammatory cytokines likely all contribute to the disease. Advances in brain neuroimaging provide a platform to assess these and other novel disease mechanisms in a non-invasive way. In the absence of controlled clinical trials, large observational cohort studies with careful documentation of NP events and their attribution, treatment and outcomes provides insight into this complex aspect of SLE. In the future, the convergence of more rigorous clinical characterization, validation of biomarkers and brain neuroimaging will provide opportunities to determine the efficacy of novel targeted therapies in the treatment of NPSLE.

S4-2

Treat to target: Endpoints and strategies for SLE

Eric Morand

Monash University, Melbourne, Australia

Conflict of interest: None

In contrast to other rheumatic conditions, only one successful targeted therapy has emerged for Systemic lupus erythematosus (SLE) in recent decades, with a lack of validated endpoints a major contributor to trial failures. As management continues to rely on glucocorticoids and non-specific immunosuppression, inadequately controlled disease activity and adverse effects of glucocorticoids contribute to irreversible end organ damage, in turn leading to early mortality. Treat to target (T2T) approaches have yielded clear benefits in many chronic diseases, especially those whose endpoints are easily measurable, such as hypertension or diabetes. T2T approaches in rheumatoid arthritis (RA), resulting in improved outcomes even without biological therapies, have been adopted in guidelines and the assessment of novel therapies. In contrast, the clinical complexity and heterogeneity of SLE has previously hindered the development of treatment endpoints and hence adoption of T2T strategies. Sustained remission in SLE is rare, and remission definitions remain in

evolution. In contrast, the Asia Pacific Lupus Collaboration (APLC) proposed the Lupus Low Disease Activity State (LLDAS), subsequently defined operationally via a nominal consensus approach. LLDAS includes domains capturing the absence of threatening disease activity and harmful treatment burden. LLDAS has begun to be tested as an outcome measure in SLE clinical trials, and evidence that its attainment is associated with improved patient outcomes has been adduced in multiple cohort studies. It is proposed that LLDAS form the basis of a T2T strategy for SLE.

S4-3

Current problems and future direction of management of systemic sclerosis

Masataka Kuwana

Department of Allergy and Rheumatology, Nippon Medical School

Conflict of interest: Yes

Systemic sclerosis (SSc) is the most difficult-to-treat rheumatic disease today. There is only a few disease-modifying treatment helpful in improving the natural course of SSc, including cyclophosphamide and mycophenolate mofetil, which were proven to show limited efficacy in interstitial lung disease (ILD). Two trials reported autologous stem cell transplantation superior to intravenous cyclophosphamide, albeit at the price of significant procedure-associated early mortality. Several reasons may explain lack of fully adequate therapies. First, it is difficult to identify “active and progressive” patients eligible for disease-modifying treatment. The majority of patients with diffuse cutaneous SSc (dcSSc) assigned to the placebo group in clinical trials experienced improvement of modified Rodnan total skin thickness score (mRSS). In addition, a number of observational studies have revealed that only 20-30% of SSc-ILD at diagnosis progress to end-stage lung disease, and the remaining patients show stable lung function throughout the disease course without treatment. Second, outcome measures that reflect long-term outcomes are not yet established. In clinical trials, mRSS (for dcSSc) or forced vital capacity (for ILD) is used as a primary endpoint, while ACR Provisional Composite Response Index for Clinical Trials in Early Diffuse Cutaneous Systemic Sclerosis (CRISS) has been proposed as a new composite measure. Finally, there is almost no drug proven to prevent excessive fibrosis. A much greater understanding of SSc pathophysiology has developed by tremendous efforts of basic researches, leading to clinically testable hypotheses. Accordingly, novel therapies towards specific molecular and cellular targets have been tested in clinical trials. These include rituximab, tocilizumab, abatacept, nintedanib, pirfenidone, riociguat, and lanabasum. This lecture features future approach to the management of SSc based on recent promising knowledge.

S4-4

Role of Jo-1 in the immunopathogenesis of the anti-synthetase syndrome

Dana P Ascherman

University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA

Conflict of interest: None

Antibodies targeting histidyl-tRNA synthetase (HRS=Jo-1) are a hallmark of the anti-synthetase syndrome, one of the most prominent subsets of idiopathic inflammatory myopathy (IIM). Although there is little evidence that these antibodies directly mediate tissue pathology, a range of clinical and epidemiological data strongly implicate Jo-1 in the immunopathogenesis of the anti-synthetase syndrome. Beyond *in vitro* studies and animal models that underscore the contribution of antigen-specific T cells to muscular as well as extra-muscular complications of this disorder, immunohistochemical studies and gene expression profiling of human muscle biopsy specimens point to an equally important role for innate immune signaling cascades. Newer animal models support these findings, demonstrating an important role for cell-surface and endosomal Toll-like receptors (TLRs) that ultimately drive NF- κ B activation and the elaboration of pro-inflammatory cytokines. Importantly, these models have begun to elucidate the pathogenic connection between dysregulated innate and adaptive immune pathways in the anti-synthetase syndrome-

-highlighting novel “checkpoints” that can be targeted through more selective immunotherapy.

S4-5

Recent Advances in the Treatment of Large Vessel Vasculitis

Yoshikazu Nakaoka

Department of Vascular Physiology, National Cerebral and Cardiovascular Center Research Institute, Japan

Conflict of interest: Yes

Large vessel vasculitis (LVV) consists of Takayasu arteritis (TAK) and giant cell arteritis (GCA) according to the classification criteria of Chapel Hill Consensus Conference 2012 (CHCC2012). Glucocorticoids (GCs), the first-line therapy for the treatment of TAK and GCA, are often associated with adverse effects when used long-term in high dose, and patients frequently relapse during GC tapering. Other immunosuppressive agents, such as methotrexate, azathioprine and mycophenolate mofetil, may be used if relapse occurs while the patient is receiving GCs; however, these agents have not demonstrated consistent clinical benefits or steroid-sparing effects. We previously reported efficacy of anti-interleukin-6 receptor antibody, tocilizumab (TCZ), for refractory TAK via conducting a pilot study in Japan (Nakaoka et al. *Int Heart J.* 54, 406, 2013). Based on these findings, we performed a phase III, double-blind, placebo-controlled multi-center, randomized clinical trial. Thirty-six patients were enrolled in this study, and all of them were randomized to 1:1 (TCZ-SC group N=18, placebo group N=18). The number of relapses were 8 (44.4%) and 11 (61.1%), the estimated relapse free rates at week 24 were 22.9% and 50.6% in TCZ-SC group and placebo group, respectively. There was no statistical significance in the primary endpoint, time to first relapse between the two groups ($p=0.0596$, log-rank test). Although the primary endpoint was not met, TCZ seemed to show favorable tendency to suppress relapses of TAK compared to placebo (Nakaoka et al. *Ann Rheum Dis*, 77, 348, 2018). In 2017, TCZ was approved for TAK in Japan. In addition, based on the results from GiACTA study, TCZ was also approved for GCA in the United States, Europe, and Japan. Like rheumatoid arthritis and inflammatory bowel diseases, new era with biologics may totally change the therapeutic scheme for LVV. In this talk, I will review the recent progress and the current perspective for the treatment for LVV.

S5-1

Multi-omics analysis of drug response in rheumatoid arthritis

Katsuya Suzuki, Tsutomu Takeuchi

Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Japan

Conflict of interest: Yes

Sustained clinical remission (CR) without drug treatment has not been achieved in patients with rheumatoid arthritis (RA). This implies a substantial difference between CR and the healthy state, but it has yet to be quantified. We report a longitudinal monitoring of the drug response at multi-omics levels in the peripheral blood of patients with RA. Our data reveal that drug treatments alter the molecular profile closer to that of healthy controls at the transcriptome, serum proteome, and immunophenotype level. Patient follow-up suggests that the molecular profile after drug treatments is associated with long-term stable CR. This high-dimensional phenotyping provides a quantitative measure of molecular remission and illustrates a multi-omics approach to understanding drug response. In this symposium, we introduce our multi-omics analysis data of drug response in RA and discuss some clues for elucidation of pathogenic mechanism of autoimmune disease.

S5-2

The Immunogenetics of Inflammatory Mechanisms by Fibroblast-like Synoviocytes form Rheumatoid Arthritis Patients

Haruka Tsuchiya¹, Mineto Ota¹, Shuji Sumitomo¹, Kazuyoshi Ishigaki², Akari Suzuki², Yuta Kochi², Yumi Tsuchida¹, Hirofumi Shoda¹, Hiroshi Inui³, Shuji Taketomi³, Yuho Kadono⁴, Sakae Tanaka³, Kazuhiko Yamamoto², Keishi Fujio¹

¹Department of Allergy and Rheumatology, The University of Tokyo Hospital, ²Center for Integrative Medical Sciences, RIKEN, ³Department of Orthopaedic Surgery and Spinal Surgery, The University of Tokyo Hospital, ⁴Department of Orthopaedic Surgery and Spinal Surgery, Saitama Medical University Hospital

Conflict of interest: Yes

Fibroblast-like synoviocyte (FLS) cooperatively expresses a wide range of inflammatory mediators (i.e., IL-6) under the complex inflammatory environment, which leads joint destruction in rheumatoid arthritis (RA). The objective of this study is to elucidate the genetic responsibility of FLS in RA pathogenesis, and to explore potential novel therapeutic targets in FLS. FLS from RA and Osteoarthritis (OA) patients (n = 30 per disease) were stimulated with cytokines (TNF- α , IL-1 β , IL-6/sIL-6R, IL-17A, IL-18, IFN- γ , IFN- α , TGF- β 1 and combination of all 8 cytokines [8-mix] which simulated the mixture of stimuli in the joint) for 24 hours. Five subsets of peripheral blood mononuclear cells were collected from the same patients. The comprehensive analysis including expression quantitative trait loci (eQTL) was performed with genome (SNP typing), transcriptome (RNA-seq) and epigenome (ChIP-seq for H3K27ac, H3K4me1, H3K4me3, Hi-C) data. By the analysis of overlapping between RA genome-wide association study (GWAS) SNPs and enhancer regions of each dataset, disease susceptibility loci were enriched in super-enhancers (SE) of 8-mix stimulated FLS and known CD4⁺T cell and B cell. SE were related to high level expression of targeted genes compared with typical enhancers (TE), and SE of 8-mix stimulated FLS (8-mix SE) formed 3D loops with the promoter of some inflammatory mediators (i.e., IL-6, chemokines). Furthermore, candidate transcription factors which bind to 8-mix SE were extracted by the motif analysis, and some of these were suggested to be regulated by disease susceptibility loci and 8-mix SE. From our research, FLS could contribute to the genetic risk of RA under the complex inflammatory environment and the control of inflammatory mediators by SE would be important for the disease course of RA modulated by the genetic background. The identification of transcription factor complex of 8-mix SE and functional analysis would lead to the development of FLS targeted treatment.

S5-3

Type I Interferon-producing mechanism in SLE

Hyota Takamatsu¹, Yasuhiro Kato¹, Jeong Hoon Park², Hachiro Konaka¹, Eri Itotagawa¹, Atsushi Kumanogoh¹

¹Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University, Japan, ²School of Medicine, Osaka University, Japan

Conflict of interest: None

Systemic lupus erythematosus (SLE) is an autoimmune disease that causes systemic organ dysfunction and occurs mostly in young women. For its pathogenesis, the failure of tolerance to nucleic acid and the accompanying excessive production of type I interferon (IFN-I) via the nucleic acid sensors including TLRs are important. Measurement of IFN-I concentration in SLE serum was difficult due to low sensitivity of ELISA. However, we successfully measured the IFN-I bioactivity in sera of SLE patients by using IFN-I-responsive reporter cells. And we found that serum IFN-I bioactivity is very high in SLE compared to other autoimmune diseases, and IFN-I bioactivity correlates with SLE disease activity. It was also found that IFN-I production is further induced by the membrane vesicles that contain dsDNA in SLE serum via the intracellular nucleic acid sensor cGAS-STING pathway in addition to IFN-I itself. Therefore, as a cell-extrinsic mechanism of IFN-I production in SLE, we have proposed an alternative mechanism, that is, the nucleic acids in extracellular vesicles induce IFN-I production via cGAS-STING pathway. Meanwhile, expectation for molecular target therapy, including IFN-I signaling, is increasing as a treatment for SLE. Anti-IFNAR1 antibody (Anifrolumab) showed efficacy in highly expressed cases of IFN-I related gene, however its effect was limited. We screened the already approved drugs and found that drug A could inhibit IFN-I production. The compound A inhibited the phosphorylation of TBK1, production of IFN-I, and expression of ISGs induced by LPS. Also the compound A reduced the mortality and proteinuria in the SLE mouse model. Therefore, we discovered the possibility that the compound A may be a therapeutic agent for SLE as IFN-I

production inhibitor, and future study of dosage suitable for SLE and clarification of pharmacological mechanism etc. are expected for practical use.

S5-4

Epigenetic regulation of T follicular helper cells in SLE

Shingo Nakayama, Yoshiya Tanaka

The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: Yes

Increasing evidence points to immunological heterogeneity that is regulated by genetic and epigenetic regulation in the pathogenesis of systemic lupus erythematosus (SLE). Indeed, targeted therapy for SLE showed considerable variability of efficacy. T follicular helper (Tfh) cells are critical for the B cell responses, but also play an important role in autoimmunity. We reported that Tfh cells may play an important role in not only promoting autoantibody production but shaping the effector response to auto-reactive lymphocytes. For example, we found that flexible CD4⁺CXCR5⁺CXCR3⁺Bcl-6⁺T-bet⁺Tfh/Th1 like cells characteristically increased in patients with SLE. Moreover, levels of serum IL-12 and expression of IL-12 receptors in memory T cells were increased in SLE. IL-12 induced the differentiation of Tfh/Th1 like cells. The loci of Bcl-6 and T-bet (master transcription factor for Tfh and Th1) were marked by bivalent histone modifications. After IL-12-stimulation, both STAT1 and STAT4 directly bound on *BCL6* and *TBX21* gene loci accompanied by suppression of repressive histone mark trimethylated histone 3 lysine 27. The findings suggest that IL-12-mediated co-activation of STAT1 and STAT4 alters histone modification, resulting in development of Tfh-Th1-like cells. This could be one of underlying mechanisms responsible for the pathogenesis of Tfh cells in SLE. Recent studies have also shown that various types of SNPs, TETs and miRNAs control phenotypic change of Tfh cells. These findings argue that the epigenomic regulation of T helper cells is a key event for the development of SLE. Thus, better understanding of the extrinsic and intrinsic signals that control stability and plasticity of Tfh cells will have important therapeutic applications to control this disease. In this symposium, we would like to highlight recent advances that pertain to this topic and the mechanisms that contribute to Tfh differentiation and the potential in the treatment of SLE.

S5-5

The role of WDFY4 gene in clinically amyopathic dermatomyositis

Yuta Kochi

Laboratory for Autoimmune Diseases, IMS, RIKEN

Conflict of interest: Yes

The progress of genetics in autoimmune diseases has enabled the identification of hundreds of loci associated with the disease susceptibility. However, unlike common autoimmune diseases such as rheumatoid arthritis, the etiology of rare autoimmune diseases is yet unknown. Among them, clinically amyopathic dermatomyositis (CADM), a subset of dermatomyositis, is of clinical importance, because this disease is often accompanied by rapidly progressive interstitial lung disease. In order to dissect the mechanism of disease, we performed genome-wide association study of CADM in Japanese and identified a significant association at the WDFY4 locus. We searched candidate causal variants and identified variants having splicing quantitative trait locus (sQTL) effect for its truncated isoform (tr-WDFY4). Moreover, we demonstrated that both WDFY4 and tr-WDFY4 interacted with pattern recognition receptors such as TLR3, TLR4, TLR9, and MDA5 and augmented the NF- κ B activation by these receptors. Because CADM is characterized by the appearance of anti-MDA5 antibody, WDFY4 may have a critical role in the autoimmune response in CADM. Interestingly, the association signals were different between Japanese and European populations, suggesting that the causal variants were different. Furthermore, the association of the WDFY4 locus was also observed in systemic lupus erythematosus and rheumatoid arthritis, but the association signals were different compared to CADM. Therefore, WDFY4 may play important roles in the regulation of innate immune responses as well the onset of autoimmune diseases, where the causal mechanism would be different among different environ-

ments and different diseases.

S6-1

Mechanisms of action of JAK inhibitors

Akio Morinobu

Rheumatology and Clinical Immunology, Department of Internal Medicine, Kobe University Graduate School of Medicine

Conflict of interest: Yes

Cytokine binding to its receptor activates the down-stream signaling cascade. Type I and II cytokines utilize JAK-STAT pathway as intracellular signaling. JAK inhibitors (JAKi) block JAK activity by binding to JAK's ATP binding pocket. JAKi are small compounds, which are orally available. JAKi suppress lymphocyte functions primarily, but also act on myeloid cells and synovial fibroblasts. The major difference between JAKi and biologics is that JAKi suppress multiple cytokines partially whereas biologics block single cytokine completely. Considering that multiple cytokines work at the site of inflammation, this property of JAKi may have the advantage to treat immune and inflammatory conditions. On the other hand, adverse events may occur due to this characteristic. Until now, however, clinical experiences have shown that JAKi are well tolerable, probably because JAKi partially inhibit JAK-STAT pathway. Cytokines that use JAK-STAT pathway involve IL-6, IFNs, IL-2, GM-CSF, and JAKi are expected to be useful in many immune and inflammatory conditions. Today JAKi are clinically used for RA and UC, and now under clinical trials for various other diseases. Broad spectrum of application of JAKi is remarkable and could be comparable to glucocorticoids, and that JAKi may change the whole concept of immune suppression strategy. JAK family consists of four members; JAK1, JAK2, JAK3, Tyk2. The current JAKi suppress couple of these, thus called pan-JAKi, while selective JAKi are being developed into clinical stages. So far selectivity depends on how they are assayed, and does not make much differences when clinically used. However, once they are tried on many diseases other than RA, selective JAKi may help understanding the cytokine regulations of each disease. In conclusion, JAKi is a new class of drugs with novel mechanisms of action. JAKi may pave the way to new strategies for the treatment of various immune and inflammatory diseases.

S6-2

Characteristics of clinical trials of JAK inhibitors in patients with rheumatoid arthritis

Tomonori Ishii

Clinical Research, Innovation and Education Center, Tohoku University Hospital

Conflict of interest: Yes

In recent years, new compounds that target specific molecules have been proposed as therapeutic agents against several systemic autoimmune diseases. In order for these compounds to be recognized as drugs, their safety and effectiveness need to be confirmed based on objective data. Clinical trials are useful for confirming the efficacy and safety of drugs. Several clinical trials have failed to establish safe and efficient drugs for most systemic autoimmune diseases, such as systemic lupus erythematosus and systemic sclerosis. One of the underlying reasons for this failure is the inability of the trial design to identify the efficiency of an effective drug. Under these circumstances, clinical trials for rheumatoid arthritis (RA) have been well organized and established among clinical trials of systemic autoimmune diseases, and several drugs have been approved in clinical practice. In clinical trials of RA, methodology is established for basic structures, such as the inclusion criteria, exclusion criteria, treatment protocols, and evaluation methods. Therefore, in most tests, the test method does not significantly change. However, in order to obtain approval for a new drug, additional usefulness beyond that of existing drugs is necessary. Therefore, new evaluation items should be added. In recent years, patient reported outcome (PRO) has been actively used as a criterion for RA evaluation. It has been adopted as an item in clinical trials that can evaluate more subjective symptoms in addition to objective data, such as joint swelling in patients and inflammatory findings on blood tests (C-reactive protein, erythrocyte sedimentation rate, etc.). In the clinical trials of JAK inhibitors targeting RA, evaluation using PRO

has been adopted, and JAK inhibitors are shown to be more useful than older drugs. Recently, several clinical trials on RA have been conducted as global trials; patients selected using the same inclusion criteria are treated with the same protocol and assessed using the same evaluation methods worldwide. Thus, it became possible to compare data obtained from patients in other countries with those from Japanese patients, clearly demonstrating the characteristics of Japanese patients.

S6-3

Future perspectives for JAK inhibitors from the Japanese all case post-marketing survey

Kunihiro Yamaoka

Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine, Japan

Conflict of interest: Yes

JAK inhibitors (JAKi) have shown similar anti-rheumatic effect with biologics. JAKi and IL-6 inhibitors gathered attention with monotherapy and is currently recommended for patients with methotrexate contraindication. The Japanese all case post-marketing survey (PMS) has revealed that JAKi is initiated as monotherapy in a fairly large amount of patients with long disease duration and failed multiple anti-rheumatic drugs. Tapering is something to consider though information is limited. In a study that discontinued tofacitinib at the time of completion of the clinical trial, 60% had flared by 52 weeks. Whereas, a tapering study with baricitinib resulted in majority maintaining their low disease activity. Due to side effects with methotrexate (MTX) especially in Japanese population, MTX-tapering is something to be considered though information with JAKi is lacking. Studies with patients under control with MTX and tocilizumab (Tcz) would be suggestive. In a study that discontinued MTX, the effect was minimum and another study that discontinued Tcz, approximately half maintained disease activity under control. Taking these results into account, tapering and/or discontinuation of MTX or tapering JAKi would be realistic. However, majority were treated with concomitant MTX. Depending on the report of PMS, tapering/discontinuation would not be suggested with those treated with monotherapy. JAKi share the fate with other anti-rheumatic drugs such as infections as their negative side. Herpes zoster is a characteristic side effect and the incident rate is doubled in the Japanese population compared to western countries. Another concern is carcinogenesis owing to the effect of JAKi on the adaptive immunity. Ten-years follow up of the tofacitinib clinical trial revealed no increase in carcinogenesis. From the PMS, patients diagnosed as cancer with metastasis was occasionally observed within 6 months following initiation, suggesting the importance of screening. Recent concern of venous thrombotic event (VTE) has been raised. Currently the incident rate is similar to that with preexisting anti-rheumatic drugs and long-term follow up is necessary. Future perspectives of JAKi will be discussed based on the observations from the PMS and previous clinical trial.

S6-4

Management of herpes zoster induced by Jak inhibitors

Shinichi Imafuku

Department of Dermatology, Faculty of Medicine, Fukuoka University, Japan

Conflict of interest: Yes

Herpes zoster is an endogenous recurrent infection of varicella-zoster virus (VZV), which develops in about 5 people / 1,000 patient-year in the whole population, but its frequency increases in immunocompromised individuals. Our study using Japanese claim database revealed that in rheumatoid arthritis patients, the incidence was as high as 9.18 / 1,000 person years. Furthermore, in rheumatoid arthritis patients treated with tofacitinib, one of the Jak inhibitors, pooled analysis of all trials including phase 2, phase 3, and open extension trials found that the incidence was extremely elevated to 39 / 1,000 PY (Cohen SB et al). In addition, severe cases (disseminated or multi-branched lesions) is 3 / 1,000 PY, thus Jak inhibitor treatment causes significant increase of incidence and severity of herpes zoster. Incidence of non-melanoma skin cancer also increases dose-dependently with other skin infections, but they are also known for other immunosuppressants such as MTX and cyclosporine.

Therefore, herpes zoster is a very specific infection characteristic of Jak inhibitors hence special attention needs to be paid to skin eruptions. Two types of vaccines have been approved for the prevention of herpes zoster in Japan, but as of November 2018, only the attenuated live vaccine, the varicella vaccine, is distributed in the domestic market. Varicella vaccine are contraindicated in immunosuppressed patients, and efficient prevention can not be expected at this point. Therefore, it is very important to diagnose herpes zoster early and treat with antiviral reagents.

S6-5

JAK-inhibitors – From targeting just another kinase to novel treatments

Gerd R Burmester^{1,2}

¹Department of Rheumatology and Clinical Immunology, Charite University Hospital, Berlin, Germany, ²Free University and Humboldt University of Berlin, Germany

Conflict of interest: Yes

For a long time, many approaches have tried using novel oral compounds to achieve similar efficacy and safety as biologics. Most of these trials have failed, especially those aiming to inhibit the MAP (mitogen-activated protein) kinase pathway where evidence suggests importance in the pathogenesis of rheumatoid arthritis (RA). However, drugs inhibiting the Janus kinase (JAK) pathways have resulted in a significant breakthrough in RA treatment. While efficacy could be anticipated due to the many cytokines that use JAKs for intracellular signaling, safety concerns were expressed, since knocking out JAK 1 or JAK 2 in rodent models were lethal and there is a human severe combined immunodeficiency disease where the gene for JAK 3 is malfunctioning. However, it appears that the doses approved in RA are usually safe, since apparently only the pathologically increased levels of JAK enzymes are reduced so that physiologic functions remain – quite analogous to the situation with biologics where the complete absence may also lead to severe diseases, yet the amounts used for treatment usually do not lead to major deficiencies (1). In many countries including the USA tofacitinib targeting JAK 1, 2 and 3 was the first drug to be approved. Finally, also EMA (European Medicines Agency) gave a positive opinion for this drug which “in combination with methotrexate (MTX) is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti rheumatic drugs” and “can be given as monotherapy in case of intolerance to MTX or when treatment with MTX is inappropriate.” EMA also granted market authorization to baricitinib, a JAK 1 and 2 inhibitor where baricitinib “is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti-rheumatic drugs” and may be used as monotherapy or in combination with methotrexate.” Both tofacitinib and baricitinib have been investigated in extensive clinical trial programs ranging from MTX naïve early RA to csDMARD inadequate responders and patients failing biologics, most notably TNF inhibitors. One trial was powered to compare baricitinib and the TNF inhibitor adalimumab in a head-to-head design showing a modest, nevertheless significantly better efficacy of the JAK inhibitor. Also, both JAK inhibitors in monotherapy were clinically more effective than MTX in early RA including the analysis of radiologic progression. In addition, the major development programs of new compounds such as upadacitinib and filgotinib (selective JAK-1 inhibitors) and peficitinib support the positive benefit/risk ratio of JAK-inhibitors. Will these novel oral anti-rheumatic drugs lead to a paradigm shift in the treatment of patients with RA? While the current EULAR recommendations place these tsDMARDs somewhat behind the biologics (Recommendation 8: “If the treatment target is not achieved with the first csDMARD strategy, when poor prognostic factors are present, addition of a bDMARD or a tsDMARD should be considered; current practice would be to start a bDMARD”), practice may change with more clinical experience, especially since the safety signals of the JAK inhibitors do not differ significantly from biologics with the exception of more herpes zoster cases, most notably in Japanese and Korean patients. Tofacitinib has safety and efficacy data from open label extension studies for more than 9 years. Nevertheless, the significant costs of these drugs will make early use in csDMARD naïve patients unlikely, and the very long experience, the extensive registry data and the availability of less expensive biosimilars with

biologics may still result in a preferred use of biologic agents in the near future. However, patient preference of oral drugs instead of injectable compounds, the possibility to use them in monotherapy and the potentially superior efficacy compared to TNF inhibition might lead to a paradigm shift in the future. Reference (1) Burmester GR, Pope JE. Novel treatment strategies in rheumatoid arthritis. *Lancet*. 2017. 389:2338-2348.

S7-1

Recent activities of the research group for the systemic autoinflammatory diseases funded by the Ministry of Health, Labour, and Welfare

Ryuta Nishikomori

Kyoto University Hospital

Conflict of interest: None

The systemic autoinflammatory diseases (SAID) are one of intractable diseases, which cause systemic inflammation resulting in damage on multiple organs. The symptoms include fever of unknown origin, rash, and arthritis which could be misdiagnosed as rheumatic diseases. Since it has been known that some of SAID show great response to certain biologics, it is very important for rheumatologists to properly diagnose and treat SAID patients. Canakinumab, or anti-human IL-1b mAb, was approved for cryopyrin-associated periodic syndrome in 2011 and the approval was extended further to TRAPS, Hyper IgD syndrome, and colchicine-resistant or -intolerant FMF in 2016. Canakinumab has provided these patients much better QOL, but at the same time the canakinumab treatment has raised some issues on its long-term effectiveness and safety. On the other hand, the diagnosis of SAID heavily relies on the genetic analysis, since SAID lack disease-specific biomarkers for diagnostic purposes. Thus, it requires nation-wide cooperation of experts on SAID in terms of clinical as well as genetic aspects. Finally, the number of SAID has been still increasing, which needs more efforts for the newly-diagnosed SAID on proper diagnosis and establishing standard patient care. To tackle these issues, we organized research group for SAID funded by the Ministry of Health, Labour, and Welfare in 2014. We have been working for patients with SAID regarding nation-wide patient care system, patient registration system, clinical guidelines, and seriousness classification. In this review talk, I will focus on the recent activities of the research group for SAID, such as introduction of genetic diagnosis system based upon newly-established genetic tests covered by health insurance, elimination of disparities on genetic diagnosis on SAID, and embarking on the “Nanbyo platform” registration system supported by AMED.

S7-2

Immunogenetics of Behçet’s disease from recent genetic findings

Masaki Takeuchi

Department of Ophthalmology, Yokohama City University

Conflict of interest: None

Behçet’s disease (BD) is a systemic inflammatory disorder vasculitis that manifests with oral ulcers, uveitis, skin inflammation, genital ulcers, and inflammation in other organs. Multiple genetic and environmental factors are believed to contribute to BD susceptibility. In 2010, we conducted the first genome-wide association study (GWAS) for BD in a Japanese population was conducted. In addition, Korean and Turkish populations were studied in the replication phase. Other genetic studies have also identified susceptibility loci. However, these genetic findings do not fully explain pathogenesis of BD. To further clarify the genetic factor of BD, we conducted the largest-ever genetic study for BD by genotyping with the ImmunoChip (Illumina), which is a custom genotyping array designed for dense genotyping of immune disease-associated loci. We genotyped 2,014 Turkish BD cases and 1,826 control subjects on the ImmunoChip and replicated the genetic findings in Japanese including 608 cases and 737 controls, and Iranian including 969 cases and 826 controls. This largest-ever genetic study with multiple populations for BD identified 6 novel loci (*IL1A-IL1B*, *RIPK2*, *ADO-EGR2*, *LAC1*, *IRF8*, and *CEBPB-PTPNI*). Our results have significantly helped expand the list of genes with common variants that influence BD susceptibility and implicate variants influencing both innate and adaptive immunity in disease patho-

genesis. The risk allele of the lead SNP in the *IL1A-IL1B* locus was associated with both decreased interleukin-1 α and increased interleukin-1 β production. Our findings suggest the possibility that a combination of the decreased barrier function of IL-1 α and increased inflammatory response of IL-1 β increases the disease risk. ABO non-secretor due to homozygosity of non-secretor SNPs for *FUT2* revealed a strong disease association. These genetic findings implicate genetic determinants of mucosal barrier function and the host response to pathogens in BD susceptibility.

S7-3

Update in clinical researches of intractable vasculitides by JPVAS

Masayoshi Harigai

Department of Rheumatology, Tokyo Women's Medical University

Conflict of interest: None

Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis (JPVAS) is in charge of the following designated intractable diseases; Takayasu arteritis (TAK), giant cell arteritis (GCA), polyarteritis nodosa (PAN), microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), rheumatoid vasculitis (RV), anti-phospholipid antibody syndrome (APS), and Burger disease. As for ANCA-associated vasculitis, three cohort studies revealed the genetic background, clinical characteristics, response to treatment, safety, risk factors for relapse, and association between ANCA positive conversion and relapse. JPVAS released the 2017 Clinical Practice Guidelines for ANCA-associated Vasculitis in February 2017, and published it in *Modern Rheumatology*. Two cohort studies for TAK and GCA are in progress, which clarified clinical characteristics and response to treatment of these diseases in Japan. JPVAS collaborated with Japan Circulation Society and revised 2017 Clinical Practice Guidelines for Vasculitides, and revised diagnosis and treatment of TAK, GCA, and Burger disease. Pediatricians are also participating in the subcommittees for large-sized vessel vasculitis and small and medium-sized vessel vasculitis. Subcommittee for clinical pathology is accepting consultation for pathological diagnosis for vasculitides from medical institutions at large. Subcommittee for international cooperation research has implemented DCVAS and PEXIVAS. It also collaborating with the Study Group on Diffuse Pulmonary Disorders to study ANCA-positive interstitial lung disease. Cross-collaboration research subcommittee has convened a series of public lectures for vasculitides and joint symposium with relevant medical societies. In this symposium, recent progress of JPVAS will be reviewed to provide a bird's-eye view of the progress and challenges of management of vasculitis.

S7-4

Efforts of research study group on autoimmune disease

Masaaki Mori¹, Takayuki Sumida², Tatsuya Atsumi³, Yoshiya Tanaka⁴, Manabu Fujimoto⁵

¹Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, ²Department of Internal Medicine, Faculty of Medicine, University of Tsukuba, ³Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, ⁴Department of First Internal Medicine, University of Occupational and Environmental Health, ⁵Department of Dermatology, Faculty of Medicine, University of Tsukuba

Conflict of interest: Yes

<Objectives> The aim of the research is to further improve its medical level with respect to 6 *designated incurable disease* such as systemic lupus erythematosus (SLE), polymyositis/dermatomyositis (PM/DM), mixed connective tissue disease (MCTD), Sjögren's syndrome (SS), adult onset Still's disease (AOSD) and juvenile idiopathic arthritis (JIA). <Method> Experts from the multiple medical fields are gathered to form a subcommittee and the following various projects are carried out in an integrated manner for children and adults; 1) verification and revision of diagnostic criteria and severity classification, and validation of international classification standards, 2) formulation and revision of clinical practice guidelines (GL), 3) educational activities for early diagnosis and treatment and medical treatment network construction for autoimmune

diseases, 4) collaboration with AMED practical research projects, and so on. <Results> 1) All diseases were verified based on diagnostic criteria and severity classification of domestic and foreign countries so far. Especially, MCTD, which resumed policy research for the first time in several years, clearly defines the concept of disease again and is discussing classification criteria and severity classification. 2) As for SLE, we decide all CQ recommended sentences, and the first comprehensive clinical practice guidelines in Japan will be released in FY 2019. Additionally, PM / DM, SS, AOSD and JIA are conducting verification for revision based on recently published criteria. 3) In cooperation with patient associations and academic societies, we are trying to hold open sessions for patients or medical consultation sessions at least every year at each subgroup and we are devoting efforts to closeness with patients. As this consultation meeting is well received, we will consider regularly and continuously holding events. 4) By coordinating with AMED practical research projects, we collect clinical information and specimens from each facility and formulate a plan for new research projects. In addition to these, from April 2018, "JIA" was registered and treated as one of designated intractable disease. <Products obtained to date> In this research, we conduct indispensable research on the above 1) ~ 4) and express outcomes leading to the future. Particularly, we were able to study children by integrating pediatric / adults is one of the results of consciousness of transition medical treatment, which is regarded as important for measures against intractable diseases.

S7-5

Investigation of the Japanese Scleroderma Research Group

Hironobu Ihn

Department of Dermatology and Plastic Surgery, Faculty of Life Sciences, Kumamoto University, Japan

Conflict of interest: None

The Japanese Scleroderma Research Group is working on "Study of diagnostic criteria, severity classification, and guidelines of systemic sclerosis and other cutaneous fibrotic diseases" supported by Japanese Ministry of Health, Labor and Welfare, and "The investigation on the efficacy of new low molecular compound for systemic sclerosis" supported by Japan Agency for Medical Research and Development. I would like to introduce the diagnostic criteria, severity classification, and guidelines of systemic sclerosis, localized scleroderma, eosinophilic fasciitis, and lichen sclerosus et atrophicus. I also would like to talk about new low-molecular compound for systemic sclerosis.

S7-6

The current status of the research committee for IgG4-related disease in Japan

Kazuichi Okazaki

Department of Gastroenterology and Hepatology, Kansai Medical University, Japan

Conflict of interest: None

IgG4 related-disease (IgG4-RD) is a fibroinflammatory disorder recognized as a novel clinical entity originally proposed from Japan, and has become specified as an intractable disease in 2015. The patients with IgG4-RD show diffuse or focal organ enlargement and mass-forming or nodular/thickened lesions with abundant infiltration of IgG4-positive plasmacytes and fibrosis in various systemic organs, and respond well to steroid treatment. The research committee for IgG4-RD consists of eight subcommittees; gastrointestinal, lacrimal and salivary (Mikulicz disease), ophthalmic, renal, pulmonary, endocrine and neural, cardiovascular, and pathological one. The committee has performed epidemiological studies, and made/updated the comprehensive and individual organ diagnostic criteria, classification of disease severity, and therapeutic guidelines. We also have established and started the registry system for the patients with IgG4-RD.

S8-1

Current and Future Osteoporosis Treatments: Mechanisms of Action

Roland E Baron

Conflict of interest: Yes

Novel therapeutic approaches for osteoporosis provide better treatment but also new insights on the cellular and molecular mechanisms by which skeletal homeostasis is regulated. Skeletal homeostasis is ensured by the balanced activities of bone resorption and bone formation in bone remodeling. Osteoclasts resorb bone, but also recruit osteoblasts (coupling) ensuring repair of resorbed areas. In turn, osteoblasts form new bone at these sites and regulate the differentiation of osteoclasts via RANKL and OPG. Consequently, inhibition of bone resorption leads also to a decrease in bone formation and remodeling. Unlike bisphosphonates, Denosumab allows continued increase in bone density and reduction in fracture risk over time, in part via bone modeling, during which bone formation continues independent of resorption, particularly in cortical bone. One can also stimulate bone formation by activating the PTH/PTHrP or Wnt signaling pathways. Daily PTH1-34 (Teriparatide) injections increase bone formation but also resorption and turnover, with a positive balance. Bone density increases, but the increase in bone resorption affects intracortical remodeling and porosity, limiting the benefits of PTH treatment. PTHrP analogs (Abaloparatide) or the combination of PTH with Denosumab partially avoids the increase in resorption, increasing bone density further. The Wnt signaling pathway is a key regulator of osteoblasts as well as their cross-talk with osteoclasts. Blockade of the inhibitor Sclerostin, secreted by osteocytes, leads to major increases in bone formation and production of OPG, reducing also resorption. Sclerostin antibodies (Romosozumab) enhance Wnt signaling and has both an anabolic and an anti-resorptive effect that, albeit limited in time, increase bone density at trabecular and cortical sites, in large part via bone modeling. Taken together, these therapeutic developments provide promising prospects for osteoporosis treatment but also insights into bone biology.

S8-2

Epidemiology of Osteoporosis, Sarcopenia, and Frailty in Japan

Noriko Yoshimura

Department of Preventive Medicine for Locomotive Organ Disorders, 22nd Century Medical and Research Center, University of Tokyo, Japan

Conflict of interest: None

Purpose: To clarify the prevalence, incidence, and mutual association among osteoporosis (OP), sarcopenia (SP), and frailty (FR) using a 4-year follow-up assessment of a population-based cohort study entitled 'ROAD.' **Methods:** The second survey of the ROAD study was conducted between 2008 and 2010; overall, 1,083 subjects (aged ≥ 60 years; 372 men, 711 women) completed all examinations on OP, SP, and FR, which were defined using the WHO criteria, AWGS, and Fried's definition, respectively. The third survey of the ROAD was conducted between 2012 and 2013; 749 of 1,083 individuals who were enrolled on the second survey (69.2%; 248 men, 501 women) completed assessments identical to those in the second survey. **Results:** The prevalence of OP, SP, and FR in the second survey were 25.0%, 8.1%, and 5.6%, respectively. The cumulative incidences of OP, SP, and FR were 1.9%/year, 2.0%/year, and 1.2%/year, respectively. After adjusting for confounding factors, logistic regression analysis indicated that OP was significantly raised the risk of the occurrence of SP, and FR. **Conclusions:** Preventing OP may help to reduce the risk of subsequent occurrence of SP and FR.

S8-3

Management of osteoporosis in diabetic patients

Ippei Kanazawa, Toshitsugu Sugimoto

Internal Medicine 1, Shimane University Faculty of Medicine, Shimane, Japan

Conflict of interest: None

Previous studies have shown that not only type 1 but also type 2 diabetes mellitus (DM) increase risk of fragility fractures. Because the estimated fracture risks based on their bone mineral density (BMD) are higher than actual fracture risks in patients with DM, the deterioration of bone

quality should be a major cause of DM-induced bone fragility. Accumulating evidence reveals the underlying mechanism of the increased risk of fractures in patients with DM; accumulation of collagen cross links of advanced glycation end products (AGEs), low bone remodeling with impaired bone formation, and microstructure alteration such as cortical porosity. Although the mechanism of DM-induced bone fragility remains unclear, we previously demonstrated that AGEs and homocysteine induce dysfunction of osteoblasts and osteocytes, which may lead to low bone remodeling and decreased bone formation. On the other hand, the increased risk of falls is also important for the incidence of osteoporotic fractures in DM patients. We previously showed that AGEs were associated with decreased myoblastogenesis and muscle reduction in type 2 DM. In clinical settings, if all of the focus is given only to BMD values, we might underestimate the fracture risks in DM. However, there are no useful markers to evaluate bone quality thus far. Therefore, we need to choose patients with a high risk of osteoporotic fracture based on clinical risk factors, and to consider intensive treatment including anti-osteoporotic drugs. Previous studies have shown that higher HbA1c levels, longer duration of DM, insulin use, and thiazolidine use (if postmenopausal women) increase the fracture risk in patients with DM. However, further studies are needed to determine a suitable assessment tool for fracture risk that supplement the insensitivity of BMD and assess fracture risk in patients with DM. In this symposium, we will review the management strategy of DM-induced bone fragility.

S8-4

Management of osteoporosis in RA patients

Tatsuya Koike

Center for Senile Degenerative Disorders (CSDD), Osaka City University Medical School

Conflict of interest: Yes

Patients with rheumatoid arthritis (RA) are known to be at higher risk for disorders of bone metabolism due to inflammation, glucocorticoid (GC) use and inactivity resulting from joint destruction. Previous researchers have reported that patients with RA had the risk of hip and vertebral fractures by about two- to six-fold compared to controls. RA is an independent risk factor for fragile fractures that has been assessed using the Fracture Risk Assessment Tool (FRAX). However, is the situation unchanged even in a new era when RA treatment has made remarkable progress? To reveal the real risk factors for osteoporosis in RA, we launched a ten-year prospective cohort in 2010, the TOtal Management Of Risk factors in Rheumatoid arthritis patients to LOwer morbidity and mortality: the TOMORROW study including 208 RA patients and age- and sex-matched 205 volunteers. The most involved in fractures is a fall. When comparing the number of falls in both groups, the percentage of subjects experiencing falls increased in the same way year by year in both groups, but the average falling number was significantly higher in RA. Moreover, a positive correlation was found between the number of falls and the amount of administered GC. Comparing the 25 (OH) D levels related to the fall, it showed a significantly low value in RA. However, there was no significant relationship with the fall. The number of existing vertebral fractures was significantly larger in RA patients and the risk factors for clinical fractures were falls and GC use. RA was not extracted as a risk factor for clinical fractures. In addition, although the risk of fracture did not decrease by reducing GC dosage, a significant reduction in fracture risk was observed in the group where GC administration could be stopped. Based on the above, we believe that administration of GC rather than RA per se is an important risk factor in fragile fractures.

S8-5

Glucocorticoid-induced osteoporosis in rheumatic diseases and other inflammatory joint disorders

Nicholas C Harvey

MRC Lifecourse Epidemiology Unit, University of Southampton, UK

Conflict of interest: None

Glucocorticoids are widely used to treat disorders such as polymyalgia rheumatica and inflammatory arthritides. The impact of glucocorticoids on fracture risk is well documented, with a rapid rise in risk follow-

ing commencement of therapy and a corresponding decline in risk after cessation. Glucocorticoids adversely affect both bone formation and bone resorption, resulting in the observed risk-time relationships. The increased fracture risk appears partly independent of BMD. Importantly epidemiological studies have demonstrated that there is no safe minimum dose below which fracture risk is not raised. National and international guidelines have been developed to address fracture risk assessment, and bone protective therapy, in patients commencing glucocorticoid treatment, for example from the International Osteoporosis Foundation and, in the UK, the National Osteoporosis Guideline Group (NOGG). Such approaches incorporate the use of the FRAX Fracture Risk Assessment Tool, which includes glucocorticoids as an input variable. Given that dose information is not considered by FRAX directly, methods for modifying the output fracture probability have been derived, and are incorporated in the UK NOGG website. In this presentation, the epidemiology and pathophysiology of glucocorticoid induced osteoporosis will be reviewed, together with current approaches to assessment and treatment, including practical messages for the clinic.

S9-1

Actual state of support system, problems, and preparation of guidance for transition support in patients with juvenile onset rheumatic diseases

Toshihiro Matsui

Department of Rheumatology, National Hospital Organization Sagami-hara National Hospital

Conflict of interest: Yes

Following the announcement of “The recommendation for the transition medicine in patients with juvenile onset disease” by the Japan Pediatric Society in 2013, “Transition support WG for pediatric patients with chronic diseases” was started to prepare guidance for transition support. In 2014, Transition support WG was established at the Pediatric Rheumatology Association of Japan. Recently, guidance for transition support for juvenile onset rheumatic diseases has been under preparation by the research project supported by the Ministry of Health, Labor and Welfare started since 2017. Interest in transition medicine is increasing year by year. In the past, places where pediatricians and adult physicians interacted were limited, but now both are participating in the same research project, cooperating with each other and discussing actively for preparing guidance for transition support in patients with juvenile onset rheumatic diseases. Nowadays, medical treatment and research on rheumatic diseases have entered a seamless era beyond the boundaries between children and adults in various aspects. At this symposium, speakers will talk about the differences between children and adults in rheumatic diseases, problems and efforts related to the transition support for patients with juvenile onset rheumatic diseases, and problems of pregnancy and childbirth. In addition, we would like to think about the medical care system in transition medicine.

S9-2

Differences between pediatric and adult rheumatic diseases

Kimito Kawahata

Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Japan

Conflict of interest: None

Clinical differences between children and adults with rheumatic diseases are unclear. Even though the names of the diseases are the same among children and adult patients, the symptoms, treatment, and prognosis of these diseases are different. To understand these differences are critical in several clinical settings. The first is the need for long-term follow-up of patients with rheumatic diseases from childhood to adulthood in the departments for adults. For example, attention to ocular complications may be required in patients with juvenile idiopathic arthritis. Furthermore, since the disease pathology does not merely change at when a patient turns 16 years old, the treatment for children may be desired for some adult patients although the symptoms start in adulthood, or likewise, the treatment for adults may be desired for some child patients even when the symptoms occur during childhood. Such phenomena have yet

to be shown in rheumatic diseases yet but are known in other diseases. For example, in acute lymphocytic leukemia, it has been shown that it is better for an adult patient to be treated with pediatric protocols until the patient reaches 25 years of age. Furthermore, even when the same symptoms and severity are observed in children and adults, it is essential to understand the variation of the influence of the treatment on living functions by performing long-term follow-ups. Future clinical studies are expected to provide insights, not only based on the differences and similarities the symptoms and complications, but also on the influence of the treatment on daily living functions in adults that have gone through the process of growth, in order to clarify the differences in the meaning of treatment for diseases with seemingly similar activities and severities. In this talk, I would like to introduce the differences between children and adults with rheumatic diseases based on the points mentioned above.

S9-3

Pathology of transitional stage of juvenile idiopathic arthritis and guidance for clinical practice

Hiroaki Umabayashi¹, Masaaki Mori²

¹Department of Rheumatology and Infectious Diseases, Miyagi Children's Hospital, Sendai, Japan, ²Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan

Conflict of interest: None

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children and young people. In a recent national epidemiological survey, it was estimated that the actual number of patients of JIA was about 3000. JIA is thought to be remission about 30% in about 10 years after onset, and many cases require an outpatient even after adulthood. Prognosis, treatment, complications and so on, are different depending on disease type. Treatment of systemic JIA is based on steroids, sometimes the treatment is completed only by that, but there are many cases that easily recurs. In patients with high steroid dependence, various adverse effects become apparent and the quality of life in transition may be affected. In a polyarthritis, MTX becomes an anchor drug like a rheumatoid arthritis in adult. Among them, in particular RF positive polyarthritis often uses biological drugs, many cases continue even in the transition period. In children who are physically and mentally growing, symptoms of JIA and long-term hospitalization may inhibit healthy growth and self-reliance as a person. To support JIA patients and families in transition, it is necessary to cooperate with pediatricians, adult medical specialists, nurses, pharmacists, psychologists etc.

S9-4

Transition support for Sjogren's syndrome and problems related to “sex”

Yuzaburo Inoue

Department of Allergy and Rheumatology, Chiba Children's Hospital, Chiba, Japan

Conflict of interest: None

Sjogren's syndrome (SS) is a chronic disease requiring medical treatment tailored to the life stage of the patient. In particular, during the transition period from childhood to puberty, adolescence, and adulthood, various problems exist including not only the simple change in medical care from pediatrics to adult healthcare, but also problems in the transition from guardian-based to self-based medical care, the influence of the physical, mental and sexual maturity of patients, and problems due to differences in the medical system for children and adults. The guidelines for transition support include a “core guide,” laying out a series of support processes necessary to satisfy the individual needs of patients as they grow, along with a “guide by disease,” demonstrating a method of providing medical support to patients based on the characteristics of individual diseases. As created in cooperation with pediatrics and adult healthcare in health labor science research, we herein introduce the guidelines on support and education for the following six categories, as the “guide by disease” to childhood SS patients: 1. psychological support; 2. self-support; 3. self-reliant medical behavior; 4. educational and occupational plans; 5. health and lifestyle, and 6. sexual health. Moreover, it is not un-

common to experience patients suffering from problems and concerns related to “sex” in the treatment of pediatric rheumatic diseases. According to a questionnaire survey targeting members of the Pediatric Rheumatology Association of Japan, approximately 60% of respondents had patients who had “troubles/issues related to sex,” while 11%, 29% and 37% of pediatric rheumatologists had patients with anxiety when it came to love, marriage, and pregnancy, respectively. Many pediatric rheumatologists had trouble regarding how to deal with this anxiety or how to talk about sexual intercourse and pregnancy originally in the clinic. Furthermore, 28% of them had experience dealing with patients who become pregnant in their teens, while 11% had experience dealing with patients who gotten married in their teens, making it by no means rare to respond to young pregnancy and young marriage. Support for troubles and problems related to “sex” is also an important issue for transition support medical care.

S9-5

Pregnancy in patients with childhood onset rheumatic disease patients

Mikako Goto¹, Kayoko Kaneko², Atsuko Murashima^{1,2}

¹The Japan Drug Information Institute in Pregnancy, National Center for Child Health and Development, ²Division of Maternal Medicine, Center of Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development

Conflict of interest: Yes

Treatment for pediatric rheumatic diseases has advanced remarkably; however, there are a certain number of cases in an adult department in which the disease developed during a patient’s childhood and continues to require treatment even after they’ve become adults. Therefore, medical care in a transitional period is an avoidable issue. Pediatric rheumatic disease is comparatively similar to its form in adults. Therefore it supposed not to be difficult to be transitioned to department of Rheumatology. However, special attention should be made to those patients. Here, we would like to consider patient’s pregnancy in this setting. First, it is necessary to check their disease condition and also to check whether or not there are any serious complications. If the patient’s condition is stable, we have to consider if it is necessary to continue the medication they are taking and also consider if the medication is possible even after pregnancy, in case they will need to continue taking it. If the disease is not stable, we have to tell the patient to concentrate on treatment, and advise them to plan to get pregnant when they are in good condition. The checklist written by Dr Ishizaki on the transition to adult includes questions on whether or not patients have consulted physicians, etc. about issues of pregnancy and childbirth. It also covers their reproductive health. In this lecture, I would like to also talk about the control of therapeutic agents while taking pregnancy into consideration, as well as to provide tips for medical treatment so that girls and females can take the initiative for realizing their reproductive health.

S9-6

Experiences of care for patients with rheumatic disease in transitional generation

Ken-ichi Yamaguchi, Masato Okada

St. Luke’s International Hospital, Immuno-Rheumatology Center, Japan

Conflict of interest: None

When a physician treats pediatric patients with chronic diseases, he may be involved various problems arise in their translational generation. Considering the importance of transitional medicine, Japan College of Rheumatology had started to create of the guideline about transition in rheumatic diseases under the cooperation of adults’ and pediatric rheumatologists. In the near future, we will provide guideline-based translational care. Even if it becomes such a time, we need solve about problems arises to patient case-by-case way in clinical medicine. This is “practical translational medicine”, which is the theme of this symposium. We treat patients from a baby to elderly people with rheumatic diseases in Immuno-Rheumatology Center, St. Luke’s International Hospital. We had been faced with various problems while treating patients in transitional age. Some patients had problems about medication under pregnancy, and some patients had problems in school life, and other patients had poor

health derived from mental problems, If a medical subject like change of the medicine accompanying pregnancy hope also occurs, a subject called the poor health which arose from the subject which arises in school life, or the mental problem is included. I hope our experiences help you in this symposium about practical translational medicine.

S9-7

What I thought in rheumatologic training of both childhood and adulthood

Mariko Mouri, Takumi Matsumoto, Fumio Hirano, Masaaki Mori
Lifetime Clinical Immunology, Tokyo Medical Dental University

Conflict of interest: None

I am a pediatrician. I could luckily have a rheumatology training in both childhood and adulthood, four years in total. During the training period, I could think about pathologic differences in childhood and adulthood. Another large crop was that I could see “pediatrics” objectively. As a pediatrician is primary physician of children, so patients will come to feel a specialist, a like pediatric rheumatologist, with a family doctor. On the other hand, the period when the pediatrician sees growth of children at the side becomes long, the bonds might be strong, and they might not want to part with the patients. There are three different points from pediatric rheumatology when I trained in outpatients of adulthood rheumatology. First, the number of patients. Second, there are many problems in one patient, but third, they have a family doctor. It is not necessary for the rheumatologist to support all of the problems, and they can concentrate on rheumatologic problems. Whereas the burdens on adult department physician come to continue increasing with of the number of patients, because there are a lot of patients whom condition is stable does not to accept with introduction to rheumatic clinic of their neighborhood. Furthermore, the adult medical care may collapse when transition patients are added. In transition medical care, it is important that pediatricians and adult internal medicine should deepen understanding of each other. A pediatric rheumatologist does not have to completely treat adult rheumatic patients, and vice versa. It is necessary for the pediatrician to realize it again about an important role to promote the independence of children.

S10-1

Overview

Yasuhiro Kondo¹, Masataka Kuwana²

¹Department of Respiratory Medicine and Allergy, Tosei General Hospital, ²Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine

Conflict of interest: Yes

Interstitial lung disease associated with the connective tissue diseases (CTD-ILD) is a challenging and crucial issue for both pulmonologists and rheumatologist. Here’s an overview of CTD-ILD. 1) Early diagnosis Pulmonologists and rheumatologist see patients with some different populations of CTD-ILD. Pulmonologist see not only ILD patients with established CTD but also see ILD with subtle or not definitive features for CTD. On the other hand, rheumatologists see patients with established CTD and then find ILD, therefore, they have chance to see mild or asymptomatic ILD. Because of these differences, collaborations of pulmonologists and rheumatologist is useful. 2) Classification The clinical course of CTD-ILD is heterogeneous; some experience stable or slowly progressive ILD; however, a significant group exhibits a more severe and progressive decline. CTD-ILD is the leading cause of death. It is crucial to make a classification with primary disease, autoantibodies, HRCT patterns, histological patterns, and biomarkers. 3) Treatment Mainstay therapies for a CTD had been corticosteroids and immunosuppressants, but recently, molecular targeted drugs for CTD are available. In patients with IPF, antifibrotic drugs roughly half the relative rate of decline of FVC. In patients with NSIP, corticosteroids and immunosuppressants are usually effective, however, they are harmful in patients with IPF. In patients with RA-ILD, DMARDs may be harmful with histopathological UIP in RA. Further studies are needed to evaluate the efficacy of these drugs in patients with CTD-ILD. 4) Future directions Many genetic factors have been identified through GWAS in CTD as well as in IPF, and evaluations

of similarities and differences of them may lead to an individualized medicine. Some molecular targeted drugs for CTD may be effective for CTD-ILD. Both pulmonologists and rheumatologists are now in desperate need for novel therapies with multidimensional approach among the broader spectrum of CTD-ILD.

S10-2

Diagnosis and treatment of interstitial lung disease associated with dermatomyositis

Shinji Sato

Tokai University School of Medicine

Conflict of interest: Yes

Interstitial lung disease (ILD) is the one of most important prognostic factors in patients with dermatomyositis (DM). Clinical course, response to treatment and prognosis of complicating ILD with DM is well known to be extremely diverse. Some are seldom progressive with no need of treatment, some are slowly progressive in a long period of time resulting in respiratory failure and some show sub-acute or acute progressive course some of which is fatal. Response to treatment is also different in each case. Therefore, correct evaluation of ILD types is very important in terms of the treatment of DM and ILD and this would lead to selection of appropriate treatment regimen and complete control of disease progression. In this aspect, autoantibodies found in patients with DM are useful for the diagnosis and treatment decision in clinical setting as well as serum ferritin or KL-6. Anti-aminoacyl transfer RNA synthetase (ARS) antibody and anti-melanoma-differentiation associated gene 5 (MDA5) antibody (anti-CADM-140 antibody) is well known as major antibodies that are closely associated with ILD accompanied by DM. Anti-ARS antibody is closely associated with ILD that shows chronic course, whereas anti-MDA5 antibody demonstrates acute or sub-acute type of ILD that is refractory and has poor prognosis. The treatment regimens of ILD with DM are still controversial and do not reach the agreement among the specialist because large multicenter prospective randomized control studies were not available in this area. In this symposium, clinical characteristics, laboratory and imaging findings, diagnosis, recommended therapy and prognosis of ILD associated with DM are reviewed.

S10-3

Interstitial lung disease in patients with systemic sclerosis

Yoshioki Yamasaki

Rheumatology and Allergy, St. Marianna University School of Medicine

Conflict of interest: None

Interstitial lung disease (ILD) is one of the common complications in patients with systemic sclerosis (SSc). ILD is detected by HRCT in up to 60% of SSc patients. Though the clinical course of ILD associated with SSc (SSc-ILD) varies from mild to severe, the disease is potentially progressive. Previous report shows that patients having extensive pulmonary disease of >20% by HRCT were associated with poor prognosis with survival rate of 43% at 10-year. Additionally, the survival in patients both with ILD and pulmonary hypertension is extremely poor (30% at 3-year). To improve the outcome in patients with SSc-ILD, proper assessment in patients having potential risk for progressive ILD and appropriate therapeutic intervention for those patients is necessary. Randomized controlled trials showed both oral cyclophosphamide and mycophenolate mofetil had the therapeutic efficacy on SSc-ILD (SLS-I and SLS-II, respectively). In stead of oral cyclophosphamide, IV cyclophosphamide is often used in clinical practice. One recent study showed that IVCY was as effective as oral cyclophosphamide. Unfortunately these traditional immunosuppressive therapies may not be enough to sustain pulmonary function in some patients with SSc-ILD. Significant interests are taken in developing new therapies based on the pathogenesis of SSc or SSc-ILD, which are now under clinical trials. Antifibrotic medications such as pirfenidone and nintedanib, which have been recently approved in patients with idiopathic pulmonary fibrosis, are included as investigational treatments. Additionally, investigation on the efficacy of pirfenidone in combination with mycophenolate mofetil was also underway (SLE-III). Tocilizumab, a humanized IL-6-receptor antibody, is now in a Phase 3 trial as a possible

treatment for SSc and its associated ILD. Rituximab might be another candidate for the treatment of SSc-ILD. In this session, the overview of SSc-ILD including recent progress in treatment will be provided.

S10-4

Statement for the diagnosis and treatment of interstitial lung disease in primary Sjögren's syndrome

Takashi Ogura¹, Noboru Kitamura²

¹Division of Respiratory Medicine, Kanagawa Cardiovascular and Respiratory Center, Japan, ²Department of Internal Medicine, Division of Hematology and Rheumatology, Nihon University, School of Medicine, Japan

Conflict of interest: Yes

S10-5

Interstitial Pneumonia with Autoimmune Features (IPAF)

Yutaro Nakamura, Katsuhiko Yoshimura, Takafumi Suda

Second Division, Department of Internal Medicine (Respiratory Medicine), Hamamatsu University School of Medicine

Conflict of interest: None

Patients diagnosed with an Idiopathic interstitial pneumonia (IIP) often have clinical features that suggest an underlying autoimmune process, and do not meet the established diagnostic criteria for any characterisable CTD. It has been proposed that the criteria and terms to describe these patients, including "undifferentiated CTD associated ILD" (UCTD-ILD), "lung-dominant CTD" or "autoimmune-featured ILD". Each term is controversial, and the lack of consensus over classification criteria limits the ability to conduct prospective studies for answering fundamental questions about these patients. The recent joint task force of the European Respiratory Society (ERS) and American Thoracic Society (ATS) proposed "interstitial pneumonia with autoimmune features" (IPAF) for this condition. A patient must meet criteria from two of the three prespecified domains to fulfill criteria for IPAF. These domains are clinical features of extrathoracic autoimmune disease, serologic evidence of autoimmune disease, and morphological criteria based on chest imaging, histopathology, or other multicompartment involvement. The concepts discussed in this research statement are intended to provide a platform for the prospective study of these patients and are not intended as guidelines for clinical care. According to the recent retrospective studies, current IPAF criteria seem to include a rather heterogeneous population. To overcome this issue, some researchers suggest requirements of multi-department with multi-center studies, and the exclusion of some specific autoantibodies. One of the main purposes of this criteria is to clarify the management and treatment of the IP patients with autoimmune features. We need prospective trials to investigate the efficacy and safety of disease-modifying antirheumatic drugs, biologic and antifibrotic agents. For a future progress in the field, there is definitely need for close collaboration between pulmonologists and rheumatologists.

S10-6

Progressive Fibrosing Interstitial Lung Disease: PF-ILD

Yoshikazu Inoue

Clinical Research Center, National Hospital Organization Kinki-Chuo Chest Medical Center, Japan

Conflict of interest: Yes

Interstitial Lung Disease (ILD), also referred to as Diffuse Parenchymal Lung Disease (Diffuse Parenchymal Lung Disease), encompass a large group of over 200 pulmonary disorders including connective tissue diseases, most of which are rare diseases. Patients with ILD have similar respiratory symptoms, pulmonary dysfunction, chest image findings, and/or pathological features, and the presence of patients who develop a progressive fibrosing phenotype instead of appropriate treatment during their clinical course has been reported. In addition, those patients can develop acute exacerbation, resulting in early death from respiratory failure. Patients with Idiopathic Pulmonary Fibrosis (IPF), a representative pulmonary fibrosis, have heterogeneous clinical features. But the prognosis of

the patients with progressive fibrosing phenotype are considered to be poor. Recently, a large-scale clinical trial for IPF using anti-fibrotic drugs (nintedanib or pirfenidone) had been conducted with the positive results. Their efficacy and safety have been also reported in a real-world setting. The effects of these anti-fibrotic drugs on the phenotype of progressive pulmonary fibrosis other than IPF are expected. "Progressive Fibrosing Interstitial Lung Disease (PF-ILD)" is a disease concept defined in the clinical trials confirming the efficacy and safety of nintedanib for such patients. PF-ILD was defined as combination of evidence of worsening lung function, worsening respiratory symptoms and/or evidence of increasing fibrosis on chest imaging, despite adequate treatment in 24 months. The clinical trial is ongoing and the results are highly expected (Flaherty KR, et al, *BMJ Open Respir Res.* 2017). Patients with connective tissue disease associated with progressive fibrosing phenotype of ILD could not be sufficiently controlled by conventional treatments and managements of underlying connective tissue disease. In order to improve QOL and prognosis of those patients, treatments and/or managements of IPF, such as anti-fibrotic drugs would be helpful.

S11-1

Joint surgery for rheumatoid arthritis aimed at improving physical function

Toshihisa Kojima

Nagoya University, Graduate School of Medicine

Conflict of interest: Yes

Drug therapy with methotrexate (MTX), and biologics (Bio) had made great progress in treatment of rheumatoid arthritis (RA) during two decades. A strategic Treat To Target aiming at a clear numerical target, that is, "remission; symptoms of arthritis remain at most one joint" is the most important for improving the outcome. Early patients with minimal joint destruction can sufficiently prevent the occurrence of ADL disorder by medication therapy. On the other hand, there are many patients who already have joint destruction and ADL disorders. Surgical therapy is an important option for these patients. According to a multi-center cohort study for the RA patient with joint surgery, which was supported by a grant from Ministry of Health, Labor and Welfare, more than half cases were operated with inflammation being almost calm. Also, approximately one third of cases were undergoing surgery in functional remission status. Therefore, current RA surgical therapy is performed not only to relief from pain but also to re-acquire physical functions. It is essential to set concrete numerical targets to achieve high therapeutic goal of improving patient's physical function. The target needs to be a daily, familiar numerical value for the patient, the medical doctor, and both. Now, we are paying attention to the range of motion of the joint and the activity speed as outcome measure to set the target. The targets should be useful for shared decision making of surgery, daily care and rehabilitation.

S11-2

Evidence of surgeries for upper extremity (Elbow/Shoulder) to improve QOL of RA patients

Yoshihisa Nasu¹, Ryozo Harada², Keiichiro Nishida², Minami Matsuhashi², Masahito Watanabe², Shunji Okita², Yohei Kiso², Hideki Ohashi², Ryuichi Nakahara³, Toshifumi Ozaki²

¹Department of Medical Materials for Musculoskeletal Reconstruction, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Science, ²Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Science, ³Department of Intelligent Orthopaedic System, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Science

Conflict of interest: Yes

The advancement of recent pharmacological therapy has dramatically changed the patients' disease characteristics of rheumatoid arthritis (RA). As results, decreasing incidence of orthopaedic surgeries have been observed in many registered populations. On the other hand, small joint surgeries for hand / foot disability have been performed more frequently in Japan. Regarding to function of upper extremity, the reconstruction of ability to reach, that is mainly affected by shoulder and elbow function is

essential to improve the QOL of RA patients. Synovectomy is rarely performed today but still important option for persistent synovitis despite of adequate therapy. Long term result should be re-evaluated in this bio era. The clinical result of shoulder arthroplasty has been remarkably improved mainly by the advancement of prosthesis design. Reverse shoulder arthroplasty is widely indicated cuff tear arthropathy. However rheumatoid shoulder with rotator cuff disorder can be also indication of reverse shoulder arthroplasty, we need careful consideration for poor bone quality and bone stock of them. Intensive drug therapy for joint inflammation and osteoporosis is expected to reduce these problems in RA patients. Total elbow arthroplasty is also important procedure for reconstruction of RA elbow. We still have to treat many patients who already have destructed elbow with severe pain, contracture, or instability. Surgeon have to select adequate implant to each case regarding to patient's factors (e.g. condition of soft tissues, age, bone stock, daily activity level). Our previous studies revealed that clinical result of TEA is significantly affected by adjacent joint involvement. In this symposium, we outline the clinical result of our TEA evaluated by several patients reported outcomes (PREE, DASH, HAND20, Boddy image assessment tool).

S11-3

Evidence that surgery for rheumatoid arthritis patients improves their quality of life Wrist and Hand

Asami Abe

Department of Rheumatology, Niigata Rheumatic Center, Shibata Niigata Japan

Conflict of interest: None

Objective: The disease activity of rheumatoid arthritis (RA) patients is improved by treatment with biological agents (Bios). We examined the surgical sites and procedures that afforded high satisfaction (EuroQol 5 Dimension [EQ-5D], Beck's Depression Inventor-II [BDI-II], Japanese version of the Stanford Health Assessment Questionnaire [J-HAQ] and Disability of the Arm, Shoulder and Hand [DASH]) in RA patients after surgery. **Methods:** We evaluated 123 RA patients for their duration of disease as well as disease stage and class. We also assessed the surgical site and type of procedure performed. The EQ-5D, BDI-II, J-HAQ and DASH were measured before surgery and at six months and one year after surgery. **Results:** A total of 123 RA patients (average age: 63.2 years old) had been affected for a mean of 16 years with a mean stage of 3.16 and class of 2.33. The surgical sites were the wrist in 76 and finger in 47. The procedure was synovectomy in 21, arthroplasty in 39, arthrodesis in 33 and joint replacement in 30. There were significant differences in the EQ-5D, BDI-II and J-HAQ scores of the wrist before and after surgery. There were also significant differences in the EQ-5D, BDI-II and J-HAQ scores between arthroplasty and arthrodesis. At all surgical sites and for all procedures, the DASH score improved after surgery. **Conclusions:** The postoperative satisfaction of RA patients was shown to be quite high at the wrist joint. The surgical procedures of arthroplasty, arthroplasty, arthrodesis and joint replacement showed a high postoperative satisfaction among RA patients. Surgeries at the wrists and fingers for RA were shown to enhance the quality of life of RA patients.

S11-4

Evidence of the knee and hip surgery for the patients with rheumatoid arthritis improved their quality of life

Yuya Takakubo^{1,2}, Michiaki Takagi²

¹Department of Rehabilitation & Orthopaedic Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan, ²Department of Orthopaedic Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan

Conflict of interest: None

Knee and hip joints play important roles for standing and walking as a human being. Reconstruction of their joints is one of beneficial therapeutic targets in surgical interventions (Ito H, et al. 2018). Biologic (BIO) therapies have been developed dramatically the treatment in RA patients. Decreasing of total numbers of surgeries for RA in BIO-era, especially synovectomy of joint and total knee and hip arthroplasties (TKA, THA) (Weiss RJ, et al, 2008, Shourt CA, et al, 2012, Momohara, et al, 2010). In our registry, the rate of orthopaedic surgeries for RA patients were de-

creased year by year compared to the trend of whole orthopaedic surgeries (Takakubo Y, et al. 2015). However, 20-30 % of RA patients using biologics are non-responders or show only minor improvement. The residual joint inflammation indicates a risk for progression of the joint destruction with osteoarthritis changes and osteoporosis (Nystad TW, et al, 2016). It has reported not to stop and prevent the progression of joint even using biologics who already has changed the joint destruction over Larsen grade 2 (Matsushita I, et al, 2017). TKA and THA is an important surgical intervention for RA patients, because they have related the improvement of ACR core set and HAQ scores (Tanaka E, et al, 2005, Ishikawa H, et al, 2018, Kojima T, et al, 2018). Because pre- and postoperative modified Harris Hip Score values were influenced by preoperative disease activity of RA due to multi-joint disorders, it is so important total management of whole joints of lower limbs for the surgical interventions (Imagama T, et al, 2018). In future, when it is possible to prevent joint arthritis and destruction at the early stage of RA, the joint preserving and re-construction surgeries which are relative contraindication until now is applied similar to non-RA patients (Yoshitomi H, et al. 2018). We will show the evidence of knee and hip surgeries for improvement of QOL in the patients with RA at this symposium.

S11-5

Foot and ankle surgery with evidence for higher QOL of rheumatoid arthritis patients

Makoto Hirao¹, Kosuke Ebina¹, Hideki Tsuboi², Takaaki Noguchi³, Shigeyoshi Tsuji³, Yasuo Kunugiza⁴, Koichiro Takahi⁵, Hideki Yoshikawa¹, Jun Hashimoto³

¹Department of Orthopedics, Osaka University Graduate School of Medicine, ²Orthopaedics/Rheumatology, Osaka Rosai Hospital, ³Orthopaedics/Rheumatology, National Hospital Organization, Osaka Minami Medical Center, ⁴Department of Orthopaedics, JCHO Hoshigaoka Medical Center, ⁵Orthopaedics/Rheumatology, National Hospital Organization, Toneyama Hospital

Conflict of interest: None

As a general-purpose rating system of the QOL, Medical Outcomes Study 36-Item Short Form-36 (SF-36) and EuroQoL (EQ-5D) are popular. These are evaluations including the mental health not only to mention an item of a function, pain, a daily living activity, the social life. There are the AOFAS score of the surgery society of the American foot and the JSSF score of the surgery society of the Japanese foot, and it is used frequently, but it is all the evaluation of pain, the function, however mental health index is not included in the treatment result criteria of a foot part, the ankle. Rheumatoid arthritis is a systemic disease, and chances for a remission state increase by dramatic progress of the medical treatment, but there is certain pain subjectively in 90%, latitude in 70%, and stiffness in 40% of a case said to be remission from a doctor notices [Rheumatic communication book, Copyright © 2018 Eli Lilly Japan K.K. All rights reserved.]. The rating system that the mental health side such as SF-36 or EQ-5D included was important, but it was said to check systematic body and mental health, and the surgery of the foot part was local treatment and focused on a foot. From these, it was able to use an evaluation using SAFE-Q rating system including the items of the mental health index. Validity and responsiveness of SAFE-Q in the rheumatic case is proved [Yano et al. *Mod Rheumatol.* 2015]. We introduce this SAFE-Q from 2014, then we compared even the severe case example such as Larsen classification 4-5 with the mild case when we performed the modified Scarf osteotomy+metatarsal shortening offset osteotomy for rheumatic forefoot deformity. There was no inferiority in severe group [JBJS.2018]. On the other hand, we knew that score was higher than case group of the biological treatment in a score of the postoperative social life-related index, as compared with non-biological group, after total ankle arthroplasty (TAA) [JBJS open access. 2017]. With progress of the medical therapy, we feel a duty and challenge for the durability improvement of the artificial ankle joint for the rheumatic case that have more activity.

S11-6

Surgical treatment of spinal lesions associated with rheumatoid arthritis

Hirota Chikuda

Department of Orthopaedic Surgery, Gunma University

Conflict of interest: None

Spinal lesions associated with rheumatoid arthritis (RA) commonly affect the cervical spine with reported incidences ranging from 40 to 80 %. Progressive destruction of the spine may cause intractable pain, loss of natural motion, and instability of the spine. Further destruction may result in compromise of spinal cord and subsequent paralysis. Recent advances in medical treatment have greatly improved care of patients with RA. Modern biologics not only suppress the progression of joint destruction but also have the potential to reduce the occurrence of spinal lesion. Nevertheless, surgical treatment will remain as treatment of choice for those presenting with advanced destruction of the spine. For the last few decades, surgical treatment of spinal lesions in RA patients has been becoming increasingly safer; the primary factors include 1) wide-use of computer navigation-assisted surgery, 2) advances in spinal instrumentation, and 3) increased awareness of potential complications. Surgical treatment of spinal lesions has the potential to substantially improve outcomes and patients' quality of life if provided at the right time.

S12-1

Trans-layer omics analysis reveals disease biology

Yukinori Okada

Department of Statistical Genetics, Osaka University Graduate School of Medicine

Conflict of interest: None

Recent development of genome sequencing technology changed the bottleneck of genomic studies from genome sequencing into interpretation of the sequenced genomes. Trans-layer omics analysis is a type of the bioinformatics analysis which integrates omics data from different samples or populations. Compared with multi-layer omics analysis which handles omics data from the same individuals, trans-layer omics analysis can handle more omics layers and larger samples with lower costs. Integration of large scale genome-wide association study results with tissue-specific epigenome information can identify key cell types causally related to disease biology. Previous trans-layer omics analysis mainly handled epigenome information such as gene expression (by RNA-seq) and chromatin information (by ChIP-seq and ATAC-seq). Recently efforts focus on integrating additional omics layers. We developed a novel statistical genetics method named MIGWAS (miRNA-target gene enrichment analysis in GWAS), which integrated large scale disease genetic data with tissue-specific expression profiles of microRNAs. Application of the non-linear machine learning method to the HLA gene variants revealed clustering patterns of white blood cell types of the Japanese population. We would like to introduce our recent researches on trans-layer omics analysis.

S12-2

AI-based drug discovery: data-driven approach to predict therapeutic effects and side-effects

Yoshihiro Yamanishi

Department of Bioscience and Bioinformatics, Kyushu Institute of Technology

Conflict of interest: None

Recent developments in biotechnology have contributed to the increase in the amounts of high-throughput data for compounds and proteins in the genome, transcriptome, proteome, metabolome and phenome. These biomedical big data can be useful resources for drug discovery and repositioning. Drug repositioning, or the identification of new drug indications (new applicable diseases of existing drugs), is an efficient strategy for drug development. The drug repositioning approach has received remarkable attention in pharmaceutical industry, because it can increase the success rate of drug development and to reduce the cost in terms of time, risk, and expenditure. In this study, we developed novel machine learning methods for predicting potential target proteins of known drugs or drug candidate compounds toward automatic drug discovery and repositioning. We performed the prediction of unknown therapeutic effects or side-effects based on various large-scale omics data of drugs, compounds, genes, proteins, and diseases in a framework of supervised network infer-

ence. Our results show that the proposed method outperforms previous methods in terms of accuracy and applicability. We performed a comprehensive prediction of new indications of all approved drugs and bioactive compounds for a wide range of diseases defined in the International Classification of Diseases. We show several biologically meaningful examples of newly predicted drug indications for cancers and neurodegenerative diseases. The proposed methods are expected to be useful for predicting therapeutic effects and side-effects of drug candidate compounds in practice.

S12-3

Cancer immunology research with novel experimental approaches

Hiroyoshi Nishikawa

Research Institute, Division of Cancer Immunology, National Cancer Center

Conflict of interest: Yes

Upon the clinical application of cancer immunotherapy, particularly immune checkpoint blockade (ICB) in which treatment efficacy is dependent on the immune system, more than half of treated patients yet fail to respond to immune checkpoint blockade, even in combination, uncovering a limited window of clinical responses. It is therefore required to develop more effective cancer immunotherapies and define biomarkers for stratifying responders and non-responders via the detailed analyses of immune responses in the patients. According to the cancer immunoeediting hypothesis, cancers select low-immunogenic tumor cells such as cells with decreased immunogenic antigens and employ multiple immune suppressive mechanisms including immune checkpoint molecules to create an immunosuppressive tumor microenvironment (TME) to escape immunosurveillance. Thus, cancers in the clinic can be divided in immunologically hot and cold tumors, and clarifying the immunological phenotypes with comprehensive genomic and immunological assays is necessary to optimize cancer immunotherapies with suitable predictive biomarkers. Certain oncogenic signals such as WNT signal reportedly control immune responses in tumors. We have found that driver mutations in EGFR promoted Treg-infiltration and inhibited effector T-cell infiltration into the TME by directly targeting chemokine expression to establish the immune suppressive TME. Thus, integrated analyses of immunological and genomic assays revealed the comprehensive immune suppressive network in the TME, leading to the optimal cancer immunotherapies.

S12-4

SKG mouse as a model of autoimmune arthritis

Keiji Hirota

Laboratory of Integrative Biological Science, Institute for Frontier Life and Medical Sciences, Kyoto University

Conflict of interest: None

The SKG strain of mice, carrying a point mutation in the gene encoding the TCR-proximal signaling molecule ZAP-70, develops CD4⁺ T cell-mediated autoimmune arthritis, which clinically and immunologically resembles rheumatoid arthritis (RA) in humans. The mice spontaneously develop the disease in a microbially conventional environment but not under a specific pathogen-free (SPF) condition. Yet the disease can be induced in SPF SKG mice by stimulation of innate immunity via TLRs, the Dectin pathway, or complement activation pathways. We previously demonstrated using SKG mice how self-reactive T cells are generated in the process of thymic positive and negative selection, become activated in the periphery by recognizing self-antigens, differentiate into arthritogenic Th17 cells upon stimulation of innate immunity, migrate into the joints, and aggress self-antigens expressed by synoviocytes. These features make this spontaneous model of autoimmune arthritis suitable for elucidating how Th17 cells mediate autoimmune diseases, especially RA, via interacting with other lymphoid and non-lymphoid cells at the inflammation site and controlling their production of inflammatory cytokines.

S12-5

Research on diseases and drug discovery by intravital imaging

Junichi Kikuta

Department of Immunology and Cell Biology, Graduate School of Medicine, Osaka University, Japan

Conflict of interest: None

Bone is the hardest tissue in the body; for this reason, it is technically difficult to visualize cellular interactions in the bone marrow of living animals. The morphology and structure of bone tissues can be analyzed using various conventional methods, including micro-computed tomography, histomorphological analyses, and flow cytometry. These methods yield information on cell shape and gene expression patterns, but not on dynamic cell movements in living bone marrow. The recent introduction of fluorescence microscopy has enabled imaging of the cellular dynamics of organs and tissues *in vivo*. Therefore, we have originally established an advanced imaging system for visualizing living bone tissues with intravital two-photon microscopy. By means of this system, we revealed the *in vivo* behavior of bone-resorbing osteoclasts and could grasp the real time-course of osteoclastic bone resorption which was finely regulated by cell-cell contact with bone-forming osteoblasts. We also found that various anti-osteoporosis drugs acted directly on mature osteoclasts during bone destruction, with different efficacies. Here we show the latest data of intravital bone imaging, and also discuss its further application. This technique facilitates investigation of cellular dynamics in the pathogenesis of bone-destructive disorders, such as osteoporosis and rheumatoid arthritis *in vivo*, and would thus be useful for evaluating the efficacy of novel anti-bone-resorptive drugs.

S13-1

Current concepts and future perspective of the treatment of rheumatic diseases

Josef S Smolen

Medical University of Vienna, Austria

Conflict of interest: None

Treatment of IMIDs of joints and spine has reached an unprecedented success, owing to early diagnosis, a strategic treatment approach and the availability of targeted therapies. Since end of last century, pathogenetic information was used to develop novel therapies, but pathogenetic information does not equate knowing pathogenesis. True pathogenetic insights come from success or failure of agents deemed to be effective by *ex-vivo* and experimental model data and, thus, still from empiric approaches. TNF inhibition is effective across many IMIDs while IL-6 inhibition is not and IL-1 inhibition fails in most. IL-17 and IL-23 directed therapies fail in RA, but are effective in psoriasis with less efficacy in PsA; IL-17 inhibition fails in Crohn's (CD), while IL-23 inhibition is inefficacious in AS. Given relationship between IL-23 and Th17, the IL-17 source and the role of IL-23 is upraised and enigmatic. While this information allows to develop a "cytokine map" of IMIDs, it does not allow drawing a "cellular map". Inhibition of pathways involved with various pathogenic cytokines, such as 38-MAPK and Syk, is not efficacious where tested, while Jak-inhibition is efficacious across many IMIDs. We still do not understand which cytokines are those whose pathway is inhibited. Activation of the interferon pathway has been assumed to be critical in SLE, but recent data shatter the interferon theory. This list reveals that we have to learn which findings constitute an epiphenomenon and which ones are of true pathogenetic relevance? this will be a major challenge of the future. Recent developments, like single cell analysis or omics approaches, may help in this regard, as might information on the role of microbiota. The fact that autoimmunity starts many years before the onset of clinical manifestations, a time point that cannot be accessed at present, reveals the complexity of approaching a true understanding of pathways to these diseases. Future perspectives will be drawn.

S13-2

Safety management of biologics learned from multiple big data in the real world

Masayoshi Harigai

Department of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

Conflict of interest: Yes

Safety data of biologics are collected during and after clinical development programs, and post-marketing surveillance programs with pre-specified objectives have been implemented for many biologics in Japan. TNF inhibitors are approved for a series of rheumatic diseases, and their safety profiles have been investigated in detail. Infection is the most frequently observed serious adverse drug reaction (sADR) of TNF inhibitors, and should be paid attention in all diseases for which TNF inhibitor is used. Risk for serious infection is strongly affected by patient background of each disease, including age, comorbidities, and concomitant drugs, especially glucocorticoid. Safety profiles are basically similar across all indications. Among non-TNF inhibitors, tocilizumab is recently approved for Takayasu arteritis and giant cell arteritis. Clinical trials of the drug for adult-onset Still's disease and systemic sclerosis has been completed, and that for microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) is currently underway. Rituximab is already approved for MPA and GPA. Infection is also the most frequently reported sADR in patients treated with tocilizumab and rituximab. When these biologics are used for systemic rheumatic diseases such as vasculitides, it is pertinent to taper concomitant glucocorticoid as fast as possible and reduce the risk for infection as much as possible. Appropriate regimens of glucocorticoid including initial dosage and tapering speed is under investigation. No new ADRs of tocilizumab and rituximab have reported in patients with vasculitides or systemic sclerosis in clinical trials. Belimumab and mepolizumab are now available for systemic lupus erythematosus and eosinophilic GPA, respectively. All-cases post-marketing surveillance programs are in progress for these biologics and the results are awaited. I would like to take this opportunity to sort out the relevant data and reflect for future challenges.

S13-3

Prevention of Inflammatory RA

Paul Emery^{1,2}

¹University of Leeds, Leeds Institute of Rheumatic & Musculoskeletal Medicine, Leeds, UK, ²Leeds Teaching Hospitals NHS Trust, Leeds, UK

Conflict of interest: Yes

That the RA phenotype is the end-point of a continuum and that patients can be identified at a phase when they are at risk, has been a major advance for RA management. There are several ways of identifying patients, including identifying those with clinically suspicious symptoms but also asymptomatic patients with presence of CCP-2 (an anti-citrullinated protein antibody). Finding these patients in primary care has been a challenge, but there is now, through a national network, a process by which patients are referred with ACPA positivity and who have a relatively short period before they progress to inflammatory arthritis. It is possible through a clinical risk score to identify those likely to progress. This score can be further improved by the use of the imaging including ultrasound. Furthermore MRI has identified that the first musculoskeletal involvement may frequently be outside the joint and unique structures involved have been defined. The presence of abnormalities of T-cell subsets (particularly reduced naïve cells corrected for age) provide further sophistication. We are now in a position to accurately stratify patients for risk. Alongside this development, there has been evidence that the primary site of initiation of autoimmunity involves the mucosa. This has been studied in the mouth, the lung and the gut. We have had a particular interest in identifying abnormalities of the oral microbiome in patients at risk and have shown that *p.gingivalis* is highly prevalent in those with autoantibodies (without synovitis) and this is true of both diseased and healthy periodontal sites. Thus, we are now in the position that clinical trials can be logically undertaken to identify the best strategy for reducing the rate of progression.

S13-4

New perspectives on non-TNF biologics for RA and other autoimmune diseases

Yoshiya Tanaka

The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: Yes

Autoimmune diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are characterized by acute and chronic inflammation leading to multiple organ manifestations and various immunologic abnormalities are involved in the diseases processes. The development of biologics targeting IL-6 and T cells as well as TNF have revolutionized treatment of RA and clinical remission and prevention of structural changes are a realistic goal for the treatment. Moreover, the indication of anti-IL-6 receptor antibody has been recently expanded to other autoimmune diseases such as idiopathic juvenile arthritis, Takayasu's disease and giant cell arteritis. In contrast, there has been less evidence of effective targeted therapies in other autoimmune diseases and corticosteroids and immunosuppressants are still the standard of care which are often associated with adverse events. Several clinical trials have demonstrated less improvement in SLE due to the clinical and molecular heterogeneity among patients. By recent genome-wide association studies, disease-associated risk loci locate not only in acquired immunity but also in innate immunity. Biologics targeting BAFF, IFN, IL-12, etc. which are produced by dendritic cells and activate T cells and/or B cells, have been emerging for the treatment of SLE. On the other hand, how multiple biologics are differentially used for the treatment of autoimmune diseases remain unclear. Psoriatic arthritis (PsA) is a chronic and progressive inflammatory arthritis and biologics targeting TNF, IL-17, IL-12/IL-23, IL-23 are approved for the treatment. Because PsA is heterogeneous, we have tried to classify PsA by phenotypic differences of peripheral lymphocytes using 8-color flow cytometry and found that PsA was divided to four types, activated Th17-dominant, Th1-dominant, both of them and neither of them, which resulted in precision medicine via the strategic selection of different biologics based on the phenotypic differences in T cells in individual patients with PsA. Taken together, a treatment strategy should be guided by molecular, cellular and/or immunological mechanisms and biomarkers and a systematic approach to design a precision medicine to autoimmune diseases should help to achieve the goal.

S13-5

Further development beyond RA and beyond biologics

Tom WJ Huizinga

Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands

Conflict of interest: None

Rheumatoid Arthritis (RA) is a chronic inflammatory and destructive disease. During the last decades insight in pathogenesis and subsequent development of targeted therapies (especially monoclonal antibodies against cytokines and surface receptor on white blood cells) have dramatically improved outcomes for patients, the major developments will be reviewed. The phases of RA development are now well defined ranging from the mere presence of genetic risk factors to full-blown persistent RA. We expect that the management of RA will change by testing intervention strategies designed to prevent the development of persistent RA. The likelihood of an individual at risk in different pre-RA phases progressing to RA is currently being defined. The subjects at the highest risk of developing arthritis (i) suffered from joint pain prior to showing typical joint swelling; (ii) experienced sick leave rising sharply already 6 months before the diagnosis; (iii) displayed elevated levels of systemic markers of inflammation and autoantibodies; and (iv) showed anatomical changes detected by advanced in vivo imaging. Most insight has been gained in the development and maturation of the autoantibody response in RA. Subsequently, the strategies to detect patients at risk have been developed. Interventional studies in undifferentiated arthritis and early RA patients aiming to reach clinical remission as defined by the absence of signs and symptoms, already showed that drug free remission can be achieved if patients are treated very early. The development of specific autoantibody profiles and the selection of B-cells specific for citrullinated antigens and subsequent specific mutations from germline sequences are now identified, opening the possibilities for more specific interventions in early disease. Examples of such interventions will be reviewed. An ideal intervention would be one that prevents the expression of the clinical entity we recognise as full-blown RA. Such intervention will halt the disease process in individuals from the 'phases' from the pre-clinical status [an individual with genetic risk factors & environmental risk factors that develops systemic autoimmunity] through the clinical phases [an individual will develop symptoms e.g. joint pain and stiffness, then arthritis fi-

nally to a disease to classified as RA.

S14-1

Guideline for management of hyperuricemia and gout in Japan 3rd edition: Important issue of revision

Ichiro Hisatome

Division of Regenerative Medicine and Therapeutics, Tottori University Graduate School of Medical Science

Conflict of interest: Yes

Evidences showing that hyperuricemia could be an independent risk factor not only for gout but also for life-style related disease, renal failures as well as cardiovascular events have been enormously accumulated since 2010 when the 2nd edition of the guideline for the management of hyperuricemia and gout has been published. Thus, the 3rd edition of the guideline for the management of hyperuricemia and gout has been published in 2018. Using the systematic reviews on reports related to outcome of 7 clinical questions, bias risk of each evidence has been estimated. Taken together with the estimation of body of evidence, patients' opinions and medical economics, the recommendation for each clinical question has been determined as follows: 1) NSAIDs, glucocorticoid and colchicine are equally recommended to be use for gout attack, 2) Lowering serum urate less than 6mg/dl is recommended to treat tophus, 3) Long term colchicine cover is recommended to treat gout patients after administration of urate lowering agents (ULAs) than short period colchicine cover, 4) ULAs is partially recommended to use for hyperuricemic patients with CKD in order to suppress their deterioration of renal function, 5) ULAs are not partially recommended to use for hyperuricemic patients with hypertension in order to improve their prognosis and suppress their cardiovascular events, 6) ULAs are not partially recommended to use for hyperuricemic patients with heart failure in order to improve their prognosis and suppress their cardiovascular events, 7) Dietary education including restriction of alcohol abuse is recommended for management of hyperuricemia and gout. In addition to recommendation against clinical questions, review papers regarding the clinical issues of hyperuricemia and gout have been published. Thus, this guideline is expected to cover the decision making against the important clinical issues on hyperuricemia and gout.

S14-2

Guidelines for management of Behçet's disease

Mitsuhiro Takeno^{1,2}, Shunsei Hirohata^{2,3}, Hiroto Kikuchi^{2,4}, Masataka Kuwana^{1,2}, Kazuyoshi Saito^{2,5}, Yoshiya Tanaka^{2,6}, Hiroko Nagafuchi^{2,7}, Tetsuji Sawada^{2,8}, Toshihiro Tono^{2,9}, Yohei Kirino^{2,10}, Ryusuke Yoshimi^{2,10}, Hiroaki Dobashi^{2,11}, Ken-ichi Yamaguchi^{2,12}, Kayoko Kaneko^{2,13}, Shuichi Ito^{2,14}, Masaki Takeuchi^{2,15}, Yoshiaki Ishigatsubo^{2,16,17}, Nobuhisa Mizuki^{2,15}
¹Department of Allergy and Rheumatology, Nippon Medical School, ²Behçet's Disease Research Committee, Ministry of Health, Labour and Welfare, ³Department of Rheumatology, Nobubara Hospital, ⁴Department of Internal Medicine, Teikyo University School of Medicine, ⁵Tobata General Hospital, ⁶The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, ⁷Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, ⁸Department of Rheumatology, Tokyo Medical University Hospital, ⁹Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine, ¹⁰Yokohama City University Graduate School of Medicine, Department of Stem Cell and Immune Regulation, ¹¹Division of Hematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University, ¹²Immunorheumatology Center, St. Like's International Hospital, ¹³Division of Maternal Medicine, Center of Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development, ¹⁴Department of Pediatrics, Yokohama City University Graduate School of Medicine, ¹⁵Department of Ophthalmology and Visual Science, Yokohama City University Graduate School of Medicine, ¹⁶Yokohama City University Graduate School of Medicine, ¹⁷Yokohama Rheumatic and Internal Medicine Clinic

Conflict of interest: Yes

Behçet's disease has a broad spectrum of clinical features including

serious organ involvement in the eye, central nervous system, vascular system, and gastrointestinal tract. The Behçet's Disease Research Committee of the MHLW, Japan generated organ based management guidelines for Behçet's disease, consisting of a total of 162 clinical questions based on the concept of "all in one". Topical steroids, colchicine, antibiotics, NSAID, and oral corticosteroid are listed for mucocutaneous lesions. Topical steroids are also recommended for ocular attacks, whereas colchicine, a small amount CS, cyclosporine (CsA), and anti-TNF antibody are recommended along the severity to prevent attacks in the posterior uveitis. Early introduction of anti-TNF antibody is encouraged for patients having poor prognostic factors such as gender of male and young aged onset. CS and immunosuppressants are recommended for both arterial and venous lesions. IVCY and anti - TNF antibody are suggested for serious cases. At surgical or endovascular interventions for impending rupture of aneurysms, concurrent immunosuppressive therapies are recommended. The Japan guidelines recommend anticoagulants for deep vein thrombosis, unlike the EULAR recommendations. The guidelines recommend 5-ASA for all intestinal lesions, and steroids and anti-TNF antibodies for refractory or severe cases with or without immunosuppressants. Gastrointestinal bleeding and perforation require surgical operations followed by postoperative immunosuppressive therapy. CS and methotrexate are recommended for acute type and chronic progressive type of parenchymal neurological involvement, respectively. Anti-TNF antibody is recommended for refractory or recurrent cases. CsA is prohibited for the neurological involvement because of the neurotoxicity. The management is tailored to each patient, considering disease phenotype and severity. The guidelines would be helpful for improving medical care for Behçet's disease in Japan.

S14-3

SLE guideline by JCR/MHLW

Tatsuya Atsumi

Department of Rheumatology, Endocrinology and Nephrology Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Japan

Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is a prototype of systemic autoimmune disease. Multiple organs and tissues are affected in patients with SLE in a different way, and such heterogeneity of clinical aspect is making difficult to standardise the management of lupus patients in clinical practice. In the history, corticosteroids (CS) dramatically improved the mortality of lupus patients; on the other hand, major or minor adverse events of CS would significantly affect to their morbidity. Recently, the potent immunosuppressants are efficiently used for the remission induction in patients with SLE. Amongst the lupus organ involvements, lupus nephritis (LN) is one of the most common and important manifestation, and the better use of immunosuppressants are described in two major guidelines for lupus nephritis. Hydroxychloroquine was described as the basic drug for all LN patients, Mycophenolate mofetil (MMF) has been recommended for the initial and maintenance treatment. Cyclophosphamide (CY) and tacrolimus (TAC) are commonly used immunosuppressants. TAC has been approved for LN in a maintenance phase of the treatment in Japan. In clinical practice, however, TAC is often considered as a partner for MMF or CY in the induction phase for cases with insufficient response for MMF or CY. JCR and MHLW have collaborated to establish SLE guideline according to the GRADE method. In this guideline, recommendation statement was classified into 3 categories; recommended, suggested and proposed. Referring another SLE guideline for British National Health System, established by BSR, we discuss the significance of the Japanese SLE guideline for our daily clinical practice.

S14-4

Treatment Guideline for pregnancy/delivery of female patients complicated with SLE, RA, JIA, or IBD

Yohko Murakawa¹, Shigeru Saito²

¹Department of Rheumatology, Shimane University Faculty of Medicine, ²Department of Obstetrics & Gynecology, University of Toyama

Conflict of interest: Yes

Recent paradigm shift in the treatments of rheumatic diseases and

IBD has brought about great changes in the managements of the woman of childbearing age (WoCBA). Since active disease harms not only the patients but also their fetuses, treatment of the WoCBA should aim to prevent disease activity with safe drug therapy for exposing fetus/child. The study group (chaired by Prof. S. Saito) published the Treatment Guideline for pregnancy/delivery of female patients complicated with SLE, RA, JIA, or IBD, in March 2018. This was developed for clinicians treating WoCBA patients with these diseases and gynecologist/obstetrician managing pregnancy. The guideline was also described for the patients. The consensus of 17 committee members were described in the guideline in light of the knowledge from manuscripts published until December 2017. Eleven clinical questions (CQ) were set and the recommendation of each CQ was described. Three levels of recommendation grade and the median value voted by Delphi method as an agreement level were described. CQs were described on i) preconception managements, ii) managements during pregnancy, iii) delivery management and newborn risks, and iv) drug information during pregnancy/ lactation. CQ1: How to explain to a patient hoping pregnancy. CQ2: State to permit a patient pregnant. CQ3: Fertility in patients with these diseases. CQ4: Effect of pregnancy/delivery on disease activities. CQ5: Laboratory tests to examine and patient obstetric management for these disease patients should be treated in advanced treatment hospital? CQ7: Delivery management of the patients. CQ8: The points to consider for neonatal care. CQ9: Use of rheumatic medications during pregnancy. CQ10: The points to consider for using biologics during pregnancy. CQ11: Use of rheumatic medications during lactation. We hope the guideline would help the clinicians and make more patients happier.

S14-5

A Clinical Practice Guidance for Pediatric Rheumatic Diseases

Kazuko Yamazaki¹, Syuji Takei², Ichiro Kobayashi³, Minako Tomiita^{4,6}, Masaaki Mori⁵

¹Department of Pediatrics, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan, ²Department of Pediatrics, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan, ³Center for Pediatric Allergy and Rheumatology, KKR Sapporo Medical Center, Sapporo, Japan, ⁴Department of Allergy and Rheumatology, Chiba Children's Hospital, Chiba, Japan, ⁵Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, ⁶Department of Pediatrics, Shimoshizu National Hospital, Yotsukaido, Japan

Conflict of interest: None

Rheumatic diseases often involve multi-organ systems and, accordingly, should be managed by rheumatologists who have enough skills as general physicians. The number of certified pediatric rheumatologists is as few as 80 in Japan and it varies from one region to another. Therefore, standardization of disease management and establishment of uniform accessibility to pediatric rheumatologists are difficult. In the absence of a pediatric rheumatologist, a pediatrician with other subspecialty may have a responsibility to the management of patients with pediatric rheumatic diseases. Also, rheumatologists take the role of consultants for pediatricians and take over the treatment when the patients come of age. In medical care for pediatric rheumatic patients, it is critical that a team of specialists share clinical information and have common clinical goals. To achieve this, four clinical practice guidance for juvenile idiopathic arthritis (2015), childhood-onset systemic lupus erythematosus (SLE) (2018), juvenile dermatomyositis (JDM) (2018), and childhood Sjogren's syndrome (SS) (2018), have been published. The three guidance (SLE, JDM and SS) were created by "Pediatric Rheumatic Diseases Research Group" under the financial support by Health and Labour Sciences Research Grants (#201610070B) in collaboration with Japan College of Rheumatology, Pediatric Rheumatology Association of Japan, and Japanese society for Sjogren's syndrome. They provide comprehensive guidance for diagnosis, treatment corresponding to the activity and severity of the diseases, and management of complications. At this symposium, we would like to describe the three guidance (for SLE, JDM and SS), emphasizing the differences between clinical features, complications, and treatment strategies in children and adults, and making comparisons with guidelines in other countries.

S15-1

Vascular Endothelial Growth Factor A (VEGF) in Osteoimmunology

Bjorn R Olsen

Harvard School of Dental Medicine/Harvard Medical School, USA

Conflict of interest: None

Vascular endothelial growth factor A (VEGF) has critical roles in cardiovascular, hematopoietic, musculoskeletal and nervous systems. The name reflects its role in endothelial-based angiogenesis, but it functioned in multicellular organisms for millions of years before cell transport channels acquired endothelial cells. To obtain insights into VEGF-dependent regulatory mechanisms, the Olsen-lab has studied endothelial, cartilage and bone disorders that include altered VEGF functions. This led to identification of the matrix-binding receptor ANTXR1 as a negative regulator of VEGF expression. Loss-of-function mutations in ANTXR1 cause high levels of VEGF in several cell types associated with a severe early aging disorder (GAPO syndrome). VEGF contributes to pathogenetic mechanisms either by interacting with cell surface receptors on target cells (paracrine signaling) or by interacting with protein complexes in nuclear or cytoplasmic compartments of the cells that produce the growth factor. Intracellular VEGF mechanisms may explain how cells in vascular-free condensations express VEGF, but angiogenesis is not induced, at early stages of endochondral ossification. In differentiated chondrocytes, VEGF expression contributes to survival in hypoxic environments and the differentiation of articular chondrocytes and is required, as a paracrine factor, for growth plate and joint development. However, once established, articular cartilage expresses low levels of VEGF, until the levels increase with age and reach disease-promoting heights in osteoarthritic joints. Differentiation of Osterix-positive bone marrow-derived stromal cells to osteoblasts during postnatal bone growth requires intracellular VEGF mechanisms. These data have led to current studies of the molecular mechanisms that may be responsible for intracellular effects of VEGF in osteoblastic and hematopoietic lineage cells.

S15-2

Mesenchymal causalities in immunity and disease

George Kollias

BSRC 'Alexander Fleming, Greece

Conflict of interest: None

Mesenchymal cells (MCs) refer to a variety of cell types, most commonly tissue fibroblasts, pericytes and mesenchymal stromal cells, which form tissue microenvironments, mediate tissue structure and function and regulate immune responses. Understanding the physiological significance of MCs, in immunological homeostasis and the pathophysiology of chronic inflammatory disease remains a great challenge. We have identified a causal role of synovial fibroblasts and tissue MCs in the development of chronic inflammatory joint diseases and comorbidities, by showing in animal models that MCs responding to TNF become necessary and sufficient orchestrators of pathophysiology. Moreover, we gained interesting new insights into the lymphoid tissue organizing role of specific subpopulations of MCs and their functions in the development of secondary lymphoid tissue. Our recent studies have also uncovered a physiologically dominant innate sensing character of MCs responding to TLR4/MyD88, NFκB and MAPK signals and mediating tissue homeostasis, inflammation and tumorigenesis. The uncovered multi-layered functions of mesenchymal cells offer exciting new links between tissue homeostasis, immunity, chronic inflammation and cancer and prove essential for the discovery of novel mechanisms in complex disease pathogenesis, patient stratification and treatment.

S15-3

Integrated bioflow in inter-organ communication between skeletal and hematopoietic systems

Yoshio Katayama

Department of Hematology, Kobe University Hospital, Kobe, Japan

Conflict of interest: None

The hematopoietic organ, bone marrow (BM), is located inside the

bone, and the hematopoietic and skeletal tissues contact directly in the endosteal region. We have been working on the mechanism how the BM hematopoiesis is regulated by the skeletal system. Through this activity, we found that bone biology is critically important to explain the phenomena observed in clinical hematology. I would like to introduce the relay of multiple biological factors in different classes (e.g. cytokine, neurotransmitter, lipid mediator, hormone) and cellular players (e.g. sympathetic nerve, osteoblast, osteocyte, macrophage, neutrophil) that regulates the transient and irreversible distortion of inter-organ network between hematopoietic and skeletal systems.

S15-4

The osteoimmune regulator, RANKL

Kazuo Okamoto

Department of Osteoimmunology, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo, Tokyo, Japan

Conflict of interest: Yes

Bone is a crucial element of the skeletal-locomotor system, but also functions as an immunological organ that harbors hematopoietic stem cells and immune progenitor cells. Additionally, the skeletal and immune systems share variety of molecules, including cytokines, receptors and signaling molecules. Osteoimmunology was created as a new interdisciplinary field to explore the shared molecules and interactions between the skeletal and immune systems. In particular, the importance of an inseparable link between the two systems has been highlighted by studies on the pathogenesis of rheumatoid arthritis, which is one of the most representative skeletal disorders triggered by an abnormal immune response. RANKL is one of the most important factors explicitly linking the two systems. RANKL plays crucial roles in not only osteoclast differentiation but also the immune system, including lymph node development, thymic epithelial cell differentiation and M cell differentiation. Furthermore, bone resorption by excessive RANKL signaling lies at the core of the pathogenesis of various inflammatory diseases such as rheumatoid arthritis, psoriatic arthritis and periodontal disease. A fully human anti-RANKL neutralizing antibody denosumab is now used in the treatment of osteoporosis and skeletal-related events by bone tumors. Furthermore, it was approved in Japan for the treatment of bone erosion associated with RA last year. Recently, the importance of RANKL inhibition has been recognized in the oncology field. RANKL biology has been widely spreading beyond the conventional framework of osteoimmunology. It can be said that it is necessary to keep the osteoimmune system in mind when we think about anything related to either the bone or immune system.

S16-1

Empower Our Society using Microsoft Technologies

Akira Sakakibara^{1,2}

¹Microsoft Japan Co., Ltd., Japan, ²Microsoft Development Ltd.

Conflict of interest: None

Artificial Intelligence (AI) that began to transcend human cognitive ability, the world where everything is connected to the Internet and can analyze various data acquired from them (IoT), and a Mixed Reality (MR) begins to penetrate all aspects of entertainment, industry, education, medicine and life by mixing up real and virtual world. We are currently changing our society drastically using these technology innovations. On the other hand, we still have big concerns such as privacy information protection issue, security risks caused by platform vulnerability, ethical perspective on AI social implementation. In this session, we can discuss how we build innovative world and how we tackle concerns that were occurred as a side effect of innovation through the prospects of technology and social future trend.

S16-2

Next Generation Genomic Medicine based on Supercomputing and Artificial Intelligence

Seiya Imoto

The Institute of Medical Science, The University of Tokyo, Japan

Conflict of interest: None

Since 2011, we have been establishing systems of clinical sequence for cancers. The recent improvement of sequencing technologies enables us to sequence our whole genome with only 1000 USD or less. By whole genome sequencing analysis, we have about one billion pieces of DNA sequence called reads whose lengths are typically several hundred. We need to use those reads to detect genomic variations of each patient, however this task requires huge computational resources. In our center, a supercomputer system called SHIROKANE, having about 560 Tera Flops (From 2019, it increases threefold) computational capacity and 30 Peta Byte high speed disk array, is implemented and we use this system for genome sequence analysis. Using SHIROKANE with our genome analysis programs, we can obtain information of several to tens thousands of mutations occurred in cancer genomes of a patient. To utilize this information to clinical site, interpretation for such huge number of mutations is a critical bottleneck. PubMed stores more than 25 million papers' abstracts. Furthermore, the number of papers rapidly increases; more than two hundred thousand every year if we only focus on cancer research. No one can read all, it is obviously beyond human ability. Therefore, in 2015, we started to use an artificial intelligence including IBM Watson for Genomics, and installed in our center in order to make clinical sequence more accurate, comprehensive and faster. In the presentation, we will introduce our achievements on cancer big data analysis and AI-based clinical sequence.

S17-1

Design Determines the Quality of Research

Shunichi Fukuhara

Kyoto University, Kyoto, Japan

Conflict of interest: None

Publication of research has been very sluggish especially in the field of clinical research (Japan's share in the number of articles published in world top journals are on averages 8% in basic medicine, whereas only 2.5% in clinical research). So, it would be fair to say that the medical academia in Japan is now standing at the turning point. Some say low productivity in clinical research can be attributed to the lack of knowledge in statistical analysis or poor English competency. However, I think this is not as a serious problem as the absence of systematic education in "research design", which is the most fundamental and serious problem. Promotion of Clinical Research is needed not just for improving the ranking in publication of articles or accumulation of evidences from Japan. It is necessary because it could animate clinicians and improve quality of health care. This would be the most important reason for promoting clinical research in Japan. Now is the time for medical academia to start encouraging clinically and socially meaningful clinical research. To do this, it is absolutely necessary to promote the education of young researchers, and at the same time, to activate the database research.

S17-2

Statistical significance and its interpretation: Understanding from clinical research papers of New England Journal of Medicine

Hisashi Noma

Research Center for Medical and Health Data Science, The Institute of Statistical Mathematics

Conflict of interest: None

I guess many clinicians are still suffering with "statistics" of clinical research papers. However, in modern medical researches, many advanced statistical techniques, e.g., significance tests, confidence intervals, logistic regression, Cox regression, have been commonly used, and we cannot understand clinical evidence from these research articles precisely if we do not have sufficient knowledge about them. In this talk, I will provide a gentle introduction for significance tests and p-values that are said as the most difficult concepts to understand "statistics" of clinical researches. The significance test is a statistical method to assess two hypotheses, null and alternative hypotheses, e.g., "the investigational drug is efficacious" and "not efficacious," and provides a reasonable answer which hypothesis is true from observed data. However, the significance test does not pro-

vide certain information concerning the magnitude of effect, e.g., efficacy of the investigational drug. From a pragmatic point of view, the concept “effect size” is also important, which measures the magnitude of effects. In this talk, I also explain its relevance in clinical researches with a related important concept “minimally important clinical difference.”

S17-3

The stumbling point of clinical research and dealing

Nobuyuki Yajima

Division of Rheumatology, Department of Medicine, Showa University School of Medicine

Conflict of interest: Yes

Unfortunately, in clinical research, the publication of Japan facilities to the top journal is not often compared to basic research. This trend is the same as in diabetes, the care and kidney area. In the Japan, there is no education of the clinical research which was systematic in the education after graduation, and there are few who go on to the public Health Graduate School to study the clinical research literacy, absence of the leader of the clinical research, lack of the consultation opportunity with the statistician, There are many possible causes, such as the lack of available databases. It seems that there are a lot of people who were not able to overcome it as a result in the road of the clinical research from the research design to the thesis in the way. As the main hurdle, I do not know the entrance of research, the complexity of the literature search, the number of samples, statistical analysis, the writing of papers, the high wall of English papers, etc. will not rise. In this lecture, we will explain the overall image of the research project, and explain how to deal with the stumbling points of the theory culture such as the liver of research planning, how to search literature, and the knack of building a multi-facility registry. It introduces the type of the thesis creation while planning it in the liver of the research design, and touches the importance of consideration of the thesis making from the time of the design. In the literature search method, I will introduce how to search in “MESH + keyword” which is a general method of the search in PubMed. In building a multi-facility registry, I would like to talk about the actual experience of building flow, rule setting, and expansion method. In April 2018, the Clinical Research Promotion Subcommittee was established in the Japan Rheumatic society. The mission of this Committee is to promote literacy and clinical research for clinical research by the members of the Society in order to disseminate higher quality clinical research from Japan. We are planning to launch seminars, lectures and consulting sessions organized by the Committee in the future, and I would like to inform you about the activities of the Committee.

S18-1

Appropriate understanding and management of axial spondyloarthritis (Axial SpA) - Overview

Shigeto Kobayashi

Department of Medicine, Juntendo University Koshigaya Hospital, Saitama, Japan

Conflict of interest: None

The statement “With increased interest in ankylosing spondylitis and awareness that the majority of cases are misdiagnosed and inappropriately treated” by Andrei Calin in 1977, *JAMA* 237;24:2613-2614, is of critical relevance even at present. Despite remarkable advancements in the understanding and management of spondyloarthritis (SpA) recently established, some controversies, pitfalls, and inappropriate comprehension have been experienced and reported in the field of clinical practice and academic research for SpA. In this symposium, the recent understanding of axial SpA will be reconfirmed, and the controversies and unexpected pitfalls will be discussed since the time Dr. Calin warned us about 40 years ago as an initiative toward the introduction of appropriate management of axial SpA in Japan.

S18-2

Ankylosing spondylitis~key points of clinical practice ~

Kurisu Tada

Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine

Conflict of interest: None

Ankylosing spondylitis (AS) is a prototype of spondyloarthritis (SpA) which is mainly affected axial joints and enthesitis and is highly associated with HLA-B27. In advanced cases, it may interfere of activity of daily life due to spinal ankylosis. In AS patients, 80 to 90 % of patients have HLA-B27 positive, but in Japanese population HLA-B27 positive people is very rare, about 0.3%, so the prevalence of AS in Japan is very small compared to overseas. The modified New York criteria which is widely used for diagnosis of AS has high specificity but low sensitivity and it is difficult to diagnose correctly in early patients who do not meet the X-ray criteria. Additionally, it is difficult to interpret the X-ray findings of the sacroiliac joints, but it also hinders correct diagnosis. To diagnose SpA patients earlier, the Assessment of SpondyloArthritis international Society (ASAS) established classification criteria for axial SpA in 2009. In this criteria, MRI of the sacroiliac joint, which can visualize inflammation from earlier than X-ray, is added as imaging arm, and other SpA features such as psoriasis and inflammatory bowel disease, is included in clinical arm. Attempts have been made to diagnose axial SpA from early stage, non-radiographic axial SpA, and to lead them to therapy earlier, but the problem of this classification criteria was discussed in recently. It is a problem to diagnose as axial SpA only by applying and meeting this classification criteria without adequate discrimination or exclusion diagnosis. At Juntendo University hospital, AS specialized outpatient clinic was established in department of orthopedic surgery and sports medicine about 25 years ago, and about 10 years ago, SpA specialized outpatient clinic was established also in department of internal medicine and rheumatology. In this session, I would like to share knowledge about this disease, the diseases to be discriminated or exclude and important point of treatment.

S18-3

What is non-radiographic axial spondyloarthritis ~ precautions for treatment ~

Yuhu Kadono, Atsuko Kanno, Hiroyuki Yoshioka, Hiromi Oda
Orthopaedic Surgery, Saitama Medical University

Conflict of interest: Yes

Recently, it becomes well known that spondyloarthritis (SpA) is a kind of umbrella inflammatory disease concept including ankylosing spondylitis (AS) and psoriatic arthritis. SpA exhibits not only arthritis or spondylitis but also enthesitis. SpA which shows sacroiliac joint or spine involvement like AS, is roughly classified into axial SpA (axSpA). We use ASAS criteria to classify axSpA, and call it a ‘non-radiographic axSpA’ when we can detect just a small radiographic change. Although there is the classification criteria, we sometimes have a difficulty to diagnose. We should distinguish inflammatory back pain from mechanical pain or fibromyalgic pain. When we find spinal fusion or hyper ossification, we should distinguish axSpA from degeneration, diffuse idiopathic skeletal hyperostosis or osteitis condensans illi. When we find STIR high lesions, we should distinguish axSpA from overuse, injury or infection. We should be careful and judge by not only cross-sectional but also longitudinal points of view.

S18-4

The prevalence of non-radiographic axial spondyloarthritis in Japan

Tetsuya Tomita¹, Yuri Matsubara², Yoshikazu Nakamura²

¹Department of Orthopaedic Biomaterial Science, Osaka University, Osaka, Japan, ²Department of Public Health, Jichi Medical University

Conflict of interest: None

The accurate prevalence, incidence rate or natural course of non-radiographic axial spondyloarthritis has been still remains unclear all over the worlds. The objective of this study is to clarify the prevalence of non-radiographic axial spondyloarthritis in Japan. A national-wide mail survey was conducted in about 20% of hospitals with beds and having orthopaedic Surgery, rheumatology and pediatrics department. The survey

required the number of patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis during last year (2017/January - December). If the hospital answered yes, we conducted the secondary mail survey in terms of the detail of the patients with AS and non-radiographic axial spondyloarthritis. In total 8459 departments, 2222 departments were extracted (the extracted rate: 26.3%). And 1344 departments responded (the response rate: 60.5%). The reported patients number for last year were 649 AS and 164 nr-ax SpA in orthopaedic surgery, 472 AS and 149 nr-ax SpA in Rheumatology, and 11 AS and 12 nr-ax SpA in pediatrics. Based upon the established survey methods, the estimated patients number of AS and nr-ax SpA in Japan were 3200 and 860 respectively. In Japan patients number of nr-ax SpA was much less compared to AS.

S18-5

Axial involvement of Psoriatic arthritis

Atsuo Taniguchi

Department of Rheumatology, Tokyo Women's Medical University

Conflict of interest: None

Axial involvement of psoriatic arthritis was reported to be 5%. However, it has been indicated that half of the patients with axial involvement did not show symptoms suggested spondylitis. The previous studies showed the differences between axial involvement of psoriatic arthritis and ankylosing spondylitis. Asymmetric sacroiliitis, non-marginal syndesmophyte, asymmetric syndesmophyte, and paravertebral ossification were more often seen in axial involvement of psoriatic arthritis. Other studies showed that the frequency of cervical spine involvement in psoriatic arthritis was more often than that in ankylosing spondylitis. The random spinal involvement has reported to be one of the characteristic findings of psoriatic arthritis. Axial involvement is important as one of the key domains of psoriatic arthritis.

S18-6

Problems involved in the treatment of axial spondyloarthritis on the standpoint of a patient-physician

Hisashi Inoue

Department of Orthopaedic Surgery, Juntendo University School of Medicine

Conflict of interest: None

Japan has been considered to be an 'underdeveloped country' for axial spondyloarthritis (AS) in view of the low incidence of this disease among Japanese. However, the academic achievements made for the disease in recent years have been quite remarkable in Japan. Through my personal experiences in the past 25 years as an AS patient myself, having been in charge of the Japan AS patients' association as well as a physician running a special AS clinic at the Juntendo University Hospital in Tokyo, I must admit that there still is a long way to go in terms of clinical aspects of the disease, namely diagnosis and treatments, especially on psychological care of the patients. The problems include erroneous diagnoses, over-diagnosis, excessive treatments, lack of tender and mindful approach to the anxious patients, etc. It is a pity to see some of the unfortunate patients tend to seek for inappropriate treatments and to become doctor shoppers, resulting in unfavorable outcomes. It is a sort of vicious cycle. Presuming that I would have been appointed as a symposist because of the above experiences, I will report the results of a questionnaire study I performed to my AS patients, and summarize my personal opinions regarding AS along with the patients' voices expressing their hope and dissatisfaction toward their physicians and treatments.

S19-1

How should we manage pneumonia in patients with Rheumatoid Arthritis?

Hiroshi Mukae

Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: None

Biological agents, such as DMARDs, now plays a vital role in caring for Rheumatoid Arthritis (RA) patients, and respiratory tract infections (RTI) have been major prognostic factors for RA, or disturbance for RA treatment. Pneumonia accounts for 23% of total death with RA patients, which is equivalent to malignancies, by Ninja Study reported in 2014. RTI screening is necessary when RA patients is scheduled the biological treatments, and sampling lower respiratory specimen is essential when airway or lung abnormalities are detected in chest CT scan. In our bronchoscopic study in RA patients, *Pseudomonas aeruginosa* accounts for 21% of pathogenic microorganisms detected in lower respiratory tract. Our findings were supported by a recent pneumonia study in RA patients, which showed that *P. aeruginosa* amount to 14% of causative microorganisms, following *Streptococcus pneumoniae*. Colonization of *P. aeruginosa* in the airway might be a risk factor for developing pneumonia and worsening prognosis of RA patients. Furthermore, those chronic RTI cause NETosis and might worsen the RA activities itself. Immunomodulatory drugs, such as macrolides may contribute to manage those diseases. Pneumocystis pneumonia (PCP) has also been increased in RA patients. It usually progresses rapidly and has high mortality. The definitive diagnosis of PCP in RA patients is difficult because the trophic forms or cysts in bronchoalveolar lavage fluid are usually undetectable, and DNA PCR result is hard to discriminate contamination. Moreover, PCP in RA often accompanied by connective tissue disease-related interstitial pneumonia, or drug-induced pneumonia, representative by methotrexate (MTX). Our recent study indicated that PCP in MTX-treated RA expressed significantly higher serum soluble IL-2R compared to PCP in MTX-untreated RA. New diagnostic markers and treatment programs specific for RA-related PCP are required in future management. In this symposium, I would like to introduce recent findings in the field and also to share our data, discussing the future management of pneumonia in RA.

S19-2

Risk and management of nontuberculous mycobacterial infection in rheumatoid arthritis patients receiving biological therapy

Shunsuke Mori

Department of Rheumatology, NHO Kumamoto Saishunsou National Hospital

Conflict of interest: None

Nontuberculous mycobacteria (NTM) are opportunistic pathogens that are ubiquitous in natural environments such as soil and water. Although over 150 different species are described, most NTM do not cause human disease. In susceptible individuals, NTM species infect the airway and lung tissue, leading to slowly progressive and destructive disease. NTM lung disease is most commonly due to *M. intracellulare* and *M. avium* (MAC). NTM disease occurs in the context of lung problem like COPD, bronchiectasis, and lung damage due to previous tuberculosis infection. The incidence of NTM disease is increasing worldwide, but there are no bactericidal anti-NTM drugs. Currently, multiple combined bacteriostatic antibiotics therapy is recommended, however, its effect is limited. The prognosis of NTM lung diseases is poor as indicated that the 5-year all-cause mortality exceeds 25%. Rheumatoid arthritis (RA) affects the immune system and is associated with lung diseases such as interstitial pneumonia and airway disease. The weak immune system and underlying lung disease are significant risk factors for NTM lung disease. Therefore, RA patients are much susceptible to NTM infection compared with the general population. In addition, biological agents, especially tumor necrosis factor inhibitors, are known to increase the risk of NTM disease. The use of biological agents has not been recommended for RA patients who have developed NTM diseases. However, we often encounter patients whose RA activity is uncontrollable without the introduction of biological therapy. Recent case reports demonstrated that under strictly supervised anti-NTM therapy, biological agents were successfully used for intractable RA patients who had NTM infection. Here, we discuss the safety of simultaneous use of biological agents in RA patients who have NTM lung disease. We also present cases of NTM disease caused by rapidly growing mycobacteria during biological therapy.

S19-3

How to assess acute-onset diffuse lung diseases in patients with rheumatoid arthritis ?

Hideto Kameda

Faculty of Medicine, Toho University, Tokyo, Japan

Conflict of interest: Yes

Lung is a vital organ where autoantibodies such as anti-citrullinated protein antibody are produced and pathological lesions including interstitial lung disease (ILD) and rheumatoid nodules develop. Among pulmonary complications, acute-onset diffuse lung diseases (AODLD) are frequently fatal, requiring the treatment in advance to the sufficient differential diagnosis procedures: they often develop as a result of immune disorder by RA, complicated by their modification by RA treatments and microorganisms. Therefore, major differential diagnoses for AODLD such as RA-ILD, drug-induced lung injury and pneumocystis pneumonia were not always mutually exclusive, and those diagnoses, including their overlap and transition, should be consistent with the treatment. Further, the concept of immune reconstruction (inflammatory) syndrome has been widely recognized, which leads to concerns about the risk of discontinuing immunosuppressive drugs upon infectious complications in patients with RA. Thus, the optimization of RA treatment discontinuation should be intensively discussed. In this symposium, the pathophysiology, diagnosis and treatment of AODLD will be discussed with recent findings and evidences.

S19-4

Pathological study of the consequences of interstitial pneumonia in the patients with rheumatoid arthritis

Tamiko Takemura

Department of Pathology, Japanese Red Cross Medical Center

Conflict of interest: None

Histopathological features of the lung with rheumatoid arthritis (RA) are very variable composed of interstitial pneumonia (IP), airway and pleural diseases. Among them, IP and bronchiolitis are thought to be the important prognostic factors of RA patients. The histological patterns of RA-IP has been applied by the classification of idiopathic interstitial pneumonias (IIPs), and the prognosis of RA-IP has been considered based on IIPs classification. However, whether this IIPs pattern exactly reflects the consequence of RA-IP has not been discussed until now. In this symposium, we present the characteristics of IP and bronchiolar disease of RA patients, and clarify the present issue. 1) Interstitial pneumonia IP in RA mainly consist of NSIP showing lymphocyte and plasma cell infiltration with alveolar wall fibrosis, and UIP with perilobular fibrosis, alternating normal alveoli and fibroblastic foci. There are some cases of UIP in RA showing cystic lesion in the lobule developed from chronic bronchiolar inflammation, resembling as honeycombing. These cystic lesions are lined by bronchiolar epithelium. Marked inflammatory cell infiltration also induced destruction of lobular structures. 2) Bronchiolar disease Hyperplasia of BALT frequently can be seen along the airways with follicular bronchiolitis. Cellular and destructive bronchiolitis, which shows loss of elastica of the bronchiolar walls, fibrosis and destruction of alveolar structures around the bronchioles, resulting in cystic change of the lobule. Sometimes, peribronchiolar metaplasia is prominent, inducing the cystic lobular change. Chronic and destructive intralobular bronchiolar inflammation in the lung with RA may induce destruction and cystic change of lobular structure. Here, we emphasize that intralobular bronchiolar inflammation and cystic consequences are important for the prognosis and treatment of RA-ILD.

S19-5

Management of rheumatoid arthritis associated with interstitial lung disease

Hitoshi Tokuda

Department of Respiratory Medicine, Tokyo Yamate Medical Center, Japan Community Health Care Organization (JCHO), Tokyo, Japan

Conflict of interest: None

Biologic agents have substantially advanced the management of rheumatoid arthritis, including its extra-articular manifestations. The only exception is lung complications, especially interstitial lung disease (ILD). RA-ILD is increasing in incidence and prevalence worldwide and now is the commonest cause of mortality of RA patients in Japan. RA-ILD includes those of slow progression (chronic ILD) and those of rapid progression (acute ILD), the latter may sometimes be caused by drug therapy or occur as an acute exacerbation of chronic ILD. The basic pathogenesis has much in common, so both should be discussed together. Chronic RA-ILD is usually classified according to the classification of idiopathic interstitial pneumonia, such as UIP pattern, NSIP pattern, and COP pattern. The latter two are usually responsive to corticosteroid therapy, resulting in favorable clinical course. UIP pattern is the problem. No effective treatment has been established in controlling the deteriorating course in some proportion of patients of this category. As for the pathogenesis of deterioration, many immunological studies have elucidated the possible participation of host immune response to pulmonary tissue containing RA specific substances such as ACPA. Thus treatment strategy should be formulated upon this knowledge including suppression of excess immune response in the pulmonary tissue. We have clarified pathologically and radiologically that in some cases of RA-UIP, the honeycomb-like structural derangement are caused by persistent inflammation and destruction of the bronchioles and surrounding lung parenchyma. Thus we propose the possibility of treatment through proper control of inflammation of the airway, utilizing inhaled corticosteroid and tacrolimus if necessary, with agile use of antibiotics in case of infection. Other immunosuppressive treatments, such as mycophenolate, rituximab, abatacept are also reported to be effective in case reports and in small case series.

S20-1

Environmental factors and rheumatoid arthritis

Yoshihiro Miyake

Department of Epidemiology and Preventive Medicine, Ehime University Graduate School of Medicine, Japan

Conflict of interest: None

In Japan, there are several clinical epidemiological investigations among patients with rheumatoid arthritis to assess prognostic factors, while no epidemiological study was performed to examine the relationship between environmental factors and the risk of rheumatoid arthritis. Some meta-analyses showed that obesity, coffee consumption, and smoking are associated with an increased risk of rheumatoid arthritis and that moderate drinking and vitamin D intake are preventive against rheumatoid arthritis. Antioxidant intake such as vitamins C and E, higher socioeconomic status, pregnancy, and statin use may be inversely related to the risk of rheumatoid arthritis. Meat intake and stress may increase the risk of rheumatoid arthritis. In a recent case-control study conducted in China, intake of mushroom, citrus fruit, and dairy products was associated with a reduced risk of rheumatoid arthritis, while intake of potato and other fruits except for citrus was positively related to the risk of rheumatoid arthritis. It is necessary to accumulate epidemiological evidence regarding risk and preventive factors for rheumatoid arthritis in Japan.

S20-2

Periodontal disease as an environmental factor in the onset of rheumatoid arthritis

Tetsuo Kobayashi¹, Satoshi Ito², Akira Murasawa², Hajime Ishikawa²

¹General Dentistry and Clinical Education Unit, Niigata University Medical and Dental Hospital, ²Department of Rheumatology, Niigata Rheumatic Center

Conflict of interest: None

Oral cavity has been considered to possess the second most complex microbiota and several different niches in human body. Dental plaque is the most microbial biofilm and causes periodontal disease (PD). PD is a chronic inflammatory disease characterized by the destruction of periodontal tissue and is classified as a lifestyle-related disease due to its association with oral hygiene and smoking. Recent evidence suggested a role for PD in systemic diseases including diabetes mellitus, vascular disorder, and rheumatoid arthritis (RA). RA is a systemic autoimmune dis-

ease triggered by a combination of genetic and environmental factors that lead to the breakdown of immune tolerance. Recently, a role for oral microbiome and PD was proposed as an environmental risk factor for RA. Studies suggest the potential mechanisms linking PD to RA as follows: 1) citrullination by oral bacteria and host peptidylarginine deiminase (PAD); 2) neutrophil extracellular traps (NETs) formation and host PAD activation by PD; 3) carbamylation by NETs components. We evaluated if *Porphyromonas gingivalis* (*P.g*) contributes to RA through its PAD activity. The results showed that serum antibody titers to *P.g* and *P.g* PAD increased and correlated with serum titer to cyclic citrullinated peptide (CCP) in patients with RA. Periodontal therapy reduced the Disease Activity Score in 28 joints (DAS28) and serum levels of anti-*P.g* titer and citrulline. The patients with high anti-*P.g* PAD titers also exhibited an inhibition in DAS28 improvements after RA medication. These suggest an association between *P.g* infection and RA. The patients further showed that serum levels of NETs and carbamylated protein (CarP) increased and correlated with PD severity. The NETs levels were related to DAS28 and serum anti-CCP titer, while the CarP levels were not. These suggest an association between serum NETs levels and PD severity, implicating a role for NETs in citrullination and autoimmune response in patients with RA.

S20-3

Supports of oral care for patients with rheumatoid arthritis by multidisciplinary team approach

Yasushi Miura

Department of Rehabilitation Science, Kobe University Graduate School of Health Sciences

Conflict of interest: None

Most of the anti-rheumatic drugs including methotrexate, steroids, biologics, and JAK inhibitors, suppress immunity. In contrast, NSAIDs render patients with RA less sensitive to dental pain. Further, the disability of upper limbs caused by joint destruction and the limited mandibular opening prevent plaque control by patients with RA. Due to these factors, patients with RA often develop and complicate periodontal diseases and dental caries, especially with lack of saliva when accompanying Sjögren's syndrome. The patients who lost their teeth by these diseases have difficulties on biting, speaking, getting proper nutrition, and swallowing and suffer from lower quality of life. Recently, *Porphyromonas gingivalis*, bacteria causing periodontal diseases, was reported to produce peptidylarginine deiminase solely and suggested to produce anti-cyclic citrullinated peptide antibody (ACPA), resulting the onset of RA or worsening the disease condition. Therefore, it is important to keep good oral condition for patients with RA to keep good treatment effects and high quality of life. For the purposes, both the professional oral care by dentists and dental hygienists and self-care by patients with RA. In addition, patient education, encouragement to visit dentists, the improvement of upper limb function by surgery, rehabilitation, and the self-help device by the multidisciplinary team are also necessary. We have been educating patients by a dental hygienist in the patient's class periodically and encouraging to visit dentists. In this symposium, the growing roles of the oral care supports by multidisciplinary team in aging society are reviewed by illustrating our experiences including the survey of oral condition of patients with RA evaluated by Adult Dental Examination Program and Health Guidance Manual by Japan Dental Association, and a study of the relationship between oral condition evaluated by Oral Health Assessment Tool (OHAT) and upper limb functions in patients with RA.

S20-4

Influence of smoking on the pathogenesis of rheumatoid arthritis

Masanori Funauchi

Department of Hematology and Rheumatology, Kindai University Faculty of Medicine

Conflict of interest: None

Relationship between smoking and rheumatoid arthritis (RA) has long been discussed, although RA has not been recognized enough as a smoking-related disease. Cigarette smoke contains various toxic substances including carcinogens and reactive oxygen species (ROS) such as

hydroxyl radical, peroxy nitrite and nitric monoxide which are associated with onset or progress of various smoking-related diseases including malignancy (laryngeal, pulmonary, gastric cancers, etc.), respiratory diseases (chronic bronchitis, emphysema, etc.), cardiovascular disorders (myocardial infarction, cerebrovascular disorder, Buerger's disease, etc.), obstetric diseases (infertility, abortion, premature birth, etc.), or periodontal disease. It is noteworthy that most of these diseases are also important as the complications of RA. Smoking is known to accelerate the onset and increase the incidence of RA as well as to exacerbate the disease activity and reduce the efficacy of anti-rheumatic drugs. Toxic substances of tobacco not only give rise to inflammation of the tissue but also modify autoantigens by activation of peptidylarginine deiminases (PADI), leading to production of anti-citrullinated peptides antibody (ACPA). On the other hand, smoking increases oxidative stress to stimulate signal transduction and apoptosis of the cell. And, it also causes changes of the microenvironment through ischemia-reperfusion injury (IRI) which increase the oxidative stress to aggravate the pathogenesis of RA. Furthermore, smoking affects the prognosis of RA by increasing the incidence of complications of the above smoking-related diseases. Since RA is influenced by smoking in many phases such as onset, disease activity, complication and prognosis, RA is absolutely one of the smoking-related diseases. Here, influences of the smoking on the pathogenesis of RA, in addition to the relationship to genetic factors, are discussed, and the effect of cessation of smoking are referred.

S20-5

Dysbiosis in rheumatoid arthritis patients

Yuichi Maeda

Department of Respiratory Medicine and Clinical Immunology, Osaka University

Conflict of interest: None

Rheumatoid arthritis (RA) is a systemic autoimmune disease, caused by both genetic and environmental factors. Recently, researchers have focused on the gut microbiota, which is thought to be one of the environmental factors affecting the development of RA. We review here the evidence from animal and human studies that supports the role of the gut microbiota in RA. We and others have demonstrated that the relative abundance of *Prevotella copri* is increased in some of RA patients. We have also produced gnotobiotic experiments to show that dysbiosis in RA patients contributed to the development of Th17 cell-dependent arthritis in gut microbiota-humanized mice. Recently, we have successfully isolated *P. copri* from rheumatoid arthritis patients. From these experiments, we could analyze precise mechanistic link between gut microbiota and human arthritis development. We believe that the endeavors to remediate dysbiosis would serve as a novel therapeutic or preventive approach in RA patients.

S20-6

Obesity, nutrition and rheumatism

Tokutaro Tsuda

Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan

Conflict of interest: Yes

According to ancient Chinese historical book "The Rites of Zhou", there were four medical professions: internalist, surgeon, veterinarian, and food physician, which is the superior to the others. The traditional Chinese medicine told that daily meals with temperance, regular lifestyle and peace of mind without greed make you live out your allotted span of life, but excessive drinking and eating, self-indulgent lifestyle and violations of the hygiene make you ill, then you would need "toxic drugs" for the treatment. The therapies for the illnesses caused by bad lifestyles must be accompanied with considerable risks, but they were regarded as a lower medicine. On the other hand, the disease preventions through improvements of whole lifestyle including daily meals were regarded as the genuine medicine. In modern rheumatology, the pathophysiology and therapeutics have made remarkable progress for these several decades. While our "weapons" such as biologics and tDMARDs are getting much stronger day by day, the risks and economical burden we take are also

getting heavier. However, the knowledges about feasible preventions remains insufficient. Recently, the comprehensive fundamental studies revealing the linkages between immunity and metabolism, and the epidemiological studies of large-scale cohorts present some evidences about the prevention. Especially, the fact that obesity has a feature of chronic tissue inflammation draws many researcher's notice. Its influence affects on the various organ systems: liver, pancreas, gut, adipose tissue, muscle and central nervous system. Among these organs, there is crosstalk mediated by cytokines, exosomes, free fatty acid, lipopolysaccharide, and so on. Based on these researches, novel promising therapies are expected to emerge. In this lecture, I will try to discuss about the prevention of rheumatic diseases which is validated by current evidences and feasible into our clinical practice.

S21-1

Overview

Kazuyuki Yoshizaki

Graduate School of Information Science and Technology, Osaka University

Conflict of interest: Yes

Since Benjamin Castleman, a pathologist in USA, had reported the enlarged lymph node, resembling thymoma with special pathological feature in 1956, it has been passed for sixty years. Pathological analysis is gradually increased. However, neither etiological and pathogenic analysis, epidemiology, treatment guideline, nor therapeutic algorithm are still unclear. Therefor, in 2015, the research study team of intractable disease on Castleman disease governed by the ministry of Health and Labor was started, and in 2017, to clear the classification of analogous diseases among Castleman disease, TAFRO syndrome, IgG4-related disease and POEMS syndrome, the another study group on above related disease has been established. Then, we are discussing about the difference and similarity among those diseases with the other study groups on IgG4-RD and POEMS syndrome. Today the professional doctors of each disease present the out line and specificity of each disease. And we propose the some cases who were hardly diagnosed. We hope you will be interesting in these rare and unclear disease. Knowing the problems and analysis of those diseases in this symposium, you will be of use in your daily clinical activity.

S21-2

Castleman disease

Hiroshi Kawabata¹, Nozomu Kurose², Shino Fujimoto¹, Yasufumi Masaki¹, Tomohiro Koga³, Atsushi Kawakami³, Toshio Kitawaki⁴, Akifumi Takaori-Kondo⁴, Hajime Yoshifuji⁵, Tsuneyo Mimori⁵, Kazuyuki Yoshizaki⁶

¹Department of Hematology and Immunology, Kanazawa Medical University, ²Department of Pathology and Laboratory Medicine, Kanazawa Medical University, ³Department of Immunology and Rheumatology, Nagasaki University, ⁴Department of Hematology and Oncology, Kyoto University, ⁵Department of Rheumatology and Clinical Immunology, Kyoto University, ⁶Graduate School of Information Science and Technology, Osaka University

Conflict of interest: None

Castleman disease (CD) is a rare non-clonal lymphoproliferative disorder; interleukin-6 plays an essential role in its pathogenesis. Clinically, CD is divided into two categories; unicentric CD (UCD) with a single lymph node lesion, and multicentric CD (MCD) with multiple lesions and systemic inflammatory symptoms. MCD is further categorized into at least 3 types; HHV-8-associated MCD commonly observed in HIV-positive individuals, POEMS syndrome-associated MCD manifesting polyneuropathy and M-proteinemia, and idiopathic MCD (iMCD). The affected lymph nodes in UCD usually show hyaline-vascular type histology, and those in MCD usually manifest either plasma cell type or mixed type histology. In Western countries, UCD is commoner than MCD, but a majority of CD in Japan are iMCD. Patients with iMCD manifest fever, malaise, anemia, lymphadenopathy, and splenomegaly; their blood tests show microcytic anemia, hypoalbuminemia, polyclonal hypergammaglobulinemia, and increased CRP levels. For making diagnosis of CD,

histopathological diagnosis is essential and excluding infectious diseases such as nontuberculosis mycobacteria infection, neoplastic diseases such as lymphomas, and autoimmune diseases is mandatory. A proportion of patients with iMCD manifest anasarca and thrombocytopenia; these symptoms are consistent with TAFRO syndrome. Thus, MCD seems to include multiple clinical entities; identification of specific markers for each entity is desired. As for treatments, UCD can be cured by complete resection of the lesions. Symptomatic patients with iMCD, especially those with pulmonary or renal involvement, should be treated with corticosteroids and/or tocilizumab (or siltuximab in US). In 2018, iMCD was registered as a designated intractable disease by Japanese government. Researchers in CD Collaboration Network are promoting researches internationally on iMCD. Further clarification of pathogenesis of iMCD and development of its novel treatments are awaited.

S21-3

TAFRO Syndrome

Yasufumi Masaki¹, Hiroshi Kawabata¹, Kazue Takai², Norifumi Tsukamoto³, Shino Fujimoto¹, Yasuhito Ishigaki⁴, Nozomu Kurose⁵, Shigeo Nakamura⁶, Sadao Aoki⁷

¹Hematology and Immunology, Medicine, Kanazawa Medical University, ²Department of Hematology, Niigata City General Hospital, ³Oncology Center, Gunma University Hospital, ⁴Medical Research Institute, Kanazawa Medical University, ⁵Department of Pathology and Laboratory Medicine, Kanazawa Medical University, ⁶Department of Pathology and Laboratory Medicine, Nagoya University Hospital, ⁷Department of Pathophysiology, Faculty of Pharmaceutical Sciences, Niigata University of Pharmacy and Applied Life Sciences

Conflict of interest: Yes

TAFRO syndrome is a systemic inflammatory disorder manifesting as thrombocytopenia; anasarca including pleural effusion and ascites; fever; reticulitis fibrosis/ renal insufficiency; and organomegaly including hepatosplenomegaly and lymphadenopathy. Its onset may be acute or sub-acute, but its etiology is undetermined. Although several clinical and pathological characteristics of TAFRO syndrome resemble those of idiopathic multicentric Castleman disease (iMCD), other specific features can differentiate between them. Some patients have been successfully treated with glucocorticoids and/or immunosuppressants including cyclosporin A, tocilizumab and rituximab, whereas others are refractory to treatment, eventually succumbing of disease. Early and reliable diagnoses and early treatments with appropriate agents are essential to enhance patient survival. We reported the 2015 updated diagnostic criteria, disease severity classification and treatment strategy for TAFRO syndrome, as formulated by Japanese research teams. We are now collecting data of patients with TAFRO syndrome, iMCD, and similar disorders, retrospectively. Establishment of appropriate medical treatment guideline is urgent business about the TAFRO syndrome which a diagnosis is difficult, and progress rapidly.

S21-4

Autoimmune Pancreatitis and IgG4-Related Disease

Shigeyuki Kawa

Department of Internal Medicine, Matsumoto Dental University, Shiojiri, Japan

Conflict of interest: None

IgG4-related disease (IgG4-RD) is a recently established systemic disease that is characteristically associated with elevated serum IgG4 levels and believed to be caused by autoimmune mechanisms. The clinical features of IgG4-RD include (i) systemic distribution, (ii) imaging findings of swelling, nodules, and/or wall thickening, (iii) high serum IgG4 levels, (iv) abundant IgG4-bearing plasma cell infiltration in affected organs, (v) a favorable response to corticosteroid therapy, and (vi) coexistence with other IgG4-RD manifestations simultaneously or in a meta-chronous fashion. The concept of IgG4-RD was established based on the culmination of specific discoveries, including a close association between autoimmune pancreatitis (AIP) and high serum IgG4 levels, massive IgG4-bearing plasma cell infiltration in pancreatic tissues affected by AIP, and systemic other organ involvements in AIP with similar IgG4-

bearing plasma cell features, which opened the gateway from AIP to IgG4-RD. Protein electrophoresis of sera of patients with AIP showed β - γ bridging, which was a polyclonal band in the rapidly migrating fraction of γ -globulins. This abnormal band was confirmed by immunoelectrophoresis to be caused by elevated serum IgG4 levels. We observed elevated IgG4 levels in 90% of patients with AIP but scarcely in other conditions, which nominated IgG4 as a sensitive and specific marker for AIP. We also described the characteristic histological features of abundant IgG4-bearing plasma cell infiltration in affected pancreatic tissues and other organs, indicating that AIP and systemic other organs shared a common pathological background. The disease spectrum of IgG4-RD seems to be capable of spreading every organ, including well-established members of AIP, lacrimal and salivary gland lesions, respiratory diseases, sclerosing cholangitis, kidney diseases, and retroperitoneal fibrosis, and other additional new members.

S21-5

POEMS syndrome

Satoshi Kuwabara

Department of Neurology, Chiba University Hospital, Chiba, Japan

Conflict of interest: None

POEMS (polyneuropathy, organomegaly, edema/effusion, M-protein and skin changes) syndrome is a rare generalized disorder characterized by plasma cell dyscrasia, characterized and overproduction of vascular endothelial growth factor (VEGF). Japanese national survey have revealed the prevalence of 0.4: 100,000, and mean onset age is 49 years. Most of the symptoms are likely to be explained by neovascularization and increased vascular permeability of VEGF, whereas multiple pro-inflammatory cytokines are upregulated in POEMS syndrome. To facilitate precise and early diagnosis, comprehensive systemic survey is essential, and we propose that current diagnostic criteria. The current first line therapy is high-dose chemotherapy with autologous stem cell transplantation (HDT with ASCT), whereas patients who are not eligible for transplantation because of high age or poor general condition, are treated with immunomodulatory drugs, such as thalidomide or lenalidomide. Prognosis of POEMS syndrome has been substantially improved by these novel interventions. This review focuses on recent advances in diagnosis, pathophysiology, and treatment of POEMS syndrome, and discusses future perspectives of therapeutic strategy.

S21-6

Differential diagnosis of IgG4-related disease, multicentric Castleman disease, TAFRO syndrome, and POEMS syndrome

Mitsuhiro Kawano

Department of Rheumatology, Kanazawa University Hospital

Conflict of interest: None

Fever and thrombocytopenia, which are representative features of TAFRO syndrome, are rarely seen in IgG4-related disease (IgG4-RD). Similarly, M proteinemia and polyneuropathy, which are important features of POEMS syndrome, rarely present in IgG4-RD. In contrast, some patients with multicentric Castleman disease (mCD) show some clinical features very similar to those seen with IgG4-RD. Frequently lymph nodes (LNs) are involved in IgG4-RD, and marked infiltration of IgG4-positive plasma cells in the LNs is a common feature between mCD and IgG4-RD. In such mCD cases, serum IgG4 levels are generally elevated. Moreover, hypergammaglobulinemia or hyper-IgGemia is a common feature shared by IgG4-RD and mCD. On the other hand, serum IgA and IgM levels are usually normal in IgG4-RD, but elevated in mCD. Although erythrocyte sedimentation rate is moderately elevated in IgG4-RD, serum CRP levels were normal or only slightly elevated (less than 1.0 mg/dL) in about 90% of patients in an analysis of 334 Japanese cases. In contrast, serum CRP concentrations are continuously elevated in mCD, and delayed treatment sometimes leads to secondary amyloidosis. Glucocorticoid responsiveness is also different between these two diseases. Good responsiveness is an important feature in IgG4-RD, while glucocorticoid responsiveness is partial, with the addition of tocilizumab therapy sometimes needed in mCD. Lungs, kidneys, skin are common extra-LN lesions in both, while pancreas, lacrimal gland or salivary gland

involvement is rarely seen in mCD. The above-mentioned features are useful for differentiating these two diseases. Finally, recently we found that serum IL-6 concentrations are continuously markedly elevated in mCD during treatment with tocilizumab. This may provide a hint to the pathogenesis of mCD.

S21-7

Approach and future prospects to clarify the pathology of idiopathic multicentric Castleman disease

Tomohiro Koga^{1,2}, Remi Sumiyoshi², Atsushi Kawakami², Kazuyuki Yoshizaki³

¹Center for Bioinformatics and Molecular Medicine, Nagasaki University Graduate School of Biomedical Sciences, ²Unit of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, ³Department of Biomolecular Science and Regulation, The Institute of Scientific and Industrial Research, Osaka University

Conflict of interest: None

Castleman's disease (CD), a heterogeneous group of lymphoproliferative disorders, is divided into unicentric CD and multicentric CD (MCD) based on the number of regions of enlarged lymph nodes with characteristic histopathologic features. The etiology of MCD remains largely unclear. The observed clinical symptoms of MCD are attributed to hypercytokinemia, including elevated levels of interleukin-6 (IL-6). The standard treatment of iMCD is glucocorticoid and humanized anti-IL-6 receptor antibody (tocilizumab), but some iMCD patients may present life-threatening complications such as respiratory failure, renal failure, liver failure, pancytopenia despite treatment with combined use with IL-6 inhibitor, high-dose glucocorticoid, and systemic chemotherapy. In addition, systemic chemotherapy is highly cytotoxic, leading to severe infection and organ disorder. Therefore, treatment development in iMCD according to the pathology is desired. Cyclosporin, a calcineurin inhibitor that suppresses activation of T cells as an immunosuppressive agent used in iMCD, is effective. In a report that examines the lymph nodes of iMCD, the percentage of T cells is higher than that of UCD, whereas the proportion of B cells is lower in iMCD suggesting the importance of T cells in the pathology of iMCD. Recent studies of the Castleman Disease Collaboration Network (CDCN) have suggested that the PI3K / Akt / mTOR pathway may be a therapeutic target for iMCD. The PI3K / Akt / mTOR signaling cascade is well known for its role in promoting cell growth and metabolism in response to growth factors by modulating S6K and 4EBP1. Accordingly, vascular endothelial growth factor: VEGF, T cell activation, and cellular proliferation can be candidates for the treatment of severe MCD. In particular, rapamycin, an inhibitor of mTOR, effectively inhibits cell proliferation of T cells and B cells. In this lecture, we will outline the latest findings on the pathology of iMCD and the possibility of mTOR inhibitor for iMCD patients.

Educational Lecture

EL1

An overview of cancer immunotherapy

Naoki Hosen

Osaka University Graduate School of Medicine

Conflict of interest: Yes

Cancer immunotherapy has become an important tool in treatment of many types of cancers. Management of immune-mediated side effects is essential for effective and safe cancer immunotherapy. In this lecture, I will summarize the state of art of cancer immunotherapy including checkpoint antibody therapy and CAR T cell therapy. In addition, I will discuss what we learn from autoimmune disease occurred after cancer immunotherapy.

EL2

Immunodeficiencies and autoimmunity/autoinflammation : the two sides of a coin

Ichiro Kobayashi

Center for Pediatric Allergy and Rheumatology, KKR Sapporo Medical Center

Conflict of interest: None

Autoinflammatory and autoimmune diseases reflect excessive immunity, whereas primary immunodeficiency syndromes are generally characterized by susceptibility to infection based on the defect of genes related to host defense. However, current classification of PID includes “diseases of immune dysregulation” which is characterized by autoimmunity or predisposition to macrophage activation. For example, defect in autoimmune regulator (*Aire*) gene which is critical to central T cell tolerance in the thymus causes multiple organ-specific autoimmunity, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED). On the other hand, mutation of *Foxp3* gene, a master key gene for regulatory T cells (Tregs) which play a critical role in peripheral T cell tolerance, causes immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome. Haploinsufficiency of CTLA-4, a functional molecule of Tregs, is clinically similar to IPEX syndrome. Defects in the function of NK cells or cytotoxic T cells lead to hemophagocytic lymphohistiocytosis similar to macrophage activation syndrome associated with systemic JIA. Because apoptosis is critical to the elimination of autoreactive clones, defects in apoptosis-related genes result in autoimmune lymphoproliferative syndrome (ALPS). Classical PIDs such as XLA or CVID are also predisposed to autoimmunity possibly based on the defects in normal receptor-editing or clonal deletion of autoreactive B cell clones. Complement deficiencies, particularly of early components of the classical pathway such as C1, C4 and C2 are also known as the causes of SLE-like diseases. To date, studies have demonstrated dysfunction or down-regulation of molecules related to the above mentioned autoimmune-prone PIDs in rheumatic diseases. The present lecture focuses on the current understanding of rheumatic diseases from the aspect of mechanisms of PID.

EL3

Treatment strategy for elderly rheumatic diseases

Takahiko Sugihara

Department of Medicine and Rheumatology, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan

Conflict of interest: None

Elderly-onset is common in polymyalgia rheumatic (PMR), giant cell arteritis (GCA), and microscopic polyangiitis (MPA). The age of onset also shifted to elderly side in rheumatoid arthritis (RA). The prevalence rates of elderly rheumatoid diseases such as systemic lupus erythematosus and dermatomyositis/polymyositis will increase in line with the increasing life expectancy. Elderly-onset cases are not rare in these rheumatic diseases. Induction therapy of elderly rheumatic diseases is challenging, because adverse events are common in elderly patients receiving corticosteroids, immunosuppressive drugs, or biologics. Maintenance

therapy is also critical problems for elderly patients. Abrogation of disease activity and its maintenance are main goal of rheumatic diseases. The pitfall of treatment of elderly patients is that drug-associated damages had great impact on the physical function and frailty, especially, long-standing corticosteroids therapy. The primary physicians are balancing risk of adverse events and relapse / recurrence of disease activity in the elderly patients with rheumatic diseases, however there are no clinical data of randomized controlled studies and observational studies are few. In this seminar, I will discuss these challenging clinical questions, mainly about treatment of PMR, GCA, and RA.

EL4

Frailty and dementia

Hiroyuki Umegaki

Department of Community Healthcare & Geriatrics, Nagoya University Graduate School of Medicine, Aichi, Japan

Conflict of interest: None

In Japan the aging of the population has progressed rapidly and the ratio of the older (>65 years old) has reached 27.3% in 2017. With aging muscle mass and performance decrease, which is called sarcopenia. Based on sarcopenia older subjects tend to decrease physical functional reserve and lead to be frail. Frailty is a syndrome that results from the accumulation of multiple age-related organic types of decline with an impairment of physiological reserve, thus increasing vulnerability to adverse health outcomes including falls, hospitalization, institutionalization and mortality. Several models for frailty have been developed and so far one of the most frequently applied is the one developed by Fried et al. According to Fried criteria the diagnosis of frailty requires three or more of the following characteristics: unintended weight loss, exhaustion, weakness, slow gait speed, and low physical activity. A number of studies have reported that frailty is associated with cognitive decline cross-sectionally and is also a risk for future cognitive decline or incidence of dementia. Although the underlying mechanism of the association of frailty and dementia have not been fully elucidated, inflammation, oxidative stress, and physical inactivity may be involved. While frailty is a risk of dementia, demented subjects often have malnutrition which may induce frailty. Therefore, the association between frailty and dementia is bidirectional. Considering the aging of the population in Japan, the understanding of frailty and dementia is necessary for all the medical providers.

EL5

Immunology Update

Sachiko Miyake

Department of Immunology, Juntendo University Graduate School of Medicine, Japan

Conflict of interest: None

Updated basic immunology will be shown and discussed. They will help you to understand the mechanisms of molecular targeted drugs for rheumatic diseases.

EL6

Two different approaches to patient safety: Safety-I & Safety-II

Kazue Nakajima

Department of Clinical Quality Management, Osaka University Hospital, Japan

Conflict of interest: None

Remarkable advances in health care have contributed to less invasiveness and improved prognosis and quality of life for patients. However, physicians are performing more difficult techniques and treating more elderly patients with multiple comorbidities, which poses new risks for patient safety. In recent years, a new approach to safety based on resilience engineering in high reliability industries such as health care and aerospace had developed because of limitations in current safety management, the enormous cost of redundancy as preventive measures, and progress in complexity science. In conventional safety management, the

objective is the reduction of failures. Events such as incidents are analyzed, related factors (e.g., people, technology, organizational culture) are identified, outcomes are explained by a linear cause-and-effect model, and preventive measures are taken for specific failures. Such an approach is called Safety-I. By contrast, Safety-II pursues proactive safety management based on resilience engineering, with the goal of promoting resilient performance of the system (e.g., health care teams, organizations), which can continue to function in varying environments with perturbations and constraints. In Safety-II, we need to understand how everyday clinical work is carried out from dynamic, non-linear perspectives, rather than to explain why things went wrong from static, linear perspectives. We also need to analyze relationships between the behavior of system components (micro level) as well as the behavior of the system as a whole (macro level), instead of capturing the performance of individuals as snapshots for retrospective evaluation. In this presentation, I will explain the theory of resilience engineering with some examples from health care. Using Safety-II, we would be able to proactively manage a dynamic and complex adaptive system and control it with more stable and responsive manners.

EL7

Recent progress in pathogenic analysis, diagnosis, and treatment for Sjögren's syndrome: 2019 Update

Hiroto Tsuboi, Fumika Honda, Saori Abe, Yuko Ono, Hiroyuki Takahashi, Yuya Kondo, Isao Matsumoto, Takayuki Sumida
Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: Yes

Sjögren's syndrome (SS) is an autoimmune disease which affects salivary and lacrimal glands, accompanied with various autoantibodies and extra-glandular manifestations (EGM). In this lecture, we introduce 1) pathogenic roles of T cells in SS, 2) comparison of different sets of diagnostic and classification criteria, 3) clinical practice guidelines for SS in all over the world, and 4) evidences of diagnostic methods and therapies for SS shown in "clinical practice guideline for SS 2017" in Japan. 1) Th1, Th2, Th17, and Tfh could induce B cells activation and plasmacytes differentiation in affected organs of SS. Moreover, infiltrated T cells directly contribute to destruction of exocrine glands via FasL and perforin. We detected anti-M3 muscarinic acetylcholine receptor (M3R) antibodies and M3R reactive Th1 and Th17 in peripheral blood of SS patients. 2) The research team of Japan MHLW (chaired by Takayuki Sumida) revealed that ACR-EULAR criteria had significantly higher sensitivity and lower specificity in diagnosis of Japanese primary SS patients, compared with the revised Japanese Ministry of Health, AECG, and ACR criteria. 3) The treatment guideline by SS Foundation in USA, the management guideline by British Society for Rheumatology, and "clinical practice guideline for SS 2017" by the guideline committee of MHLW are currently available. 4) In "clinical practice guideline for SS 2017", unstimulated whole saliva, Saxon and Gum test, labial salivary gland biopsy, and anti-SS-A/B antibodies are recommended for diagnosis of SS. Salivary gland swelling, purpura, and low C3/C4 levels are recommended as significant risk factors for development of malignant lymphoma in SS. Although cevimeline and pilocarpine are recommended for the treatment of dry mouth, it is suggested that corticosteroid cannot improve salivary and lacrimal secretion. For biologics, it is suggested that rituximab and abatacept can improve both glandular and EGM, while belimumab can improve only EGM.

EL8

Mechanism, prevention and treatment of herpes zoster

Shinichi Imafuku
Department of Dermatology, Faculty of Medicine, Fukuoka University, Japan

Conflict of interest: Yes

Herpes zoster (HZ) is an endogenous recurrent infection of varicella-zoster virus (VZV). Most of the HZ presently seen are seen as unilateral painful erythema and vesicles in adults who were infected with natural varicella at childhood. HZ develops at about 5/1000 person year, but the incidence doubles in elderly people. Also, in immunosuppressed patients,

the incidence increases. Our claim database study revealed that incidence of HZ tripled in SLE patients and doubled in rheumatoid arthritis patients. Although HZ heals spontaneously, HZ burdens patients with severe pain, skin lesions such as vesicles, crusts, and ulcers, and the like, involvement of important adjacent organs (ocular complications and facial nerve palsy, etc.), and most importantly postherpetic neuralgia (PHN). It is known that the incidence of PHN is proportional to the age, severity of eruption at first visit. In immunosuppressed patients, the frequency of hospitalizations due to PHN and other complications significantly increase. Herpes zoster is easily diagnosed from clinical symptoms. Acute onset, unilateral edematous erythema, monotonous papules/vesicles, etc. However, but in atypical cases needs to be distinguished from herpes simplex, impetigo, or contact dermatitis etc. In 2018, a quick kit with excellent sensitivity and specificity was released, and definitive diagnosis became available on the spot. Serologically, it is difficult to diagnose. Almost all adults with a history of varicella has serum anti-VZV-IgG antibody but the titer is low. VZV-IgG become elevated after onset of herpes zoster, but it rises immediately or as late as 2 weeks after onset, depending on cases. Elevated antibody confirms the diagnosis, but it is important that low titer does not deny the diagnosis. Early administration of antiviral drugs is most important in treating HZ. Representative antiviral drugs such as valacyclovir, or famciclovir were a nucleic acid analog and its serum concentration is dependent on renal function. Amenamevir is a helicase primase inhibitor, appeared in 2017 in Japan, and is metabolized in the liver, therefore, safe options for those with impaired renal function. Incidence of HZ was proved to be suppressed by the same vaccine against varicella in a large clinical trial in US and labeled for prevention of HZ in Japan, too. But because it is a live vaccine, its administration to immunosuppressed patients is contraindicated. Meanwhile, a subunit vaccine against HZ was also developed and approved. Clinical trials have demonstrated that the subunit vaccine have an extremely high preventive effect on HZ, and it is expected for immunocompromised individuals.

EL9

Approach to the Patient with Fever/Inflammation of Unknown Origin

Noboru Hagino
Division of Hematology and Rheumatology, Teikyo University Chiba Medical Center, Japan

Conflict of interest: None

Rheumatologists sometimes act as a "last resort" to diagnose difficult case of prolonged fever or inflammation. To diagnose a rheumatic disease, physician must rule out other conditions which may mimic rheumatic disease before applying "classification criteria". Thus, exclusion of infectious diseases, oncologic diseases, and other "mimickers" is of paramount importance for the diagnosis of fever/inflammation of unknown origin. For example, infectious disease such as tuberculosis or syphilis is an "old foe" as they are difficult to prove via culture. Chronic infectious diseases also make the diagnosis of rheumatic disease the difficult one. In the field of oncology, various types of lymphoma present with fever, and some of them, including intravascular lymphoma, mimic rheumatic diseases such as adult-onset Still's disease. In our field, autoinflammatory diseases have attracted attention as the cause of fever/inflammation of unknown origin, and adult-onset cases are more common than ever believed. This lecture aims to provide overview of the approach to fever/inflammation of unknown origin from the adult rheumatologist's viewpoint, in the form of case-based discussion.

EL10

Antiphospholipid syndrome: diagnosis and treatment

Shinsuke Yasuda
Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University

Conflict of interest: Yes

Antiphospholipid syndrome (APS) is an autoimmune disorder in which the persistent presence of antiphospholipid antibodies (aPL) is associated with recurrent thrombotic events and pregnancy morbidities.

Pathophysiology of APS has been intensively investigated since 1990. aPLs play a role in activating monocytes, endothelial cells and platelets, being recognized as pathogenic autoantibodies. Complement activation is also one of the pathogenic features observed in patients with APS. We recently found elevated anti-C1q antibodies that activate classical pathway of complement system, as well as decreased factor H that results in activation of alternative pathway. T/B cell subpopulations are also altered in APS patients, characterized by increased Th2, Th17, and plasmablasts and decreased Tregs, Bregs, and memory B cells. Diagnosis of APS is made based on clinical symptoms such as arterial thrombosis, venous thrombosis, and/or pregnancy morbidities, with persistent presence of the following aPLs: IgG/M anticardiolipin antibodies (aCL), IgG/M anti-beta2-glycoprotein I antibodies (aβ₂GPI), and lupus anticoagulant (LA) (the Sydney-revised Sapporo criteria). To make aPL screening simple, we propose the measurement of non-criteria aPLs: anti-aβ₂GPI domain I antibody (aDI) and phosphatidylserine-dependent antiprothrombin antibodies (aPS/PT) tests for the diagnosis of APS. Treatment strategy for APS focuses on the prevention of recurrences, in which anticoagulation and/or anti-platelet therapies are mainstay. For the prevention of arterial thromboses, our retrospective analysis suggests dual antiplatelet therapy (DAPT) has an advantage comparing to anticoagulant, single antiplatelet therapy or combination of anticoagulant with an antiplatelet agent. Xa inhibitor may not be sufficient for the prevention of thrombotic events in patients with high-risk APS. I would like to discuss recent advancement in the clinical and translational aspects of APS.

EL11

How to improve patient satisfaction after total knee arthroplasty

Ken Okazaki

Department of Orthopedic Surgery, Tokyo Women's Medical University

Conflict of interest: Yes

Although the long-term results of total knee arthroplasty (TKA) has significantly improved, patient-reported satisfaction after TKA is not always high. It has been reported 10 to 20% of patients were not very satisfied with their replaced knees. Number of studies have been reported with factors affecting patient satisfaction using patient-reported outcome measures (PROM). Coronal alignment, rotational alignment and range of motion after TKA correlate with the PROM. As the coronal alignment, severe varus or valgus alignment after surgery would deteriorate the PROM while slight varus would show the comparable results with the neutral alignment. Regarding the ligament balancing, loose medial tension in flexion would deteriorate the clinical results whereas slight loose tension at the lateral side would be accepted. Therefore, care should be taken to obtain the medial stability in all the range of motion and not to extensively release the medial ligaments. Pain control after TKA is also important factor to reduce the residual pain. Although residual pain can be caused by many factors such as, malposition of the component, inappropriate soft-tissue balancing, infection, subcutaneous nerve injury, unexplained pain after TKA still exists. Pain sensitization may present in some patients. Patient selection and education are also important.

EL12

Assessment and management of the rheumatoid foot

Takumi Matsumoto

Department of Orthopaedic Surgery, Faculty of Medicine, The University of Tokyo

Conflict of interest: None

Dramatic improvement in rheumatoid arthritis (RA) control due to the development of powerful drugs has significantly changed the therapeutic strategy for joint destruction and deformity in RA patients. Especially, decreased involvements of large joints in lower limbs have come to shed light on the magnitude of functional impairment by foot deformity and wide range of needs for resolution of foot trouble. For human being achieving bipedal walking, the defect of foot could be directly linked to gait impairment. In the first place, the foot lesion is one of the most favorite sites of joint involvements in RA from its early stage. Foot and ankle involvement increases with duration of the disease process, and more than 90% of patients with RA have foot and ankle symptoms at later

stages. It is not surprising that more focus has been on the foot as a result of decreased involvements of large joints. Higher demand for quality of life by patients than ever before also highlight the problems in foot. The most common RA-related foot deformities are splayed foot, flat foot, and hindfoot valgus; however, in practice, we face a wide variety of deformities which cannot be expressed only with these words. Moreover, the intensity of symptoms and the severity of deformity do not necessarily correlate with each other. Because of these situations, there might be a lot of physicians who feel difficulty in assessing RA foot deformity. In addition to the knowledge about the pros and cons of each intervention, understanding the pattern of destruction and its future prospect is essential to construct an appropriate treatment strategy for RA foot. This instructional lecture will present the way how to grasp the characteristic foot deformity and patients' complaints dividing the foot lesions into forefoot, midfoot, hindfoot, and ankle. And also, the cross relationship of deformities among these lesions and the pattern of deformity progression will be discussed. It is essential to understand that the progression of RA foot deformity is affected by both factors including disease activity and mechanical load. This concept will help you to select the way or timing to intervene in RA foot deformity.

EL13

Actual use of biological products in pediatric rheumatic diseases

Masaaki Mori

Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University

Conflict of interest: Yes

The fact that this common inflammatory pathogenic factor is an inflammatory cytokine was proved by inhibiting a single inflammatory cytokine function leading to inflammation with monoclonal antibodies against specific inflammatory cytokines or specific receptors as therapeutic agents. At the same time, it was also found that the type of cytokines leading the inflammatory pathology is different depending on the disease, even in the same inflammatory condition. In juvenile idiopathic arthritis (JIA), a typical disease of rheumatic diseases of childhood, there are various inflammatory cytokines production and mechanisms for mutual induction have been found, but in fact it is thought that there is a leading cytokine specific to disease, and by blocking that cytokine, inflammation can be brought to the end. Systemic JIA is forced to use a long-term massive amount of steroid against strong systemic inflammation and is suffering from side effects such as obesity, growth disorder, osteoporosis, compression fracture of the vertebral body, femoral head necrosis and steroid diabetes. In this way, the life of patients was extremely restricted. As a treatment with biological preparation, it was found that tocilizumab as an anti-IL-6 inhibitor was approved through clinical trials earlier in the world, it was found that it had high effectiveness and side effects were relatively slight, and it is used as an essential therapeutic agent. Also, in July 2018, canakinumab, which has a proven anti-IL-1 inhibitory action in Europe and the United States, has been approved in Japan and has been shown to be effective in clinical practice. Anti-TNF therapeutic agents such as etanercept / adalimumab are used for types in which arthritis remains even if systemic symptoms improve. On the other hand, in articular JIA, the anti-TNF inhibitor etanercept / adalimumab and the above tocilizumab were approved in Japan and abatacept, which inhibits costimulatory signals between antigen presenting cells and T cells located upstream of the onset of inflammation, has also recently received approval as a result of clinical trials. In this lecture, I focus on systemic JIA in which an abnormality of innate immunity is involved in pathogenesis, and articular JIA in which excessive adaptive immunity induces arthritic symptoms, and finally I will outline the actual use of biological preparation and the mechanism that has been elucidated so far.

EL14

Basic Philosophy of Research Ethics and Regulation Rules in Japan

Tsunakuni Ikka

Center for Public Health Sciences, Bioethics and Healthcare Law Research Division, Healthcare Law Section, National Cancer Center Japan

Conflict of interest: None

I am going to speak on Basic Philosophy of Research Ethics and Regulation Rules in Japan. The main subjects are “Clinical Research Act” and “Ethics Guideline on Medical Research”.

EL15

Mechanism of the rheumatoid hand deformity

Ryuichi Nakahara

Department of Intelligent Orthopaedic System Development, Okayama University Graduate School of Medicine Dentistry and Pharmaceutical Sciences, Okayama, Japan

Conflict of interest: Yes

Due to the remarkable improvement of drug therapy of rheumatoid arthritis (RA), severe rheumatic hand deformed patients are decreasing. However, the patient with rheumatic hand deformity does not disappear. Rheumatoid hand deformity often progresses asymptotically and starts with minute image changes that are difficult to evaluate clinically. If we know the mechanism of the rheumatoid hand deformity, we can predict the progression of deformity from radiographic and ultrasonographic findings. Synovitis of the wrist joint occurs in all of the distal radioulnar joint, radiocarpal joint, intercarpal joint, carpometacarpal joint, and tenosynovitis may also develop in extensor tendon and flexor tendon. For examining these findings, guideline for musculoskeletal ultrasound in rheumatology published by college of rheumatology is useful. These lesions progress to wrist deformity via carpal rotation, supination deformity, ulnar carpal shift, dorsal dislocation of the distal ulna and palmar carpal subluxation. Synovitis of radioulnar joint and mechanical irritation by bone deformity progress to tendon rupture. Ulnar deviation derived from synovitis of MCP joint and carpal rotation (zig-zag deformity). Attention should be paid because the ulnar deviation may progress gradually even once occurred. Boutonniere deformity results when the central slip of the extensor tendon of a digit are disrupted. Swan neck deformity develops from either tightening of intrinsic muscle or overpull of the extensor mechanism on the proximal phalanx or instability of the distal phalanx. In this way, the synovitis and bone destruction of each joint are closely related to the rheumatoid hand deformity. In this lecture, we outline the rheumatoid hand deformity focusing on image finding and anatomical structure.

EL16

The treatment of glucocorticoid-induced osteoporosis

Ikuko Tanaka¹, Shigenori Tamaki²

¹Imaging Center, Nagoya Rheumatology Clinic, Japan, ²Nagoya Rheumatology Clinic

Conflict of interest: None

Glucocorticoid-induced osteoporosis (GIO) is the most important adverse effect caused by the glucocorticoid therapy, as bone fractures occur in 30 to 50% of the patients receiving long-term glucocorticoid therapy. The loss of bone mineral density is as high as 8 to 12% in the first few months after initiation of glucocorticoid therapy. Fracture risk already increases before bone mineral density decreases. These findings suggest that it is necessary to cope with GIO promptly after starting glucocorticoid administration. The primary prevention is to be considered. For autoimmune diseases, there are many patients in adolescence from young people, and many patients with childbearing age. In the treatment of autoimmune diseases, glucocorticoids are drugs that are still used in large amounts and for a long time. It is necessary to choose treatment for GIO while considering the characteristics of the original disease, the characteristics of glucocorticoid treatment, and the patient's own needs. Since the appearance of Methotrexate and biologics, glucocorticoids were less used for treatment of rheumatoid arthritis. However, in the EULAR Update of 2016, it is recommended that glucocorticoids be used in the initial treatment. Guidelines and recommendations about glucocorticoid treatment in many inflammatory and autoimmune diseases have been published in Europe, United States, and other countries. Glucocorticoid will continue to be a frequently used drug for rheumatoid arthritis in the future. The pathophysiology and the treatment of GIO will be discussed in this lecture.

EL17

Molecular mechanism of osteoclast differentiation and function

Naoyuki Takahashi

Institute for Oral Science, Matsumoto Dental University, Japan

Conflict of interest: None

We have established a mouse co-culture system of osteoblastic cells and hematopoietic cells to examine osteoclast differentiation in vitro. In 1992, we proposed a hypothesis that osteoblastic cells express osteoclast differentiation factor (ODF) in response to bone resorption-stimulating factors. In 1998, RANKL [receptor activator of NF- κ B (RANK) ligand] was discovered as an osteoclast differentiation factor ODF. This discovery of RANKL triggered the identification of nuclear factor of activated T cells c1 (NFATc1), a master transcription factor for osteoclast differentiation. Furthermore, the significance of immunoreceptor tyrosine-based activation motif (ITAM) signal as a costimulatory signal of RANK has been demonstrated. Thus, understanding of the molecular mechanisms regulating osteoclast differentiation has greatly progressed over the past 20 years. On the other hand, the analysis of osteoclast function started from experiments using osteoclasts isolated from bone tissue in the 1980's. Experimental systems to obtain a large number of osteoclasts were established in the 1990's, and the mechanism of osteoclast function has been analyzed in more detail. Osteoclasts adhere to bone via α v β 3 integrin and p130Cas in osteoclasts recognizes the hardness of bone as a mechanosensor. It is proposed that p130Cas recognizing bone hardness is phosphorylated by c-Src and its phosphorylation sends a signal to induce ruffled border formation. In addition to the adhesion signal, signals from RANKL and Wnt5a have also been shown to be necessary to promote ruffled border formation in osteoclasts. In my presentation, I would like to summarize the molecular mechanisms that regulate osteoclast differentiation and function.

EL18

Diagnosis and Treatment in Idiopathic Inflammatory Myopathies

Takahisa Gono

Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine

Conflict of interest: None

Idiopathic inflammatory myopathies (IIMs) is one of the autoimmune diseases, characterized by muscle weakness and extramuscular lesions including dermatitis, arthritis, interstitial lung disease (ILD) and cardiomyopathy. IIMs is classified into the followings based on the new EULAR/ACR IIM classification criteria: dermatomyositis (DM), amyopathic DM, polymyositis (PM), immune-mediated necrotizing myopathy (IMNM) and inclusion body myositis (IBM). The important things which physicians should pay attention to in diagnosis of IIMs are presence or absence of cutaneous features associated with DM, distribution of muscle weakness and muscle atrophy, clinical course of muscle symptoms, and pathohistological finding of the muscles. First of all, physicians should carefully examine the skin. When patients don't have any skin rashes related to DM, infection, drug, thyroid diseases, muscular dystrophies and metabolic myopathies should be considered as differential diagnoses beside IIMs. The distribution of muscle involvement is usually proximal predominant in PM/DM and IMNM. On the other hand, finger flexor muscles are involved in IBM. Muscle atrophy is also often revealed in patients with IMNM or IBM. Clinical courses of myositis depend on each form of IIMs; muscle weakness develops in months in PM/DM, in weeks in subacute form of IMNM, and in months/years in chronic form of IMNM or in IBM. Pathohistological evaluation of the muscles is critical to diagnose in myositis patients. Infiltration of CD8-positive T cells which surround and invade non-necrotic muscle fibers, necrosis and regeneration of muscle fibers with pauci-infiltrating lymphocytes, and accumulation of proteins in vacuoles within muscle fibers are specific for PM, IMNM and IBM, respectively. In addition, physicians should also investigate complications of ILD, cardiomyopathy and malignancy in IIMs patients. I will give a lecture regarding diagnosis and treatment for IIMs, focusing on clinical issues in daily practice.

EL19

Ten common mistakes in the management of systemic sclerosis- part 2

Masataka Kuwana

Department of Allergy and Rheumatology, Nippon Medical School

Conflict of interest: Yes

Systemic sclerosis (SSc) remains an intractable disease with poor outcomes because of underlying mechanisms mainly caused by excessive fibrosis, which is often irreversible, and almost lack of treatment proved to be effective by randomized clinical trials. In addition, adverse outcome is attributable, in part, to poor understandings of natural disease course and highly variable clinical presentation of the disease by healthcare providers. It is useless and meaningless without full understandings of unique clinical features of SSc, and discussion of treatment responses in observational cases without adequate controls is always inadequate and often leads wrong prejudice. Recent advances in basic researches successfully lead to implementation of a number of clinical trials of potential anti-fibrotic agents in SSc patients. Before the dawn of SSc-treatment era, this lecture features fundamental knowledge required for daily clinical practice of SSc patients, highlighting 10 common mistakes in the management of SSc, listed below: 1. The absence of Raynaud's phenomenon judged solely by history taking of color changes of fingers 2. Skin thickness scoring based on whether skin can be easily pinched or not 3. Exclusion of SSc diagnosis based on the absence of skin thickness 4. Exclusion of SSc diagnosis based on negative anti-nuclear antibody test 5. Transition of patients with limited cutaneous SSc to diffuse cutaneous SSc 6. Treat sicker patients more intensively 7. Evaluation of upper gastrointestinal involvement using endoscopy 8. Initiate upfront combination of pulmonary vasodilators in patients diagnosed as having pulmonary arterial hypertension 9. Wait for initiating disease-modifying treatment until functional impairment becomes apparent 10. Avoid high-dose corticosteroids to treat overlapping myositis or vasculitis because of increased risk of renal crisis Extra. Use of tocilizumab to treat patients with early dcSSc

EL20

Physical joint examination: what we learn from ultrasound

Kei Ikeda

Department of Allergy and Clinical Immunology, Chiba University Hospital

Conflict of interest: None

Physical joint examination for arthritis provides information on both the current inflammation and the structural damage but this lecture focuses on the inflammation. 4 signs of inflammation (i.e. redness, warmth, tenderness, swelling) are important in physical joint examination; however, each sign has its advantage and disadvantage. Redness and warmth are highly specific to inflammation but are detected only when acute, severe inflammation is present, and their sensitivity is very low. Tenderness is more sensitive but less specific to inflammation and may reflect non-inflammatory (e.g. mechanical, neuropathic, psychosocial) pain. Swelling, on the other hand, has well-balanced sensitivity/specificity and plays an important role in the assessment of chronic inflammation. In addition, joint swelling has been shown to correlate with joint inflammation in patients with rheumatoid arthritis in a stable state. In inflamed synovial tissues, the amount of synovial fluid increases and the volume of synovial tissues also increases due to cellular infiltration and angiogenesis. We need to discriminate between these synovial changes and other soft tissues by physical examination. In addition, we may want to discriminate synovial fluid from synovial hypertrophy, the latter is more specific to inflammation. Ultrasound visualizes the extent of synovial fluid and hypertrophy and dynamic scanning can further differentiate their properties (i.e. compressibility and displaceability). These pieces of visual information help with improving physical examination skills. In this lecture, real ultrasound images/videos of synovitis will be presented and general/joint-specific tips in palpitation will be provided. In addition, how to guide treatment based on these physical examination findings will be discussed.

EL21

Updates of genetic studies of rheumatoid arthritis

Chikashi Terao

Laboratory for Statistical Analysis, RIKEN Center for Integrative Medical Sciences

Conflict of interest: None

Rheumatoid arthritis (RA) is a complexed disease and both genetic and environmental factors are associated with onset of RA. Twin studies have revealed heritability of rheumatoid arthritis (RA) as around 60% in both European and Japanese, supporting significance of genetic studies in RA to identify susceptibility genes beyond populations. Enormous progress has been made since completion of the Human Genome Project in 2003. Genetic association studies especially genome-wide association studies (GWAS), where we comprehensively genotype single nucleotide polymorphism (SNP) throughout the genome in a hypothesis-free manner, have greatly contributed to this progress. As far as we focus on inherit variants in genetic studies, significant signals indicate that they are causes of the diseases and not results of the diseases. This is a big advantage of genetic studies over non-genetic studies. Genetic studies have revealed that there are more than thousands of associated variants with weak effect sizes. The HLA region is an exception and shows strong multiple signals. Previous studies have identified significant amino acid positions of HLA proteins and showed that significant amino acid positions were different in subsets of RA. Genetic studies have identified more than 100 susceptibility loci for RA. With the use of summary statistics of GWAS results, critical cell types, molecular networks and pathways in RA were identified. While next-generation sequencer (NGS) can identify variants not in GWAS arrays and difficult to impute, association studies to focus on rare variants with the use of NGS were not successful so far. Aside from onset of diseases and its genetic associations, numerous efforts have been made to analyze genetic components associated with disease progression or responsiveness of treatment and some of which are successful. Some researchers are trying to combine latest technologies such as CyTOF with sequence results by NGS to understand the basics of RA.

EL22

Update on Diagnosis and Assessment of Systemic Lupus Erythematosus

Yasuhiro Katsumata

Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: None

The most widely used classification criteria for systemic lupus erythematosus (SLE) are those developed by the American College of Rheumatology (ACR). These classification criteria were published in 1982 and revised by a committee in 1997. The 1982 ACR criteria have been validated, but not the 1997 revision. In addition, multiple concerns have arisen in the current ACR classification: possible duplication of highly correlated cutaneous lupus terms (such as malar rash and photosensitivity) and the absence of inclusion of many other lupus cutaneous manifestations; omission of many SLE neurologic manifestations; the need to utilize new standards in the quantification of urine protein; and the omission of low complement (Arthritis Rheum 2012;64:2677). Most of all, there were concerns about patients without any immunologic criteria being classified as SLE. The Systemic Lupus International Collaborating Clinics (SLICC) group revised and validated the ACR criteria in 2012. We also evaluated the performance of the SLICC criteria on classifying SLE in an uncontrolled multi-centered study with real-life scenario of the patients in Japan (Mod Rheumatol 2018;28:642). Compared to the ACR criteria, the SLICC criteria had a higher sensitivity (0.88 vs. 0.99) and lower specificity (0.85 vs. 0.80). However, the SLICC criteria has never been used in clinical trials or officially approved. On the other hand, at the 2017 ACR Annual Meeting, a draft of new EULAR/ACR endorsed criteria for SLE were presented. Although the criteria were based on the SLICC criteria, they were fine-tuned and simplified, using ANA of $\geq 1:80$ as entry criterion and a classification threshold of 10. In this seminar, update on diagnosis and assessment of SLE, including the pitfalls of the SLEDAI and SLICC damage index, is to be discussed. The Asia Pacific Lupus Collab-

oration (APLC) has proposed the Lupus Low Disease Activity State (LLDAS). The LLDAS and other remission criteria for SLE are also to be discussed.

EL23

Measures Against Infectious Diseases in Patients with Rheumatoid Arthritis and Collagen Disease

Norio Ohmagari

Department of Infectious Diseases, National Center for Global Health and Medicine Hospital

Conflict of interest: Yes

Patients with rheumatoid arthritis have a high risk of infection. This is considered to be due to the use immunosuppressive drugs such as steroids and methotrexate in treatment. Rheumatoid arthritis patients also have opportunistic infections such as legionellosis, nocardiosis and pneumocystis pneumonia. Decrease in cellular immunity due to the effects of rheumatoid arthritis therapy is thought to contribute to this. In order to appropriately treat these infectious diseases, the causative microorganisms must be identified. However, these microorganisms are often difficult to detect by common bacterial tests. Therefore, it is necessary to accurately list up the possible causal microorganisms from the condition of the patient's immunity and lung lesions, etc., and to individually select examination methods for identifying those microorganisms. Prevention of infectious diseases is important because respiratory virus infections such as influenza can become severe in immunocompromised individuals. First, they should be advised to maintain the rhythm of life as far as possible and to manage their physical condition. Patients' wearing a surgical mask is effective in preventing acute respiratory tract infections. Oral care will also become more important from the viewpoint of preventing infections such as pneumonia. Immunization is also important, such as influenza and pneumococcal vaccines. Although there is a view that the effect of a vaccine is insufficient in immunocompromised patients, even so, for the surrounding family and others try to prevent infection by getting vaccinated is a useful measure against infection of the patient. Oral administration of TMP/SMX is effective for prevention of pneumocystis pneumonia, but the conditions of patients vary and it is necessary to consider individually which patients need it. Patients using biological products also have an increased risk of developing tuberculosis, so evaluation beforehand and treatment of any latent tuberculosis are necessary.

EL24-1

ICD-11 revision and its implementation in Japan

Koki Abe, Emiko Oikawa, Kaori Nakayama, Kei Mori

International Classification and Information Management Office to the Director-General for Statistics, Information Policy and Policy Evaluation, Ministry of Health, Labour and Welfare, Japan

Conflict of interest: None

The International Classification of Diseases and Related Health Problems (ICD) was originally adopted in 1900. It has been implemented in Japan since the same time and applied to various statistical studies, including mortality statistics. In Japan, the "Statistical classification of diseases, injuries and causes of death" is stipulated as a statistical standard under the Statistics Act, and is applied to producing official statistics including the Vital Statistics or the Patient Statistics and used in management of medical records in medical institutions. In the global ageing where especially Japan enters a high-mortality society, it is important to prepare effectively by constructing a sustainable health and medical system. Statistics and information foundation constitutes the basis of this and its maintenance and utilization will become required even more while the newly released ICD-11 and related international classifications are expected to fulfil its role to assist such framework. From now on, we would like to verify the legal system issues and the usage environment in cooperation with stakeholders and work toward the implementation in Japan smoothly.

EL24-2

International Classification of Diseases-11 in the field of rheumatology

Masayoshi Harigai

Department of Rheumatology, Tokyo Women's Medical University

Conflict of interest: None

Classification of rheumatic diseases have been drastically changed through the revision of International Classification of Diseases-10 (ICD-10) to ICD-11. Rheumatic diseases has been assigned to Chapter XIII, Disorders of the musculoskeletal system or connective tissue, in ICD-10, but has been separated into two chapters, Chapter IV Diseases of the immune system and Chapter XV Disorders of the musculoskeletal system or connective tissue. Rheumatoid arthritis, psoriatic arthritis, polymyalgia rheumatica, Adult-onset Still's disease, Juvenile idiopathic arthritis, gout, other crystal-induced arthritis were categorized into 'Inflammatory arthropathies' and belong to Chapter XV together with osteoarthritis and infection-related arthropathies, which include infectious arthritis, reactive arthritis, and others. Chapter IV has primary immunodeficiencies and acquired immunodeficiencies, followed by non-organ specific systemic autoimmune disorders (NOSSAD) and Autoinflammatory disorders. NOSSAD includes major collagen diseases such as systemic lupus erythematosus, idiopathic inflammatory arthritis, systemic sclerosis, vasculitis, mixed connective tissue disease, and anti-phospholipid syndrome. Autoinflammatory disorders contains monogenic autoinflammatory syndromes, SAPHO syndrome, Behcet's disease, and others. In this educational lecture, classification of rheumatic diseases in ICD-11 will be reviewed and some tips and traps will be provided.

EL25

HSCT for the treatment of refractory autoimmune diseases

Takahiko Horiuchi

Department of Internal Medicine, Kyushu University Beppu Hospital, Japan

Conflict of interest: None

Treatment for autoimmune diseases has made remarkable progress in recent years, however there still remain many difficult-to-treat diseases. Systemic sclerosis (SSc) is one of the refractory diseases. The efficacy of immunosuppressive therapy, such as corticosteroids and cyclophosphamide, for SSc is limited. Therefore, SSc patients with severe skin sclerosis and/or major organ involvement have a poor prognosis with a 5-year estimated survival rate of ~50%. In Europe and the US, Hematopoietic stem cell transplantation (HSCT) was introduced for the treatment of refractory autoimmune diseases, multiple sclerosis and inflammatory bowel diseases from the 1990s. In Japan, HSCT has also been tried to refractory autoimmune diseases from 2000. Recently, three prospective randomized trials (RCTs) for the treatment of SSc have been published; The American Scleroderma Stem Cell versus Immune Suppression Trial (ASSIST), The Autologous Stem Cell Transplantation International Scleroderma (ASTIS), and Scleroderma: Cyclophosphamide or Transplantation (SCOT). These trials revealed a significant long-term, event-free survival benefit, improved skin sclerosis and forced vital capacity. Based on the beneficial effect of HSCT for SSc, Update of EULAR recommendation for the treatment of SSc published in 2017 announced that HSCT should be considered for treatment of selected patients with rapidly progressive SSc at risk of organ failure. In Japan, autologous HSCT for severe SSc was approved as advanced medical care by the Ministry of Health, Labour and Welfare to perform at Kyushu University Hospital in August, 2017. In this presentation, I would like to address the current situation and issues as well as the attempt to predict the prognosis of the HSCT.

EL26

Differences between Takayasu arteritis and giant cell arteritis: Drafts of revised classification criteria

Hajime Yoshifuji

Department of Rheumatology and Clinical Immunology, Kyoto University, Kyoto, Japan

Conflict of interest: None

In 2009, it was proposed that Takayasu arteritis (TAK) and giant cell arteritis (GCA) are the same disease with a spectrum by age of onset (Maksimowicz-McKinnon, *Medicine*, 2009). However, TAK and GCA are different in geoepidemiology (Asia vs. Western countries) and comorbidities (ulcerative colitis vs. polymyalgia rheumatica), and the difference can be explained by the difference of associated HLAs. In histopathology of the aorta, it is pointed out that the outer layer of the media and the adventitia are dominantly affected in TAK, whereas the middle or inner layer of the media are dominantly affected in GCA (Stone, *Cardiovasc Pathol*, 2015). TAK and GCA have different responsiveness to several drugs. A randomized controlled trials (RCT) with abatacept for TAK and GCA were performed, and it showed significant relapse-prevention effects on GCA, whereas, disappointingly, real drug is inferior to placebo for TAK. Three single-arm tests with TNF inhibitors for TAK showed favorable effects, whereas three RCTs with TNF inhibitors for GCA all failed. The importance of Th1 and Th17 cytokines is known for both diseases. In the analysis of PBMC from TAK and GCA with the same protocol performed by Saadoun et al. (*Arthritis Rheumatol*, 2015), the expression of both Th1 and Th17 cytokines is markedly enhanced in TAK, whereas both the cytokines showed relatively milder elevation in GCA; only expression of IL-23 was significantly more enhanced in GCA. Taken together, it is reasonable that TAK and GCA are distinct diseases which differ in epidemiology, histopathology, symptoms, and cytokine profiles. In ACR2018, separated drafts of revised classification criteria for TAK and GCA were presented. Regarding the age, the committee proposed inclusion criteria, in which the criteria of TAK is considered when the age at diagnosis ≤ 60 years, and the criteria of GCA is considered when the age at diagnosis ≥ 40 years. They also proposed new items that have not adopted before. The strengths and weaknesses of the proposed drafts are discussed.

Meet the Expert

MTE1

Lumbar lesions in patients with rheumatoid arthritis: An underrecognized problem

Hirota Chikuda

Department of Orthopaedic Surgery, Gunma University

Conflict of interest: None

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder characterized by polyarticular synovitis that can lead to structural damage and deformation of joints. While the involvement of the cervical spine in RA has been well documented, lumbar lesions have received much less attention. Recent studies have revealed that half of RA patients have lumbar lesions, including disc narrowing, spondylolisthesis, and scoliosis. Despite its high prevalence in aged populations and the potential impact on patients' quality of life, lumbar lesions in RA patients remain underrecognized, which might lead to a misdiagnosis or a delay in treatment. Lumbar lesions in RA patients are categorized into three groups according to the underlying pathology. First, inflammation due to RA itself can cause erosion of the lumbar spine, especially in the facet joints and endplates, which may destabilize the spine. Second, severe osteoporosis, particularly in patients receiving glucocorticoid therapy, may result in multiple vertebral fractures and consequent spinal deformity. Finally, with the improved life expectancy, RA patients are increasingly presenting with common degenerative spinal disorders, such as canal stenosis. A patient with RA may present with one or a combination of these three categories. Physicians encountering RA patients who present with gait disturbance or leg pain are advised to be alert for not only arthritis in the lower extremities but also potential lumbar lesions.

MTE2

Footwear and custom orthotic interventions for rheumatoid foot in combined-modality therapy of surgical, pharmaceutical and rehabilitation

Jun Hashimoto

Department of Rheumatology and Allergology, National Hospital Organization Osaka Minami Medical Center

Conflict of interest: Yes

Principle of footwear and custom orthotic interventions for rheumatoid foot is simple. Cautious selection of shoes, prevention of concentrated plantar pressure and the friction due to plantar sliding, stabilization of damaged joints and realignment of the shifted mechanical axis are required. Principle of shoes selection is also simple. Large toe box that is provided by shoes 2-3 cm bigger than foot length, well-fixation of foot in shoes by fixing belt or shoestring and well-fitting of heel to quarter are required. After cautious selection of shoes, we prescribe the insole for various pathological condition of rheumatoid foot. The difficulty of footwear and custom orthotic interventions lies in point other than these principles. Despite the prevalence of footwear and custom orthotic interventions, unrecovered or remaining gait disturbances are frequently overlooked. Their poor functional prognosis due to overlapping age-related disability could burden them sooner or later. In the case of disabled patients using foot orthosis, we must return them to a lifestyle with less disability with timely indicated appropriate surgical intervention. Since we are now short of the specialists of foot and ankle surgery whose techniques catch up with rapidly advanced pharmacotherapy, the well-organized cooperation with foot and ankle surgeon who have high expertise in rheumatoid foot is possible solution. On the other hand, some patients tolerate the improper footwear or orthotics and are led into reduced walking distance and impaired health-related quality of life. Patients' reasons for this tolerance are complex but include high price of custom foot orthotics, difficulty in size and shape adjustment after purchase of ready-made shoes, strongly opinionated shoes size choice of foot length and low demand of recovery from disability. Provision of dedicated foot care service including shoes adjustment is required, however that remains to be prepared in our team. Rapidly advanced pharmacotherapy and rapid improvement of longevity in the elderly including aged patients with RA inevitably increase the importance of non-pharmaceutical management such as rehabilitation and surgery. This course aimed to improve skill in

footwear and orthotics fitting and interpretability of the whole series of rheumatoid foot treatment for increasing daily steps counted by pedometer in patients with RA.

MTE3

Chasing molecular and cellular dynamics using genome editing and robotic technologies

Nozomu Yachie

RCAST, The University of Tokyo

Conflict of interest: None

Mammalian development, tumorigenesis and other dynamic progressions of heterogeneous biological systems remain largely unclear. The molecular landscapes of cells have been rapidly unveiled by fast-developing sequencing and mass-spectrometry technologies, which however all require destruction of the samples and limit us to analyze the dynamics of single cells or individuals. One can analyze the spatiotemporal dynamics of molecules and cells by microscopic observation with fluorescent proteins or probes, but only for a limited number of objects. Not surprisingly, the above-mentioned technologies only allow us to examine the events that occur at the time of observation. This fact prevents global analyses of heterogeneous molecular dynamics in a complex system. We do not have a time machine. To address this kind of issues, our team has been developing several cell-embedded dynamic DNA memories using genome editing and DNA sequencing technologies. I will first talk about our progress in developing a dynamic DNA memory that continuously recodes cellular lineage and molecular event information, and then another DNA memory that enables time-course omic analyses of a target clone buried in a complex cell population. I will also briefly discuss the need for robotic technologies to promote biology of the next decades.

MTE4

Giant cell arteritis and Polymyalgia rheumatica

Eiichi Suematsu

Division of Internal Medicine and Rheumatology, National Hospital Organization Kyushu Medical Center, Fukuoka, Japan

Conflict of interest: None

Polymyalgia rheumatica (PMR) is an inflammatory disorder characterized by pain and stiffness in shoulders, neck as well as girdles. The markedly significant uptake of FDG has been reported in ischial tuberosities, greater trochanters, iliopsoas bursas and spinous processes, suggesting the great value of FDG-PET/CT for the diagnosis with PMR. Giant cell arteritis (GCA), previously known as temporal arteritis is classified as a large-vessel vasculitis. Almost all patients who develop GCA are over the age of 50. Common signs and symptoms of GCA due to the involvement of the temporal arteries and other medium-sized arteries of the head and the neck are visual disturbances, headache, jaw claudication, neck pain, and scalp tenderness. General manifestations, such as fatigue, malaise, and fever, are also present. GCA is diagnosed based on the American College of Rheumatology 1990 classification criteria. Because the disease is relatively uncommon, and the disease can cause so many different symptoms, the diagnosis of GCA can be difficult. Actually, GCA is classified into three types: classic temporal arteritis type (cranial GCA); large-vessel type (LV GCA), affecting the aorta and its major branches without temporal arteries; generalized type, affecting both temporal arteries and large vessels. ACR 1990 classification criteria for large-vessel GCA were satisfied in only small portion of LV GCA patients. Recently new classification criteria for GCA has been proposed. PMR occurs in 30~50% of patients with GCA, and 15~30% of patients develop GCA, thus these two diseases might be the same disease with different clinical aspects. In this section, we would like to discuss the clinical subtype and characteristic manifestations of GCA, and the relation between GCA and PMR.

MTE5

Diagnosis and treatment for pain in extremities in children

Shuichi Ito

Department of Pediatrics, Yokohama City University Graduate School of

Medicine

Conflict of interest: Yes

Pain in extremities in children is common chief complaint in outpatient clinic. However, diagnosis and physical examination is often challenging. Orthopedic trauma and growth pain are major causes, but infection, rheumatic diseases, metabolic diseases, hemato-oncological diseases, congenital bone, cartilage and connective tissue diseases could be the cause. Anatomically-based careful physical examination and radiological evaluation are useful to focus on site of the pain, leading to the diagnosis. Additionally, family and developmental history taking is essential to diagnosis inborn disorders. Meanwhile, somatoform disorder, malingering and fibromyalgia syndrome are also put in the list of differential diagnosis. Psychosocial problems are frequently associated with such disorders, so-called "heart pain". In this lecture, you can learn physical examination, differential diagnosis and treatment of pain in extremities in children.

MTE6

Clinical and immunological characteristics of macrophage activation syndrome: From the results of serum cytokine profile analysis

Masaki Shimizu

Department of Pediatrics, School of Medicine, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University

Conflict of interest: Yes

Macrophage activation syndrome (MAS) is defined as secondary hemophagocytic lymphohistiocytosis related to rheumatic diseases. Excessive activation and expansion of cytotoxic T cells and macrophages, and overproduction of proinflammatory cytokines play a central role in the pathogenesis of MAS. Although MAS has been associated with most rheumatic diseases, in pediatrics it is most common in systemic juvenile idiopathic arthritis (s-JIA). The genetic defects contributing to the development of cytolytic dysfunction including perforin, and chronic interleukin (IL)-6 and IL-18 exposure inducing secondary suppression of cytolytic function are also closely associated to the development of MAS. A trigger of MAS such as infection activates macrophage by interferon- γ , further amplifies the inflammatory response, leading to excessive production of cytokines and ultimately creating cytokine storm. Clinical features of MAS are characterized by fever, hepatosplenomegaly, lymphadenopathy, profound depression of all 3 blood cell lines, deranged liver function, hyperferritinaemia and evidence of intravascular coagulation. Bone-marrow examination reveals numerous morphologically benign macrophages exhibiting hemophagocytic activity. MAS is a potentially fatal complication, and a proper diagnosis of MAS is essential to start appropriate therapeutic interventions. Once the complication of MAS is suspected, careful monitoring of platelets counts, serum AST, ferritin levels and coagulation test is necessary. We analyzed serum cytokine profile in patients with MAS associated with s-JIA. Serum IL-18 levels in patients with s-JIA were extremely high, in particular, in those with MAS. These levels reflected disease activity of s-JIA and MAS. Serum IL-18 levels were useful to predict MAS development. There were two distinct subsets on the basis of serum IL-6/IL-18 levels in s-JIA. Serum neopterin and sTNFR1/II ratio were useful for the diagnosis of MAS. In this lecture, we will learn the pathogenesis of MAS. Furthermore, we will discuss how we should diagnose MAS and how we should treat the patients with MAS through the case presentations.

MTE7

Psychiatric symptoms in patients with neuropsychiatric systemic lupus erythematosus (NPSLE): A management strategy for rheumatologists

Katsuji Nishimura

Tokyo Women's Medical University, Japan

Conflict of interest: None

Neuropsychiatric systemic lupus erythematosus (NPSLE) is associated with poor prognosis, extensive cumulative organ damage, and low quality of life. Therefore, rheumatologists consider adequate management

of NPSLE important for patient outcome. However, it is often difficult to evaluate and manage psychiatric symptoms in patients with SLE. Typically, the psychiatric differential diagnosis of medically ill patients includes syndromic and etiologic components. Regardless of the etiology, psychiatric manifestations are classified into 4 major syndromes: cognitive, including delirium and dementia; psychotic; mood; and anxiety. These categories were adopted by the American College of Rheumatology in 1999 to define NPSLE cases. The second step, the etiologic differential diagnosis, is often very difficult in SLE patients for the following reasons: (1) it is difficult to distinguish NPSLE from psychiatric disorders due to other etiology, such as corticosteroid-induced psychiatric disorders, solely on the basis of symptoms; (2) no disease-specific diagnostic markers or gold standard for NPSLE has been established; and (3) NPSLE may occur independently of the systemic activity of SLE. Therefore, the first step of the etiologic diagnostic work-up should involve excluding non-SLE-related conditions. The correct diagnosis is derived from careful analysis of the clinical, laboratory, and imaging data on a case-by-case basis. The choice of psychotropic drug for symptomatic treatments is based on the above-mentioned syndromic diagnosis. However, patients with SLE often develop stress-related psychological distress that manifests as depression or anxiety and requires stress management or supportive psychotherapy. This program reviews the status of the diagnosis and management of psychiatric symptoms in SLE patients, which will be useful for rheumatologists to establish a management strategy for NPSLE. The beneficial collaborative partnership with psychiatrists is also discussed.

MTE8

Questions in daily clinical practice for patients with Behçet's disease

Mitsuhiro Takeno

Department of Allergy and Rheumatology, Nippon Medical School

Conflict of interest: Yes

The Guidelines for management of Behçet's disease released from Behçet's Disease Research Committee, MHLW and 2018 update EULAR recommendations for the management for Behçet's syndromes would be helpful for daily clinical care of the patients. Although a number of the disease susceptible genes have been identified, the cause is still unknown. The diagnosis remains dependent on symptomatology with no disease-specific biomarker. Of note, it is important to assess individual symptoms appropriately, as the Japan criteria mention "Atypical findings in both major and minor symptoms should not be counted." This session discusses issues of Behçet's disease in daily clinical practice. 1. What is the definition of "recurrent" oral aphtha? 2. What conditions should be excluded from folliculitis- and acne-like eruptions? 3. What relation is found between genital ulcer and menstrual cycle? 4. What features are found in uveitis of Behçet's disease? 5. When should visual acuity be assessed? 6. Is it appropriate to pick up gastrointestinal lesions other than ileocecal ileum at the diagnosis? 7. What vascular lesions are associated with poor survival prognosis? 8. When should CSF IL-6 be measured to make the diagnosis of neurologic chronic progressive type? 9. What are the differences between the Japan criteria and other sets of International criteria? 10. Why is HLA-B 51 a reference finding on the diagnosis? How is it different from the significance of HLA-B27 in ankylosing spondylitis? 11. How is the disease activity assessed? 12. Which should be selected, steroids or anti-TNF antibodies, in given conditions? 13. Is anticoagulation therapy acceptable for deep venous thrombosis? 14. How have been the clinical pictures of Behçet's disease changed in Japan?

MTE9

Ultrasound assessment of disease activity in rheumatoid arthritis patients

Michihiro Ogasawara

Department of Internal Medicine and Rheumatology, Juntendo University Faculty of Medicine, Tokyo, Japan

Conflict of interest: None

In routine practice, we mainly refer to the number of tender and swollen joint, CRP, ESR, patient's VAS, which are components within the composite measure such as DAS, SDAI, CDAI. and investigate the

condition of rheumatoid arthritis. It is common to judge roughly, however, each component cannot judge the disease condition of RA properly, such as when the findings of affected joints are mild, when suffering from infection, individual difference in pain range value, etc. In such a case, using joint ultrasound examination, it becomes possible to detect abnormal findings such as synovitis with high sensitivity through high-resolution ultrasound images and correct disease activity judgment. On the day of lecture, tips and pitfalls of ultrasound examination, how do you select and judge joint position and number of ultrasound examination necessary for RA activity evaluation? The inspection timing and interval? How do you interpret the obtained findings? How to strengthen treatment using ultrasound image? We will acquire the fundamental knowledge that is indispensable for exploiting the joint ultrasound examination in RA monitoring.

MTE10

Methods for evaluating idiopathic inflammatory myopathies

Ken Yoshida

Division of Rheumatology, Department of Internal Medicine, Jikei University School of Medicine

Conflict of interest: None

Idiopathic inflammatory myopathy (IIM) is an autoimmune disorder with a diverse phenotype characterized by chronic inflammation of the muscle, skin, or lung. The treatment response and prognosis differ depending on the phenotype. It is thus important to comprehensively evaluate the disease condition early for an appropriate treatment. I will first describe the differences between the latest 2017 EULAR/ACR IIM classification criteria and conventional classifications, such as the Bohan & Peter criteria for polymyositis (PM)/dermatomyositis (DM), 2015 diagnostic criteria for PM/DM set by the Ministry of Health and Welfare in Japan, and European Neuromuscular Centre classification criteria focusing on muscle pathology. Furthermore, for the treatment of IIMs, clinicians must evaluate the disease activity, extent of disease, complications, and prognostic factors using various evaluation methods including imaging tests. Magnetic resonance imaging (MRI) and ultrasonography are particularly useful noninvasive modalities, in contrast to the more invasive electromyogram and muscle biopsy, and allow for the accurate assessment of myositis and fasciitis. I will therefore show the utility of imaging tests in IIMs and discuss the relationship between the MRI findings and myositis-specific antibodies. Finally, I would like to describe the prognostic factors in clinically amyopathic DM (CADM). Anti-MDA5 antibody-positive CADM with rapidly progressive interstitial lung disease leads to a poor outcome. Therefore, it is critically important to assess the prognostic factors in CADM for early intervention.

MTE11

The assessment of nailfold capillary changes in clinical settings

Yoshihide Asano

Department of Dermatology, University of Tokyo Graduate School of Medicine

Conflict of interest: Yes

Systemic sclerosis (SSc) is a multisystem autoimmune disease characterized by vasculopathy and fibrosis of the skin and various internal organs. Although its etiology still remains unknown, recent clinical and basic studies have achieved a progress in the understanding of its developmental process. SSc-associated organ fibrosis occurs as a result of constitutive activation of dermal fibroblasts followed by vasculopathy and autoimmune inflammation; therefore the assessment of vasculopathy is quite useful for the early diagnosis of SSc without fibrotic changes, as well as for evaluating its disease stage and severity. SSc vasculopathy consists of the functional and structural abnormalities, the latter of which can be evaluated by looking at nailfold capillaries. Generally, skin vasculature forms capillary loops in the papillary dermis, which runs parallel to the epidermis in the areas around nailfold. The nailfold capillary changes associated with SSc vasculopathy is characterized by capillary dilation or loss, which can be observed by naked eyes when the changes are severe. Dermoscopy and capillaroscopy help us observe the nailfold capillary changes much more precisely. Especially, there is a scoring system of

naifold capillary changes, and also the evaluation of blood flow velocity is possible in capillaroscopy-based evaluation. Indeed, we experienced the improvement of numeric parameters in capillaroscopy-based assessment in SSc patients treated with disease-modifying drugs, suggesting that capillaroscopy may be useful for evaluating disease modifying effects of new drugs against SSc. In my talk, I will present our cases who were longitudinally followed up with capillaroscopy, and also explain the underlying pathogenesis of SSc vasculopathy.

MTE12

Synovial fluid hands-on workshop: “one-drop assessment” by physicians

Naoto Yokogawa¹, Takayasu Kise¹, Yuji Miyoshi¹, Yoshiki Nagai¹, Masako Utsunomiya¹, Ikuko Masuda²

¹Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, ²Juho Takeda Rehabilitation Hospital, Center for Rheumatic Diseases

Conflict of interest: Yes

Crystal arthritis is the most important differential diagnosis in the assessment of inflammatory arthritis but misdiagnosed very frequently. Crystal identification by microscopy is a classic, simple diagnostic procedure but remains to be a gold standard for the definitive diagnosis. Microscopic examination of a drop of synovial fluid can provide a prompt assessment of the presence or absence of inflammation and crystals and help avoiding excessive tests and treatments. In Japan, crystal identification is not performed routinely and often sent outside laboratories. In cooperation with ACR and EULAR synovial fluid workshop, we organized the first JCR synovial fluid workshop for rheumatologists. Teaching points 1) A clinical diagnosis of crystal arthritis is provisional. The definite diagnosis of crystal arthritis should be made by microscopic examination of the synovial fluid. 2) Physicians should look at every synovial fluid by microscopy. It is very important that rheumatologists become acquainted with crystal analysis; besides becoming able to diagnose crystal arthritis at the first visit, they search with knowledge of the clinical picture, and their interest in the search is clearly higher than that of a lab technician. Centrifuging is not necessary. Important clinical information such as presence or absence of inflammation, monosodium urate (MSU) and calcium pyrophosphate (CPP), will be obtained immediately. 3) Ordinal microscopy is acceptable. By the ordinary microscope, crystals are well distinguished and identified as MSU or CPP easily by shape. There is always a microscope fitted with polarized filters in Pathology departments. The polarizing light observation is helpful, showing the strong brilliance of most MSU crystals and the weak to absent of CPP. Use of the compensator may be useful for isolated or very occasional crystals. Acknowledgement: Dr. Eliseo Pascual (EULAR), Dr. Brian F Mandell (ACR), Dr. Ralph H Schumacher.

MTE13

Pathological aspects of vasculitides

Akihiro Ishizu

Department of Medical Laboratory Science, Hokkaido University, Faculty of Health Sciences

Conflict of interest: None

Vasculitis is a disease in which vessels are affected primarily. Since vasculitis is apt to affect vessels segmentally, it is desirable to cut the vessels in round slices as many as possible for histological examination. By the same reason, it is recommended to examine deeper sections when there is no remarkable finding in the first section in spite of the clinical suspicion. The major histological aspects of vasculitis are granulomatous vasculitis and necrotizing vasculitis. The specific stain of elastic fibers can be useful to elucidate the vascular injury. Granulomatous vasculitis is characteristic of Takayasu arteritis (TAK) and giant cell arteritis. Multinuclear giant cells that capture the degraded elastic fibers in the cytoplasm are sometimes present in the lesion. In TAK, the granulomatous inflammation characteristically invades the tunica media from the adventitial side. On the other hand, necrotizing vasculitis occurs in polyarteritis nodosa, anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, anti-glomerular basement membrane disease, IgA vasculitis,

etc. Infiltration of neutrophils (eosinophils in case of eosinophilic granulomatosis with polyangiitis) is present, and leukocytoclastosis is sometimes observed. Additionally, the presence of neutrophil extracellular traps in the lesion is the feature of ANCA-associated vasculitis. These histological characteristics are considered to reflect the pathogenesis. Thus, an exact recognition of pathological findings is important for understanding the pathophysiology of vasculitides. In this lecture, I will introduce the textbooks of vasculitis, the consultation system of Pathological Diagnosis of Vasculitides, which have been established by the Subcommittee of Clinical Pathology in the Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis, and the workshops of vasculitis. I hope to contribute useful information for diagnosis of patients with vasculitis.

MTE14

Approach to SpA diagnosis for rheumatologists

Shigeyoshi Tsuji

NHO Osaka Minami Medical Center

Conflict of interest: None

SpA is classified into Axial SpA (axSpA), Peripheral SpA (pSpA) by the ASAS classification (Assessment of Spondylo Arthritis international Society) from the superiority of its body axis lesion, peripheral lesion, and non - radiographic axial SpA nr - axSpA) has been proposed. On the other hand, from the concept of disease / diagnosis, prototypes such as ankylosing spondylitis (AS), reactive arthritis (ReA), psoriatic arthritis (PsA), juvenile SpA, enterocolitis related spondylarthritis (IBD - SpA) SpA (uSpA), and ReA, IBD-SpA, uSpA, etc. are representative, mainly PsA, as diseases classified as pSpA. This seminar will outline the physical findings and image findings which are important findings in the process of conducting PsA diagnosis in “SpA diagnosed by rheumatologist”.

MTE15

Clinical utility of anti-nuclear antibody testing in patients with connective tissue diseases

Takao Fujii

Department of Rheumatology and Clinical Immunology, Wakayama Medical University

Conflict of interest: None

Connective tissue diseases (CTDs) are well known as systemic autoimmune disorders, because high tiers of anti-nuclear antibodies (ANAs) are frequently observed in sera from CTD patients. Actually, lots of ANA tests, of which clinical significance is clearly identified, are available in clinical practice. 1) ANAs associated with disease diagnosis Anti-Sm and dsDNA antibodies (Abs) in systemic lupus erythematosus (SLE), and anti-topoisomerase I Abs in systemic sclerosis are ‘marker ANAs’. These Abs are highly specific and included in the international classification criteria. 2) ANAs associated with specific manifestations Anti-U1RNP Ab may be one of the critical risk factors for pulmonary arterial hypertension and aseptic meningitis. Anti-aminoacyl tRNA synthetase (ARS) Abs including anti-Jo-1, autoantigens of which are cytoplasmic proteins and are usually recognized in polymyositis/dermatomyositis. Patients with anti-ARS Abs, however, often show the similar clinical manifestations (anti-synthetase syndrome), which include fever, Raynaud’s phenomenon, polyarthritis, interstitial lung disease (ILD) and/or myositis. 3) ANAs associated with disease activity Anti-DNA Ab titer correlate with disease activity in SLE and should be repeatedly determined until clinical remission. 4) Autoantibodies associated with severe and/or life-threatening manifestations Anti-melanoma differentiation-associated gene 5 (MDA5) Abs are closely associated with life-threatening ILD, particularly in clinically amyopathic dermatomyositis. Also, anti-transcription intermediary factor 1- γ (TIF1- γ) are linked to the cancer-associated dermatomyositis, so clinicians should check the malignancy before an immunosuppressive treatment. In the present seminar, we can discuss the best way to use autoantibody testing according to the International recommendations for the assessment of autoantibodies to cellular antigens referred to as anti-nuclear antibodies (Agmon-Levin N, *et al. Ann Rheum Dis* 2014;73:17-23).

MTE16

Statistical Analysis for Clinical Research based on Database

Eisuke Inoue

St. Marianna University

Conflict of interest: None

There is a type of clinical research that utilizes a database as its platform (DB-research). For example, a research following up a group of subjects with a specific medicine, capturing a natural course of a certain disease for a long period of time, building a registry of a rare disease along with clinical information are included as this type of research. Results from DB-research have great influence on various aspects and have contributed to progress in medicine in various forms since sample size and observation period of DB-research are often enormous. In order to publish correct results from DB-research, there are two key components: designing appropriate data collection system and conducting reliable statistical analysis. In this session, we consider and discuss methods of statistical analysis to report information appropriately from DB-research. Analysis of DB-research requires attention to confounding. One solution is to collect lots of factors of possible confounding and incorporate them into the analysis. However, imposing an impossibly large amount of data collection will affect increasing missing data or continuity of research project. It is inevitable to discuss the data collection first enough. In DB-research, it is necessary to deal with missing values appropriately. In multivariate analysis, missing data will affect loss of information directly since a subject with even one missing data item will be excluded from analysis. There is no gold standard method to handle missing values. Therefore, it is necessary to analyze data from various aspects using several currently available methods and evaluate sensitivity to those methods.

MTE17

Pharmacoeconomics in Rheumatoid Arthritis

Eiichi Tanaka

Institute of Rheumatology, Tokyo Women's Medical University Hospital, Tokyo, Japan

Conflict of interest: None

The recent introduction of biologics has resulted in significant advances in treatment strategies for rheumatoid arthritis (RA). On the other hand, rising healthcare costs have caused concern, placing a heavy burden on society as well as RA patients. The IORRA study has also shown that RA patients' financial burden is increasing and that direct and indirect costs associated with progression of functional impairment or decline in quality of life (QOL). This suggests that inhibiting the progression of functional impairment through aggressive control of RA may help reduce lifetime healthcare costs. Pharmacoeconomics is the scientific discipline that evaluates both the clinical benefits and economic efficiency of a drug to determine whether it is worth the cost. Mainly in Europe, pharmacoeconomic evaluation of expensive drugs has been widely used. In Japan, cost-effective assessment was started on a pilot basis for some expensive anticancer and hepatitis C drugs in April 2016. In pharmacoeconomic studies for chronic diseases like RA, cost-utility analysis is mainly used, in which "cost" and "effectiveness" are separately quantified for the study and control health technologies to evaluate the incremental cost-effectiveness ratio (ICER). Effectiveness is usually expressed in quality-adjusted life years (QALYs). We have analyzed the cost-effectiveness of biologics in the treatment of RA and found that the use of biologics in Japanese RA patients is justified in the long term from a health economic perspective. These results suggest that, although biologics are expensive, their proper use in eligible RA patients may also be socially beneficial by helping maintain QOL for a long period of time and allowing patients to have a social life including workforce participation without difficulty. At this Meet the Expert seminar, I will first share health economic issues and the importance of pharmacoeconomic evaluation and then explain cost-effectiveness in real-world settings.

MTE18

Basic knowledge of orthopedic diseases for RA treatment and diagnosis

Toshihisa Kojima

Nagoya University, Graduate School of Medicine

Conflict of interest: Yes

Rheumatoid arthritis (RA) is characterized by multiple arthritis which causes bone destruction. There are many orthopedic diseases that cause pain in the hand fingers, wrist joints, feet, and other limb joints that are particularly frequent in arthritis by RA. Along with advances in drug therapy, an early diagnosis before the appearance of bone destruction and tight control of inflammation is required. Therefore, in order not to misdiagnose these conditions as RA and also to evaluate the disease activity correctly during treatment, it is necessary to know representative orthopedic diseases. The following are representative orthopedic diseases due to routine medical treatment that causes pain in the limb joints. These diseases can understand pathology from the anatomical structure and function of the site. Hand fingers, wrist joints: 1) finger tendonitis and de Quervain tenosynovitis, 2) osteoarthritis (Heberden nodule, Bouchard nodule, CM arthropathy) 3) ulnar plus variance, triangular fibrocartilage complex injury Foot: 1) plantar fasciitis, 2) Achilles tendinopathy Elbow: 1) lateral epicondylitis (tennis elbow) Shoulder: 1) frozen shoulder 2) bicipital tenosynovitis Knee: 1) osteoarthritis, 2) popliteal cyst In elderly onset RA, there are many cases where osteoarthritis is present. Multiple arthritis is an important feature of RA. It should be taken into consideration, in the elderly, there are many pain sites. Plantar fasciitis and pain around the heel are also important to diagnose spondylarthritis. In this lecture, we aim to deepen our knowledge including diagnosis of these diseases, pathology, examination methods, differences from RA.

MTE19

Total ankle arthroplasty through a lateral approach

Katsunori Ikari

Department of Orthopaedic Surgery, Tokyo Women's Medical University

Conflict of interest: Yes

In 2018, new total ankle arthroplasty (TAA) system has been launched in Japan. It is to be used through a lateral transfibular approach. The existing TAA systems in Japan have been performed through an anterior approach, but it is subject to soft-tissue complications. On the other hands, a lateral transfibular approach provides direct visualization of the center of rotation of the ankle, allowing less bone resection with anatomically curved resections as well as more accurate reconstruction of the joint alignment. It requires an external alignment frame that is a rigid coordinate system for bony resections. The purpose of this program is to show the surgical technique for the new TAA system.

MTE20

Examination and treatment for RA hand

Natsuko Nakagawa

Department of Orthopaedic Surgery, Rheumatology & Collagen Disease Center, Hyogo Prefectural Kakogawa Medical Center

Conflict of interest: None

(Introduction) In rheumatoid arthritis (RA), wrist and finger joints are often affected. According to National Survey for rheumatoid arthritis patients- Ryumachi Hakusho, initial symptoms of RA are mainly wrist joint arthritis (37.7%) or finger joint arthritis (52.1%). Persistent arthritis could cause joint destruction or deformity. For this reason, the treatment of RA hand has become essential recently. (Examination of RA hand) As it is required to confirm the presence of finger or wrist joint synovitis, careful examination is essential. In addition, it is necessary to get in-depth information, joint destruction, range of motion, pinch power, and grip power. As the joint synovitis that is not detected by palpation may be confirmed by ultrasound test, it is necessary for additional inspection. As checking if tenosynovitis exist is important because of the risk of tendon rupture, it should not be missed. (Conservative treatment of RA hand) Joint steroidal injection makes some synovitis improve, therefore it

is important as conservative treatment of RA hand. It is desirable to consider resting-purpose orthotics for arthritis. If an orthotic suitable for individual hand deformity is considered, the benefits were significant. (Surgical treatment of RA hand) Small joint surgeries are predicted to increase, and joint-preserving RA hand surgery has been more indicated recently. If conservative treatment such as a joint injection is not effective, the synovial resection is recommended. For destructive joint cases surgical intervention is needed. Especially for RA patients, hand deformity is big problem. Therefore, we need to explain that surgical treatment is also effective for advanced hand deformity. (Conclusion) In addition to drug treatment, a local approach to remaining arthritis is also thought to be essential. Especially for the problem of RA hand, combination of conservative and surgical treatment is thought to be even more important.

MTE21

How to assess plain X-ray imaging for rheumatic diseases

Shintaro Hirata, Eiji Sugiyama

Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital

Conflict of interest: Yes

Recent progress in clinical imaging technology with novel modalities have contributed to diagnosis and management, as well as investigation of pathophysiology in rheumatic diseases. Indeed, plain X-ray is a "legacy" modality utilized for more than 120 years since discovery of X-ray by Wilhelm Conrad Röntgen in 1895. Nevertheless, plain X-ray is the most frequently used modality at both diagnosis and follow-up, especially for bone/joint and chest, in rheumatology to date, since plain X-ray is simple, inexpensive, and suitable for repeated test. Various findings are identified on bone/joint X-ray in rheumatic diseases. Erosion, joint space narrowing, and luxation/subluxation are common in rheumatoid arthritis (RA); especially, erosion is highly diagnostic. van der Heijde's modified total Sharp score (vdH-S score, mTSS) has been the standardized index for joint destruction in clinical trials for RA. Pencil-in-cup appearance, sacroiliitis, or bamboo-spine are characteristic for spondyloarthritis (SpA) including psoriatic arthritis (PsA) and ankylosing spondylitis (AS). Linear calcification in joint space is characteristic for pseudogout. Various findings are observed on chest X-ray, as well. Interstitial lung diseases (ILDs) are common in several connective tissue diseases; however, degree of infiltration and fibrosis varies; infiltration is dominant in polymyositis/dermatomyositis (PM/DM) whereas fibrosis is dominant in systemic sclerosis (SSc). Pleuritis and pericarditis are often observed in systemic lupus erythematosus (SLE), airway lesions including bronchiolitis are often found in RA. Indeed, chest X-ray is quite important for screening infectious disorders including tuberculosis and pneumocystis at initiation and follow-up of immunosuppression with DMARDs or glucocorticoids, etc. In the session, active discussion with attendees will be encouraged about assessment of plain X-ray imaging for rheumatic diseases, viewing representative images.

MTE22

Early treatment of tenosynovitis with conventional synthetic disease-modifying antirheumatic drugs other than methotrexate prevents the progression of preclinical rheumatoid arthritis

Tomomasa Izumiya

Higashisendai Rheumatic Disease Clinic

Conflict of interest: None

I have a dream that one day Japan would lead the world in treating preclinical rheumatoid arthritis (pre-RA). However, there is a theoretical dilemma in treating pre-RA: As pre-RA can only be retrospectively defined in the absence of currently available clinical definition, presumable cases cannot be verified as being pre-RA when the treatment is effective and the would-be RA resultantly stops progressing to established RA. Mankia *et al.* have reported that many patients who possess a risk to progress to established RA actually do not. I have experienced a case in which the patient progressed to established RA after a very long period of 37 years from his seroconversion of rheumatoid factor. Such a case indicates us that it is impossible to distinguish those who progress from those not. Therefore, a revolutionary change in the definition of pre-RA is re-

quired. Since RA is a syndrome of systemic synovial inflammation, arthritis is not necessarily its essential component. Accordingly, its treatment must aim at systemic synovitis instead of just arthritis. For example, tenosynovitis can be an initial symptom and can cause erosions of adjacent bones. Thus, this pathology can be useful in making an early diagnosis of RA and itself can be a treatment target in the pre-RA stage. Tenosynovitis can cause severe pain and morning stiffness especially when it affects flexor tendons of hands. At our clinic conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) other than methotrexate (MTX) are effective in treating such cases. Ultrasonography is especially useful in diagnosing tenosynovitis and this technique is widely available in Japan. Further, many csDMARDs other than MTX including Bucillamine, Igaratimod and Tacrolimus can be used in this country. Taking advantage of these, I hope that we can lead the world in detecting and treating pre-RA and preventing its progression to established RA.

MTE23

Treatment of Shoulder Pain in Patients with Rheumatoid Arthritis

Kazuya Tamai¹, Yuichi Nagase², Masashi Naito², Sakae Tanaka³

¹Department of Orthopedics, Tohto Bunkyo Hospital, ²Rheumatology and Connective Tissues Department, Tokyo Metropolitan Tama Medical Center, ³Department of Orthopaedic Surgery and Spinal Surgery, The University of Tokyo Hospital

Conflict of interest: None

The goal of this lecture is to provide knowledge for: 1) functional anatomy of the shoulder, 2) possible causes of shoulder pain in patients with RA, 3) intraarticular injection, 4) physical therapy, and 5) surgical options. <Functional anatomy> The basic function of the shoulder is to move the hand to a specific position in the space. The shoulder motion is a sum of scapulothoracic and glenohumeral motions. The stability of the glenohumeral joint depends on the rotator cuff. <Shoulder joint in RA> In advanced RA, the glenohumeral as well as the acromioclavicular joint show destructive changes in half of cases. Rotator cuff tear occurs frequently in RA because the insertion of the rotator cuff is located close to the bare area. The impairment of shoulder function has a great impact on the health-related QOL in RA patients. <Treatment of shoulder pain in RA> The JCR clinical guideline (2014) describes intra-articular corticosteroid injection, physical and occupational therapy, and total shoulder and hemiarthroplasty as a recommended treatment for RA patients. 1) Intra-articular corticosteroid injection: This is known to improve pain VAS and active shoulder flexion, and to decrease inflammation/hypervascularity in the synovium. My preference of injection technique is from posterior in a sitting patient. 2) Rehabilitation: It is known that aerobic exercises and resistance muscle training are useful for RA patients. For the shoulder joint, isometric exercises of the rotator cuff muscles and relaxation of the scapulothoracic muscles are recommended. 3) Surgery: Anatomical total shoulder arthroplasty is recommended when a rotator cuff function is preserved because it shows satisfactory clinical outcome as well as longevity of the implant. In contrast, hemiarthroplasty is not preferred now because it often causes glenoid erosion. Reverse total shoulder arthroplasty is now an attractive option in patients who have both joint destruction and rotator cuff insufficiency.

MTE24

Musculoskeletal ultrasound makes our RA practice style aggressive one!~Excellent procedure for Rheumatologist make it possible to depict the sharp answer in clinical setting~

Kenta Misaki

Department of Rheumatology, Kita-Harima Medical Center

Conflict of interest: Yes

Ultrasound technique have played a pivotal role for diagnosis and evaluation of treatment efficacy since 1949 when K.T. Dussik firstly introduced it in clinical settings. The reason why ultrasound is surprisingly spread in clinical field is that it is easy and non-invasive imaging procedure to patients. Remarkable innovative revolutions for ultrasound probe make it possible for Rheumatologists to put into clinical setting. However, many patients also including co-medicals are no where insight about adaptations of ultrasound to connective tissue disease (CTD). Musculo-

skeletal ultrasound (MSKUS) is mostly used for Rheumatoid arthritis (RA) in Rheumatology. The contribution of MSKUS for both diagnosis and evaluation of treatment efficacy is quite high as expected. In particular, high specificity (93.7%) in 2010 ACR/EULAR-RA classifications was shown by using MSKUS compared with that (79.4%) of palpation method from our country. The algorithm for RA diagnosis also including the validation of both therapeutic effect and remission, and the final definition of enthesitis were reported from EULAR recently. These excellent reports suggested that MSK is crucial examination for daily medical practice, moreover MSKUS is very useful to not only RA but also the differential diagnosis similar to connective tissue disease. In this session, I am going to introduce the latest evidence of MSKUS in addition to the real-cases diagnosed by MSKUS, and focus upon the educational systems to sonographers and nurse in our institution.

MTE25

An introduction to statistical analysis for clinical researches using R and EZR

Hisashi Noma

Research Center for Medical and Health Data Science, The Institute of Statistical Mathematics

Conflict of interest: None

In the Symposium 17, I provided an introductory talk about the worrisome “statistics,” and I’d ask again, “Are you still suffering with “statistics” of clinical research papers?” However, in modern medical researches, many advanced statistical techniques, e.g., significance tests, confidence intervals, logistic regression, Cox regression, have been commonly used, and we cannot understand clinical evidence from these research articles precisely if we do not have sufficient knowledge about them. In addition, we cannot write a clinical research article if we can use statistical software actually. It is said that these software cannot be used if the user is not familiar with programming skills and most of these software are expensive. In this session, I conduct a hands-on seminar about a free statistical software R (R Foundation for Statistical Computing, Vienna, Austria) and its add-in EZR for statistical analysis for clinical researches, which resolve all of the problems mentioned above. R is a well-known statistical software that has been widely adopted in clinical researches published in international medical journals, and has rich and reliable functions for data analyses. R itself is difficult to use if the user acquires programming skills for the R language, but EZR enables easy-to-conduct statistical computations like as spreadsheet software, e.g., Microsoft Excel. In this seminar, you can experience statistical computations of p-values, confidence interval, and multivariate analyses that are widely used in international medical journals actually.

MTE26

How to Write a Paper in English 2 - The Structure of Logic and Figures -

Tetsuo Koyama

Department of Rehabilitation Medicine, Nishinomiya Kyoritsu Neurosurgical Hospital

Conflict of interest: None

In medical science, research papers are published primarily in English. I provide some useful ideas to write a research paper in English in terms of the structure of logic and figures. In both English and Japanese, logical composition is most important in writing a paper. Scientific papers are not highbrow literature, esoteric philosophy, or advanced mathematics. The required logical composition is therefore very simple; the keys are “abstract and specific,” “parallel and contrast,” and “comparison and integration.” Japanese sentences often put main focus on predicates and allow null subjects, whereas English sentences require definite subjects and predicates in principle. English is thus beneficial in providing a well-organized logical structure. A good hint for writing a paper in English can be found in modern/contemporary artworks. Not a few modern paintings, including those of Édouard Manet, are based on past artworks. Scientific papers are similar to these artworks in that they are prepared referencing past papers. Another hint comes from the use of ready-mades in artworks. For instance, Marcel Duchamp placed a mass-produced porcelain urinal

in an art museum as Fountain (1917), and Andy Warhol attracted public attention with Campbell’s Soup Cans (1962). Similarly, most figures and tables presented in a beautiful array in scientific papers are prepared using the format of Excel and other statistical software. The use of “ready-mades” in modern/contemporary art gives a great hint on the preparation of figures and tables, which have pivotal roles in scientific papers. In summary, the keys to write a research paper in English are: 1) to find a point for discussion in the context of past papers; 2) always to be mindful of subject-oriented logical structure; and 3) to create a beautiful array of figures and tables using “ready-mades.”

Luncheon Seminar

LS1-1

Current treatment for spondyloarthritis

Naoto Tamura

Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine

Conflict of interest: Yes

Spondyloarthritis (SpA) is a group of diseases showing common clinical features, such as axial and peripheral arthritis, enthesitis, dactylitis, and extraarticular involvement, including uveitis. There are now two types of SpA, peripheral dominant peripheral SpA and axial dominant axial SpA, and psoriatic arthritis and ankylosing spondylitis are representative diseases, respectively. Patients with psoriatic arthritis often have enthesitis and/or dactylitis other than peripheral arthritis that are critical for the diagnosis. Family history of psoriasis, examination of nail disease, and finding hidden psoriatic lesions, in scalp, buttocks and other places, are also important. Axial disease is not rare in psoriatic arthritis. It usually can be distinguished from ankylosing spondylitis due to asymmetrical appearance, lack of sacroiliac involvements, and non-marginal ossification. Modified New York criteria has been used for classification of ankylosing spondylitis and also for diagnosis of an intractable disease supported by Ministry of Health, Labour, and Welfare. On the other hand, a classification criteria for axial spondyloarthritis proposed by ASAS is now commonly used. It includes MRI and HLA-B27 to classify early disease as non-radiographic axial SpA. However, only a part of non-radiographic axial SpA becomes to ankylosing spondylitis. Although early intervention is required for SpA to improve its outcome, appropriate diagnosis is necessary. In axial disease and enthesitis, conventional anti-rheumatic drugs are not effective and then biologics should be used in case of active diseases with NSAIDs. Recently, "Treat to target (T2T)" is recommended as a therapeutic strategy for SpA, and new medicines for SpA have been appearing. In this session, we will discuss about update of diagnosis and treatment of SpA.

LS1-2

Pathophysiology of Spondyloarthritis : the role of IL-17A in inflammation, enthesitis, and new bone formation

Dirk Elewaut

VIB Inflammation Research Center, Ghent University and Department of Rheumatology, Ghent University Hospital, Ghent, Belgium

Conflict of interest: Yes

Enthesitis is a hallmark of spondyloarthritis. Despite this, relatively little is known about the immunobiology of enthesitis. The enthesitis is composed of stromal cells, tendon structures and a rare population of innate like T cells composed primarily of gamma delta T cells. Curiously, these rare cells respond vividly to IL-23 by secreting IL-17A, IL-22 and other inflammatory mediators leading to enthesitis. It should be noted that there may be other means how enthesitis occurs including by tissue resident cells. The overall immunobiology of enthesitis will be discussed with special emphasis on IL-17A as a key driver of inflammation and tissue remodeling.

LS2-1

Clinical features of eosinophilic granulomatosis with polyangiitis compared to other ANCA-associated vasculitis

Ken-ei Sada

Dentistry and Pharmaceutical Sciences, Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine

Conflict of interest: Yes

Eosinophilic granulomatosis with polyangiitis (EGPA) is classified into antineutrophil cytoplasmic antibody (ANCA) associated vasculitis along with microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) in Chapel Hill Consensus Conference 2012. EGPA is characterized by eosinophil-rich and necrotizing granulomatous inflam-

mation and necrotizing small vessel vasculitis, and hypereosinophilia, and occurs in individuals with asthma and allergic rhinitis. A previous national survey in Japan reported that younger disease onset than patients with other ANCA associated vasculitis, high frequency of neurological manifestations, and 50% of positivity of myeloperoxidase-ANCA. This report also showed that ANCA-positive patients had renal involvement, mucous membrane or ophthalmological symptoms, and ENT symptoms more frequently, whereas cutaneous lesions and cardiovascular involvement were less common. Interestingly, neurological symptom revealed no dependence on ANCA positivity. Glucocorticoids generally showed good treatment response for EGPA. For refractory cases, cyclophosphamide and azathioprine have been used concomitantly as with the treatment of other ANCA associated vasculitis. Recently, B-cell depleting therapy with the anti-CD20 antibody rituximab has proved beneficial for the treatment of MPA and GPA, and avacopan, selective C5a receptor inhibitor, has been developed as a new treatment option. For EGPA, the efficacy of IVIG for refractory neurological symptoms and efficacy of mepolizumab, anti-IL-5 inhibitor, for refractory EGPA were reported additionally. In this seminar, we focused on the clinical features of EGPA compared to MPA and GPA based on recent epidemiological studies and clinical trials.

LS2-2

Mepolizumab, an anti-IL5 monoclonal antibody, improves disease outcomes in Eosinophilic granulomatosis with polyangiitis

Peter Howarth^{1,2}

¹Global Medical Expert, GlaxoSmithKline, UK, ²Allergy and Respiratory Medicine, University of Southampton, UK

Conflict of interest: Yes

Mepolizumab add on therapy was assessed in the treatment of EGPA in a randomized, placebo-controlled, double-blind, parallel-group, multicenter study in patients with a history of relapsing or refractory disease on stable therapy with prednisolone/prednisone ≥ 7.5 - ≤ 50 mg/day with or without additional immunosuppressive therapy for ≥ 4 weeks (Wechsler et al NEJM 2017;376:1921-1932). Mepolizumab 300mg subcutaneously or matching placebo was given every 4 weeks, in a 52 week study. Co-primary endpoints were, accrued duration of remission (Birmingham Vasculitis Activity Score [BVAS]=0, prednisolone/prednisone dose ≤ 4 mg/day) over 52 weeks and the proportion of patients in remission at both Weeks 36 and 48. Secondary endpoints included average glucocorticoid dose during weeks 48-52 and time to first EGPA relapse. Safety was also assessed. There were 136 randomized patients (mepolizumab n=68, placebo n=68). Duration of remission accrued over 52 weeks was significantly prolonged with mepolizumab vs placebo (odds ratio: 5.91 [95% confidence interval [CI]: 2.68,13.03]; p<0.001); a significantly higher proportion of patients were in remission at Weeks 36 and 48 (32% vs 3%, respectively, odds ratio: 16.74 [95% CI: 3.61,77.56]; p<0.001). Significant reductions in average daily glucocorticoid dose during Weeks 48-52 were seen with mepolizumab vs placebo (odds ratio: 0.20 [95% CI: 0.09,0.41]; p<0.001). Time to first EGPA relapse was significantly longer with mepolizumab vs placebo (hazard ratio: 0.32 [95% CI: 0.21,0.50]; p<0.001). Rates of adverse events (AEs) and serious AEs were similar for mepolizumab and placebo. This study thus demonstrates consistent and meaningful clinical benefits of mepolizumab in patients with EGPA.

LS3

Utilization of Biomarkers targeting Remission in RA Treatment - Making use of Autoantibody and MMP-3 Assays -

Eiichi Tanaka

Institute of Rheumatology, Tokyo Women's Medical University Hospital, Tokyo, Japan

Conflict of interest: None

In recent years, the treatment of Rheumatoid Arthritis (RA) has been significant advances with the introduction of biologics. The treatment goal is shifting from "Reduce disease activity" to "Prevent bone and joint destruction", and remission is now a realistic treatment target. The Institute of Rheumatology Rheumatoid Arthritis (IORRA) study has demon-

strated clear improvement in patient outcome. In order to assure better patient outcomes, early diagnosis and intervention based on Treat to Target recommendations, as well as Tight Control through careful monitoring are necessary. When planning such an RA treatment strategy, biomarkers provide invaluable objective information. Biomarkers used in the treatment of RA can largely be divided into two categories, auto-immune antibody tests and tests for markers of inflammation. Auto-immune antibody tests include rheumatoid factor (RF) and anti-citrullinated peptide antibody (ACPA). These are given significant weight in the ACR/EULAR new classification criteria for early diagnosis, as they may be positive even prior to the onset of joint inflammation. On the other hand, markers of inflammation include serum CRP and ESR for the evaluation of disease activity, and Matrix Metalloproteinase-3 (MMP-3) as an indicator of the degree of synovitis. As these reflect the effectiveness of treatment, they are important in the Tight Control of disease activity. These biomarkers are also noted as "Guidance of medical care" for the treatment of Juvenile idiopathic arthritis (JIA), a pediatric rheumatoid disease. This seminar will cover the basics of biomarkers which are reimbursable under the Japanese national health insurance system and are currently being utilized in Japan, along with presenting some of the evidences that has been published in recent years. In addition, the MBDA scoring system which shows high correlation with RA disease activity and has been used in the United States will also be covered.

LS4

Nurse education for total care of rheumatoid arthritis

Mie Fusama

Nursing Department, NTT West Osaka Hospital

Conflict of interest: None

Rheumatoid arthritis (RA) therapy has made dramatic progress with the spread of MTX and biologics, and the need for total care by nurses has increased. Total care is indispensable in order to improve QOL so that patients can receive optimal treatment and live their own lives while aiming to achieve remission. Total care for RA that nurse think about is as follows: · As a medical staff, aiming to maximize the treatment effect while considering the physical, psychological and social aspects of the patient · Stay closer to the patient who lives everyday while suffering from diseases, improve the quality of medical care while sharing goals with the patient We need to provide information (about diseases, treatment, side effects, etc.) that patients can understand their illnesses and can make "Shared decision making" with medical staff. Self-management guidance is also important. In order to alleviate the patient's anxiety and to make better communication, we should acquire the basic attitude (such as listening comprehension and empathic understanding) necessary for psychological support. However, in reality, nurses themselves often find it difficult to master and practice these diverse tasks. Therefore, comprehensive nurse education from patient assessment to treatment / self-management, monitoring and follow-up is necessary. In this seminar, we will consider current situation, issues and perspectives, including the activities of Asia-Pacific Initiative for Rheumatology Nurse Education (ASPIRE), which we are collaborating with Asian countries on nursing education to support total care of RA.

LS5

Early diagnosis and evaluation of the disease activity for systemic sclerosis -Where are we and where are we going? -

Hidekata Yasuoka

Division of Rheumatology, Department of Internal Medicine, Fujita Health University School of Medicine

Conflict of interest: None

Hidekata Yasuoka Division of Rheumatology, Department of Internal Medicine, Fujita Health University School of Medicine Systemic sclerosis (SSc) is a systemic fibrotic disease characterized by microvascular injury and autoantibody production. In usual wound healing, the process proceeds as follows; 1) injury as a trigger, 2) succeeding infiltration of immune cells to the lesions, 3) tissue damage and repair, and 4) healing or regeneration of the tissue. However, the healing step is insufficient or abnormal, it will go to 5) residual of damage and remodeling. In patients

with SSc, most of the cases were diagnosed during the course to the phase 5, and the causality of SSc can be explained by the abnormality of any of these steps. Thus, it is easy to understand that less patients are detected at the phase 2, inflammatory phase. And also, evaluation of disease activity is difficult, since the process of damage and repair is mixed in phase 4. Moreover, since SSc is a systemic disease with multiple organ involvements, remodeling process of each organ is different, which makes complicate to evaluate the "systemic" activity of the disease. There is no available treatment to halt the process of fibrosis or remodeling and prognosis of SSc is still poor. Therefore, the trial for the development of novel treatment approach is an urgent and important issue in SSc. Thus, I would like to discuss the approach for early detection of SSc to improve the prognosis, and evaluation methods for the disease activity to establish better outcomes for clinical trials. For now, it is important for us to recognize that there are 2 disease types, limited-cutaneous and diffuse-cutaneous SSc, which of these have different natural courses. And then, we should be aware of the early signs for SSc, referring the 2013 new classification criteria for SSc, which might be clues to reach the early diagnosis of SSc. For evaluation of disease activity of SSc, modified Rodnan skin score is still useful. Including the information presented, these points will be discussed in this session.

LS6

IGRA practice in rheumatoid arthritis

Shigeto Tohma

Department of Rheumatology, National Hospital Organization Tokyo National Hospital

Conflict of interest: None

Infliximab (IFX) was approved and reimbursed for Crohn's disease (CD) in 2002 and for Rheumatoid arthritis (RA) in 2003. Since then, a variety of Biologics has been clinically developed for inflammatory diseases such as inflammatory bowel disease (IBD) and psoriasis with better outcome. At the same time these drugs usage has increased the opportunistic infection risk such as tuberculosis due to their immunosuppressive nature. This risk has been strongly informed via "Biologics practice guideline" and "Biologics and Respiratory disease, practice guideline", insisting the importance of thorough evaluation by quaternary, chest X-ray, IGRA/TST. Thanks to these efforts TB SIR has been decreasing in RA with slight increase at the early phase. In IBD and psoriasis TB development has also been well controlled. The newly diagnosed TB case number has been decreasing down to 13.9 in 100,000 in 2016. The characteristic feature of TB case is increasing number of TB development from latent TB infection (LTBI) among elderly people those were TB infected at their younger age. These people are likely to develop active TB due to age associated weak immune status and immunosuppressive treatment for their underlying disease. It is necessary to design TB treatment plan for these patients considering the following points; 1. Extrapulmonary tuberculosis is more often, difficult and tend to delay the TB diagnosis, 2. The underlying disease is likely re-activated during prior TB treatment, 3. IRIS likely occurs when stop Biologics treatment. Therefore, it is critical to fully screen LTBI by X-ray and IGRA and perform prophylaxis TB treatment if necessary. Also important is to closely monitor an early symptom of TB development during the course of Biologics by distinguishing inflammation by underlying disease progression from TB infection/reactivation. To access the risk/likeness of TB development from LTBI some predictive markers has been investigated such as neutrophil, CD8 count, lymphocyte subset analysis, and Monocyte/Leukocyte ratio. The clinical utility of these predictive marker has to be investigated if it works well under immunosuppressive therapy.

LS7-1

Baricitinib overturn the treatment concept of RA! ~Musculoskeletal ultrasound depicts the novel utility of BAR in clinical practice~

Kenta Misaki

Department of Rheumatology, Kita-Harima Medical Center

Conflict of interest: Yes

The clinical indication of Biologics (Bio) for Rheumatoid arthritis (RA) has caused the paradigm shift, and it had also approved under the

medical insurance in Japan since 2003. Bio make it possible to improve the RA prognosis as a clinical remission, however we often encounter the cases unfortunately led to drastic radiographic destruction after achieving clinical remission, and those refractory to multiple Bio. It is easily suggested that good outcome is only brought to the RA patients triggered by particular cytokine as we expected because the target of Bio is just for one-focused cytokine. As it is still difficult to apply the tailored medicine for RA in clinical setting, the treatment of Bio sometimes produce a poor cost-effective result and unexpected bone destruction during the Bio switching. JAK inhibitor (JAKi) induced the efficacy for RA patients under the mechanism of working in upper RA inflammatory pathway, inhibiting the multiple cytokine signaling. JAKi has been also available in Japan since 2013, it is noteworthy JAKi was approved all the same time in all over the world. Now, 2 kinds of JAKi including Baricitinib (BAR) are focused as one of the novel therapeutic items. RA treatment strategy is not only the administration of Bio/JAKi, but also the achievement of sustained radiographic remission. One of the useful procedures for monitoring the RA disease activity is musculoskeletal ultrasound (MSKUS). Recently MSKUS is shared the spotlight as a pivotal non-invasive examination tool for Rheumatologist as well as Bio/JAKi. The collaboration between MSKUS and Bio/JAKi will enable to early diagnosis, early treatment induction, early achievement of remission and finally reduce/withdraw various DMARDs. I am going to introduce the utility of BAR and MSKUS in dairy clinical setting with current topics and evidence in this session.

LS7-2

Expectation of Baricitinib in the treatment of rheumatoid arthritis

Kensuke Oryoji

Center for Rheumatic Diseases, Matsuyama Red Cross Hospital

Conflict of interest: Yes

Baricitinib is the second JAK inhibitor approved in Japan. The mechanism of action is inhibition of JAK 1/2 and is different from Tofacitinib previously approved with or without JAK 3 inhibitory action. IL-6, IFN γ and GM-CSF are representative of cytokines that are particularly well inhibited by JAK 1/2 inhibition. The importance of IL-6 in rheumatoid arthritis is obvious. Because the disease activity of rheumatoid arthritis correlates with the amount of macrophages in joints, we believe that it is attractive to be able to selectively inhibit IFN γ and GM-CSF, cytokines that activate macrophages. Although it seems that they are not suppressed as much as the cytokines mentioned above, it seems that the JAK1 inhibition seems to be well balanced to moderately suppress cytokines such as type 1 IFN, which is thought to be difficult to suppress in existing biological preparations. In this presentation, we outlined the pathological condition of rheumatoid arthritis, autoantibody and temporal phase and clinical trials of Baricitinib (RA-BEAM; noninferiority to adalimumab, RA-BEACON; efficacy on bio failure, RA-BEGIN; efficacy on almost seropositive early RA) and the expectation for the future will be described.

LS8

Selectivity and Specificity in the treatment of RA

John D Isaacs

Institute of Cellular Medicine, Newcastle University Faculty of Medical Sciences

Conflict of interest: Yes

Following recent advances in the understanding of downstream signaling pathways, janus kinase (JAK) inhibitors have been developed as a novel approach for treating rheumatoid arthritis (RA). JAK inhibition constitutes the first major breakthrough since the advent of biologic DMARDs. As with tumor necrosis factor inhibitors, we must appreciate that JAK inhibitors have unique pharmacokinetic, pharmacodynamic, and clinical characteristics that have important implications for efficacy and safety. We will explore the JAK isoforms and their functional roles in inflammation, define JAK selectivity, and consider the potential advantages and disadvantages of inhibiting one JAK over another.

LS9-1

Recent progress in the treatment of ANCA-associated vasculitis

Masayoshi Harigai

Department of Rheumatology, Tokyo Women's Medical University

Conflict of interest: Yes

Primary goal of treating patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis is optimizing health-related quality of life through abrogating disease activity and minimizing accrual of disease-related and treatment and comorbidity-related damage. The treatment is consisted of remission-induction and remission-maintenance therapies. According to the 2017 Clinical Practice Guidelines for ANCA-associated Vasculitis published in February 2017, the standard remission-induction therapy for microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) is glucocorticoid (GC) plus cyclophosphamide. Rituximab (RTX) can be an alternative treatment if an attending physician is an expert with enough knowledge and experience for treating vasculitis. Efficacy of RTX for MPA and GPA has been established by RAVE study and RITUXVAS study, but evidence is still limited and a prospective observational study is in progress by JPVAS. Almost all of patients achieve remission by remission-induction therapy, but majority of them relapse unless they receive remission-maintenance therapy. Standard remission-maintenance therapy is low-dose GC and azathioprine (AZA), but a better regimen has been investigated by various clinical trials. In MAINRITSAN trial where GC plus RTX was compared with GC plus AZA in patients with MPA and GPA, relapse rate of RTX by Month 28 was significantly lower than that of AZA, and serious adverse events were similar. MAINRITSAN2 trial compared fixed and on-demand treatment with RTX in patients with MPA and GPA; no difference was observed in relapse rate by Month 28 between the two treatment arms, and the on-demand group received significantly less RTX than the fixed treatment group. I would like to take the advantage of this opportunity to organize most recent evidence of treatment for MPA and GPA to consider future treatment strategy.

LS9-2

Recent advances in the management of Takayasu arteritis

Mitsuaki Isobe

Sakakibara Heart Institute

Conflict of interest: Yes

The clinical guideline for management of vasculitis syndrome had been revised and published in 2018. The diagnostic accuracy of Takayasu arteritis has been greatly improved based on the development of imaging modalities including CTA and MRA. ^{18}F -FDG-PET is useful for diagnosing the extent and degree of inflammation. As for treatment corticosteroid is the first line immunosuppressive agent and effective to subside inflammation. However, more than 60% of patients show recurrence during the tapering of corticosteroid. Various agents have been used for the second line immunosuppression. Regarding the utility of tocilizumab, Steroid dose reduction can be achieved in about 80% of patients under tocilizumab coverage. One problem is the diagnosis of recurrence during tocilizumab treatment since CRP does not show elevation even in the presence of inflammation. Precise clinical and physical assessment is required for detection of recurrence during tocilizumab treatment.

LS10

Update on Therapeutic Approaches for Myositis Associated with Interstitial Lung Disease

Takahisa Gono

Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine

Conflict of interest: None

Polymyositis/dermatomyositis (PM/DM) is a autoimmune disease, characterized by inflammation and progressive weakening of the skeletal muscles. Skin rash, arthritis, interstitial lung disease (ILD), and cardiomyopathy are also accompanied as extramuscular manifestations in patients with PM/DM. ILD is one of the leading causes for mortality in pa-

tients with PM/DM. Thus, physicians need to manage patients with PM/DM-associated ILD (myositis-ILD) appropriately in clinical practice. Clinical courses and response to treatment are highly variable in patients with myositis-ILD. The most useful and reliable predictor for treatment response and prognosis is the myositis-specific autoantibodies (MSAs). Anti-MDA5 and anti-ARS antibodies are strongly related to development of myositis-ILD. Patients with anti-MDA5 usually present with clinically amyopathic DM (CADM). They frequently develop rapidly progressive ILD (RP-ILD). Thirty percent of them die due to respiratory failure related to RP-ILD in despite of intensive immunosuppressive therapy. On the other hand, patients with anti-ARS present with PM, DM, or CADM. They develop ILD gradually, from several months to six months. Although initial response to treatment with corticosteroid is good for myositis-ILD, eventually, supplement of oxygen therapy is required and/or acute exacerbation of ILD develops during long-term observation in some of patients with anti-ARS. Physicians should plan a treatment strategy in each patient with myositis-ILD, based on comprehensive evaluation of predictive prognostic factors such as age, progressive speed and extent of ILD, partial pressure of oxygen in arterial blood, forced vital capacity, serum biomarkers including CRP, ferritin and KL-6, and MSAs. I would like to give a lecture regarding update on therapeutic approaches for myositis-ILD, showing the results of postmarketing surveillance of the safety and effectiveness of tacrolimus in Japanese patients with myositis-ILD.

LS11

Early diagnosis and treatment of ssc-associated pah

Masato Okada

Immuno-Rheumatology Center, St. Luke's International Hospital

Conflict of interest: None

Connective Tissue Disease associated Pulmonary Arterial Hypertension (CTD-PAH) is a major manifestation of Anti-Nuclear Antibody associated Syndromes, such as systemic sclerosis, mixed connective tissue disease, systemic lupus erythematosus, dermatomyositis/polymyositis, Sjogren's syndrome. Early diagnosis and treatment is crucial to improve the outcome and prompt upfront combination or rapid sequential introductions of PAH specific medications including Selexipag has become standard. Systematic screening method of CTD-PAH and treatment with immunosuppressant and pulmonary arterial dilators are discussed based on cases on selexipag and other regimens.

LS12-1

Strategy of pregnancy in patients with rheumatoid arthritis

Atsuko Murashima

National Center for Child Health and Development

Conflict of interest: Yes

"A sound baby in a sound maternity" is a creed of obstetric medicine. The importance of pre-conception care is becoming important as age of pregnancy is becoming high. It is important that women with chronic diseases are required further premedication care to maintain their remission status with drugs that are not harmful to both mothers. However, considering the risk of pregnancy complications such as pregnancy deterioration and pregnancy hypertension syndrome, it is important to take medical treatment with a policy that "treatment of primary disease should be given priority, but not pregnant. In pregnancy of patients with rheumatoid arthritis, it is most important to keep them for pregnancy while suppressing disease activity for fertility, maintaining remission during pregnancy, and good results of pregnancy. So, the usage strategy of disease modifying anti-rheumatic drugs is essential. Most of the labeling of medicine drugs for the pregnant women / lactating women are written with reference to reproductive experience results, but there are limits to applying the results of animal experiments to humans. It is appropriate to judge whether or not it is safe to use it in human experience, but epidemiological research outcome in Japan is hard to be reflected in the labeling. FDA classification has been used in Japan, but in 2015 this classification method was shifted to the description formula. In Japan as well, the description method of the labeling was changed for the first time in 20 years. Under such circumstances, I believe that the obstetrics and gynecologic

clinical practice guideline will be a reliable tool. I will explain the method of safety evaluation during pregnancy / breast feeding and the concept of medication treatment based on it.

LS12-2

Treatment strategy of Rheumatoid Arthritis in WoCBA (Women of Child-Bearing Age) patients

Hiroaki Dobashi

Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University

Conflict of interest: None

The treatment strategy of Rheumatoid Arthritis (RA) had greatly advanced with the development of many therapeutic drugs including csDMARDs, bDMARDs, and tsDMARDs. A lot of efficacy and safety evidence for such drugs has been established, which also contributed to this advancement. However, the RA treatment strategy should be decided for individual patients based on not only his/her disease activity, but also other factors such as comorbidities, as stated in the overarching principles of 2016 EULAR Recommendation for RA Treatment: "Treatment of decisions are based on disease activity and other patient factors, such as progression of structural damage, comorbidities and safety issues." This is also very important for WoCBA (Women of Child-Bearing Age) patients. It is necessary to pay much attention when deciding a treatment strategy for a WoCBA patient because of various characteristics they are associated with. A treatment strategy for a WoCBA patient should be decided individually for each of the three pregnancy phases (preconception, during pregnancy, after pregnancy). This talk will present typical characteristics and necessary considerations in WoCBA patients and a proposal for the treatment strategy in such patients. As a result, this talk aims to discuss about "how to support RA patients who hope to become a mother." A patient wish is written down in the ACR draft guideline of reproductive health of ACR as "My rheumatologist knows me better than gynecologist." I hope this seminar will be helpful for the audience to meet this wish of WoCBA patients.

LS13-1

Significance of Treatment Continuation Rate in Drug Therapy for Rheumatoid Arthritis: Review of Etanercept

Yuji Hirano

Department of Rheumatology, Toyohashi Municipal Hospital

Conflict of interest: Yes

In Japan, Etanercept (ETN) was approved for RA in 2005. Some studies have provided answers to a wide range of clinical questions regarding ETN. The TEMPO trial showed suppression of disease activity and prevention of joint destruction in patients with long-standing RA. The COMET trial showed suppression of disease activity and prevention of joint destruction in patients with disease duration less than 2 years after onset. The PRESERVE trial showed the effects in achieving bio-free remission and tapering BIO. Although some anti-TNF antibody drugs are associated with reduced effect due to production of neutralizing antibodies and development of adverse events, ETN has less immunogenic potential and is not associated with such concerns. ETN is effective even after anti-TNF antibody drugs are switched to ETN. Data on the incidence of adverse events indicate that ETN is associated with lower risks of serious infection and recurrent tuberculosis than other anti-TNF antibody drugs. In actual clinical practice, ETN may be characterized by its favorable long-term continuation rate. Studies using data from the European registries, such as DAMBIO, DREAM, RABBIT and SCQM-RA, have demonstrated that ETN is associated with a better long-term continuation rate than anti-TNF antibody drugs. In 209 patients who initiated ETN therapy at least 10 years earlier at facilities affiliated with the Nagoya University, the long-term continuation rate was 40.5% at 10 years. In the other countries, registry studies following patients for 10 years or more have revealed favorable continuation rates for ETN therapy. The treatment continuation rate appears to reflect a combined measure of efficacy and safety. In this seminar, the clinical studies and actual clinical data on ETN are reviewed, and the significance of the continuation rate of BIO therapy is discussed.

LS13-2

Biosimilar will bring about new treatment option

Hiroaki Matsuno

Matsuno Clinic for Rheumatic Diseases, Toyama, Japan

Conflict of interest: Yes

The therapeutic effect of biologics in rheumatoid arthritis (RA) is excellent, but the cost is prohibitive, with biosimilar versions costing much less. We conducted a phase 3 study of etanercept biosimilar (ETN-BS) in Japan and the Republic of Korea (ROK). When ETN-BS was compared with etanercept-reference product (ETN-RP) in a phase 1 study, the total area under the curve (AUC_t: 90% confidence interval [CI], 0.87 to 1.06) and maximum drug concentration (C_{max}: 0.92 to 1.13) were within the acceptable range of equivalence (0.80 to 1.25). To unify study conditions between the two countries, the maximum dose of methotrexate (MTX) was set at 16 mg/week; however, in the ROK, as only 2.5 mg MTX tablets were available, the maximum dose was set at 15 mg/week. The primary endpoint was change in Disease Activity Score 28-Erythrocyte Sedimentation Rate (DAS-ESR) at week 24 after start of treatment. We determined the acceptable range of comparability with ETN-RP as -0.6 to 0.6, because the European League against Rheumatism criteria state that a change > 0.6 in DAS28-ESR is clinically relevant. The target sample size was calculated backward from this acceptable range, using a simulation. Thus, the success rate of the study would be 90% or higher when the two-sided 95% CI of the between-group difference and the point estimate of the difference between the Japanese and Korean groups was within the acceptable range of equivalence. A comparative study of 296 patients (148 in each group) would be needed to confirm comparability using DAS28-ESR. Based on a predicted drop rate of 20%, a double-blind study protocol with 372 patients was submitted to the PMDA and eventually approved. The numbers of patients in the primary efficacy analysis set at week 24 were 164 in the ETN-BS group and 165 in the ETN-RP group. The changes in DAS28-ESR were -3.009 (95% CI, -3.198 to -2.820) for ETN-BS and -2.859 (-3.05 to -2.667) for ETN-RP, and the between-group difference was -0.150 (-0.377 to 0.078). As this was within the acceptable range of equivalence, the comparability of the 2 biologics was demonstrated. In addition, the incidence of all adverse reactions during the study period was 51.3% in the ETN-BS group and 62.0% in the ETN-RP group. Furthermore, the frequency of anti-drug antibody generation in the ETN-BS group did not exceed that in the ETN-RP group. Thus, we believe that ETN-BS can be used for RA therapy.

LS14

The immunomodulating effects of abatacept correlate with clinical effectivity

Tom WJ Huizinga

Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands

Conflict of interest: Yes

Rheumatoid Arthritis (RA) is a chronic inflammatory and destructive disease with the subset of RA patients autoantibodies have the worst prognosis. The development of specific autoantibody profiles and the selection of B-cells specific for citrullinated antigens and subsequent specific mutations from germline sequences have been identified as the hallmark of RA development. Based on the presence of specific mutations in the germline sequences and based on the presence of IgG isotypes, the production of ACPAs by B cells is T-cell-dependent and costimulation is a necessary biological process for T-cell development necessary for mutations in the germline and for isotype switching. Therefore the inhibition of costimulation by Abatacept is predicted to interfere in this process. Indeed it is shown in intervention studies in early RA that Abatacept can interfere in the development of the ACPA response. Since presence of ACPAs is associated with increased radiological damage and disease progression, it is expected that interfering with ACPA development leads to better outcomes for patients. Indeed in post-hoc analysis of head to head studies between TNF-blockade and costimulation blockade it is observed that in the high titer ACPA group, costimulation is the most effective therapy. Detailed analysis of the ACPA response including the RA-specific feature of glycosylation in the antigen binding site will be discussed.

LS15-1

Medical economic issues of biological DMARDs in rheumatoid arthritis and future prospects

Eiichi Tanaka

Institute of Rheumatology, Tokyo Women's Medical University Hospital, Tokyo, Japan

Conflict of interest: None

The introduction of biologics has resulted in significant advances in treatment strategies for rheumatoid arthritis (RA). On the other hand, rising healthcare costs have caused concern, placing a heavy burden on society as well as RA patients. The IORRA study has shown that RA patients' financial burden is increasing and that direct and indirect costs associated with progression of functional impairment or decline in quality of life (QOL). This suggests that inhibiting the progression of functional impairment through aggressive control of RA may help reduce lifetime healthcare costs. Pharmacoeconomics is the scientific discipline that evaluates both the clinical benefits and economic efficiency of a drug to determine whether it is worth the cost. We have analyzed the cost-effectiveness of biologics in the treatment of RA and found that the use of biologics in Japanese RA patients is justified in the long term from a health economic perspective. These results suggest that, although biologics are expensive, their proper use in eligible RA patients may also be socially beneficial by helping maintain QOL for a long period of time and allowing patients to have a social life including workforce participation without difficulty. Under these circumstances, biosimilars for anti-TNF inhibitors have been developed with the expectation of further reducing economic burden. Biosimilars have biosimilarity (equivalence and homogeneity) to reference biological products. Approved biosimilars can be used in the same methods as reference product. Shares of biosimilars are expanding rapidly, especially in the European countries. In Japan, infliximab and etanercept biosimilars are available. Since their drug prices are approximately 60 to 70% of reference product, economic impact is expected to be large. In this Luncheon Seminar, I would like to share the medical economic issues in RA as well as the importance of pharmacoeconomics, and also discuss the future prospects for biosimilars.

LS15-2

Optimization of Biologic Treatment for Rheumatoid Arthritis

Kazuhisa Nakano

The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: Yes

Treatment of rheumatoid arthritis (RA) has recently reached a major turning point due to the introduction of biologics targeting specific molecular aberrations, which has redefined the major treatment goals to (1) induce remission, (2) control the progression of joint destruction and functional disorders, (3) maintain remission, and (4) improve life prognosis. In Japan, 10 drugs for RA are covered by the National Health Insurance including 8 drugs with 3 different modes of action, i.e., TNF inhibition, IL-6 receptor inhibition, and T-cell co-stimulation inhibition, and 2 biosimilars which may be regarded as generic versions of biologics. When a biologic is to be administered at our institution, a clinical pathway is utilized, thereby the patient is required to be hospitalized, a screening test including CT scan is conducted, and a fecal occult blood test and a sputum test are additionally conducted depending on the case to control adverse reactions. Thereafter, the final decision on administration is made, and the First registry is created to monitor effectiveness and safety. Meanwhile, to select a biologic, various considerations are necessary in terms of efficacy as well as safety, cost, convenience in the route and intervals of administration, etc. Based on the data from the First registry, we have studied: 1. how to quickly determine the effectiveness of the biologics, 2. possibility of dose reduction or discontinuation, 3. optimization of biologics switching, etc. I would like to present a summary of these studies and prospects for biosimilars increasingly used to offer some ideas for optimization in RA treatment.

LS16

From basic of JAKs to the JAKinibs in the clinic

Kunihiro Yamaoka

Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine

Conflict of interest: Yes

Janus kinase (JAK) is an intracellular protein that is activated immediately after the cytokine binds to the cognate receptor expressed on the cell surface. More than one JAK inhibitors have demonstrated similar efficacy to biologics, highly specific to the extracellular inflammatory cytokines. Interestingly, these two drugs belonging to two different class possess totally different mechanism of action. Biologics are highly specific to a single molecule with a long half-life and on the other hand JAK inhibitors are selective to certain JAKs, not necessarily specific with a short half-life. Thus, off-target effect should be kept in mind for JAK inhibitors. In this seminar, I will briefly introduce the basics of JAKs and how and why JAKs were targeted. In addition, I would like to discuss on what has been observed with in vitro experiments and analysis of patient specimens treated with JAK inhibitors to elucidate the mechanism of action.

LS17

Bridging the gap between patients and health care providers in Rheumatoid Arthritis with Motivational Interviewing - Making recommendations asked for by patients, and no more pushy sales

Hiroaki Harai

Harai Clinic Harai Consulting&Training Inc. Japan Association of Motivational Interviewing

Conflict of interest: None

Motivational Interviewing (hereinafter referred to as MI) is effective when proposing a new treatment method to patients in the field where new drugs are developed one after another within a relatively short period of time. Even though an effective drug is launched, it is meaningless unless patients actually try it. Healthcare professionals (HCPs) tend to simply show only the facts to their patients, or explain by saying "this works extremely well" or "the evidence is so and so" based on the view point of experts. When a patient makes a decision to change the familiar treatment method to something else, it is desirable to provide information from the patient's standpoint. Now, MI is a useful technique that strategically and intentionally brings out the feeling of the patients themselves to change. The more HCPs are the cutting edge, the more they are experts, the more they want to use new and the best treatment methods and they think it is natural for patients to follow the best treatment. If a patient does not follow the treatment, they think the patient will do so if they explain in further detail. However, the method that a HCPs teaches what they want to teach is not always useful for anyone. Offering more information to a patient who resisted when the information was given the first time would be counterproductive. If information is provided and is not appropriate for the patient's desire to "know", it strengthens the patient's feeling, i.e., "I don't want to know". Ultimately, if a HCPs comes to feel that "this patient is stubborn and bigoted", there is a huge gap that cannot be overcome between a HCPs and patient. What can we do to avoid creating such a gap? How can patients themselves be guided to change their behavior without using forcible guidance? I would like to talk about an overview of MI and actual clinical examples to show you that with MI you can lead the conversation with patients in constructive direction without going around and around.

LS18

Management of pain and osteoporosis of patients with rheumatoid arthritis

Isao Matsushita, Hiraku Motomura, Tomoatsu Kimura

Department of Orthopaedic Surgery, University of Toyama

Conflict of interest: Yes

In recent year, the treatment for rheumatoid arthritis (RA) has improved drastically. According to this change, disease activities of RA have been steadily decreasing. National Database of Rheumatic Disease

in Japan (NinJa) showed rates of patients with DAS28 remission were 18.2% and 57.2% in 2002 and 2016, respectively. The mean of patient's pain VAS of 2002 and 2016 were 3.6 and 2.4, respectively. Pain VAS is also gradually improved, but the tendency of the improvement slows down. Though objective indexes are improved, pain VAS, which is subjective index, is not improved enough. There are several reasons why the pain continues to exist. Subclinical inflammation and/or residual joint damage might induce pain. Many elderly RA patients who are complicated with osteoarthritis might show arthralgia. Rheumatologists identify the cause of the pain and must cure. Osteoporosis is serious complication for patients with RA. It was reported that the RA patient with the past of the vertebral fracture showed significantly higher HAQ-DI than the patient without the past history. Subanalysis of BeSt study indicated that use of bisphosphonate was independent factor of the maintenance of bone mineral density. And it was reported that frequency of fracture did not decrease though disease activity was improved. Rheumatologists have to practice dual T2T aiming at suppression of disease activity and inhibition of bone mineral density loss in order to maintain ADL and QOL of RA patients during long-term period.

LS19-1

Tremfya's usefulness on PsA

Shigeyoshi Tsuji

National Hospital Organization Osaka Minami Medical Center

Conflict of interest: Yes

Psoriasis is the typical disease of inflammatory keratosis, and its incidence rate in Japan reach 0.34%. Psoriatic arthritis, characterized by inflammation of a joint, spondylitis, inflammation of digit, enthesitis appear approx. 10-15% of psoriasis and it causes high possibility of generating comorbidity¹⁾ which related to metabolic syndrome (adipositas 26%, hyperlipidemia 43.9%, diabetes 15.1%, hyperuricemia 20.9%, high blood pressure 23.2%, liver enzyme abnormality 29.2%) compare to the case of having only psoriatic exanthema lesion. It's regard as problem that there is high ratio of cardiac infarction especially in younger generation. Also, since approx. 30% of psoriatic arthritis complicate with spondylitis, without proceeding an appropriate therapeutic intervention at the earliest timing, it causes bony ankylosis and disturb patients' QOL badly, therefore Rheumatologists need to consider psoriatic arthritis as one of diagnostic criteria for patients who claim chronic lower back pain or arthritis without specific cause/reason. What is the best treatment method for patients with psoriatic arthritis to obtain better QOL? Firstly, by giving patients a basic guidance of better living, exercise therapy, nutritional guidance, etc. it can improve their comorbidity related to metabolic syndrome, and this improvement will maximize an efficacy of pharmacotherapy to contribute to increase persistency rate. I consider that this is one of the key. The other treatment method is pharmacotherapy. In 2010, biological products against psoriasis/psoriatic arthritis became applicable to insurance in Japan and this fact changed the treatment method for psoriasis/PsA drastically and contributed to improve patient's QOL. And, in 2018 Tremfya, anti-human IL-23p19 monoclonal antibody product became applicable to insurance against psoriasis/PPP as well. This addition can broad option of pharmacotherapy. In this lecture I would like to introduce the latest knowledge of psoriatic arthritis, and positioning/possibility of Tremfya.

LS19-2

Medical care for PPP, from the view of dermatologist

Tadashi Terui

Division of Dermatological Science, Department of Dermatology, Nihon University School of Medicine

Conflict of interest: Yes

In Japan, approx. 150,000 people are suffering by PPP (palmoplantar pustulosis) which is intractable, chronic disease causes pustules mainly appearing on the palms of the hands or soles of the feet. It is similar to generalized pustular psoriasis, however PPP forms blisters first followed by pustules while generalized pustular psoriasis forms pustules without blisters. Additionally, there are cases that tonsilla, dental focus, focal infection, dental metal allergy, etc. trigger PPP. Symptoms on skin appear all over on the palm, the sole. Especially center of the palm towards to

thenar, and anti thenar on the hand and the arch towards to edge, heel on the sole. Pustules eventually became crust and desquamate, sometimes it cause crack by forming inflammatory keratosis after repeating inflammatory reaction. In PPP, there are patients who have osteoarticular symptoms which is called as Palmoplantar pustulotic Arthro-Osteitis. Osteoarticular symptoms often is observed in chest rib joint, but sometimes appears in sacroiliac articulation, peripheral joint. Symptoms of PPP appears on the hand where is seen always by the others, and patients feel pain by soaking their hands with water while taking bath, doing dishes, feel pain in their sole while they walk, or feel pain in their joint if patients have osteoarthritis. This is a disease which can easily destroy QOL. Up to present, basic medical care of PPP are causal therapy such as focal infection treatment, symptomatic treatment by using external medicine, oral agent, phototherapy, or giving guidance of better living ex. quit smoking. There are only a few suitable medicine for symptomatic treatment, and it cause difficulty sometimes for medical care. November last year, Guselkumab which is IL-23p19 inhibitor approved as biologic medicine for PPP for the first time. In this lecture session, we will explain clinical pathophysiology, characteristics along with introduction of clinical test result of Guselkumab and would like to study positioning of treatment of PPP.

LS20-1

Surgery for rheumatoid arthritis in the era of biological DMARDs and targeted synthetic DMARDs

Katsunori Ikari

Department of Orthopedic Surgery, Tokyo Women's Medical University

Conflict of interest: None

Rheumatoid arthritis is the most common autoimmune disease characterized by progressive joint damage. Clinical outcomes have improved dramatically and remission is possible for many patients because of advances in medical treatment in these 20 years. There were many reports that showed a decrease in RA-related surgical procedures. However, certain number of patients still need RA-related surgeries. Combination therapy consisting of medical treatment and surgical intervention is thought to be effective in improving the quality of life for RA patients who have joint destruction. I will show you recent trends in RA-related orthopedic surgery in Japan.

LS20-2

Effectiveness of bDMARDs by analyzing big claimed data

Katsuhiko Takabayashi^{1,2}

¹Sanwa Hospital, ²Department of Medical Informatics, Chiba University Hospital

Conflict of interest: None

Rheumatoid arthritis is a systemic autoimmune disease with arthritis as the main symptom. The joint destruction with the synovitis progresses from the early stage. Since the irreversible physical dysfunction is caused by the joint destruction, the precise diagnosis and treatment from the early stage are necessary. Recently, in addition to the development of biologics (bDMARDs) targeting cytokines that influence in pathogenesis and low molecular medicine targeting JAK as an intracellular tyrosine kinase, the treatment to target and maintain remissions with the conception of Treat to Target (T2T) contributed to the control for the destruction of joint structures and the functional disorders. Any drug is expected to be effective in 1st Line treatment, however it is necessary to treat with considering the difference between real world data as clinical practices used in various patients and clinical trials conducted in limited patients. CISA (Clinical Information Statistical Analysis) is the medical statistics data accumulated from the claimed data by the cooperation of 13 national university hospitals. CISA is widely utilized for clinical pharmaceutical research, efficacy investigation of the drug, medical needs investigation, and so on. The result is helpful for the Japanese medical treatment. and CISA as a database is useful for the people. The National Database (NDB) is stored and constructed from Japanese health insurance claims Data and specific Health checkups data and Specific health Guidance data. It is going to be used as a big database for epidemiology and clinical research as investigation for preparation, implementation and evaluation

of medical cost optimization plans. In this seminar, I would like to focus on the efficacy and safety of RA treatment by analyzing these databases.

LS21

Managing Remission in RA

Paul Emery^{1,2}

¹University of Leeds, Leeds Institute of Rheumatic & Musculoskeletal Medicine, Leeds, UK, ²Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, UK

Conflict of interest: Yes

Remission is the target of all guidelines for the management of RA. It is now more frequently achieved due to more aggressive treatment approaches and the early use of very effective drugs: a treatment strategy is now required for these large numbers of patients reaching remission. An initial trial of methotrexate with steroids is probably not optimal for all. Guidelines suggest that patients should be tapered, but there is a lack of objective evidence of which ones are appropriate. Initial studies suggested that with early use of biologics and methotrexate it was possible to stop the biologic. This will be discussed, although there is little evidence that biologics can be stopped in late disease except in specific cases. Tapering of the biologic, however, has been successful in many randomized controlled trials. One problem with remission is the lack of agreement on a definition of either remission or flare. All composite scores suffer from the disadvantage that joint counts are inaccurate when patients are close to remission. Therefore, attempts have been made to use more objective measures; these include imaging and immunological measures (in particular T-cell sub-sets). A recent study has shown that for csDMARDs seropositivity, HAQ, quality of life and presence of power Doppler are all predictive of flare on tapering, whereas for bDMARDs only low T-regs and quality of life were predictive. Other studies have shown that sustained deep remission was an effective predictor of successful stopping of etanercept. Thus there is increasing evidence that one can predict the likelihood of individual's flaring on tapering and stopping. These should now be tested in randomized controlled studies.

LS22-1

Disease burden of psoriatic arthritis and its overcome by anti-TNF therapy

Hideto Kameda

Faculty of Medicine, Toho University, Tokyo, Japan

Conflict of interest: Yes

Psoriatic arthritis (PsA) is the most common disease among predominantly peripheral spondyloarthritides. Patients with severe PsA experience impaired quality of life (QOL) due to mutilans joint deformity or axial joint ankylosis mimicking ankylosing spondylitis. The primary pathophysiology of PsA includes enthesitis, which is believed to develop secondary synovitis, dactylitis and nail changes. And the repairing process to the micro-injury at enthesis leads to osteoproliferative changes, while osteoclast activation by the adjacent synovitis leads to bone erosion: A complicated joint structural change in PsA is likely to thus develop. Tumor necrosis factor (TNF) is one of the critical cytokines involved in the joint disease of PsA, and its neutralization by biological agents such as adalimumab (ADA) enables PsA patients to achieve the treatment goal such as remission or minimal disease activity (MDA). In ADEPT trial, patients receiving ADA showed significantly better improvement in skin and joint diseases as well as QOL examined by SF-36 than those receiving placebo. Further, patients receiving ADA showed significantly less radiographic progression defined by modified total Sharp score than those receiving placebo, and MDA was achieved in 33.3% of the ADA group, which was significantly higher than 3.2 % in the placebo group. In addition, a work productivity and activity impairment (WPAI) study in the postmarketing surveillance of PsA patients in Japan demonstrated significant decrease of the overall work impairment score by ADA treatment for 24 weeks, providing an evidence supporting the benefit of ADA therapy for WPAI.

LS22-2

TNF alpha inhibitor in the treatment of ankylosing spondylitis

Yuho Kadono

Orthopaedic Surgery, Saitama Medical University

Conflict of interest: Yes

Recently, it becomes well known that spondyloarthritis (SpA) is a kind of umbrella inflammatory disease concept including ankylosing spondylitis (AS) and psoriatic arthritis. AS involves not only sacroiliitis or spondylitis but also coxitis or enthesitis. AS exhibits inflammatory back pain which is one of the major clinical aspects, uveitis, psoriasis, or inflammatory bowel disease. Since TNF α is a major cytokine in the pathogenesis, TNF alpha inhibitor shows effectiveness in treatment of AS. We sometimes have difficulties to diagnose AS. We should distinguish it from mechanical pain or fibromyalgia. When we find out spinal involvement in images, we should distinguish it from diffuse idiopathic skeletal hyperostosis or osteitis condensans illi. If the inflammation was not well controlled, spinal fusion would progress. Spinal fusion leads to impairment of activity of daily living, ADL. The goal of AS treatment is to control disease activity monitoring BASDAI or ASDAS, to inhibit the progression of bone change, and to protect from ADL impairment. NSAIDs is the first choice, and TNF α inhibitor would be considered when NSAIDs were insufficient.

LS23

Treatment of rheumatoid arthritis in the new era

Tsutomu Takeuchi

Division of Rheumatology, Keio University School of Medicine

Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has made an innovative progress in the last decade. In 2010, new RA classification criteria developed by the American College of Rheumatology/European League Against Rheumatic Diseases (ACR/EULAR) were introduced which allowed for early diagnosis with higher sensitivity. In 2011, the ACR/EULAR new remission criteria for RA were proposed to establish more stringent clinical remission criteria that directly related to improvement in the outcome, prevention of joint destruction. In addition, the "Treat-to-Target" strategy has been recognized globally and, the treatment recommendations were renewed by the EULAR in 2013 and by the ACR in 2014, and also in Japan. Furthermore, the EULAR recommendations were updated in 2016. These changes that occurred after 2010 are the most drastic in the history of RA treatment. These changes are the results of the review of the overall treatment flow, "diagnosis-treat to target-clinical remission-improvement in outcome", in order to preserve long term quality of life of the patients. Denosumab is a fully human IgG2 monoclonal anti-RANKL antibody that inhibits the binding of RANKL to RANK. It suppresses bone resorption by inhibiting the generation, function and survival of osteoclasts. In Japan, denosumab has been applied in clinical practice as an anti-osteoporotic agent since 2013. Furthermore, in 2017, denosumab was approved for the inhibition of the progression of bone erosion associated with RA, thereby a new treatment option targeting joint destruction has become available in addition to csDMARDs, bDMARDs and tsDMARDs. This session will review the role and action of denosumab as the new treatment option in RA treatment, including the results of a long-term observational study in Japanese patients.

LS24

Management of Infections and Respiratory Complications That Rheumatologists Should Know - Practical side of Diagnosis, Treatment, and Prevention -

Kazuyoshi Saito^{1,2}

¹Center for Rheumatic Disease, Tobata General Hospital, ²The First Department of Internal Medicine, University of Occupational & Environmental Health

Conflict of interest: None

Autoimmune diseases such as rheumatoid arthritis (RA) are treated with anti-inflammatory and immunosuppressive drugs to normalize self-

reactive lymphocytes. Infliximab, the first anti-TNF α antibody approved in Japan for RA, and other biological agents have contribute to high clinical efficacy and caused paradigm shift in RA treatment. These drugs are highly efficacy, but they often cause infection diseases and respiratory complications, resulting in the difficulty to continue RA treatment. Therefore, infection management in RA is critical to improve patient outcomes. Tuberculosis patients were increased rapidly in the initial administration of anti-TNF treatment, for whom latent tuberculosis (LTBI) reactivation were strongly suspected. Therefore, LTBI screening and a primary prevention with INH before administration of anti-TNF inhibitor became the urgent needs, after that prophylactic treatment with INH is effective for LTBI suspected patients. Interferon- γ release assay is very useful in LTBI screening, but needs comprehensive judgment, including that of image findings and interview, are required for interpretation of the result (negative/positive/indeterminate/invalid) under immunosuppressive treatment. As per a PMS on actual use of biologic drugs, infections, including bacterial pneumonia, *Pneumocystis* pneumonia, and herpes zoster, along with tuberculosis, occurred at a certain rate. The Department of First Internal Medicine, University of Occupational and Environmental Health, Japan (UOEH), has planned and implemented criteria for primary prevention based on screening conducted at introduction of registry (FIRST registry) of RA patients who introduced biological drugs and actual condition survey of infections, and has increased effects on onset inhibition. Better treatment outcomes will be obtained through proper management of them.

LS25

Reconsidering remission induction and maintenance of therapy in patients with rheumatoid arthritis

Isao Matsumoto

Division of Rheumatology, Department of Internal Medicine, University of Tsukuba

Conflict of interest: Yes

Recent therapies for rheumatoid arthritis (RA) were dramatically progressed continuously, we need to diagnose earlier, and intensive therapy aimed to clinical remission and its maintenance are strongly recommended especially in active RA. A lot of biologics targeting inflammatory cytokines (TNF α and IL-6), T cells-co stimulator and JAK are available in Japan. From the view of the effective therapy with new molecular, immunological and genetic studies, the etiology of RA has been reconsidered. But we have faced primary and secondly disabled to these drugs, and comorbidities in patients with RA limits the choice of effective drugs due to conceivable side effects. Eight kinds of biologics (plus two bio similars) are approved in Japan, and five out of eight are TNF inhibitors. In this seminar, we discuss remission induction and maintenance regulated by TNF inhibitors which have history of more than 15 years, and updated mechanisms by TNF α regulation in arthritis. In addition, we also discuss about new biomarker of RA such as citrullinated proteins in serum, recently identified by us, for monitoring disease activity, diagnosis and pathogenesis.

LS26-1

Adult hypophosphatasia: a disguised adult bone metabolic disease in rheumatic outpatients

Nobuaki Ito

Division of Nephrology and Endocrinology, The University of Tokyo Hospital

Conflict of interest: None

Hypophosphatasia: HPP is a bone metabolic disease with impaired bone calcification due to *ALPL* mutation. While neonatal severe type of HPP shows devastating bone malformation, adult HPP develops chronic bone/muscle pain, recurrent and prolonged pseudofracture/fracture, muscle weakness and fatigue. The most prevalent pathogenic mutation of *ALPL*: c1559delT is recognized at one in 480 in Japanese. Heterozygotes of pathogenic mutations are seen at one in 100~200. In Europe, the prevalence of symptomatic adult HPP is reported to be one in 6370. The screening method for osteomalacia including HPP simply consists of serum ALP, Pi, Ca, Alb. When serum ALP is under low-normal range in

symptomatic patients or in normal range in existence with overt pseudo-fracture/fracture, the genetic test for *ALPL* should be considered. When the adequate diagnosis of adult HPP is made, Asfotase Alpha is useful to improve the symptoms in qualified patients. However, most adult HPP patients who visited rheumatologists or orthopedists complaining above mentioned symptoms were misdiagnosed as having rheumatoid arthritis, fibromyalgia, polymyositis, ankylosing spondylitis, primary osteoporosis, plantar fasciitis and so on, because recognition rate of this disease among rheumatologists or orthopedists is still very low and pseudofracture is often elusive in X-ray imaging. After all, most of these adult HPP patients lose opportunities to be correctly diagnosed and adequately treated. Meanwhile, in adult HPP patients like other osteomalacia patients, the use of bisphosphonates and the other bone antiresorptive drugs is practically contraindication as it could develop more atypical fractures in these patients. Furthermore, intensive physical therapy itself could also cause pseudofractures. Therefore, patients presenting chronic bone/muscle pain, pseudofracture/fracture and osteoporosis should be screened for HPP and hypophosphatemic osteomalacia in order to avoid misguided medical and physical therapy.

LS26-2

Consideration of adult type hypophosphatasia from the viewpoint of a rheumatologist

Kenji Yoshida

Immuno-Rheumatology Center, Matsuyama Red Cross Hospital

Conflict of interest: None

Have you ever heard of a disease called hypophosphatasia (HPP)? While awareness of this disease has been increased among obstetricians and pediatricians, HPP is unknown by physicians in specialties for adult patients. HPP is an inherited metabolic bone disorder caused by decreased alkaline-phosphatase (ALP) activity due to mutations of the *ALPL* gene that encodes ALP involving bone mineralization and as a result, skeletal, muscular, and dental manifestations are developed. Additionally metabolic disorders of calcium pyrophosphate cause ectopic calcification which can lead to pseudogout. On the one hand the majority of patients with HPP in Japan have been detected in newborns and juveniles, on the other hand patients who onset HPP in adulthood, called adult form of HPP, have rarely been diagnosed. This is possibly related to low awareness of the disease among physicians who may encounter adult HPP patients. HPP in adult population may get overlooked because symptoms and severity vary among patients. It is also known that adult patients with HPP suffer from unexplained systemic pain, joint pain, musculoskeletal pain, muscular weakness, chondrocalcinosis and stress fractures, which impairs their ADL and quality of life. Therefore rheumatologists and orthopedists would have opportunities to see HPP patients. Once HPP is aware, it can be relatively easily suspected from medical history and low ALP activity and diagnosis is confirmed by gene mutation analysis. We present a case of 69 years old male diagnosed as HPP, particularly the process of diagnosis from the perspective of a rheumatologist.

LS27

Evolution of IL-6 Inhibition therapies in rheumatoid arthritis-Sarilumab, a fully human monoclonal antibody against IL-6 receptor-

Motomu Hashimoto

Department of Advanced Medicine for Rheumatic Diseases, Kyoto University

Conflict of interest: Yes

IL-6 is one of the key cytokines involved in both autoimmunity and inflammation of rheumatoid arthritis (RA) pathology. IL-6 inhibitors not only inhibit bone destruction but also improves the subjective symptoms of RA patients, so it shows excellent efficacy and continuity rate in clinical practice. There are various methods for inhibiting IL-6 signaling, such as IL-6 inhibition and IL-6 receptor inhibition, classical IL-6 signaling inhibition and IL-6 trans-signaling inhibition, or gp130 and Jak-Stat pathway inhibition. Inhibition of the IL-6 receptor is one of the most effective methods among them. In order to “evolve” the bDMARDs by obtaining the antibody with higher affinity and lower immunogenicity, various at-

tempts have been made including the phage-display method or immunizing transgenic containing human immunoglobulin genes. Sarilumab is a “fully human” monoclonal antibody that targets the IL-6 receptor. Sarilumab is a so-called “hybrid” bDMARDs that inherited functional characteristics of IL-6 receptor inhibition from tocilizumab with manufacturing method inherited from Golimumab. It is welcome that now we have a second option to inhibit IL-6 signaling by bDMARDs in RA. In this presentation, the role of IL-6 in RA pathology and the history of “evolution” of therapeutic methods to inhibit IL-6 signaling will be reviewed, with the introduction of therapeutic strategy using Sarilumab in clinical practice.

LS28-1

Considering the positioning of Igaratimod from its pharmacological action

Kosuke Ebina

Graduate School of Medicine, Department of Orthopaedic Surgery, Osaka University

Conflict of interest: Yes

It has been confirmed that Igaratimod (IGU) exhibits unique pharmacological actions as follows. In vitro 1. IGU suppressed TNF- α production from mouse and rat macrophages when stimulated with zymosan or lipopolysaccharide (LPS), and inhibited inflammatory cytokines production such as TNF- α , IL-1 β , IL-6, IL-8 and MCP-1 upon stimulation of human macrophages with LPS. 2. In the clinical blood concentration at human administration, IGU suppressed IgG production from B cells as well as methotrexate (MTX). 3. IGU suppressed the production of IL-6, IL-8, IL-17, RANKL, MMP-3 upon stimulation of human RA synovial cells with TNF- α , IL-1 and IL-6. 4. IGU suppressed RANKL-induced differentiation of RAW264.7 cells into osteoclasts, and promoted differentiation of osteoblasts in cooperation with rhBMP-2. Based on these evidences, IGU may be effective not only in suppressing inflammation of arthritis but also in suppressing bone and joint destruction. In vivo 1. IGU in corporation with MTX suppressed arthritis and bone-joint destruction in collagen-induced arthritis of rats. 2. IGU reduced the combined dose of glucocorticoid by suppressing macrophage migration inhibitory factor (MIF) in autoimmune disease model mice. 3. IGU inhibited osteoclast differentiation and bone loss in postmenopausal osteoporosis model mice. 4. IGU improved the pain threshold of the sciatic nerve entrapment model rat. Based on these evidences, IGU is expected not only to protect bone joints from destruction, but also to reduce concomitant glucocorticoid dosing and to improve pain of RA. Taken together, IGU can be adapted to patients who have difficulty in using sufficient amount of MTX, difficulty in controlling pain, high RF value, high risk of joint destruction progression, and difficulty in reducing glucocorticoid dosing. Further development of clinical evidence and application is expected in the future.

LS28-2

New development of RA treatment with csDMARDs ~ Igaratimod~

Masato Okada

Immuno-Rheumatology Center, St. Luke's International Hospital

Conflict of interest: Yes

In recent years, there is no doubt that biologic disease modifying anti-rheumatic drugs (bDMARDs) have reached their peak in rheumatoid arthritis (RA) treatment. Although bDMARDs are very useful agents, their usefulness is supported by an appropriate combination with conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs). Igaratimod (IGU) is one of the csDMARDs with anti-inflammatory and immunomodulatory actions. It suppresses production of cytokines such as IL- β , TNF- α , IL-6, IL-8, and also immunoglobulin. In Japan, it has been used for patients with RA especially in early stage, its importance in clinical practice is increasing. In past randomized control studies, the efficacy of IGU has been demonstrated, but its tolerability is not clearly known. Therefore, we conducted a retrospective study on 456 patients who received IGU. In this study we examined the tolerability of IGU in clinical practice and the relationship between IGU retention rate and complications such as malignancy, tuberculosis infection and interstitial lung disease. We examined the reasons for termination for patients who

discontinued IGU, the main reasons for discontinuation due to adverse events were renal damage 22.8% (26/114), liver dysfunction 22.8% (26/114), gastrointestinal disturbance 18.4% (21/114), etc. However, the extent of these adverse events was mild and quickly recovered after discontinuation of IGU administration. In addition, when examining whether or not there is a difference in retention rate of IGU depending on the presence or absence of complications such as malignancy, tuberculosis, and interstitial lung disease, no significant difference was observed. In conclusion, IGU shows adequate considerable retention rate and good tolerability in clinical practice.

LS29-1

Importance of quantitative evaluation of quality of life in patients with systemic lupus erythematosus and usefulness of Japanese LupusPRO as a disease-specific instrument for measuring quality of life

Mitsuyo Inoue

Department of Nursing, Hyogo University of Health Sciences

Conflict of interest: None

Symptoms of systemic lupus erythematosus (SLE) may present in various way and are difficult to predict. These not only have negative impacts by restricting daily life functions and interpersonal relationships with others, but can also interfere with life events such as school attendance, employment, pregnancy, and childbirth. SLE patients experience continually declining health even when they proactively protect themselves against ultraviolet rays and avoid fatigue. It is also difficult for others to understand the effects of SLE patients. The sum of these issues decreases SLE patients' quality of life (QOL). A previous study found QOL of SLE patients was difficult to measure with conventional QOL-related instruments. However, the Japanese LupusPRO (Inoue et al., Lupus, 2017), a specific QOL questionnaire for SLE, was developed. This enables measurement of QOL in SLE patients. The original English LupusPRO (Jolly et al., Smin Arthritis Rheum., 2012) is a patient-reported outcome questionnaire for measuring 12 aspects of QOL of SLE patients. That original has been translated into many languages and international comparisons are possible. In this seminar, we will examine the importance of quantitative evaluation of QOL in SLE patients and the usefulness and specific tasks of the Japanese LupusPRO, based on clinical trial data and interviews with SLE patients.

LS29-2

Long-term management of SLE patients to improve the quality of life

Nobuyuki Yajima

Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan

Conflict of interest: Yes

The prognosis for systemic lupus erythematosus (SLE) is improved, and the patient's quality of life (QOL) is garnering attention. The goal of the treatment is to be able to be conscious of the QOL of patients twenty to thirty years ahead. Not only organ failure of SLE, but the side effects of drugs, anxiety about diseases, and deviations from women's lifestyles are all related to the patient's QOL. Organ failure of SLE is affected by the severity of the organ failure and the number and degree of relapse; it is essential how can prevent the flare. While there is too much treatment to be aware of the relapse prevention, the risk of the occurrence of side effects of the drug rises, the Treat to Target recommendation, which was published in 2014, mentions corticosteroid tapering and adjustment of immunosuppressive agents. In the quality indicator that created in 2009, modification of corticosteroids and immunosuppressive agents when more than PSL10 mg was described. Also, the criteria for remission, such as LLDAS definition and DORIS definition, are being discussed, and while long-term management is being paid attention, it is still up to each physician where to set the goal goals in real clinical. In this lecture, I will talk about the Treat to Target recommendation with SLE, particularly appropriate corticosteroid dose, steroid tapering, and long-term management to prevent flare. In addition, I will introduce our pregnant women management in our department for maternity outpatient, and I would be more than happy if my speech could be of some reference to you all. The

PLEASURE-J Study, which is a registry of SLE, is also introduced. It is the first disease Registry of JCR, and it collects the information of SLE patients at 6-40 years old and plans to expand to facilities nationwide from April 2019. Features of this registry are that patient-reported outcome (PRO), such as Lupus Pro, SF12, sleep, exercise is included abundantly. It will be a good opportunity to pay attention to the importance of the QOL of SLE.

LS30

The management of connective tissue disease associated pulmonary arterial hypertension - How will it have changed after WSPH2018? -

Masaru Kato

Department of Medicine II, Hokkaido University Hospital

Conflict of interest: Yes

The poor prognosis of connective tissue disease associated pulmonary arterial hypertension (CTD-PAH), particularly that of systemic sclerosis associated PAH (SSc-PAH), is one of the issues to be solved in the management of rheumatic diseases. Early diagnosis and treatment using a detection program have been shown to be the most effective way to improve the prognosis of SSc-PAH. In World Symposium on Pulmonary Hypertension 2018 which was held in Nice, pulmonary hypertension was suggested to be redefined from mean pulmonary arterial pressure (mPAP) of ≥ 25 mmHg to that of >20 mmHg. Moreover, SSc patients with mPAP of >20 mmHg, pulmonary arterial wedge pressure of <15 mmHg, and pulmonary vascular resistance of >3 WU are supported by recent data to be potentially treated with pulmonary vasodilators. Since current programs, such as the DETECT algorithm, are for mPAP ≥ 25 mmHg detection, new programs to predict mPAP of >20 mmHg are desired. Although PAH patients are usually treated with upfront combination therapy with two or more pulmonary vasodilators, initial monotherapy has a potential role in some specific PAH subsets, including elderly patients, patients with cardiopulmonary comorbidities, patients with suspicion of pulmonary veno-occlusive disease/pulmonary capillary hemangiomas, and patients with very mild disease. SSc-PAH is frequently complicated with left heart disease, interstitial lung disease, and/or pulmonary veno-occlusive disease and may therefore benefit from initial monotherapy more than other forms of PAH. SSc patients with $20 < \text{mPAP} < 25$ mmHg may also be treated with initial monotherapy. In this seminar, we introduce our recent study on the detection of "very early SSc-PAH", our treatment regimen for SSc-PAH, and finally the latest evidence on immunosuppressive therapy for CTD-PAH.

LS31

The current strategy of ANCA-ASSOCIATED VASCULITIS management

Hiroaki Dobashi

Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University

Conflict of interest: Yes

The primary systemic vasculitides (PSV) are characterized by inflammation of many vessels. PSV often could cause multiple organ damage which is strongly associated with prognosis. Chapel Hill nomenclature is widely used to define different forms of vasculitis according to the size of the predominantly affected vessels. Recently among small vessel vasculitis, Vasculitis associated with the presence of anti-neutrophil cytoplasm antibody (ANCA), termed AAV, advances have been made in understanding its pathogenesis and evidence for treatment. However in AAV, morbidity and mortality are still very high, in the induction phase because of high disease activity and infections, in maintenance phase due to major flares of AAV, cardiovascular disease and complications of malignancies. AAV is classified into three major forms: granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). In diagnosis of AAV, ANCA is a major diagnostic biomarker. However not all AAV patients are positive for ANCA. Additionally, the frequency of positivity of ANCA (c-ANCA or p-ANCA) in Japanese AAV patients is different from those of other countries such as Europe or USA. We should pay much attention about ANCA positivity at the diagnosis of AAV. In treatment of AAV at the induction

phase, the use of high dose corticosteroids and cyclophosphamide (CY) should be recommended strongly. Additionally, CY could be replaced by rituximab (RTX). Both of recent EULAR and Japanese guidelines on therapy for AAV indicate that cyclophosphamide or rituximab (plus glucocorticoid) is the mainstay of remission induction therapy. However, safety or efficacy evidences of RTX are still not confirmed in Japan. In maintenance therapy after remission, azathioprine (AZA) or methotrexate (MTX) is recommended, and reducing doses of glucocorticoids. Recently the effectiveness of rituximab treatment for maintenance is also being established. These evidences for effectiveness is clear for MPA and GPA. In this seminar, we reconfirm and discuss about these issues of management in AAV especially in RTX treatment for AAV.

LS32

A Review and Update to the Comprehensive Treatment of Rheumatoid Arthritis [RA] - from the Past to the Future

Kunihiro Yamaoka

Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine

Conflict of interest: Yes

Since the successful introduction of the biological disease-modifying anti-rheumatic drug class [bDMARD] that first launched in 2001, RA treatment outcomes have made both significant and remarkable progress. It is widely believed that patient treatment starts with the conventional synthetic disease-modifying anti-rheumatic drug class [csDMARD]. From here, many patients transition to combination therapy involving bDMARD or targeted synthetic DMARD [tsDMARD], especially if or when the disease activity does not achieve the targeted remission. Remission evaluation is focused on the Treat to Target (T2T) strategy. While this is a realistic and achievable goal for RA patients, approximately 50% do not achieve goal and therefore require further treatment strategy modification. Several unique targets are under development in order to bridge the T2T gap, with the hope of further progress for positive treatment outcomes. For this presentation, I would like to offer a review and summary of the key landscape assets, and discuss the future patient treatment optimization with RA.

LS33-1

Pathophysiology and treatment strategy of knee osteoarthritis

Shuichi Matsuda

Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Conflict of interest: Yes

Osteoarthritis is a disease that causes pain and dysfunction of the knee joint with degeneration of the articular cartilage but the disease state is not the same in all patients and it is necessary to construct a treatment strategy according to the individual disease condition. One of the most important exercise therapies is muscle training, but muscular strength training is less effective for the patients with sufficient muscle strength. Attempts to change exercise therapy by the presence or absence of muscle weakness, lateral thrust, obesity, etc also proceed. For orthotic therapy, foot insole and unloader knee brace are used. Although it has been reported that the adduction moment and the clinical symptoms are also reduced, from now on, it is necessary to investigate to which patient the effectiveness of the orthotic therapy is high. Artificial cartilage, synovial membrane, and subchondral bone are conceivable as targets of drug therapy. Intraarticular injection of hyaluronic acid etc. is used for degeneration of articular cartilage, but it is currently difficult to suppress the degeneration of articular cartilage and promote repair only by medication therapy. Inflammation of the synovial membrane is an exacerbating factor of pathological condition also in osteoarthritis of the knee, oral administration of nonsteroidal antiinflammatory drugs, topical drugs for external use, intraarticular injection of steroid, etc. are used. However, patients with osteoarthritis are not always strongly inflamed, and the results of studies so far revealed that patients with injections of steroid joints are effective. It is thought that anti-inflammatory treatment should be limited at the time of strong inflammation. Not only articular cartilage and synovium but also subchondral bone status are known to affect the pa-

thology of osteoarthritis. On the other hand, various results have been obtained on the method of managing pain. Although weak opioids have also come to be used frequently, there are many unclear points about side effects and dependency in long-term use, and easy prescription should be avoided. Serotonin / noradrenaline reuptake inhibitor (SNRI) and acetaminophen can also be used. Our options have been increasing, but establishing an appropriate method of administration is a future task.

LS33-2

Mechanism and treatment of chronic musculoskeletal pain from perspectives of pain clinic

Masako Iseki

Department of Anesthesiology and Pain Management, Juntendo University School of Medicine, Japan

Conflict of interest: Yes

Pain is defined as 'An unpleasant sensory and emotional experience' by International Association for the Study of Pain. Chronic pain is defined as 'pain that extends beyond the expected period of healing or progressive pain due to non-cancer diseases.' Pain is necessary for people as an alarm signal of the body, however its protraction can lead to lower quality of life. Comprehensive Survey of Living Conditions by Ministry of Health, Labour and Welfare in Japan reported that, of top five health-related subjective symptoms, three are painful symptoms in men (low back pain, shoulder pain, and joint pain), and four in women (low back pain, shoulder pain, joint pain, and headache). Protraction of pain, which reduces the productivity of young and middle-aged people, and prevents the independence of the elderly, is increasingly becoming a major problem in Japan where the population is rapidly aging and birthrate is declining. There are many patients suffering chronic musculoskeletal pain, and they are longing for appropriate alleviation of pain to secure quality of life. With regard to preservation treatment in general, pharmacotherapy is usually the first choice. Drugs are selected based on the type of pain; nociceptive, neuropathic, or mixed pain. However, when the pain exacerbates with movement or hold of body, it is sometimes difficult to alleviate with drugs only. Moreover, environmental factors around each patient can affect the pain. Thus, there are many factors and issues to be considered in the clinical practice. This talk will cover standard treatment of musculoskeletal pain, particularly focusing on pharmacotherapy.

LS34-1

Benlysta (R): a potential novel therapeutic agent for Systemic Lupus Erythematosus

Susumu Nishiyama

Rheumatic Disease Center, Kurashiki Medical Center, Okayama, Japan

Conflict of interest: None

Statements of treat to target for systemic lupus erythematosus (SLE) recommend that the treatment target of SLE should be remission of systemic symptoms and organ manifestations, and that prevention of flares is a realistic target in SLE and should be a therapeutic goal (van Vollenhoven RF et al. *Ann Rheum Dis* 2014;73: 958-967. doi:10.1136/annrheumdis-2013-205139). The introduction of corticosteroids in the 1950s improved survival rate of lupus patients remarkably; however, a new issue arose about corticosteroid-related organ damage, such as atherosclerosis and osteoporosis in long-term. Therefore, the best way to prevent damage accrual at this moment is treating patients with minimum, necessary, and sufficient amount of steroids so as not to cause a flare-up. Belimumab (trade name Benlysta), anti B lymphocyte stimulator (BlyS) antibody, is a novel therapeutic agent for SLE. This molecular targeted therapy suppresses B lymphocyte activation and decreases autoantibodies including anti-DNA antibody. Clinical trials revealed disease activity significantly subsided in Belimumab group compared to placebo (Zhang F, et al. *Ann Rheum Dis* 2018;77:355-363. doi:10.1136/annrheumdis-2017-211631) and long-term prevention of flares over seven years in lupus patients with Belimumab treatment (Furie RA, et al. *Arthritis Rheum* 2018;70:868-877. doi:10.1002/art.40439). Belimumab is indicated for the treatment of active, autoantibody-positive adult patients with SLE who are receiving standard therapy. In order to draw out its full potential, use the drug as early as possible before organ damage appears

in early phase and keep stable state without flare in long-term.

LS34-2

SLE and pregnancy

Atsuko Murashima

National Center for Child Health and Development, Tokyo, Japan

Conflict of interest: Yes

The development of treatment for women with systemic lupus erythematosus (SLE) leads to be able to wish for pregnancy. Taking remission with medicines that can be used during pregnancy, evaluating severe organ lesions, anti-SS-A antibody · antiphospholipid antibody, blood pressure and glucose tolerance, osteoporosis and taking measures are important as a pre-conception care in SLE. Pregnancy in remission is a prerequisite for obtaining good pregnancy outcome. The treatment with steroids has been standard in SLE patients during pregnancy, but steroids should be decreased as they increase the risk of gestational diabetes, pregnancy hypertension, infections and premature rupture. In that case, combined use of an immunosuppressive agent and hydroxychloroquine is also useful. Azathioprine, cyclosporine, tacrolimus were contraindicated for pregnant women on the basis of animal tests, but teratogenicity was considered negative from the experience of transplant patients and it became capable to be used during pregnancy in 2018. Mycophenolate mofetil, one of the immunosuppressants, is teratogenic and it is necessary to instruct contraception during use. It is estimated that the anti-SS-A antibody retains about 1%, and it is frequent as a specific antinuclear antibody. Congenital cardiac block related to this antibody is about 1%, but it is a serious disease condition and it is a troublesome task to be done on countermeasures. On the other hand, there are cases where good results can not be obtained with the policy of prevention of thrombus formation in pregnancy of anti-phospholipid antibody carriers. On the pregnancy management method of these antibody holders, based on the results of the research group so far, we will present the best possible countermeasures. Sometimes evidence is poor as a major reason for pregnancy to be difficult. As a foundation for creating evidence from Japan to the world at the same time as improving such a situation, the Japanese Rheumatology Association says, "A prospective cohort study on long-term and short-term prognosis including young SLE patients in Japan, and outcomes of pregnancy: PLEASURE-J study "started. We have already cooperated from many facilities, but we would like to ask for your continued support and cooperation.

LS35-1

Diagnosis and Treatment of autoinflammatory syndrome in adult

Koichiro Ohmura

Department of Rheumatology and Clinical Immunology, Kyoto University Graduate School of Medicine

Conflict of interest: None

Since autoinflammatory syndrome is a hereditary disease, many of the patients show their symptoms in childhood. However, some develop the disease after they become adults. We physicians have to know the characteristics of the popular autoinflammatory diseases such as Familial Mediterranean Fever (FMF), TNF receptor-associated periodic syndrome (TRAPS), and Cryopyrin-associated periodic syndrome (CAPS). CAPS consists of 3 different diseases depending on their severity, FCAS, Muckle-Wells Syndrome (MWS), and CINCA. MWS is most often found in adults. Typical clinical symptoms of FMF is the short duration of fever (0.5-3 days) and serositis presenting severe abdominal pain. Usually colchicine is effective. TRAPS shows long duration of fever (> 7 days) and serositis (abdominal pain) and rash with muscle ache are the typical symptoms. Conjunctivitis and periorbital edema are also found frequently in TRAPS patients. CAPS (MWS) shows urticarial eruptions and arthralgia typically. Progressive sensorineural hearing loss and chronic aseptic meningitis are also important complications. Colchicine is usually ineffective to TRAPS and CAPS, but moderate to high dose corticosteroid is effective. Recently kanakinumab was admitted to use for CAPS, TRAPS and treatment-resistant FMF and it is very effective for such diseases who are resistant to the conventional therapy or hard to decrease the corticosteroid dose. I will overview the differential diagnosis points of autoin-

flammatory diseases in adults with some of case records.

LS35-2

Positioning and practice use of biologics in systemic juvenile idiopathic arthritis

Masaaki Mori

Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University

Conflict of interest: Yes

Canakinumab (CAN) is a recombinant human IgG1 monoclonal anti-interleukin-1 β (IL-1 β) antibody, and it binds to IL-1 β then suppresses inflammation by neutralizing its activity. In Japan, CAN was approved for systemic Juvenile Idiopathic Arthritis (sJIA) in 2018 July as additional indication. It was 5 years behind US approval in 2013 May and EU approval in 2013 August. CAN is administered subcutaneously with 4 mg/kg (maximum dose is 300 mg) every 4 weeks. CAN achieved improvement in sJIA clinical symptoms and tapering of glucocorticoid (GC) in clinical studies, but serious adverse event may occur in the administration. Pediatric Rheumatology Association of Japan developed a guidance for post-marketing surveillance of CAN upon the approval for sJIA to ensure appropriate use and sufficient safety. The guidance was created based on the results of clinical studies to date. CAN administration is considered for the following sJIA patients: 1) patients don't show improvement in clinical symptoms such as fever, rash, arthritis, and inflammation, 2) patients cannot achieve tapering of GC, or have concern of side effects with long-term of GC, 3) patients have no or insufficient efficacy to, or not tolerant to anti-IL-6R antibody, tocilizumab. When macrophage-activation syndrome occurs, methylprednisolone pulse and dexamethasone therapy (off-label use), and continuous infusion of cyclosporine (off-label use) should be used, then CAN shouldn't be administered until the condition is stable. Besides, MHLW Insurance Bureau issued an important notification upon the approval of CAN in sJIA, indicating 1) basically CAN administration should be considered for patients who have insufficient efficacy to other biologics, 2) the followings need to be specified in the notes of medical remuneration claims (1) Name and duration of used other biologics, (2) reason (s) to consider CAN administration is necessary. In short, CAN cannot be used essentially as first biologics from health insurance aspect in Japan. This session will overview positioning and evidence of CAN in sJIA outside of Japan also approach for appropriate use of CAN in Japan.

LS36-1

Diagnosis and pathogenesis of Sjögren's syndrome - From the viewpoint of a dermatologist -

Yoshinao Muro

Department of Dermatology, Nagoya University Graduate School of Medicine

Conflict of interest: None

Sjögren's syndrome (SS) is a systemic autoimmune inflammatory disease characterized by secretory gland dysfunction leading to oral and ocular dryness and by various kinds of autoantibodies. SS can be primary or secondary to other systemic autoimmune diseases, i.e., rheumatoid arthritis, systemic lupus erythematosus (SLE), and systemic sclerosis. Japan has been promoting research of intractable diseases and financially supporting patients with these diseases. The number of designated intractable diseases (DID) was expanded from 56 to 306 by July 2015 where SS has also been included. We should increase social recognition of SS more than ever. A recent Japanese survey with questionnaires for patients with SS clarified that dry mouth contributes to painful experiences and quality of life impairment in many patients. They often meet difficulties in conversation, eating, and sleep. Early detection and early effective treatment should be provided to the disease. In Japan, the revised criteria for the diagnosis of SS proposed by the Japanese Ministry of Health have been used commonly in daily clinical practice and clinical studies, and also used as certification criteria for the national registry of DID. New ACR-EULAR classification criteria for primary SS (pSS) were published in 2016, and a recent Japanese study showed that this criteria had significantly higher sensitivity in diagnosis of pSS than the Japanese criteria. In

the ACR-EULAR criteria, labial salivary gland (SG) histology and anti-SS-A/Ro tests have higher scores than the other items. In this lecture, recent studies on these two items are shortly reviewed as well as on SG ultrasonography. In SS, a lot of kinds of immunocompetent cells and cytokines are key players. Recent studies on biomarkers of SS using large cohorts are showing high heterogeneity such as comparable to SLE. For example, various manifestations of skin involvement also can be found which is one of domains of ESSDAI.

LS36-2

Sjögren's syndrome: evidence review

Atsushi Kawakami

Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Japan

Conflict of interest: Yes

Sjögren's syndrome (SS) is an autoimmune disease the prominent symptoms being dry eye and dry mouth. It preferentially occurs in female subjects older than middle age. SS is categorized into primary SS (pSS) which is not associated with other well defined connective tissue diseases (CTDs), and secondary SS (sSS), which is associated with other well defined CTDs such as rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE). Moreover, pSS is further subdivided into the glandular form, with involvement of the exocrine glands only, and the extra-glandular form, with the involvement of organs other than exocrine glands including lung, kidney, joint, muscle and nervous systems. The Research Program for Intractable Disease of the Ministry of Health, Labor and Welfare (MHLW) has conducted epidemiological study for SS and revealed that the ratio of primary to secondary is 6:4, glandular form to extra-glandular form in pSS 7:3, 60% of underlying diseases of sSS RA and SLE, respectively. Thus, the requirement of measure of dryness, organ damages, underlying diseases and complications including malignant lymphoma is necessary in clinical practice of SS. SS includes varying pathological conditions and Research Team for Autoimmune Diseases, the Research Program for Intractable Disease of MHLW, has developed clinical practice guideline (CPG) for SS 2017. This consists of 38 clinical questions (CQ) documented by integrating the body of evidence for each outcome, based on the systematic review report and evidence evaluation sheets produced by the systematic review team members including diagnosis, complications, treatment of glandular form and extra-glandular form, management of pregnancy and delivery. Regarding to treatment, CPG states about dry mouth (CQ24), salivary gland swelling (CQ25), eyedrops (CQ26), punctual plug (CQ27), corticosteroid (CQ28, CQ29), immunosuppressants (CQ30, CQ31), biologics (CQ32, CQ33), pediatric patients (CQ34, CQ35, CQ36). Investigations of SS has been developing and Japanese society of SS has also published and revised the manual textbook regarding SS. SS is certified as a designated intractable disease by the MHLW in January 2015 and become to be popular in clinical field. However, EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) does not include glandular symptoms (dryness) and no biologics are yet approved though several clinical trials has progressed. The evidence of SS will be reviewed in this seminar.

LS37-1

This is my strategy how to use Abatacept!~The clinical position of Biologics focus on T cell interaction~

Kenta Misaki

Department of Rheumatology, Kita-Harima Medical Center

Conflict of interest: Yes

Biologics (Bio) have been approved under the medical insurance in clinical setting since 2003 in Japan. It would not be exaggeration to say that the clinical adaptation of Bio brought a distinct paradigm shift concerned with drastic improvement of Rheumatoid arthritis (RA) disease activity. Initially one after another anti-TNF inhibitor (TNFi) were approved, and additionally non-TNF agents were come to the fore in 2008 in our country. Abatacept (ABT): CTLA4-Ig interacted between innate and adaptive immunity was adapted in clinical setting in 2010. At the same time, the first EULAR recommendation was published with the

treatment strategy that TNFi were confirmed as first Bio, revised version of the recommendation in 2013 were mentioned the ABT was advocated as part of the first Bio for RA. Rheumatologist is capable to obtain the treatment options of First Bio. Moreover JAK inhibitor was added as our clinical option for RA treatment in 2013 and the theory of Treat to Target made it possible to indicate the RA treatment goal. Based on the above, it is possible for us to achieve the radiographic remission besides the reduction or withdraw of therapeutic agents. As it is pity to miss the best treatment opportunity by means of excellent Bio, early diagnosis of RA and appropriate First Bio combined with DMARDs are now required for Rheumatologist. RA pathogenesis is diverse, however musculoskeletal ultrasound (MSKUS) is one of the most useful clinical procedures to detect the subclinical synovitis and subtle bone erosion not depicted in X-ray film without harm. MSKUS is gradually applied to dairy clinical practice. It is suggested the Duet dance performance between Bio and MSKUS make it possible of achievement of radiographic remission and drug withdraw. In this session, I am going to introduce the efficacy of ABT as first Bio to RA patients in our institution and the clinical adaptation of MSKUS.

LS37-2

Importance of clinical data in RA treatment

Naoki Ishiguro

Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine & Faculty of Medicine

Conflict of interest: Yes

Clinical studies are roughly divided into two types, interventional studies and observational studies. Interventional research is a study to obtain results from artificially determining treatments according to certain conditions. Observational research is a research method to observe practical clinical practice. A typical example of intervention studies is a development trial of drugs performed by drug company. What is formed by observational research based on actual clinical practice becomes knowledge called real world data. Clinical studies are divided into two types, prospective and retrospective studies. For prospective studies, data is gathered according to purpose, which is considered to be more reliable. Clinical trials are prospective studies, in most cases taking the form of intervention studies in which a control group is established. By doing random assignment, we are conducting research work with elimination of artificial bias in enrolled cases. It is well accepted as a situation of high fairness, and it is regarded as an indispensable research for drug development. On the other hand, by manipulating inclusion standards, it is common for research to be conducted on a group of patients whose medicinal effect is likely to differ. Most of clinical trials that is said to be EBM-like high quality from blindness and the presence of control treatment is this kind of studies. Real world data is generally originated from the observational research work after marketing, so it is natural that the bias to be referred to as doctor's preference is given to the case of administration. It may be possible to reduce the preference bias of doctors rather than single facility research by multicenter collaborative research. The primary advantage of clinical observational studies is the observation period. Therefore, in actual clinical studies it is required to observe the enrolled cases as long as possible over the long term, and it is important that the target cases are followed up as precisely as possible. It is not preferable that there are many dropout cases that are not subject to analysis. Meanwhile, in a clinical trial such as blinding and placing a placebo control group, there is always a problem of loss of treatment opportunities for participants, and a long research term causes human rights problems. Here is the reason why the blinded period of clinical trials with control group stays in the short term within 6 months. High quality observational research that require long-term observation is important for resolving some clinical questions.

LS38

Interstitial lung disease associated with systemic sclerosis: natural course and prediction of disease progression

Masataka Kuwana

Department of Allergy and Rheumatology, Nippon Medical School

Conflict of interest: Yes

Interstitial lung disease (ILD) causes major morbidity and mortality in patients with systemic sclerosis (SSc). A number of observational studies have revealed that only <30% of SSc-ILD at diagnosis progress to end-stage lung disease and resultant poor mortality. The remaining patients show stable lung function throughout the disease course without treatment. Because of difficulty in prediction of future progression of SSc-ILD, symptomatic patients, especially those with worsening dyspnea, or patients exhibiting progressive restrictive lung impairment are currently eligible for treatment and clinical trials. Since tissue distortion caused by excessive fibrosis is irreversible, it is difficult to achieve normal lung function by delayed intervention. Extensive stage based on global lung involvement attributable to SSc-ILD on high-resolution computed tomography (HRCT) and/or present predicted forced vital capacity $\leq 70\%$ is used to identify patients who are likely to develop end-stage lung disease in clinical practice, but patients in the extensive stage are obviously those with progressive ILD who already have irreversible lung damage. Therefore, it is critical to identify patients at greater risk of progression at early phase when lung function is normal without irreversible damage. To identify patients with progressive SSc-ILD early in the disease course, fibrotic score on HRCT, early diffuse cutaneous SSc with rapidly progressive skin thickening, and circulating biomarkers, such as KL-6 and CCL18, are shown to be useful. Before the dawn of SSc-treatment era, this lecture features basic knowledge required for management of SSc-ILD, highlighting how to identify patients with progressive disease, who are eligible for treatment.

Evening Seminar

ES1-1

Safety and Effectiveness of Abatacept for Rheumatoid Arthritis-Safety First-

Mitsumasa Kishimoto

Immuno-Rheumatology Center, St Luke's International Hospital

Conflict of interest: Yes

For rheumatoid arthritis (RA), availability of various DMARDs including MTX and biological DMARDs and targeted small molecules, has increased treatment options, improving both short-term and long-term outcomes and QOL. Appropriately-tailored treatment of individuals with RA in daily practice, however, depends on an accurate differential diagnosis and evaluation of patient's co-morbidities before starting these effective treatment, but is still often based on experientially-derived clinical judgement. One of the common co-morbidity in RA is an interstitial lung disease (ILD) which is associated with poor prognosis in RA patients. Treatments such as methotrexate or anti-TNF agents, have been implicated in the exacerbation of an ILD. Abatacept is a biological DMARDs that has demonstrated a lower risk for infection in comparison with other bDMARDs among RA patients. At first, I introduce the data presented in EULAR 2018; the potential cost differences associated with the reduced risk of infection among RA patients treated with abatacept vs. other tDMARDs is discussed here. Secondly, I would show a new clinical data regarding RA patients complicated with ILD treating with abatacept or tocilizumab, and it's basic study in chronic graft-versus-host disease (cGvHD) mouse model. In daily clinical practice, these data re-assured our knowledge on safety profile in treatment of RA with abatacept.

ES1-2

Optimization of Rheumatoid Arthritis therapy: current issues and outlook for the future

Tsutomu Takeuchi

Division of Rheumatology, Keio University School of Medicine

Conflict of interest: Yes

There have been many advances and innovations in the diagnoses and treatment of Rheumatoid Arthritis (RA) in the past few years. There has been numerous amendments to treatment recommendation and guidelines, such as ACR, EULAR and Treat to Target (T2T). It goes without saying that one of the factors is the development of biological disease-modifying ant-rheumatic drugs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs). With the development of these drugs, Clinical remission is the primary goal in the treatment of the disease and both structural and functional remission have become possible. It greatly contributes to the improvement in the patient's Quality of Life (QOL). On the other hand, there are many kinds of issues, such as how to treat patients appropriately and monitor the patients, and how to predict the reduction in dose until medication is no longer necessary. We need to understand the characteristics of each bDMARD and tsDMARD as well as the patient's background so as to maximize the effectiveness and minimize any adverse events with medical therapy. There are 15 bDMARDs and tsDMARDs for RA in Japan, divided into 4 class clusters, TNF inhibitors, IL6 inhibitors, T-cell co-stimulate and Jak inhibitors. Based on clinical evidence, the effectiveness of each drug is nearly equivalent. However, some patients have not yet reached the ideal therapeutic goal. In recent years, the population of the world has been aging. This is especially true for Japan, which has the highest rate of aging. This trend is expected to continue. It shows that we require more care regarding the prevention of adverse events when using bDMARDs and tsDMARDs on patients over 65 and have lung complications in our RA study group (cohort). For our treatment strategy, understanding the background of each patient as well as the characteristics of each drug is of the utmost importance. This seminar will outline the current issues with RA and the latest evidence regarding ABT in Japan and consider the optimization of RA therapy.

ES2-1

Treatment standardization of systemic lupus erythematosus

Tatsuya Atsumi

Department of Rheumatology, Endocrinology and Nephrology Faculty of Medicine and Graduate School of Medicine Hokkaido University, Hokkaido, Japan

Conflict of interest: Yes

Systemic lupus erythematosus (SLE) affects multiple organs and tissues in a different way, and such heterogeneity of clinical aspect is making difficult to standardise the management of lupus patients in clinical practice. In the history, corticosteroids (CS) dramatically improved the mortality of lupus patients; on the other hand, major or minor adverse events of CS would significantly affect to their morbidity. Recently, the potent immunosuppressants are efficiently used for the remission induction in patients with SLE. Amongst the lupus organ involvements, lupus nephritis (LN) is one of the most common and important manifestation, and the better use of immunosuppressants are described in two major guidelines for lupus nephritis. JCR and MHLW have collaborated to establish SLE guideline according to the GRADE method. In this guideline, recommendation statement was classified into 3 categories; recommended, suggested and proposed. Referring another SLE guideline for British National Health System, established by BSR, we discuss the significance of the Japanese SLE guideline for our daily clinical practice.

ES2-2

The problem of glucocorticoids in SLE, and pathways to a solution

Eric Morand

Monash University, Melbourne, Australia

Conflict of interest: None

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease. Uncontrolled disease activity, observed in 60% of patients despite standard of care therapy, leads to the accrual of irreversible organ damage, which in the case of renal, central nervous system (CNS), and cardiovascular systems can have fatal consequences. Thus patients with SLE, the majority of whom are young women, face chronic illness, loss of health, reduced work participation, and a very significant risk of premature death. Because of a lack of significant advances in therapy, the majority of patients still receive acute and/or chronic treatment with glucocorticoids, a drug class unchanged since the 1950s. Severe, predictable, dose-dependent metabolic adverse effects accompany glucocorticoid use, and the continued use of glucocorticoids despite their toxicity reflects a failure to discover tractable alternatives. The well-established adverse consequences of chronic glucocorticoid therapy are now recognized as significant contributors to the accrual of irreversible organ damage in lupus patients. Indeed, reduction in glucocorticoid dose is recognized as a vital marker of efficacy in clinical trials of novel therapies in SLE, and is cited as an important goal of therapy by the US FDA. In this presentation, data on the negative effects of glucocorticoids will be reviewed, their impact on treat to target approaches in SLE described, and recent discoveries in the mechanisms of action of glucocorticoids that may unveil new therapeutic targets discussed. In particular, recent discoveries on the protein GILZ, a potential glucocorticoid mimic, will be outlined.

ES3-1

Immunopathology and recent epidemiology in Behçet's disease

Mitsuhiro Takeno

Department of Allergy and Rheumatology, Nippon Medical School

Conflict of interest: Yes

This seminar summarizes current understanding of the immunopathology of Behçet's disease and reviews recent epidemiology in Japan. Behçet's disease has a unique epidemiology feature that the patient distribution form the Mediterranean area to the Middle East Asia and East Asia, where coincide with high frequent areas of HLA-B51 positive individuals. A couple of epidemiological analyses in immigrants from the prevalent areas to other areas suggest that both the genetic and environmental factor are involved in the etiology. Before 2000, one of favorable

hypotheses is that microbial agents trigger autoimmune responses in hosts having genetic predispositions, resulting in the development of the disease. However, lack of the disease-specific autoantibodies, abnormal innate immune functions, clinical manifestations with attacks and remissions, rather suggest features as an autoinflammatory disease. GWAS and subsequent detail genetic analysis have identified the disease susceptible genes in both innate and acquired immune systems, suggesting the mixed features of autoimmunity and autoinflammation. Furthermore, epistasis between HLA-B51 and *ERAP-1* suggests that the disease belongs to recently proposed MHC-I-opathy along with ankylosing spondylitis and psoriasis. Epidemiological data showed that patients receiving medical support as the specific intractable disease had been rising from 1972 to 2000, thereafter reached the plateau. Recent chronological changes were summarized aging, decreasing frequency of ocular lesion and HLA-B51 positive patients, and increasing female patients and intestinal type. Early diagnosis and early treatment due to the spread of the revised diagnostic criteria might partly contribute to the chronological changes. Rather, our studies suggest that patients with Behçet's disease are classified into several clinical subgroups and that the proportions of individual subgroups have been changing presumably through the gene-environment interaction.

ES3-2

Diagnosis of special type of Behçet's disease and the latest treatment

Hiroto Kikuchi

Department of Internal Medicine, Teikyo University School of Medicine

Conflict of interest: None

Intestinal, vascular, and central nervous system (CNS) lesions are present in special types of Behçet's disease (BD). Intestinal lesions may develop anywhere from the esophagus to rectum, but typically, round-oval deep ulcer is formed in the ileocecum and induces symptoms such as abdominal pain, diarrhea, and bloody feces. Medium-to-large dose steroid administration is the main treatment for remission induction, and mesalazine and salazosulfapyridine are often used concomitantly. The effect of TNF inhibitor alone is insufficient in many cases of intestinal BD, and combination with an immunosuppressor is necessary. Vascular lesions develop in various blood vessels from the aorta to veins, with a frequency of about 5-10% in patients with BD. Colchicine and nonsteroidal anti-inflammatory drugs do not inhibit inflammation sufficiently in many cases, and steroids, cyclophosphamide, azathioprine, methotrexate (MTX), and infliximab are required. In Japan, complication by deep vein thrombosis-associated pulmonary thromboembolism is often encountered, for which antithrombotic drugs are concomitantly administered, in addition to immunosuppressors. CNS lesions are divided into acute type and chronic progressive type. Headache, fever, and local nerve symptoms develop in the acute type neuro BD (ANB), and an increase in the number of cells in cerebrospinal fluid (CSF) is useful, if CNS infections are excluded. In the chronic progressive type neuro BD (CPNB), cognitive impairment, character change, truncal ataxia, and dysarthria progress, and a persistently high level of CSF IL-6 and brain stem atrophy are the characteristic findings. ANB is dealt with separately for acute phase and prevention of recurrence. Acute phase is treated with steroids that are rapidly administered at a medium or high dose when cerebral local signs progress. Response to steroids is favorable, but symptoms may recur even in ANB. Colchicine is recommended for prevention. Acute phase in CPNB is also treated with high-dose steroids. CSF IL-6 transiently decreases after administration, but increases again with steroid dose reduction. MTX has been shown to decrease CSF IL-6 and inhibit progression of mental and neurologic manifestations. In a study of long-term outcomes of the CPNB in Japan, the mortality and rate of patients who became bedridden were significantly lower in the MTX treatment group. For intractable cases in which the effect of MTX is insufficient and cases in which use of MTX is difficult, administration of infliximab should be considered.

ES4

Importance of Shared Decision Making (SDM) in the practice of EBM

Takeo Nakayama¹, Yuko Kaneko², Ayano Hayashi³

¹Department of Health Informatics, Kyoto University School of Public

Conflict of interest: None

Recent medical advancements have expanded treatment options and due to this, it is becoming increasingly important for doctors to communicate sufficiently with patients and their families to reflect their values in treatment decisions. Informed consent (IC) is widely known as the basis of consensus building between doctors and patients. In IC, patients are provided with information to make an autonomous decision to either select, agree to or reject treatment based on their understanding. However lately in the clinical practice, doctors tend to *provide information in order to gain consensus*, rather than *providing information to empower the patient to make a treatment decision*. This is a deviation from the initial purpose of IC, and is becoming a growing concern. Now, shared decision making (SDM) is emerging as the new approach to decision making and consensus building. What is the difference between SDM and IC? SDM focuses on sharing the treatment decision process of all potential treatments, enabling both parties to make a decision and form a consensus simultaneously. The dramatic advances in RA treatment has enabled many patients to reach and sustain remission. Having multiple treatment options are favorable for patients, while it puts pressure on HCPs to identify the right option for patients. Furthermore, HCPs are expected to practice evidence based medicine (EBM), which cannot be achieved in isolation from SDM. EBM defines that evidence is a critical factor for decision making, however to make a comprehensive decision, all other factors cannot be neglected. The aim of this seminar is to explore SDM and its true values. For a deeper understanding of SDM, we shall start by looking at the association between EBM and SDM, and how to connect SDM with practice guidelines. After introductions of specific case studies, a panel discussion will be held to explore how SDM should be implemented to the field and the important key points that must be followed in practice.

ES5-1

Benefit of Interleukin-6 inhibition in rheumatoid arthritis

Kunihiro Yamaoka

Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine

Conflict of interest: Yes

Considerable experience has proven the usefulness of biological DMARDs (bDMARDs) not only in rheumatoid arthritis (RA) but also a wide range of inflammatory diseases. However, it has also become clear that there are few diseases like RA in which similar efficacy can be observed with tumor necrosis factor (TNF) and interleukin-6 (IL-6) inhibition contributing to understand the RA pathology. During the recent years, tocilizumab (TCZ) has revealed the efficacy in Takayasu's arteritis and giant cell arteritis and an additional new IL-6 receptor antibody has been approved for RA. Janus kinase inhibitor (Jakiniib) an orally available DMARD that has demonstrated similar efficacy with bDMARD is known to suppress both IL-6 production and IL-6 signaling with variety of other mechanism of action. According to the latest ACR/EULAR recommendation, IL-6 inhibitors and Jakiniibs have some advantages in monotherapy that make one believe that these drugs have different feature compared to TNF inhibitors. Recently, tapering and/or cessation of concomitant csDMARDs or bDMARDs have been conducted in patients in remission. The results of these studies (ACT-TAPER, COMP-ACT, SURPRISE) have suggested that tapering or cessation of MTX in TCZ combo therapy would be the feasible strategy in clinical practice. Although Jakiniibs and bDMARDs possess evident difference in mechanism of action, the anti-rheumatic effect is similar. Elucidating the changes by these drugs in whole body and local joint inflammation could lead toward precision medicine. In this lecture, we will focus on the effectiveness of IL-6 inhibition and future positioning.

ES5-2

Treatment optimization in RA - For Patients -

Andrew Östör

Conflict of interest: None

Rheumatoid arthritis (RA) is autoimmune disease that is associated with a reduced quality of life (QOL) by systemic inflammation, disability by progressive bone destruction, early death by poor management of comorbidities, and socioeconomic costs by loss of work. The primary objective for RA treatment is to maximize QOL through early diagnosis and intervention with optimal therapeutics. As a consequence medication adherence is essential for RA patients. However, medication adherence rates may be as low as 30% in patients with RA thus increasing of the cost of care and leading to poor patient outcomes. Currently, rheumatologists usually prescribe conventional synthetic DMARDs (csDMARD) for RA, progressing to biologic DMARDs (bDMARD) to improve the short- and long-term outcomes. Currently, bDMARD added to MTX is gold standard therapy for patients with moderate to severe RA and an inadequate response to csDMARDs. Meanwhile, approximately one-third of patients discontinue or are non-compliant with MTX because of preference or toxicity. Taking these facts into consideration, strategies for the appropriate use of biologics as monotherapy is needed to adequately manage RA. Tocilizumab (TCZ), which is anti-interleukin 6 receptor antibody, can reduce the signs and symptoms of RA in combination with a csDMARD and as monotherapy in MTX-intolerant patients or patients for whom MTX is ineffective or inappropriate. Furthermore, we investigated whether TCZ plus a tapering MTX dose had comparable efficacy and tolerability compared with TCZ plus a stable MTX dose in patients with severe RA and an inadequate response to MTX who had achieved a EULAR response after TCZ combination therapy. The results of this clinical study increases the treatment strategies available to patients with active severe RA and allows for individualized, tailored therapy. I will focus on the optimization of current RA treatment for patients in this symposium.

ES6

Diagnosis and treatment of CTD-PAH with lung involvement – Challenges for the future –

Masaru Kato

Medicine II, Hokkaido University Hospital, Japan

Conflict of interest: Yes

Pulmonary arterial hypertension (PAH, group 1 PH) and pulmonary hypertension due to lung disease (group 3 PH) develop through different pathological mechanisms but exhibit similar hemodynamic abnormalities including increased pulmonary vascular resistance. Interstitial lung disease (ILD) is frequently detected by high resolution computed tomography of the chest in patients with connective tissue disease (CTD) associated PAH, particularly with systemic sclerosis (SSc) associated PAH, there is however no consensus on the definition of moderate-to-severe ILD to classify a patient in group 3 PH. In most of the clinical trials on PAH, patients with ILD and forced vital capacity (FVC) of <60% were excluded and classified in group 3 PH or "group 3 dominant" PH. Conversely, patients with ILD and mean pulmonary arterial pressure (mPAP) of >40 mmHg are generally thought to have group 1 dominant PH, so called "out of proportion", since only mild elevation of PAP occurs in "pure group 3" PH. In SSc-PAH, given the less elevation of PAP as demonstrated in the previous studies, differentiating PAH and group 3 PH is rather more complex. A recent study demonstrated a lower survival rate in SSc-PAH-ILD patients but did not find a difference in hemodynamic measurements, NT-proBNP levels, FVC/DLCO ratio, 6MWD, WHO FC, and scleroderma specific autoantibody levels. The impact of ILD, even with FVC of >60%, on the mortality of SSc-PAH patients was also shown. Given the high mortality rate and the possible unwanted effect of aggressive vasodilation through an increase of ventilation-perfusion mismatch, the treatment regimen for CTD-PAH coexisting ILD, particularly moderate-to-severe ILD, may differ from that for other PAH. In this seminar, we discuss what needs to accurately evaluate the proportion of group 3 PH in CTD-PAH and to provide optimal treatment for those patients.

ES7-1

Tofacitinib as a standard therapy in rheumatoid arthritis

Akio Morinobu

Section of Rheumatology, Department of Internal Medicine, Kobe University Graduate School of Medicine

Conflict of interest: Yes

Rheumatoid arthritis (RA) is an autoimmune disease characterized by synovitis, which eventually causes joint damage. Various cytokines play a critical role in the synovitis and anti-cytokine therapies have been developed for the clinical use. Monoclonal antibodies against TNF α and IL-6R have proved the importance of these cytokines in the pathogenesis of RA and lead to new therapeutic concepts and strategies in the treatment of RA. Tofacitinib (TOFA) is the first JAK inhibitor (JAKi) which comes 5 years old as another anti-cytokine drug for rheumatoid arthritis. JAKs are tyrosine kinases within cells. When a cytokine binds with its receptors, JAKs are activated to in turn activate STAT molecules. JAKi is an oral drug with low molecular weight and inhibits the kinase activity of JAKs. Thus JAKi inhibits signaling of cytokines that utilize JAKs. Because JAKi inhibits signaling of multiple cytokines which belongs to type I and II cytokine families, the mechanisms of immunosuppression should be different from biologics which blocks a specific cytokine. Today, 2 JAKi are used in clinical settings. The two JAKi possess different selectivity on JAKs, which may lead to different clinical effects. Various clinical trials have proved the clinical efficacy of TOFA. ORAL STEP has shown that TOFA is as effective as adalimumab when used in combination with MTX. ORAL SOLO has shown clinical usefulness of TOFA as a monotherapy. A clinical advantage of TOFA is that it is an orally available drug, because some patients prefer oral agents to injections. Another advantage of TOFA is that it reduces patient pain score quickly. These features of TOFA has made the drug widely used in the world.

ES7-2

Safety Information Update: Tofacitinib for Rheumatoid Arthritis Treatment

Keishi Fujio

Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo

Conflict of interest: Yes

Tofacitinib citrate approved for the indication for “rheumatoid arthritis (RA) inadequately responsive to the existing treatment” in Japan on March 25, 2013 is an oral drug with an action mechanism to modulate the activated cytokine network by inhibiting the transduction via the janus kinase (JAK) pathway of multiple cytokine-mediated signals in RA patients. While tofacitinib was a promising RA treatment option because of its novel immunoregulatory function, it has been under a Special Drug Use Surveillance (all-case surveillance) in RA patients to evaluate its safety due to associated safety concerns, specifically, the occurrence of serious infections and malignancies. In 2018, it has been 5 years after the launch, and the safety profile of tofacitinib has been elucidated under the post-marketing actual use in over 8,000 RA patients. According to the current interim report (Proper Use Information vol. 11), the incidence status of serious infections is significantly higher in patients in the XELJANZ group compared those in the control group. In the Proper Use Information vol. 11, the incidence of adverse reactions at 6-month observation and the baseline patient background information were tabulated for patients enrolled in the Special Drug Use Surveillance (all-case surveillance) in RA patients with their data fixing by November 5, 2017 (safety analysis set; 3,929 patients in the tofacitinib group and 1,789 patients in the control group). Changes in incidence rates (100 person-years), which were cumulative (from the start of treatment until 24 months later), and which were stratified by observation category (the start of treatment until 1 month later, from Month 2 to until 3 months later, from Month 4 until 6 months later, from Month 7 until 12 months later, from Month 13 until 18 months later, from Month 19 until 24 months later), of significant adverse reactions to XELJANZ (“serious infections”, “herpes zoster”, “malignancy”, and “interstitial pneumonia”) were also reported since the data fixing of patients observed for up to 24 months have progressed. In this lecture, the follow-up report on the Special Drug Use Surveillance (all-case surveillance) in RA patients will also be presented.

ES8-1

Modern rheuma-surgery under disease control-management of peri-operative DMARDs and patient-reported outcome

Keiichiro Nishida

Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

Conflict of interest: None

The treat-to-target (T2T) approach for rheumatoid arthritis (RA) has focused on the reduction of inflammation to prevent the joint destruction and functional disability, and better prognosis. After the clinical introduction of biologic DMARDs, disease activity of patients has been much improved, and the number of synovectomy and total joint replacement surgeries for large joints has declined. Despite the modern pharmacologic treatment, however, a significant population of patients still experience pain, fatigue, mental health symptoms, such as anxiety or depression, and reduced social and work participation, which all would negatively influence the health-related QOL. It has also been reported that RA patients consider the improvement of pain and fatigue, maintenance of physical function and HR-QOL as more important aspects in disease care than disease progression or goal-corresponding outcomes. Recent reports on the efficacy of DMARDs include the positive results on physical, mental, and QOL improvement assessed by FACIT-F, EQ-5D, BDI-II, EQ-5D, and SF-36. Under these circumstances, Rheuma-Surgery has been also changing. For residual deformity, correction osteotomy or partial arthrodesis has been selected for forefoot and wrist joints, respectively. Pain/functional disorders due to deformation of foot and fingers are good treatment target of the surgery, and the number of artificial joint replacement of the ankle, wrist joint and finger joint under the control of disease activity are increasing. As the result, new problems such as how to deal with unmet needs such as pain, fatigue and psychological problems with surgical treatment and how to manage perioperative DMARDs have been raised. Disease activity of preoperative patients in our department has been improving over time, and the degree of depression after surgery and the degree of psychosocial improvement to the body image are higher in patients with better disease control. These results strongly suggest the importance of the combination therapy of pharmacologic therapy and Modern Rheuma-Surgery towards social remission of RA patients.

ES8-2

Best use of each biological disease-modifying antirheumatic drug in patients with rheumatoid arthritis

Takao Fujii

Department of Rheumatology and Clinical Immunology, Wakayama Medical University

Conflict of interest: Yes

Biological disease-modifying antirheumatic drugs (bDMARDs) can be widely used in the treatment for rheumatoid arthritis (RA) and treatment strategy and classification criteria had newly developed or revised. Notably, as well as other systemic diseases (e.g., diabetes mellitus and hypertension), treatment target is determined by using numerical composite measures such as DAS28 and SDAI. In addition to control RA inflammation strictly and suppress joint injury, deterioration of quality of life could be prevent by treat-to-target strategy. bDMARD is one of the most important agents in the recent treatment for RA. To date, we can use 13 bDMARDs (TNF inhibitors 10, IL-6 signal inhibitors 2, and CD80/86 inhibitor 1). Recently, five of biosimilar DMARDs (bsDMARDs) were newly developed as TNF inhibitors. Two kinds of JAK inhibitors (targeted synthetic DMARD, tsDMARD) were also available in Japan. We, rheumatologists, should choose the best agent among bDMARDs of different mode of actions for each patient. In this seminar, clinical features of each bDMARD including recent evidences are shown and the best decision for bDMARD use will be discussed.

ES9-1

Pustulotic arthro-osteitis and SAPHO syndrome: how do we dermatologists consider those disorders?

Toshiyuki Yamamoto

Fukushima Medical University, Fukushima, Japan

Conflict of interest: None

Palmoplantar pustulosis is relatively frequent in Japanese population. Among the extra-cutaneous manifestations associated PPP, arthralgia is the most common comorbidity, termed as pustulotic arthro-osteitis (PAO). Chest wall is the most frequently involved, and the ratio of PAO in PPP is observed in nearly 30% in the university hospitals. By contrast, SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, osteitis) is extremely rare in Japanese population. Skin eruption of SAPHO syndrome is not limited to PPP, but acne inversa (hidradenitis suppurativa) is also rarely observed. In addition, acne of SAPHO syndrome is not usual acne but severe acne (acne conglobata, cystic acne, etc). Looking at the papers outside Japan, cases of PPP and arthralgia are diagnosed as SAPHO syndrome. If we diagnose such cases as SAPHO syndrome, we have many Japanese cases of SAPHO syndrome. PPP, as well as PAO, is closely related to focal infection, and treatment aiming at focal infection, such as tonsillectomy or dental caries treatment, dramatically improves skin and joint manifestation. By contrast, SAPHO syndrome, and also CRMO syndrome, are suggested to belong to autoinflammatory syndrome. In this talk, the concept of PAO, and difference between PAO and SAPHO syndrome, will be presented from dermatological perspective.

ES9-2

Differential diagnosis of non-radiographic axial spondyloarthritis

Yuhō Kadono

Orthopaedic Surgery, Saitama Medical University

Conflict of interest: Yes

Recently, it becomes well known that spondyloarthritis (SpA) is a kind of umbrella inflammatory disease concept including ankylosing spondylitis (AS) and psoriatic arthritis. SpA exhibits not only arthritis or spondylitis but also enthesitis. SpA which shows sacroiliac joint or spine involvement like AS, is roughly classified into axial SpA (axSpA). We use ASAS criteria to classify axSpA, and call it a 'non-radiographic axSpA' when we can detect just a small radiographic change. Although there is the classification criteria, we sometimes have a difficulty to diagnose. We should distinguish inflammatory back pain from mechanical pain or fibromyalgic pain. When we find spinal fusion or hyper ossification, we should distinguish axSpA from degeneration, diffuse idiopathic skeletal hyperostosis or osteitis condensans illi. When we find STIR high lesions, we should distinguish axSpA from overuse, injury or infection. We should be careful and judge by not only cross-sectional but also longitudinal points of view.

ES9-3

Diagnosis and management of functional pain syndrome which is mistaken for SpA

Kenji Miki^{1,2,3,4}, Masao Yukioka⁴

¹Faculty of Health Science, Osaka Yukioka College of Health Science,

²Center for Pain Management, Orthopaedic Surgery, Hayaishi Hospital,

³Pain Medicine & Research Information Center (NPO-PMRIC), ⁴Department of Rheumatology, Yukioka Hospital

Conflict of interest: Yes

Functional pain syndrome falls under the concept of "Functional Somatic Syndrome" proposed by Simon Wessely, and has become recognized as "central dysfunctional pain." The definition of pain is "an unpleasant **sensory and emotional experience** associated with actual or potential tissue damage, or described in terms of such damage." Also, "Many people report **pain in the absence of** tissue damage or any likely pathophysiological cause; usually this happens for **psychological reasons**... Activity of nociceptive pathways is not pain, which is always a **psychological state**." A total of 175 outpatients with a chief complaint of chronic pain were classified as fulfilling the diagnostic criteria of fibromyalgia (FM), spondyloarthritis (SpA), or neither. There were 83, 14 and 82 patients in the FM, SpA and chronic widespread pain group, respectively. Approximately 30 percent of patients with SpA met the diagnostic criteria of FM, a functional pain. (Chronic pain disease: difference in the treatment response between FM and rheumatic SpA. *The Journal of Japan Spondyloarthritis Society* 2 (1): 79 -87 2010). Although it is most

important to eliminate organic diseases from functional pain, organic diseases which appear as pain, numbness, trembling, etc. are often difficult to diagnose. Patients with chronic pain are said to become chronic due to how they are supported by health professionals. Communication skills, etc. of health professionals are important also from the standpoint of medical ethics. A paradigm shift of healthcare from "giving" to "supporting" in the management of patients with chronic pain is important. In workshops for healthcare professionals at Pain Medicine & Research Information Center (NPO-PMRIC), communication skills, cognitive behavioral therapy, and overall chronic pain knowledge can be learned. Multi-disciplinary medical care becomes possible if all health professionals including nurses, PTs and others acquire the skills to act on behalf of busy physicians.

ES10-1

Prevention and measures for frailty and sarcopenia

Hidenori Arai

National Center for Geriatrics and Gerontology

Conflict of interest: Yes

Aging is a global issue and patients with rheumatoid arthritis (RA) are getting older because of the improvement of medical management. Therefore, we need to deal with various problems associated with aging. Among them, geriatric syndromes such as sarcopenia and frailty are often found in RA patients and are associated with various outcomes such as falls, bone fractures, decreased quality of life and declines in daily living activities (ADL). Sarcopenia is a disease associated with outcomes such as falls and fractures due to a decrease in skeletal muscle mass and muscle strength associated with aging, and the proportion of sarcopenia in RA patients is extremely high. Meanwhile, frailty is considered to be a condition which is liable to cause dysfunction in daily life functions in response to acute stressors. Although it is a syndrome that can occur to anyone with aging, its evaluation is important because frailty is a determinant of prognosis in older RA patients. Regarding diagnosis, grip strength, walking speed, limb skeletal muscle mass are used for sarcopenia, while Cardiovascular Health Study's criteria are often used for evaluation of frailty, but measurement of grip strength and walking speed is common. On the other hand, the kihon checklist developed in Japan is 25 self-answered questionnaires, and if there are more than 8 items, the risk of needing long-term care insurance certification significantly increases. Therefore, it is considered to be an effective index for evaluating the presence or absence of frailty. What is important for the intervention of sarcopenia and frailty is the intake of protein and vitamin D with sufficient energy intake; additionally, combination of resistance training and aerobic exercise is recommended. For RA patients, due to the presence of arthritis, adequate consideration is required for resistance training. In this symposium, I would like to discuss about the concepts, implications, diagnosis and interventions for frailty and sarcopenia, which are an important problem in older rheumatoid arthritis patients.

ES10-2

Treatment strategy for elderly RA patients accompanied with sarcopenia

Motomu Hashimoto

Department of Advanced Medicine for Rheumatic Diseases, Kyoto University

Conflict of interest: Yes

Patients with rheumatoid arthritis (RA) exhibit a characteristic body composition abnormality called "Rheumatoid Cachexia", in which the muscle mass decreases and fat mass increases due to the influence of inflammatory conditions and physical dysfunction. Therefore, RA patients have increased prevalence of sarcopenia compared to the general elderly, leading to high risk of falls and fractures. Furthermore, some RA patients exhibit "sarcopenic obesity", who accumulate visceral fat mass even in normal body weight and have high risk of arteriosclerosis. Since inflammatory cytokines such as TNF- α and IL-6 are deeply involved in such characteristic body composition abnormalities in RA, the use of biological DMARDs which directly inhibit these cytokines could decrease sarcopenia in RA patients. On the other hand, the use of steroids acts to re-

duce inflammation and decrease sarcopenia if short-term and small amount, but if used at long term / high dose, it could promote sarcopenia by inducing steroid myopathy. Therefore, if we could achieve clinical remission using biological DMARDs reducing steroid use, it could decrease sarcopenia, improve the metabolic abnormalities, and greatly improve ADL / QOL of RA patients. Elderly RA patients not only have sarcopenia but also have various problems such as deterioration of cognitive function and medical complications. In this presentation, the treatment strategy for elderly RA patients accompanied with sarcopenia will be discussed.

ES11-1

Treat-to-target (T2T): strategic effectiveness and challenges in the new decade

Josef S Smolen

Department of Internal Medicine 3, Medical University of Vienna, Austria

Conflict of interest: Yes

T2T is part of RA/PsA management recommendations. Stringent clinical remission conveys best outcomes (damage, function). Imaging remission is not better than clinical remission, except higher costs, drug use and adverse events. Thus, clinical remission is gold standard for T2T. ACR and EULAR have provided stringent remission definitions not affected by types of therapy, particularly CDAI (no acute phase reactant). Remission defined by DAS28 shows damage progression and erroneously high responses when IL-6 or Jak-inhibitors are used (many patients “in remission” have high activity). Changing cutpoints for DAS28 remission does not help. ACR-EULAR Boolean definition is often missed due to PtGA > 1cm. One can develop remission definitions excluding patient input; modifications of SDAI were similar to traditional SDAI. But excluding patient perspectives in remission definition has to be evaluated against consequences of ignoring patient perspectives. Rather a slightly higher threshold for PtGA when defining remission may suffice. Just like classification criteria for one disease should not be used for another disease (e.g. RA classification for patients with SLE), clinical scores should not be used for patients with another disease (e.g. CDAI for patients with fibromyalgia). T2T recommendations account for patient factors when defining treatment target or using scores. With CDAI remission, PtGA is counterbalanced by lack of joint swelling and tenderness. Low disease activity by CDAI and SDAI is a good alternative, especially in patients with long-standing disease. DAS28-LDA is not ideal, because upon IL-6 or Jak-inhibition erratic results are seen (especially DAS28-CRP vs DAS28-ESR). The biggest challenge for T2T is implementation in practice. Given that targeting a good clinical outcome is as good as targeting imaging outcome, the implementation of assessing joints and indices in practice is not only timely but also urgently needed.

ES11-2

Significance of T2T treatment strategy reconsidered from new evidence

Tsutomu Takeuchi

Division of Rheumatology, Keio University School of Medicine

Conflict of interest: Yes

“Treat to Target: T2T”, an approach that sets a treatment target and optimizes treatment in the pursuit of that target has brought a major advancement in the treatment of rheumatoid arthritis (RA). The treatment strategy was widely recognized, including Japan, through global dissemination activities and based on this new approach, treatment recommendations were revamped by EULAR and ACR, and additionally the treatment guidelines in Japan were also revised. However, during dissemination and educational activities of T2T in Japan, there was not enough evidence to suggest that patient outcome was improved in daily clinical practice. Therefore, in cooperation with over 100 facilities in Japan to which rheumatologists affiliate, targeting early stage RA patients scheduled to begin treatment with methotrexate (MTX) and MTX without the use of biologic preparation, we examined the influence of T2T in daily clinical practice on outcome of RA patients, using HAQ as an indicator (HAQ study). Also, especially at an early stage of 2 to 3 years since the onset of RA,

joint destruction progresses quickly, and when bone erosion is recognized, deformation occurs in a few years, so a treatment strategy for preventing joint destruction progression in this phase is essential. Therefore, in early RA, more powerful tight controls aiming for clinical remission are desired. However, in daily clinical practice these goals are not easy to achieve. In order to achieve early clinical remission, it is critical that MTX, which is considered as the first-line treatment for RA, and biologics that have powerful clinical and radiographic efficacy, are introduced at an appropriate timing according to the patients' background. In this seminar, we will reconsider the realities of RA treatment in Japan and the significance of T2T treatment strategy based on the HAQ study results, and also deepen our consideration of the treatment strategy to maximize the outcome for RA patients.

ES12

Respiratory infection risk in rheumatic disease patients with the topic of pneumococcal vaccine

Sadatomu Tasaka

Department of Respiratory Medicine, Hirosaki University Graduate School of Medicine

Conflict of interest: None

The introduction of biologics is changing rheumatoid arthritis (RA) therapy. However, infectious complications are related to immunosuppressant therapy. Early diagnosis, appropriate treatment, and prevention are important. Pneumonia commonly causes hospitalization of RA patients, and respiratory infections are frequent and often severe. Complications such as interstitial pneumonia and alveolar hemorrhage make it difficult to diagnose respiratory infections in patients with rheumatic disease. Respiratory disease can occur regardless of RA activity such as joint symptoms. Drug-induced pneumonia is related to MTX or biologics. Differentiating non-infectious respiratory disease is a challenge. RA and SLE are risk factors for infections themselves, as well as drugs and complications. Prednisolone, MTX, and TNF inhibitors with anti-inflammatory and immunosuppressant actions may re-activate occult infections to induce opportunistic infections. Pneumonia is the most frequent infection in RA patients as said earlier. Pneumococcus is the most frequently isolated pathogen in community-acquired pneumonia. Pneumococcal vaccination can prevent pneumococcal pneumonia. It is recommended along with influenza vaccination in immunosuppressed adult patients, such as RA patients, by the American College of Rheumatology (ACR) and the European Congress of Rheumatology (EULAR). In Japan, pneumococcal vaccination is recommended in the guideline for the treatment with MTX and the guidelines for the use of TNF inhibitor, tocilizumab, and abatacept for RA of the Japan College of Rheumatology. Two types of pneumococcal vaccines, 23-valent pneumococcal polysaccharide vaccine (PPSV23) and 13-valent pneumococcal conjugate vaccine (PCV13), are currently available for use in adults (≥ 65 years) in Japan. I will present the mechanism of onset, characteristics, epidemiology, prevention, and diagnosis of respiratory infections in rheumatic diseases such as RA and discuss preventive vaccination.

ES13-1

A strategy to treat Psoriatic arthritis: Rheumatologist's point of view

Mitsumasa Kishimoto

Immuno-Rheumatology Center, St Luke's International Hospital

Conflict of interest: Yes

The prevalence of psoriatic arthritis (PsA) among Japanese psoriasis patients is thought to be less than those in Western countries. However, in keeping with our clinical experience that the prevalence of PsA among Japanese patients may actually be higher, we reported prevalence rates of up to 20.4% among Japanese psoriasis patients. Further improvements in awareness of this disease entity is necessary to allow patients to receive early and appropriate care. Awareness of clinical characteristics of PsA, including both articular and extra-articular manifestations, is essential for this process, especially because clinical characteristics of PsA are highly variable across patients. In this session, at first, we aim to characterize the distinguishing clinical features of PsA in patients, which will allow us to improve both under-diagnosis and misdiagnosis of the increasingly treat-

able disease, and emphasize the need for early diagnosis and appropriate differential diagnosis. Secondly, the treatment guideline and recommendation for PsA is changing constantly with the advent of new therapies in the EULAR, ACR, and GRAPPA internationally, and I would introduce a current treatment strategy “T2T” and its limitation. Furthermore, therapeutic strategies of how to set the treatment target should be determined through a shared decisions between physicians and patients in consideration of the disease activity and the characteristics (presence or absence of complications) of each patient. I will present a clear exposition of significance to choose oral DMARDs in treatment of PsA including the new oral DMARDs. Apremilast is a new oral DMARDs, and Phosphodiesterase 4 (PDE4) inhibitor which inhibit proinflammatory enzyme/cytokine including IL12, TNF α , and IL1 via degradation of cAMP. Finally, I would introduce its mechanism of action and the long-term efficacy and safety data in PsA programs.

ES13-2

Therapeutic strategy using apremilast for psoriasis and psoriatic arthritis

Yukie Yamaguchi

Yokohama City University Graduate School of Medicine

Conflict of interest: Yes

Psoriasis is a chronic auto-inflammatory disease in which IL-23/IL-17 plays a pivotal role. Nowadays, seven different biologics against to TNF α (infliximab, adalimumab), IL-12/23p40 (ustekinumab), IL-23p19 (guselkumab), IL-17A (secukinumab, ixekizumab), and IL-17RA (brodalumab) became therapeutical options for psoriasis in Japan. Moreover, an oral PDE4 inhibitor, apremilast, was also approved for psoriasis in 2017. Apremilast is effective for psoriasis, especially cases accompanied by pruritus, scalp psoriasis, and nail psoriasis, which remarkably improves patient's QOL. In addition, apremilast may be considered at first for active PsA patients with enthesitis if patients prefer an oral therapy. In this seminar, we will discuss best cases for apremilast therapy in psoriasis and PsA treatment.

ES14

Switching from reference product to biosimilar is not inherently dangerous

Hiroaki Matsuno

Matsuno Clinic for Rheumatic Diseases, Toyama, Japan

Conflict of interest: Yes

While tumor necrosis factor- α (TNF- α) inhibitors including reference product (RP) comprise a major strategy for the treatment of rheumatoid arthritis (RA) and other intractable autoimmune diseases, their high cost creates an economic burden in various countries and regions, including Japan. Thus, there is an increasing demand for the development of biosimilar drugs to increase cost-effectiveness. NI-071 has been developed as a biosimilar to RP by Nichi-Iko Pharmaceutical Co., Ltd. in Japan. We conducted a phase III study in Japanese RA patients to compare the efficacy and safety of BS with those of RP in a double-blind manner using DAS28-ESR (disease activity score in 28-joint count based on erythrocyte sedimentation rate as a primary efficacy parameter. Following the double-blind period, the BS administration was continued for another 24 weeks to evaluate the drug's long-term safety. Here, we present the data obtained in this phase III study taking into account certain factors of infliximab biosimilar. The disease activity score in 28-joint count based on erythrocyte sedimentation rate or C-reactive protein and the American College of Rheumatology 20/50/70-based efficacy profiles of BS were similar to those of RP during Period I (30 weeks) including evaluations at Week 14, a critical time point. BS efficacy was maintained throughout the 54-week study period. BS efficacy profile matched the RP profile until Week 54 after the drug switch from RP to BS at Week 30. The safety profiles of BS and RP were comparable and the long-term safety of BS was confirmed. BS demonstrated equivalent efficacy and safety to RP at treatment weeks 14 and 30, and long-term safety until Week 54 in Japanese RA patients.

ES15-1

Clinical impact of recent advances of molecular biology on rheumatoid arthritis: from bench to bedside

Keishi Fujio

Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo

Conflict of interest: Yes

In the treatment of rheumatoid arthritis (RA), treatment results are dramatically improved by the use of biological products, and clinical remission can be achieved in about half of patients. However, in about half of the remaining cases, the therapeutic effect is insufficient, and we often experience patients who are refractory to multiple biologic preparations and show rapid progress of bone destruction. Therefore, for better medical care, it is necessary to advance the elucidation of further pathological conditions of RA and select appropriate treatment. The heterogeneity of the therapeutic reactivity of RA makes it possible to speculate that various immunocompetent cells and immunological pathways are involved in the disease state. Various analytical methods have become applicable to human specimens in recent years. Mass cytometry, single cell analysis, and functional genome analysis are being applied to analysis of RA. As a result, evidence of the involvement of various immunocompetent cells in RA has been accumulated based on the peripheral blood immunocompetent cells, the local histology of inflammation and genetic risk. Epigenomic control of lymphocytes and synovial fibroblasts, which has not been previously clarified, is also becoming apparent at a deeper level. Classification of the pathological condition of RA will enable us to stratify the treatment and prognosis. Questions to be addressed are what kind of pathways are related to therapeutic reactivity and, how immune cells are modified in relation to the disease duration. With multi-subset transcriptome analysis, we have found that certain innate immunity pathways are related to therapeutic response of RA. We also address the nature of epigenomic modification unique to RA synovial fibroblasts. Further research is necessary until stratification that can be clinically applied. In this seminar, based on the latest knowledge of integrated analysis in RA, I would like to discuss the pathogenesis and treatment of RA.

ES15-2

The future of rheumatoid arthritis therapies: from life-changing to life-saving

Gurkirpal Singh

Division of Gastroenterology and Hepatology, Stanford University, USA

Conflict of interest: Yes

Recent advances in therapy of rheumatoid arthritis have led to major improvements in clinical and quality-of-life outcomes. Early aggressive treatments with “treat to target” strategies have resulted in considerably better disease control and less joint destruction. Indeed, therapies with biologic agents have been shown to reverse joint destruction, an outcome unheard of just a few years ago. We have changed lives of patients. I believe the future of rheumatoid arthritis therapies is to save lives. It is well-known that patients with RA have considerable excess mortality compared to age and gender-matched cohorts, with coronary heart disease (CHD) accounting for the largest excess. At the same time, recent studies in pathogenesis of CHD in the general population have emphasized the role of inflammation. It is now believed that the major effects of statins in reducing morbidity and mortality relate to their effects on inflammation rather than just cholesterol reduction. It is possible that the excess coronary CHD incidence in RA is likely because of high levels of circulating cytokines that enhance inflammation in the vulnerable plaque. Indeed, our work and that of others have identified RA as a CHD-equivalent risk factor, similar to diabetes. Essentially, this means that patients with RA need to be assessed as having CHD even if there are no other risk factors, just as is the practice with diabetes. However, these issues are still not widely recognized, unlike in diabetes care. Our work has shown that while CHD mortality in diabetes has declined dramatically in the US, there has not been a similar significant change in RA. In my lecture, I will further explore the factors leading to premature death in RA and how we can change assessment, monitoring and treatment of our patients in order to reduce this risk. Time has come for us to move to the next step of “saving lives” from just “changing lives”.

ES16

Biotechnology-based drugs and molecularly targeted drugs in treatment of rheumatoid arthritis

Atsushi Kawakami

Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: Yes

Establishment of 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) rheumatoid arthritis (RA) criteria, development of disease-modifying antirheumatic drugs (DMARDs), that of clinical practice guideline (CPG) and recommendation, spread of magnetic resonance imaging and ultrasonography have resulted in significant progress regarding to diagnosis as well as therapy of RA. Molecularly targeted drugs markedly contribute to anti-rheumatic therapy development of RA and divided into biological DMARDs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs). bDMARDs significantly suppress inflammation as well as joint destruction and are recommended to introduce in clinical practice in Phase II in case conventional synthetic DMARDs (csDMARDs) such as MTX and sulfasalazine (Phase I) does not achieve improvement at 3 months and target at 6 months or Phase III bDMARDs or Jak-inhibitor does not achieve the goal at 3/6 months stated in Japan College of Rheumatology (JCR) RA CPG 2014 as well as EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. bDMARDs of RA include TNF-inhibitors, abatacept, IL-6 receptor blocker and rituximab (not approved in Japan) and their efficacy is approved by clinical trials and studies toward csDMARDs-incomplete responder (IR) and TNF-inhibitors-IR (except TNF inhibitors). Jak-inhibitors, tofacitinib and baricitinib, are classified as tsDMARDs and the clinical trial data has been piled up towards MTX-naïve subjects, csDMARDs-IR and TNF-inhibitors-IR. Jak-inhibitors are recommended to introduce in Phase II or Phase III in EULAR recommendations 2016 update whereas Phase III in JCR RA CPG 2014. Efficacy of bDMARDs and Jak-inhibitors is excellent whereas molecularly targeted drugs are in some cases difficult to be introduced by high cost. Recently, efficacy as well as safety of biosimilars have been proved in clinical trials and the use of biosimilars is stated in the literatures including EULAR recommendations. The introduction of biosimilars into clinical practice will significantly improve the financial cost of RA treatment. The evidence of molecularly targeted drugs, including biosimilars, in RA treatment, will be discussed in this seminar.

ES17-1

Usefulness of baricitinib in RA treatment

Hideto Kameda

Faculty of Medicine, Toho University, Tokyo, Japan

Conflict of interest: None

The development and maintenance of rheumatoid arthritis are achieved through the network of various immune-related cells via the secretion of cytokines and cell-cell interaction. There are several ways to inhibit cytokine activity; the use of biologics which bind to the cytokine itself or its receptors and inhibit their activity on the surface or outside of immune-related cells; or the use of small-molecule kinase inhibitors which inhibit the intercellular cytokine signaling. For the former, due to its high “specificity”, it is important to administer the sufficient dose of biologics to completely inhibit the function of the targeted single cytokine. Therefore, it is difficult to identify the optimal dose for the amount of cytokine expression level of every patients. The latter, on the other hand, as the word “selectivity” indicates, partially inhibits the function of several cytokines with the limited dosing options to avoid off-target cellular toxicity. Baricitinib is a Janus kinase (JAK) inhibitor characterized by its high selectivity for JAK 1 and JAK 2 over JAK 3. Although the primary dosage has been set to 4mg daily administration because of its excellent potential for remission induction, 2mg daily administration is also possible according to the patient conditions. The usefulness of baricitinib will be explored in this symposium by both basic and clinical data of it.

ES17-2

The JAK Era has Come

Gerd R Burmester

Department of Rheumatology and Clinical Immunology, Charite University Hospital, Berlin

Conflict of interest: Yes

In 2016 EULAR Recommendation update, JAK inhibitors were recommended to be used in phase 2 of the treatment algorithm after cDMARD, however, with a note that biologics may still have advantage due to robust real-world experience. Since then, we have gathered enough real-world experience with JAK inhibitors for us to be able to see what benefits JAK inhibitors can bring to RA treatment, which may exceed the outcome with past treatment. In this presentation, I will discuss when JAK inhibitors might be used in 1st line therapy after cDMARDs, and also the characteristics of patients who would benefit most with JAK treatment.

ES18-1

Potential pathogenicity of autoantibodies in rheumatoid arthritis

Masataka Kuwana

Department of Allergy and Rheumatology, Nippon Medical School

Conflict of interest: Yes

A variety of autoantibodies are detected in patients with connective tissue diseases, and are utilized in clinical practice in making diagnosis and clinical subsetting. However, there has long been believed that those autoantibodies are produced as an “epi-phenomenon” reflecting ongoing pathogenic process, and lack pathogenicity by themselves, unlike autoantibodies detected in organ-specific autoimmune diseases. Autoantibodies related to RA include anti-citrullinated protein antibody (ACPA) and rheumatoid factor (RF), which are useful for making diagnosis and are thus included in the classification criteria. Recently, it has been shown that production of ACPA/RF precedes many years before onset of synovitis, and a new term “pre-RA” has been proposed as a condition of positive RA autoantibodies without any joint symptom or inflammation. RA autoantibodies are produced in genetically susceptible individuals by accumulation of environmental factors, such as smoking and periodontitis, leading to onset of synovitis through increase in antibody titers and epitope-spreading. On the other hand, high levels of RA autoantibodies are known as prognostic factor, which predict rapid joint destruction, as well as efficacy of some molecular-targeting anti-rheumatic drugs such as abatacept. Recently, a number of basic researches have revealed that ACPA is indeed involved in pathogenic process and contributes to joint destruction, through promoting differentiation of precursors into osteoclasts and triggering production of inflammatory cytokines such as TNF α , IL-6, and IL-8 by formation of immune complexes. Immunological remission is now proposed as a concept of disappearance of RA autoantibodies beyond clinical, functional, and imaging remission as the most challenging treatment goal. This lecture features recent insights into pathogenicity of RA autoantibodies and their clinical significance.

ES18-2

Biomarker of Rheumatoid Arthritis and Its Application to Treatment Selection

Yoshiya Tanaka

The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: Yes

The introduction of biological products resulted in a paradigm shift in the treatment of rheumatoid arthritis (RA), which is closely linked to the presence of standard measurements as a background factor, enabling precise and objective evaluation of disease activity and treatment response. Such measurements must be excellent in terms of versatility, economy, and reproducibility. In this manner, the disease activity index including DAS28 and SDAI satisfies these conditions. Biomarkers such as MMP-3 and multi-component markers such as MBDA are also applicable based on the state of the disease. Widely accepted imaging evalua-

tion, such as modified Total Sharp Score by joint X-ray and magnetic resonance (MR) imaging scoring, aimed for strict structural assessment, also resulted in great achievement in setting therapeutic goals. Meanwhile, no disease-specific marker, such as HbA1c for diabetes mellitus, has been identified for rheumatoid arthritis. However, in TNF inhibitor treatment, it is believed that the serum level of its ligand TNF is useful for determining drug selection and/or treatment response. In the TSUBAME Study, the association between the level of serum TNF and IL-6 was analyzed before and at 24 hours after treatment, and DAS 28 (ESR) at 12 weeks after treatment when certolizumab pegol (CZP) was additionally administered to 85 patients with RA where sufficient response to MTX had not been obtained. At 24 hours after treatment, the blood level of CZP varied widely, and the median value was 9.4 (0.2-31.8) µg/mL, while the serum TNF and IL-6 levels had significantly decreased. In addition, the serum CZP level had a strong negative correlation with the serum TNF level at 24 hours later. DAS28 (ESR) was significantly improved from 5.5 ± 1.3 to 3.4 ± 1.5 at 12 weeks after treatment. Remission at 12 weeks later was not associated with the serum TNF or IL-6 level before treatment, but with lower serum TNF level, lower IL-6 level, and higher CZP level at 24 hours after treatment according to univariate analysis, whereas it was associated only with lower serum TNF level at 24 hours later according to multivariate analysis. These findings suggested that the blood level of CZP was negatively correlated with the serum level of the ligand, TNF at 24 hours after treatment, and that the lower serum TNF level at only 24 hours after treatment predicted the treatment response at 12 weeks later. At present, biological products have been applied for various collagen and rheumatic diseases, resulting in therapeutic breakthroughs in each area. The introduced biological products targeting TNF, IL-17, and IL-12/IL-23 result in innovative efficacy in psoriatic arthritis, associated with progressive spinal joint damage, as is the case with rheumatoid arthritis. It is found that using different biological antirheumatic drugs targeting either IL-12, IL-17, or TNF leads to a high treatment response in patients with psoriatic arthritis classified into four immunological phenotypes according to the expression pattern of peripheral lymphocyte chemokine receptor. This suggested the potential of precision medicine, optimized target therapy using lymphocyte immunological phenotype as a biomarker. The achievements mentioned above are expected to contribute to the establishment of a novel therapeutic system and strategy.

ES19-1

RA hand surgery in T2T era~ from the basics to difficult cases~

Natsuko Nakagawa

Department of Orthopaedic Surgery, Rheumatology & Collagen Disease Center, Hyogo Prefectural Kakogawa Medical Center

Conflict of interest: None

The treatment of rheumatoid arthritis (RA) has remarkably progressed. Tight control of RA disease activity makes it possible to inhibit the progression of the joint destruction. For this reason, small joint surgeries are assumed to increase in number, and RA hand surgery to be more important. On the other hand, because of this era, unsolved problems of RA hand could accumulate significantly in the near future. This study group seminar, which has been held annually since 1999, celebrates the 21st seminar this year. We are planning to have two sessions, which are audience-participating case study using Answer Pad and a special lecture with the theme of "RA hand surgery in T2T era ~from the basics to difficult cases~". In case study, we will present some cases, and we would like to discuss with participants how to treat with them applying the basic concepts. For the special lecture, Dr. Keiichiro Nishida will give a lecture on surgical reconstruction of rheumatoid wrist-basic procedures and management of difficult cases-. In this seminar, we would like to make this workshop useful for clinical practice of all participants with all our effort.

ES19-2

Surgical reconstruction of rheumatoid wrist- basic procedures and management of difficult cases-

Keiichiro Nishida

Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

Conflict of interest: None

The wrist is one of the most frequently affected joint during the process of rheumatoid arthritis (RA). It is reported to be involved in the first two years of the disease in about 50% of the patient, increasing up to nearly 90% after 10 years, often including both sides. Bone erosion and bone marrow edema detected by MRI, and ultrasonographic synovitis provide useful information for early diagnosis of RA, and radiographic bone erosion and joint space narrowing have been used for the evaluation of progression of joint destruction. It has been also reported that the major joint areas that most frequently contributed to Δ J-HAQ score were the wrist joint (31%), followed by shoulder (21%), knee (13%), and ankle (10%) joint. The mal-alignment of the wrist joint is minimum in Osteoarthritis type and Ankylosis type of Schluthess classification. However, in the Disintegration type, it starts with radial rotation of the carpal bones and dorsal subluxation of the ulnar head, followed by supination, ulnar deviation, and palmar subdislocation of the carpus. From the viewpoint of surgical treatment, the wrist joints are divided into mid-carpal joint (MC joint), radiocarpal joint (RC joint), and distal radio-ulnar joint (distal radio- DRUJ). Mainstay surgery for RC joint, when mobility remains in MC joint, is radio-lunate partial arthrodesis, which allows realignment of lunar bone to lunar fossa of radius. Basic surgery for DRUJ is the Sauvé-Kapandji (SK) method, which also stabilize the RC joint by creating the ulnar shelf. Darrach procedure is safely indicated to stable Ankylosis type. In some cases of advanced wrist joint destruction such as Disintegration type and mutilance arthritis, it might be often difficult to deal with only the basic procedures described above, and modified SK method, radio-lunate-triquetrum arthrodesis, tendon arthroplasty, total wrist fusion, or total wrist arthroplasty are used as appropriate, but still there are many problems and no clear criteria for indication. In the current presentation, I will show basic surgical techniques and discuss how to manage difficult cases.

Annual Course Lecture Luncheon Seminar

ACL-LS

Proper use of methotrexate based on the latest incidence of adverse reactions

Yasuo Suzuki

Division of Rheumatology, Department of Internal Medicine, Tokai University School of Medicine, Japan

Conflict of interest: Yes

Methotrexate (MTX) is globally considered as the anchor drug for the treatment of RA even in the biologic era. Therefore, MTX is used in more than 80% of RA patients by monotherapy or combination therapy. High-dose MTX up to 16 mg/week was approved in 2011. The PMS results showed the percentage of patients who achieved remission nearly tripled in cases of MTX more than 8 mg/week. The MTX guideline 2016 update recommends that a target of dose increase is 10 to 12 mg/week based on the recent evidences and referred rapid dose escalation for the patients who have poor prognostic factors. On the other hand, 730 fatal cases possibly associated with MTX were reported by December 2017 after the marketing approval for MTX and among them, 175 patients died after 2011. Deaths associated with infections or neoplasms (lymphoproliferative disorder, LPD) are increasing, specifically, infections in 25.1% and LPD in 21.7%. The demographic analysis of patients who died of infections showed 75% of patients were aged 70 years or above, 35% of patients were treated with MTX 10 mg/week or above, and about a half of the patients were treated for 2 years or longer. Since 2014, more than 60% of patients with serious infections, were treated with concomitant biologics or JAK inhibitors, and 36.7% were treated with oral MTX 10 mg/week or above. Common serious infections included pneumonia and pneumocystis pneumonia. Chronic opportunistic infections such as TB, fungal infection, herpes infection, and nontuberculous mycobacterium infection are also increasing. Patients who died of neoplasms (LPD) since 2011 were also mostly elderly: 87.1% were aged 60 years or above. Patients treated with MTX 10 mg/week or above were only 15.3% while those treated for 2 years or longer were 54.4%. Of 457 patients with LPD, 88.0% were treated with MTX for 2 years or longer. Attentions are required for elderly patients treated with oral MTX for a long time. Outcomes of the latest RA treatment have been dramatically improved because of the use of high-dose MTX as the anchor drug and the proactive concomitant use of molecular-targeted drugs in patients inadequately responsive to MTX. Considering the recent trend of adverse reactions and the aging of RA patients, however, immunosuppression relief after long-term remission should be required.

Workshop

W1-1

Calcineurin Inhibitors for the Treatment of Polymyositis /Dermatomyositis-associated Interstitial Lung Disease (PM/DM-ILD)

Takahisa Gono¹, Naoshi Nishina², Shinji Sato³, Masataka Kuwana¹

¹Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, ²Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, ³Division of Rheumatology, Department of Internal Medicine, Tokai University

Conflict of interest: None

[Objective] We investigated the efficacy of calcineurin inhibitors (CNIs) in patients with PM/DM-ILD using a large JAMI cohort database. [Methods] A total of 491 patients with adult-onset PM/DM-ILD were selected, and survival rates were compared between the patient groups, followed by additional comparisons using propensity score (PS) matching. [Results] Cumulative 5-years survival rate in 402 patients treated with CNI was 78%, which was significantly lower ($P = 0.03$) than 80% in 89 patients treated without CNI. Anti-MDA5 antibody, a higher level of ferritin, and a higher initial dose of corticosteroid (CS) were identified as parameters associated with CNI use by multiple logistic regression analysis. After PS matching employing these three factors, the 5-years survival rates were 90% and 67% in patients treated with and without CNI, respectively ($P = 0.17$). In comparison of clinical backgrounds between patients treated with CsA and TAC, anti-MDA5 antibody and CS pulse therapy were associated with CsA use. After PS matching employing these two factors, survival rates were similar between patients treated with CyA and TAC (78% versus 80%, respectively; $P = 0.59$). [Conclusions] CNI in combination with CS-based regimens is potentially effective for PM/DM-associated ILD.

W1-2

The efficacy and the safety of tacrolimus for polymyositis and dermatomyositis complicated with interstitial lung disease

Hirofumi Toko, Yuya Kondo, Taihei Nishiyama, Shota Okamoto, Masaru Shimizu, Fumika Honda, Mizuki Yagishita, Ayako Ohyama, Izumi Kurata, Saori Abe, Hiroyuki Takahashi, Atsumu Osada, Masahiro Yokosawa, Hiroto Tsuboi, Isao Matsumoto, Takayuki Sumida

Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: None

<OBJECTIVE> To clarify the efficacy and the safety of tacrolimus (Tac) on polymyositis (PM) and dermatomyositis (DM) complicated with interstitial lung disease (ILD). <METHODS> We included 50 cases of PM/DM (24 PM and 26 DM) complicated with ILD diagnosed in University of Tsukuba hospital in this study. We retrospectively evaluated 1) characteristics, 2) efficacy of Tac on myositis and ILD, 3) safety profile. <RESULTS> 1) Twenty three cases were treated with Tac. 2) In 17 out of 23 cases treated with Tac for remission induction, levels of CK and KL-6 were significantly decreased from one month and six months after Tac was initiated. Dose of prednisolone (PSL) was also reduced after one month. In 17 out of 27 cases treated with cyclosporine for remission induction, levels of CK and KL-6 and dose of PSL were similarly decreased. 3) One case treated with Tac died due to renal failure while seven cases treated without Tac died due to exacerbation of ILD (3 cases) and infection (4 cases). Number of death tended to be fewer in cases treated with Tac than without ($p=0.09$). Adverse events appeared within 48 months were comparable. <CONCLUSION> The concomitant use of Tac was effective for PM/DM complicated with ILD and there was no significant difference compared to cases treated without Tac.

W1-3

Significance and Predictive Factors of Recurrence in Anti-Aminoacyl-tRNA Synthetase Antibodies-Interstitial Lung Disease treated with corticosteroids and calcineurin inhibitor

Reoto Takei, Yasuhiko Yamano, Yasuhiro Kondo

Respiratory Medicine and Allergy, Tosei General Hospital

Conflict of interest: None

[Object] Anti-aminoacyl-tRNA synthetase (anti-ARS) antibodies related interstitial lung disease (ILD) often recurred. Our objective was to clarify the efficacy of initial treatment with corticosteroids (CS) and calcineurin inhibitor (CNI), significance of recurrence, and predictive factors for recurrence in patients with ARS-ILD. [Methods] We retrospectively identified consecutive ARS-ILD patients treated with CS and CNI from 2006 to 2017. [Results] Fifty-seven patients were included and 53 improved by one year initial treatment. KL-6 changed with disease behavior. Thirty-two recurred in maintenance therapy. No significant difference was obtained between baseline patients' characteristics with or without recurrence. KL-6 at recurrence increased from remission in all patients. In the recurrence group, respiratory function declined over the clinical course. In the multivariate analysis, KL-6 increase rate from remission and CNI discontinuation were independent predictive factors for recurrence. No relationship was observed between CNI continued period and recurrence. [Conclusions] In ARS-ILD, CS and CNI were well responded. It is important to predict recurrence by measuring KL-6 and continuation of CNI.

W1-4

Successful rituximab therapy for refractory rapidly progressive interstitial lung disease in a patient with anti-MDA5 antibody-positive dermatomyositis

Shogo Kodama, Takashi Ozaki, Tatsuhito Umeki, Yuichi Omura, Masataka Torigoe, Chiharu Imada, Keisuke Maeshima, Koji Ishii, Hirotaka Shibata

Department of Endocrinology, Metabolism, Rheumatology and Nephrology, Faculty of Medicine, Oita University, Oita, Japan

Conflict of interest: None

Introduction: It is well known that patients with anti-MDA5 antibody (MDA5-Ab)-positive dermatomyositis (DM) could follow a lethal course despite intensive immunosuppressive therapy with steroids, calcineurin inhibitors, and intravenous pulse cyclophosphamide (IVCY). Herein, we report a case with MDA5-Ab-positive DM who developed refractory RP-ILD that was markedly relieved after rituximab (RTX) treatment. **Case report:** A 54-year-old man with several months' history of skin rash and muscle pain was admitted in another hospital and diagnosed with MDA5-Ab-positive DM complicated with ILD. He was immediately given pulse methylprednisolone, followed by oral prednisolone (1mg/kg/day) combined with tacrolimus (TAC) and IVCY. Nevertheless, his CT showed ILD progression. Moreover, he developed deep neck abscess and he was transferred to our institution on 24th day. Therapeutic plasma exchange was added to combination therapy with steroids, TAC and IVCY, which was ineffective for progressive ILD. Consequently, RTX therapy (375mg/m²/W for 4 weeks) was initiated on 39th day. A follow-up CT after RTX administration demonstrated marked improvement and he was discharged on the 165th day. **Conclusions:** RTX treatment might be potential therapeutic option for refractory RP-ILD in MDA5-Ab-positive DM.

W1-5

Efficacy of plasma exchange for patients with anti-melanoma differentiation antigen 5 antibody-positive dermatomyositis at our hospital

Yukiko Iwasaki¹, Aya Nishiwaki¹, Haruka Takahashi¹, Akito Kawamura¹, Risa Yoshihara¹, Haruka Tsuchiya¹, Toshihiko Komai¹, Norio Hanata¹, Bunki Natsumoto¹, Yusuke Sugimori¹, Akihiko Matsumoto², Rei Isshiki², Yumi Tsuchida¹, Yasuo Nagafuchi¹, Oh Sasaki¹, Hiroaki Harada¹, Shuji Sumitomo¹, Hirofumi Shoda¹, Kanae Kubo¹, Masaomi Nangaku², Keishi Fujio¹

¹Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, ²Purification Unit, The University of Tokyo Hospital

Conflict of interest: None

[Object] In IIM, CADM with anti-MDA5 antibodies is famous for its high prevalence of rapidly progressive interstitial pneumonia (IP). Although the intensive regimen of combination therapy with high-dose cor-

ticosteroids, calcineurin inhibitor, and IVCY is frequently chosen at early phase of treatment because of its poor prognosis, treatment-resistant cases still exist. In 2017-2018, we applied plasma exchange (PE) with the immunosuppressive treatment to 7 inpatients at our hospital. Here we reported the effectiveness of the therapy. [Methods] 2 males and 5 females. The interval of their diagnosis after onset ranged from 1-6 months. PE was immediately chosen for one and remaining 6 started 1-2 months after they entered to our hospital. At the induction phase, 2-3 times per week were taken and then gradually reduced. Total number of PE was 21.4±8.3 times on average. [Results] In October 2018, over 1-year survival cases were 2, over 150-days survival cases were 4, although 1 case died of disease control failure. [Conclusions] 1 case of death started the therapy at the other hospital and the progression of IP had already appeared at the transfer to our hospital. PE is one of the promising therapies and we need further investigation to select the proper cases at proper timings.

W1-6

Therapeutic apheresis therapy for rapid progressive interstitial pneumonia of clinically amyopathic dermatomyositis with anti MDA-5 antibody

Maki Kagitani¹, Hidehiko Makino², Shogo Matsuda³, Takaaki Ishida², Youhei Fujiki², Kenichiro Hata², Tohru Takeuchi², Shigeki Makino³, Shigeki Arawaka²

¹Blood Purification Center, Osaka Medical College Hospital, ²Department of Internal Medicine IV, Osaka Medical College, ³Division of Immunology and Rheumatology, Osaka Medical College, Mishima Mini-ami Hospital

Conflict of interest: None

[Object] Interstitial pneumonia (IP) of clinically amyopathic dermatomyositis (CADM) with anti MDA-5 antibody typically shows rapid progress and high mortality in spite of several immunosuppression agents. [Methods] About seven cases who were performed therapeutic apheresis therapy, we assess the efficacy by some clinical functions, and outcomes. [Results] Seven cases who were given therapeutic apheresis therapy; PE/PMX 1, SePE/PMX1, PMX 2, PE/SePE 1, PE1, SePE 1. At 1year after apheresis therapy, 4 cases are alive, 2 are dead by reactivation and one is dead by laryngeal cancer. The anti-MDA5 Ab titer was decrease in three all cases those its titer was detected. A-aDO₂ and P/F ratio were also resolved. All cases were recovered from critical situation. [Conclusions] Therapeutic apheresis therapy is effective in controlling CADM-IP with anti MDA-5 antibody.

W2-1

Prognosis and causes of deaths of polymyositis and dermatomyositis patients with interstitial pneumonia

Shigeki Makino¹, Takuya Kotani², Takeshi Shoda³, Hidehiko Makino², Youhei Fujiki², Tohru Takeuchi², Shigeki Arawaka²

¹Division of Internal Medicine, Osaka Medical College Mishima-Minami Hospital, Takatsuki, Osaka, Japan, ²Department of Internal Medicine IV, Osaka Medical College, Takatsuki, Osaka, Japan, ³Division of Rheumatology, Yodogawa Christian Hospital, Osaka, Japan

Conflict of interest: Yes

[Background] We aim to know the influence of interstitial pneumonia (IP) involvement on prognosis of polymyositis and dermatomyositis (PM/DM). [Methods] We reviewed clinical data concerning about prognosis and causes of deaths of PM/DM-IP patients of our institute from August 2008 to July 2018. [Results] Total PM/DM-IP patients are 197 (57 males, average 64.1 years). Comparing PM/DM patients without IP (69cases, 23 males, average 58.9 years), PM/DM-IP patients were older and female dominant. Total dead cases were 39 (18males). 5-year survival rate of PM/DM-IP patients was 73.9%, 10-year survival rate was 51.9%. Deaths within 1 year were 23 (59%). Concerning about the causes of deaths of PM/DM-IP patients, early IP deaths were 21 cases, chronic progression of IP were 4, acute exacerbation of IP were 3, lung cancer were 1, other malignancy were 4, infection were 5. Total death due to IP were 28 (72%). [Conclusions] PM/DM-IP patients of our institute were older and female dominant compared to PM/DM patients without IP. 5-year survival rate of RA-IP patients was 73.9%, 10-year survival rate was 51.9%.

Deaths within 1 year were 23 (59%). Total death due to IP were 28 (72%). So IP of PM/DM profoundly influence on prognosis of PM/DM-IP patients.

W2-2

Clinical features and prognosis of interstitial pneumonia associated with anti-MDA5 antibody positive dermatomyositis

Ai Umeda, Takako Hashimoto, Natsuko Watanabe, Masashi Suzuki, Tatsuaki Naganawa, Konomi Ashihara, Megumi Kurumizawa, Daisuke Hirano, Jo Nishino, Shusaku Fukaya, Shunji Yoshida, Hidekata Yasuoka
Division of Rheumatology, Department of Internal Medicine, Fujita Health University School of Medicine

Conflict of interest: None

[Object] To examine clinical features and prognosis for anti-MDA5 antibody positive dermatomyositis associated interstitial pneumonia (DM-IP) patients. [Methods] We investigated clinical features and prognosis retrospectively for anti-MDA5 antibody positive DM-IP patients hospitalized in our hospital between January 2010 and October 2018. [Results] In 19 cases (7 males), the average age at diagnosis was 54.9 years. There were 8 deaths. Male mortality rate was high (85.7%). In all death cases, triple combination therapy (steroid, calcineurin inhibitor and IVCY) was performed. In two death cases, other immunosuppressants were added to triple therapy. On the other hand, no additional immunosuppressants other than triple therapy was required in the surviving cases. Serum ferritin levels before treatment were significantly higher in the death group. In long-term survival cases, 2 of 10 cases required reintroduction with IVCY due to IP relapse. [Conclusions] Although the ferritin levels before treatment is useful for the prognosis prediction, the case of poor response to the initial treatment was difficult to rescue even with a strong immunosuppressive combination therapy. In long-term survival cases there may be recurrence, but re-induction can be introduced by resuming IVCY.

W2-3

Change in serum ferritin levels during therapy is related to disease activity in patients with anti-MDA5 Antibody-positive dermatomyositis

Satoko Arai, Kazuhiro Kurasawa, Yuta Takamura, Tomoyuki Miyao, Junya Nagasawa, Ryutaro Yamazaki, Takayoshi Owada, Reika Maezawa, Masafumi Arima
Department of Rheumatology, Dokkyo Medical University

Conflict of interest: None

[Object] To determine whether serum ferritin levels during the therapy are related to disease activity and predicts prognosis in patients with anti-MDA5 Ab + dermatomyositis (DM). [Methods] Subjects were consecutive 20 anti-MDA5 Ab + DM patients who admitted Dokkyo Medical University hospital from 2009 to 2015. The relation between serum ferritin levels during treatment for DM and prognosis of patients was analyzed. [Results] Of 20 subjects, 19 developed ILD, 17 of which was rapidly progressive ILD, 9 survived and 11 died. Time of death was 16 to 64 days (median; 41 days). Within 2 weeks starting therapy, serum ferritin levels were increased in all patients with poor prognosis, while 4 out of 7 survivors showed the increase. After 2 week-therapy, none of the survivors did not show the increase of serum ferritin levels. In contrast, the continuous rise of ferritin levels were found in 6 of 7 patients with poor prognosis. The peak of serum ferritin levels was in 0-3 weeks (median: 0 week) in the survivor, but at 2-5 week (4 week) in dead patients. [Conclusions] Patients were poor in prognosis, when ferritin levels continuously increase, the decrease of ferritin levels was slow, or ferritin levels show re-elevation.

W2-4

Increased serum leucine-rich alpha2-glycoprotein (LRG) levels are correlated with the disease activity, progression, and prognosis of interstitial pneumonia in patients with dermatomyositis

Takaaki Ishida¹, Takuya Kotani¹, Minoru Fujimoto², Tohru Takeuchi¹, Shigeki Makino³, Shigeki Arawaka¹, Tetsuji Naka²

¹Department of Internal Medicine IV, Osaka Medical College, Osaka, Japan, ²Center for Intractable Immune Disease, Kochi Medical School, Kochi University, Kochi, Japan, ³Internal Medicine, Osaka Medical College Mishima-Minami Hospital, Osaka, Japan

Conflict of interest: None

[Objective] To investigate whether leucine-rich α_2 -glycoprotein (LRG) can be a biomarker for interstitial pneumonia (IP) in patients with dermatomyositis (DM). [Methods] Correlations between the clinical findings and serum LRG levels were investigated in 46 patients with DM-IP (33 with acute/subacute IP [A/SIP] and 13 patients with chronic IP [CIP], including 10 fatal cases of IP). [Results] The median levels of serum LRG at baseline, and 2 and 4 weeks after the initiation of treatment in patients who died were significantly higher than those in surviving patients ($P = 0.026, 0.029, 0.008$). The median level of serum LRG in the DM-A/SIP patients than was significantly higher than that in the DM-CIP patients ($P = 0.0004$), and that in the anti-MDA5-Ab-positive group was slightly higher than that in the anti-ARS-Ab-positive group. The serum LRG levels were significantly correlated with the serum levels of LDH, CRP, ferritin, AaDO₂, %DLco, and the total GGO score. The survival rate after 24 weeks in patients with an initial LRG level of ≥ 17.6 pg/mL was significantly lower than that in patients with an initial LRG level of < 17.6 pg/mL ($P = 0.0009$). [Conclusions] The serum LRG level may be a promising marker of the disease activity, progression, and prognosis in patients with DM-IP.

W2-5

Retrospective analysis on the relapse of polymyositis / dermatomyositis after achieving remission

Akiko Shibata, Yusuke Okada, Kentaro Chino, Takahiko Kurasawa, Hirofumi Takei, Tsuneo Kondo, Koichi Amano
Division of Rheumatology/Clinical Immunology, Department of Internal Medicine, Saitama Medical Center, Saitama Medical University

Conflict of interest: None

[Object] To elucidate the current situation of polymyositis (PM) /dermatomyositis (DM) after achieving remission in our department. [Methods] 71 PM/DM patients who have visited our department from October 2017 to October 2018 and had been diagnosed and initiated treatment in our hospital after April 2005, were enrolled and clinical information were analysed retrospectively from medical records. [Results] 15 cases experienced relapse (relapse rate 21%). There was no significant difference in the background features of 56 patients who were maintenance group and relapse group between 2 groups. The mean initial daily PSL dose for remission induction therapy in both groups was 47 mg and 52 mg, and immunosuppressant was used in 66% and 100% respectively and the difference was not significant. In the relapse group, 6 cases had recurrence of myositis after achieving remission (average period was 45 months), and 9 cases had worsening of interstitial pneumonia after remission (average 72 months). [Conclusions] Relapse was seen in 21% of PM/DM patients who achieved remission. Relapse rate of interstitial pneumonia was higher than that of myositis. There was no significant difference in clinical features or initial treatment between remission maintenance group and relapse group.

W2-6

An analysis for detecting a poor prognostic factor in polymyositis and dermatomyositis in the modern period -The result of a single-center cohort study -

Hiroshi Oiwa¹, Kei Araki², Yohei Hosokawa¹, Masamoto Funaki³

¹Department of Rheumatology, Hiroshima City Hiroshima Citizens Hospital, ²Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, ³Medical Corporation JR Hiroshima Hospital

Conflict of interest: None

[Objective] To detect a poor prognostic factor in polymyositis and dermatomyositis (PM/DM) in the modern period. [Method] All the newly-diagnosed myositis cases, seen between April 2014 and June 2018, were included. Probable or definite cases based on the Bohan & Peter cri-

teria, or possible cases with myositis-specific antibody were included. We investigated clinical parameters including the myositis pattern, interstitial lung diseases (ILD), malignancy, anti-ARS, anti-MDA5, anti-Tif1- γ antibodies to predict poor survival. The presence of ILD was based on CT of the chest, and that of malignancy was defined as its onset within three years of myositis. Each parameter was evaluated by using Logrank test. Statistical analysis was done with EZR, with statistical significance of p value of <0.05. [Results] Thirty cases newly diagnosed with PM/DM/Clinically amyopathic dermatomyositis (CADM) (7/16/6) were included. Ten were male, and the median age was 67 years old. ILD and malignancy were found in 57% and 27%, respectively. Ten cases died of ILD (5), malignancy (4), and sudden death (1), during the median observation of 352 days. Anti-MDA5 antibody only predicted poor survival ($p < 0.01$). [Conclusion] Anti-MDA5 antibody was the only predictor of poor survival in our cohort.

W3-1

Vascular ultrasound findings in assessing disease activity of Takayasu Arteritis (TAK)

Kasumi Takagi¹, Yuichiro Shirai¹, Takashi Nawata^{1,2}, Shunsuke Uchiyama¹, Seiji Kobayashi¹, Takahisa Gono¹, Mitsuhiro Takeno¹, Ikuyo Takagi³, Masataka Kuwana¹

¹Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, ²Department of Medicine and Clinical Science, Yamaguchi University Graduate School of Medicine, Yamaguchi, Japan, ³Department of Cardiology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan

Conflict of interest: None

[Background] Regarding a need for a method of monitoring disease activity under treatment, we report two cases of TAK in which ultrasound (US) findings have changed over time. [Case1] A 18-year-old Japanese man with fever and fatigue showed bilateral carotid bruit and laterality of blood pressure. Computed tomography (CT) revealed wall thickening of ascending to abdominal aorta and its branches. He was diagnosed as having TAK. Treatment with prednisone (PSL) (30 mg/day) and tocilizumab was started. One month later, he had a relapse when we tapered PSL to 15 mg/day, with carotidynia, CRP elevation (<0.03 to 0.12mg/dL), and increased intima-media thickness (IMT) of left carotid artery (2.44 to 2.61mm) by US. After PSL was increased, symptoms improved. [Case2] A 18 year-old Japanese man with fever and weight loss showed upper abdominal bruit. CT revealed wall thickening of thoracic and abdominal aorta, and superior mesenteric artery (SMA). He was diagnosed as having TAK. Treatment with PSL (50 mg/day) and azathioprine was started. One month later, upper abdominal bruit was inaudible and US revealed reduction of IMT of SMA (1.7 to 1.3mm). [Discussion] US can detect the lesion of large vessel vasculitis noninvasively and repeatedly. It could be a useful tool for assessing disease activity.

W3-2

Carotid ultrasonography was useful in evaluating the activity of Takayasu arteritis treated with Tocilizumab (TCZ)

Ryutaro Yamanaka, Kazuya Matsumoto, Shoichi Nawachi, Reika Hayashi, Hidetoshi Kagawa
Department of Internal Medicine, Japanese Red Cross Himeji Hospital

Conflict of interest: None

A 27 year-old woman admitted to our hospital because of high grade fever and neck pain. We diagnosed Takayasu arteritis with MRI, carotid ultrasonography showed common carotid artery wall thickening. We started treatment with PSL 50 mg/day. When we reduced PSL to 20 mg/day, the CRP value elevated. Therefore, PSL was increased to 30 mg/day, and MTX was started in combination. The CRP value again elevated, when we increased MTX to 12 mg/w and reduced PSL to 20 mg/day. We considered relapse and started using TCZ. After we used TCZ, we gradually decreased PSL, because the CRP value remained negative. After decreasing PSL to 7.5 mg/day, exacerbation of the wall thickness of the common carotid artery was observed by carotid ultrasonography, so we increased to PSL 20 mg/day again. While TCZ is in use, there is a possibility that the activity still remains even though the CRP is normal. There

is a risk that the finding of relapse may be delayed if activity is evaluated only by blood test. When TCZ was used, it was considered that it is necessary to periodically evaluate the activity in the imaging test. As in this case, if the active lesion is confined to the neck, it seems that evaluation by ultrasonography is useful even from the viewpoint of radiation exposure and cost.

W3-3

Usefulness of the detection of carotid artery wall blood flow signal by Superb Micro-vascular Imaging (SMI) for the assessment of silent vasculitic disease activity of Takayasu arteritis

Yusuke Okada, Akiko Shibata, Kentaro Chino, Takahiko Kurasawa, Hirofumi Takei, Tsuneo Kondo, Koichi Amano
Department of Rheumatology and Clinical Immunology, Saitama Medical Center

Conflict of interest: Yes

Objectives: To investigate the usefulness of the detection of carotid artery (CA) wall blood flow signal by SMI for the assessment of vasculitic activity of Takayasu Arteritis (TAK). Methods: Four patients who had been newly diagnosed in our department from May 2015 to October 2018 and had received SMI to detect CA wall blood flow signal were retrospectively analyzed. Results: All patients were female, mean 26 years old, mean CRP 8.13 mg/dl, CA wall thickening had been confirmed by ultrasonotomography and contrast CT and the SMI signal was detected. After treatment with Steroid, CRP returned to negative and no exacerbations in CT and MRI findings in all 4 cases. In cases 1 and 2 had been treated with 1 mg/kg/day of PSL, the SMI signal remained detected after 2 weeks of treatment. Two weeks after the addition of tocilizumab, the SMI signal decreased in case 1, and disappeared in case 2. In case 3 had been treated similarly with 1 mg/kg/day of PSL, the SMI signal became undetected after 2 weeks, and continued to be undetected every several months until month 30. In the fourth patient with aortic regurgitation who underwent steroid pulse therapy, the SMI signal disappeared at week 2. Conclusions: SMI is useful as a method of evaluating latent vasculitic activity of TA with CA lesion.

W3-4

Myocardial FDG-PET/CT findings in children with Takayasu arteritis

Kenichi Nishimura, Seira Hattori, Ai Ohnishi, Ryoki Hara, Shuichi Ito
Department of Pediatrics, Yokohama City University Graduate School of Medicine

Conflict of interest: Yes

[Object] To analysis the FDG-PET/CT (PET/CT) findings in children with Takayasu arteritis (TA) except for vascular lesions. [Methods] This is a single-center retrospective observational study. We evaluated 9 children with TA and compared them with 10 children with other rheumatic disease (systemic juvenile idiopathic arthritis; 5, polyarticular juvenile idiopathic arthritis; 1, juvenile dermatomyositis; 1, Crohn's disease; 2, Kikuchi's disease; 1) (control group). All children were underwent PET/CT before treatment from April 2015 to March 2018. [Results] Median age of performed PET/CT was 13.9 (range; 11.1-14.9) years old in TA children and 5.4 (1.4-12.4) years old in control group. Both group includes 6 females. FDG accumulation in left ventricular myocardium was observed in 8 TA patients (89%) but in 3 (30%) of control group ($p=0.02$). Six TA children received follow-up PET/CT. Myocardium FDG accumulation was continued in 3 children, but resolved in 2. TA children with persistent accumulation in myocardium had ascending aorta dilation later. [Conclusions] FDG accumulation in left ventricular myocardium would be a characteristic findings in children with TA, and possibly related to later ascending aorta dilation.

W3-5

The availability of temporal artery ultrasound and temporal artery biopsy in giant cell arteritis

Yasuhiro Nohda, Saori Hatachi, Saki Mukohara, Norihiko Amano, Katsuhiko Yoneda, Soshi Takahashi, Miwa Nishida, Shunichi Kumagai

Conflict of interest: None

[Object] Temporal artery biopsy (TAB) has long been the gold standard for the diagnosis of giant cell arteritis (GCA), but we need more accessible and less invasive tool. Recently, the availability of temporal artery ultrasound (TAU) is widespread. We examined the correlation between TAU and TAB. [Methods] We examined the results of TAU and TAB in 16 patients who fulfilled the 1990 ACR classification criteria for GCA between April 2010 and October 2018. [Results] Five patients had already received immunosuppressant therapy. All patients presented with new headache, temporal artery abnormality and elevation of erythrocyte sedimentation rate. In TAU, 15 patients had wall thickening, and 8 of whom had also hypo-echoic halo. In TAB, 13 patients had a positive biopsy. All 8 patients who had hypo-echoic halo in TAU demonstrated multinucleated giant cells and fragmentation of lamina in TAB. On the other hand, in 7 patients who had nonspecific wall thickening in TAU, 5 patients had a positive but 2 had a negative biopsy. [Conclusions] TAB may not be necessary if hypo-echoic halo is observed in TAU. On the other hand, TAB is useful in case who had only nonspecific wall thickening in TAU.

W3-6

Consideration of picture images and establishment of foundation knowledge for eradicate blindness about Giant cell arteritis

Toshio Kawamoto¹, Michihiro Ogasawara¹, Souichiro Nakano², Yuko Matsuki-Muramoto¹, Masakazu Matsushita¹, Kenjiro Yamanaka³, Ken Yamaji¹, Naoto Tamura¹

¹Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan, ²Internal Medicine and Rheumatology, Juntendo Tokyo Koto Geriatric Medical Center, ³Internal Medicine and Rheumatology, Juntendo University Koshigaya Hospital

Conflict of interest: None

[Object] In the 2018 EULAR recommendations, IVUS and MRI are the first-choice diagnostic methods, while CTA and PET/CT are considered alternative methods. Since IVUSs and CTAs may be as useful as biopsies or PET/CTs in the diagnosis of GCA, we evaluated multiple cases. [Methods] The clinical and serological characteristics, imaging findings, and biopsy findings from 14 cases of GCA from our hospital, within the past 5 years were compared and evaluated. [Results] With respect to the aggregated results of the findings obtained from our hospital over the past 5 years, CTA sensitivity for GCA diagnoses was 84%, and CTAs were considered to have favorable clinical utility. Four out of 6 cases had positive biopsy results and positive CTA findings, and cases with negative CTA findings also had negative findings as a result of other imaging tests, indicating that biopsy is indispensable in cases involving negative imaging findings. [Conclusions] We believe that the use of CTA, in conjunction with noninvasive IVUS, is useful as a diagnostic imaging method for GCA. We propose a GCA diagnostic approach that considers the usage of a temporal artery biopsy. We are going to establish foundation knowledge for eradicate blindness by constructing GCA hotline with neurology and ophthalmology.

W4-1

Change in immune phenotype by the treatment of large vessel vasculitis

Shingo Nakayamada, Yusuke Miyazaki, Hiroko Yoshinari, Akio Kawabe, Ipei Miyagawa, Satoshi Kubo, Shunsuke Fukuyo, Shigeru Iwata, Kazuhisa Nakano, Yoshiya Tanaka
The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: Yes

[Object] The pathogenesis of large vessel vasculitis (LVV) such as Takayasu arteritis (TAK) and giant cell arteritis (GCA) consists of an immune abnormality; however, little is known about pathological immune cell subsets in LVV. [Methods] PBMC were obtained from 18 LVV patients (TAK 6, GCA 12) and 14 healthy donors (HD). Phenotype of im-

mune cells was defined by flow cytometric analysis. [Results] The proportion of activated Th17 cells, Tfh cells in TAK and that of activated Th17 cells and Th1 cells in GCA were higher compared with HD. The immunosuppressive therapy improved the disease activity in all patients. The frequency of Tfh cells in TAK and that of Th1 cells in GCA was reduced by 24-week treatment with high dose glucocorticoid (GC). However, the frequency of Th17 cells was not changed by high dose GC. Of note, tocilizumab decreased the proportion of activated Th17 cells and increased the proportion of Treg cells in both TAK and GCA. [Conclusions] These results imply that IL-6 blockade may alter the balance of Th17/Treg cells by reducing Th17 but increasing Treg cell in LVV patients.

W4-2

Clinical features of large vessel vasculitis

Yui Kosumi, Hiroyuki Nakamura, Hiroshi Iesaka, Toshiyuki Watanabe, Tetsuya Horita
Tomakomai City Hospital, Tomakomai, Japan

Conflict of interest: None

[Object] To clarify clinical features of large vessel vasculitis (LVV). [Methods] Consecutive patients who were diagnosed with giant cell arteritis (GCA) or Takayasu arteritis (TA) from 2010 to 2018 were enrolled in this retrospective study. We clarified clinical characteristics and evaluated efficacy of radiographical and pathological examination for the diagnosis of LVV. [Results] A total of 32 patients were diagnosed with LVV (GCA; 26, TA; 6). Median age was 69 and 26 years old, respectively. Nineteen (73%) patients with GCA and all with TA were female. Fever was the most frequent symptom, which was found in 16 (62%) patients with GCA and 5 (83%) with TA, followed by headache in 12 (46%) with GCA and melalgia in 3 (50%) with TA. Out of 21 patients who were performed with temporal artery biopsy, 11 were diagnosed with biopsy-proven GCA. Seven out of 11 biopsy-proven GCA patients had neither headache nor under jaw claudication. All patients with GCA and TA were treated with glucocorticoids. Due to the lack of treatment efficacy, immunosuppressive agents were added to 9 and 4 patients with GCA and TA, respectively. [Conclusions] Temporal artery biopsy might be recommended for patients with suspicion of GCA regardless of head symptoms.

W4-3

Validation of a score for assessment of radiologic damage in large-vessel vasculitis (Combined Arteritis Damage Score, CARDS)

Daiki Nakagomi^{1,2}, Kei Kobayashi^{1,2}, Shunsuke Furuta³, Kimie Harama⁵, Shunichiro Hanai^{1,2}, Takeyuki Kanzaki⁵, Takao Sugiyama⁴, Hiroshi Nakajima³, Kenichiro Kitamura^{1,2}

¹Third Department of Internal Medicine, University of Yamanashi Hospital, ²Center for Clinical Immunology and Rheumatology, University of Yamanashi Hospital, ³Department of Allergy and Clinical Immunology, Chiba University Hospital, ⁴Department of Rheumatology, Shimoshizu Hospital, National Hospital Organization, ⁵Department of Internal Medicine, Yamanashi Prefectural Central Hospital

Conflict of interest: None

Objective This study aimed to validation a radiologic damage score in large-vessel vasculitis (LVV) which was proposed to determine the optimized weight of imaging findings. Methods We identified 59 TAK and 62 GCA patients from four Hospitals in Japan. We evaluated stenosis, occlusion and aneurysm in 25 arterial regions from carotid artery to iliac artery with enhanced CT or MRI / MRA. We calculated the "Combined Arteritis Damage Score (CARDS)". That was number of mild stenosis, $<50\% \times 0.6 +$ number of moderate to severe stenosis, $50-99\% \times 1.2 +$ number of occlusions $\times 1.6 +$ number of aneurysms $\times 0.8$. We compared CARDS to patient background. Results Mean age at onset in TAK was 29 years and GCA was 70 years. Female was 83% in TAK, 74% in GCA. The median of delay from symptom onset to diagnosis was 7 months in TAK, and 3 months in GCA. Median CRP and ESR level at diagnosis was 7.6mg/dl and 70mm/h in TAK, and 8.5mg/dl and 80mm/h in GCA. Frequency of arterial lesion including stenosis, occlusion and aneurysm were higher in TAK than GCA. As a result, median CARDS was higher in TAK than GCA. Conclusion TAK was severer than GCA in radiologic damage in Japanese cohort. This results supports that TAK and GCA in

LVV are different diseases.

W4-4

Study on the relationship between serum ALP and giant cell arteritis

Shogo Furukawa, Kumiko Shimoyama, Daisuke Suzuki, Noriyoshi Ogawa

Division of Immunology and Rheumatology, Hamamatsu University School of Medicine

Conflict of interest: None

[Object] Vasculitis has few biomarkers (e.g. CRP, ESR), and there are cases in which diagnosis and treatment are difficult. It is reported that serum ALP is elevated at the time of diagnosis of large-vessel vasculitis and normalized in response to treatment. Therefore, we examined the relationship between vasculitis and ALP in Japanese patients with large-vessel vasculitis. [Methods] We studied 19 cases of giant cell arteritis diagnosed from 2000 to 2019. We examined these cases retrospectively by dividing two groups, ALP elevated group (ALP group) and the control group. [Results] There were 4 cases (21%) in the ALP group. The CRP level was higher (14.3 vs 8.39 mg/dL) as compared with the control group. ESR (120.7 vs 103 mm/h) and the platelet count (50.2 vs $36.6 \times 10^4 / \mu\text{L}$) were also higher. AST (38.7 vs 25 U/mL) and ALT (61.2 vs 24.0 U/mL) were slightly higher in the ALP group. There was only one case in both groups that showed loss of visual acuity. Serum ALP decreased promptly in response to the treatment in the all 4 cases of ALP group. [Conclusions] The mechanism of ALP elevation and the pathological significance in large-vessel vasculitis are not clear. ALP could be a novel biomarker for large-vessel vasculitis, further accumulation of cases is necessary.

W4-5

The risk of cranial ischemic complications due to giant cell arteritis is related to the period of clinical manifestations

Yusuke Yoshida, Kei Araki, Hiroki Kohno, Tomohiro Sugimoto, Kazutoshi Yukawa, Tatsuomi Kuranobu, Tadahiro Tokunaga, Katsuhiro Ohi, Sho Mokuda, Keisuke Oda, Takaki Nojima, Shintaro Hirata, Eiji Sugiyama

Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan

Conflict of interest: None

[Object] To clarify the risk factors of cranial ischemic complications (CICs) such as ischemic optic neuropathy or stroke in patients with giant cell arteritis (GCA) [Methods] Patients diagnosed with GCA at our hospital were consecutively registered from January 2009 to September 2018. The diagnosis of GCA was made by 1990 ACR criteria for GCA. [Results] A total of 19 patients were diagnosed with GCA. The mean age was 75.8 years old and 10 were males. Temporary artery (TA) abnormality on examination, positive for TA ultrasound, positive for TA biopsy and the complication of polymyalgia rheumatica (PMR) and CICs were observed in 73.7%, 70%, 87.5%, 42.1% and 26.3%, respectively. The mean period from the onset of PMR symptoms, such as arthralgia or myalgia, or general symptoms to the diagnosis of GCA was 6.4 months. And that of GCA symptoms, such as new onset of headache, awareness of TA abnormality or jaw claudication, was 1.9 months. All of the patients who were within 2 weeks from GCA symptom onset to GCA diagnosis didn't develop CICs, but the patients over 10 months from the onset of PMR or general symptom to GCA diagnosis developed CICs more frequently. [Conclusions] The long period from the onset of symptoms to the diagnosis can be a risk factor of CICs in patients with GCA.

W4-6

Outcome of 115 patients with polymyalgia Rheumatica (PMR)

Akiko Ueno, Kei Hirose, Manami Hirata, Yuriko Yamamura, Noriya Momoki, Masahiro Yamamura

Department of Rheumatology, Okayama Saiseikai General Hospital

Conflict of interest: None

[Object] To invest the outcome of PMR patients diagnosed with 2012 EULAR / ACR PMR classification criteria [Methods] We have followed up 115 patients diagnosed with 2012 EULAR/ACR criteria of PMR. [Results] Male / female ratio: 1: 1.26, age of onset 73.9 ± 9.9 years old, observation period 44.5 ± 26.1 months, 6 out of 115 patients diagnosed as cancer within 2 years, 7 of whom died did. Three patients had spondyloarthritis, three had rheumatoid arthritis, one had ANCA-associated vasculitis, and one had unexploded arthritis and diagnosis changed. There was no change in PMR diagnosis for 101 other people. 41 out of 101 people recurred, 30 additional MTXs, 8 additional TCZs, outcome on the left: 47 healing cases. Maximum amount of steroids and platelets was high, and cases with low IgA were highly flared. [Conclusions] These results indicate that other diseases were merged or diagnosed during the course of 12.1%, and reexamination of the diagnosis / condition at the time of relapse was important.

W5-1

Risk factors for clinical fracture in RA patients

Shuko Tsumoto¹, Kentaro Inui², Yuko Sugioka², Tadashi Okano², Masahiro Tada³, Tatsuya Koike⁴, Hitoshi Yoshimura¹, Hiroaki Nakamura²
¹Saiseikai Nakatsu Hospital, Osaka, Japan, ²Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine, Osaka Japan, ³Department of Orthopedic Surgery, Osaka City General Hospital, Osaka, Japan, ⁴Shirahama Hamayu Hospital Orthopedic Surgery, Osaka Japan

Conflict of interest: None

[Object] We examined how bone quality would influence the rate of clinical fracture with 8 year cohort study. [Methods] Using the date of cohort study (TOMORROW, UMIN00003876), we examined risk factors for clinical fracture using multiple regression analysis. We measured BMD and also pentosidine/non-carboxyl osteocalcin/homocysteine as the marker of bone quality. [Results] Comparing RA patients (RA) and volunteers (Vo), the level of bone quality marker was higher in RA, but number of fractures showed no difference. Comparing fracture group (Fx), and non-fracture group (nFx), age (average age Fx;58.2 years, nFx;62.9 years) and urine pentosidine (average Fx;60.2 $\mu\text{g}/\text{mg}/\text{Cr}$, nFx;75.6 $\mu\text{g}/\text{mg}/\text{Cr}$) was significantly higher, BMD was significantly lower in Fx. Age (OR;1.05, 95%CI 1.02-1.09, $p < 0.001$) was a significant risk factor for fracture by logistic multi regression analysis including existence of RA/age/sex/BMI. BMD was an inhibitor of fracture (OR;0.04, 95%CI 0.004-0.51, $p = 0.013$). Bone quality marker and BMD rate of change were not the predictive factors for clinical fracture. [Conclusion] The rate of clinical fracture of RA was same as the Vo. It is also revealed that bone quality marker are not the predictive factor and BMD rate was the suppressive factor for clinical fracture.

W5-2

Influence on disease activity and inflammatory biomarkers provided by orthopedic reconstruction surgery in patients with rheumatoid arthritis

Junji Hayashi, Sachiko Araki, Satoshi Nakamura, Yukihiko Sato
Joint Reconstruction & Rheumatic Center, Niizashiki Central General Hospital

Conflict of interest: None

[Object] To examine the effect of orthopedic reconstruction surgery on disease activity and inflammatory biomarkers in patients with rheumatoid arthritis. [Methods] 87 patients who were passed 2years after surgery and did not undergo other orthopedic surgery in the past 2years were investigated. We investigated the transition of DAS28, CRP, MMP-3, mHAQ before and 2years after surgery. In addition, we classified it into two groups, a treatment strengthening group which started, increased and switched bDMARDs after surgery, and another treatment maintenance group, and examined the transition in the same way. Logistic regression analysis was also performed for each parameter between the two groups. [Results] DAS28, CRP, MMP-3, and mHAQ were significantly lower after surgery than before surgery. In both DAS28 and MMP-3, both groups were significantly decreased after surgery. Significant differences were found between the two groups in terms of age, MTX use, DAS28, CRP

and MMP-3 at the time of surgery, and knee joint surgery. [Conclusions] Orthopedic reconstruction surgery alone can improve disease activity, inflammatory biomarkers. However, when knee joint surgery is performed for younger patients with high disease activity and inflammatory biomarkers, there is a high possibility that treatment will be strengthened

W5-3

Relation between radiographic findings before total joint arthroplasty and backgrounds in rheumatoid arthritis patients

Nobuyuki Asai^{1,2}, Shuji Asai², Toshihisa Kojima², Nobunori Takahashi², Takuya Matsumoto², Yasumori Sobue², Tsuyoshi Nishiume², Mochihito Suzuki², Naoki Ishiguro²

¹Department of Orthopaedic Surgery and Rheumatology, NHO Nagoya Medical Center, Nagoya, Japan, ²Department of Orthopedic Surgery, Nagoya University School of Medicine, Nagoya, Japan

Conflict of interest: None

[Object] The present study was undertaken to investigate relation between radiographic findings before total joint arthroplasty and backgrounds in RA patients. [Methods] This study included 317 RA patients who underwent primary total joint arthroplasty (knee, hip, elbow, and ankle) in Nagoya University Hospital from 2007 to 2017. We conducted multivariate analysis for patient characteristics between osteophyte group (n = 229) and non-osteophyte group (n = 88). [Results] Disease duration (17 vs 13 years), rate of TEA (14% vs 6%), and rate of CRP negative (48% vs 28%) were significantly higher, and prednisone use (45% vs 63%) was significantly lower in osteophyte group than non-osteophyte group. Multivariate analysis showed disease duration (OR: 1.04, 95% CI: 1.01-1.07), prednisone use (OR: 0.49, 95% CI: 0.29-0.83), and CRP negative (OR: 2.16, 95% CI: 1.25-3.73) contributed to osteophyte formation. [Conclusions] In RA patients without use of prednisone and with CRP negative, radiographic findings show osteophyte formation before total joint arthroplasty.

W5-4

Are clinical symptoms related with hindfoot alignment after hindfoot fusion in rheumatoid arthritis?

Hiromu Ito, Ryo Sugita, Takuya Tomizawa, Koichi Murata, Shuichi Matsuda

Department of Orthopaedic Surgery, Kyoto University Graduate School of Medicine

Conflict of interest: Yes

[Object] Hindfoot arthrodesis is the major operative treatment for destructed joints and disability of the hindfoot in patients with rheumatoid arthritis (RA). However, the relationship between clinical outcome and postoperative alignment remains unveiled. [Methods] We conducted a prospective comparative study in a hindfoot operation cohort. A total of 37 hindfoot arthrodesis conducted for RA patients out of 80 total operations were followed for at least one year with a complete data set and were eligible for further analyses. Clinical outcome was compared between OA and RA patients using JSSF ankle/hindfoot scale, and the association between the scale and postoperative alignment was analyzed. [Results] Clinical outcome significantly improved from 40.8 to 56.4 postoperatively. However, the outcome was better in non-RA patients with the score of 70.1, postoperatively. The postoperative alignments were significantly worse in Calcaneal pitch in RA than in OA. Patients with flatfoot deformity showed worse outcome than non-flatfoot patients both in RA and non-RA patients, and RA group had more flatfoot patients than non-RA group. [Conclusions] Flatfoot deformity could be a contributing factor for worse clinical outcome in RA patients who underwent hindfoot arthrodesis.

W5-5

Surgical outcome of lumbar spinal instrumented and fusion in patients of lumbar spinal disorders with rheumatoid arthritis

Hiroshi Takahashi, Arata Nakajima, Masato Sonobe, Manabu Yamada, Shiho Nakano, Koichi Nakagawa

Department of Orthopaedic Surgery, Toho University Sakura Medical

Center

Conflict of interest: None

[Object] To evaluate the surgical outcome of lumbar spinal instrumented and fusion in patients of lumbar spinal disorders with rheumatoid arthritis (RA). [Methods] 10 patients of RA who underwent lumbar instrumented and fusion surgery from 2011 to 2017 (RA group) and 31 consecutive patients of non-RA patients who underwent TLIF from 2016 to 2017 (C group) were included. We evaluated the rate of screw loosening (RA group: 90, C group: 138 screws), fusion rate using X-ray and CT at the final follow-up, and clinical outcome using VAS and ODI. [Results] The rate of screw loosening was 23.3% (21/90) in RA group whereas 5.8% (8/138) in C group that indicated a significant increase of screw loosening was observed in RA group compared with that in C group (p<0.01). Especially in the RA group, the rate of screw loosening of 6 patients using steroid is 27.3% (24/88). On the other hands, the fusion rate was 70% (7/10) in RA group whereas 83.8% (26/31) in C group that did not show significant difference. VAS and ODI showed significant improvement in RA group as well as C group. [Conclusion] In the lumbar spinal instrumented fusion of patients with RA, screw loosening occurred at a high rate. However, the fusion rate and clinical improvement in RA group was favorable compared with non-RA group.

W5-6

Perioperative management in RA treated with Tofacitinib

Tomomitsu Hashiguchi, Seiichi Kawamura, Kenichi Seo
The Department of Orthopedic Surgery, Japanese Red Cross Oita Hospital

Conflict of interest: None

[Object] Tofacitinib (TOF) inhibits the multiple cytokines involved in the inflammatory cascade, hence there is concern over the side effect of infection. The perioperative management of RA treated with TOF is a major concern among orthopaedic surgeons. On the other hand, it is unknown about delayed wound healing (DWH) and surgical site infection (SSI), flare up of rheumatic symptoms in RA treated with TOF during the perioperative period. The purpose of this study is to investigate DWH/SSI and flare up of the disease in patients with RA to make an useful perioperative guideline. [Methods] Between January 2015 and October 2018, we experienced 23 operations in RA patients treated with TOF. The average pre-operative TOF discontinuation period was 2.3 days. Oral administration of TOF was restarted after removal of stitches and the total perioperative discontinuation of TOF was 18.7 days on an average. [Results] In this study, 2 of 23 cases had DWH, and Flare up of RA occurred in 9 of 23 cases on average 13.3 days after discontinuation of TOF. [Conclusions] We require further investigation about DWH/SSI and flare up of rheumatic symptoms during perioperative period in RA treated with TOF.

W6-1

Bone mineral density in postmenopausal women correlates with body mass index for lumbar spine, while it correlates with muscular volume for proximal femur

Ichiro Yoshii¹, Tatsumi Chijiwa², Naoya Sawada³

¹Rheumatology and Musculoskeletal Medicine, Yoshii Hospital, ²Department of Rheumatology, Kochi Memorial Hospital, ³Department of Rheumatology, Dohgo Spa Hospital

Conflict of interest: None

[Object] Factors that influence on bone mineral density (BMD) for postmenopausal women in each part of lumbar spine and proximal femur were analyzed statistically. [Methods] BMD was measured for 426 postmenopausal women from May to August 2018. Their BMD were re-calculated for the correction of age, and each of these values in lumbar spine (LS), femoral neck (FN), greater trochanter (GT), and whole femur (WF) was set as dependent variant, while creatinine cystatin-C ratio (Cr/CysC), rheumatoid arthritis suffered (RA), body mass index (BMI), history of spinal compression fracture or severe deformity due to osteoarthritis (DS), glucocorticoid steroid administration for more than three months

(GCS), were set as independent variant. Then statistical evaluations were performed with multivariate linear regression analysis. Significant level was set within 5%. [Results] LS correlated with RA and BMI, while FN, GT, and WF correlated with Cr/CysC and RA, significantly. [Conclusions] There is different mechanism influencing on BMD between LS and femur. In LS, BMI, namely gravity has influence on BMD, while muscular volume had influence in proximal femur. Common factor was RA.

W6-2

Factors that affect bone mineral density in rheumatoid arthritis patient Different factors work separately on each of lumbar spine and femur

Ichiro Yoshii¹, Tatsumi Chijiwa², Naoya Sawada³

¹Rheumatology and Musculoskeletal Medicine, Yoshii Hospital, ²Department of Rheumatology, Kochi Memorial Hospital, ³Department of Rheumatology, Dohgo Spa Hospital

Conflict of interest: None

[Object] Factors that influence on bone mineral density (BMD) for rheumatoid arthritis (RA) patient in each part of the lumbar spine and proximal femur were analyzed statistically. [Methods] BMD was measured for 197 postmenopausal women from May to August 2018. Each BMD in lumbar spine (LS) and femoral neck (FN) was set as dependent variant, while age, sex, glucocorticoid administration for more than 3 months (GCS), creatinine cystatin-C ratio (Cr/CysC), 28-joints disease activity score (DAS28), modified Health Assessment Questionnaire (mHAQ), each component of EuroQol 5-dimensions (EQ-5D) were set as independent variant. Then statistical evaluations were performed with single and multivariate linear regression analysis (SLR and MLR). Significant level was set within 5%. [Results] Significant factors in LS were age, sex, GCS, DAS28, mHAQ, and gait, prepare and activity of EQ-5D with SLR, and sex, DAS28, and mHAQ with MLR, while age, sex, GCS, Cr/CysC, mHAQ, and pain of EQ-5D with SLR, and age and sex with MLR. [Conclusions] There is different mechanism influencing BMD between LS and femur in RA patient. In treating osteoporosis for RA patients, attention to their age, sex, and BMD in each bone area must be paid.

W6-3

Risk factors for lumbar and femoral bone loss in patients with rheumatoid arthritis (RA)

Noriko Sasaki, Takayuki Wakabayashi, Yasuo Suzuki

Division of Rheumatology, Tokai University Hachioji Hospital, Tokyo, Japan

Conflict of interest: None

<Objective and methods> To clarify the risk factors for lumbar and femoral bone loss, we measured bone mineral density (BMD) of lumbar spine (L2-4) and femoral neck and investigate the following factors; age/gender, BMI, duration of RA, stage/class, disease activity (DAS), RA therapy in 263 patients with RA (male 34, female 229, mean age 68.7). Among them, 139 patients were taking glucocorticoid (GC). Influence of RA activity and therapy for osteoporosis was investigated in 145 patients whose BMD was measured at more than 2 points. <Results> The patients who showed lower lumbar BMD (<80% YAM) also had lower BMD of femoral neck and distal radius. However, lower femoral BMD was not associated with lower lumbar and radial BMD. Old age, female, and BMI were identified as risk factors for both lumbar and femoral bone loss. In contrast, loss of femoral BMD was associated with high disease activity with elevated ESR and CRP, the duration of RA, and advanced stage. About a half of patients who were not taking medicine for osteoporosis showed reduction of BMD at both sites. About 80% and 60 % of the patients who were treated with denosumab and bisphosphonates respectively, showed an increase in femoral BMD. femoral BMD in RA patients.

W6-4

Early efficacy of bisphosphonate and denosumab on bone microstructure in rheumatoid arthritis

Ikuko Tanaka¹, Takashi Kato², Motokazu Kai³, Kunikazu Ogawa³,

Hiroaki Mizuno¹, Hisaji Oshima⁴, Shigenori Tamaki¹

¹Nagoya Rheumatology Clinic. Nagoya, Japan, ²Department of Radiology, National Center for Geriatrics and Gerontology, Obu, Japan, ³Mie Rheumatology Clinic. Suzuka, Japan, ⁴Department of Connective Tissue Disease. Tokyo, Japan, Tokyo Medical Center

Conflict of interest: None

[Object] Rheumatoid arthritis (RA) is a risk factor for osteoporosis. In this study, the early effect on bone microstructure by osteoporosis treatments was examined in RA patients using HR-pQCT. [Methods] 16 subjects treated with Bisphosphonate (group B) and 6 patients treated with Denosumab (group D) who examined with HR-pQCT within 3 to 6 months after starting administration were included. [Results] Total volumetric Bone Mineral Density (Tt.vBMD) was significantly higher in Group D compared to Group B (P <0.05) in the pre-treatment measurements. In the comparison before and after treatment, there was a significant increase in cortical vBMD (Ct.vBMD) in Group B (p <0.01), while in Group D, Tt.vBMD (P <0.01), Ct.vBMD (P <0.05), inner trabecular vBMD was significantly increased (P <0.05). In the comparison of the changes before and after the administration, Tt.vBMD (P <0.01), the cortical area (P <0.05), trabecular vBMD (P <0.05), the meta trabecular vBMD (P <0.05) of D group increased significantly. [Conclusions] In RA patient using HRpQCT, both Bisphosphonate and Denosumab showed an increase in Ct.vBMD in the early stage of administration, and Denosumab showed effects in trabecular bone.

W6-5

Study on early effect of daily teriparatide with HR-pQCT in rheumatoid arthritis patients with marked reduction in cancellous bone

Ikuko Tanaka¹, Takashi Kato², Motokazu Kai³, Kunikazu Ogawa³, Hiroaki Mizuno¹, Hisaji Oshima⁴, Shigenori Tamaki¹

¹Nagoya Rheumatology Clinic. Nagoya, Japan, ²Department of Radiology, National Center for Geriatrics and Gerontology, Obu, Japan, ³Mie Rheumatology Clinic. Suzuka, Japan, ⁴Department of Connective Tissue Disease, Tokyo Medical Center, Tokyo, Japan

Conflict of interest: None

[Purpose] In this study, we examined the change in bone microstructure 3 month after administration of daily teriparatide (dPTH) to RA patients with remarked reduction of cancellous bone at the distal radius using HR-pQCT. [Subject and method] The bone microstructure of 6 patients (group P) treated with dPTH and 12 patients (group B) treated with bisphosphonate were analyzed. [Result] There was no significant difference in total bone mineral density (BMD) and cortical BMD, and the cancellousBMD was significantly lower in group P (15.4 ± 17.2 mg / cm³) than in group B (55.7 ± 22.1 mg / cm³) before treatment. Changes before and after treatment were examined. In group P, there was a significant increase with total BMD (p = 0.0073), cortical BMD (p = 0.0004), inner cancellous BMD (p = 0.0318), trabecular bone width (p = 0.013). In group B, there was a significant increase in cortical BMD (p = 0.0012), cancellous BMD (p = 0.0039), inner cancellous BMD (p = 0.0007), mean cortical pore size (p = 0.0326), trabecular number (p = 0.0373). Group P significantly increased with BMD (p = 0.043) as compared with the group B. "Conclusion" Improvement was observed both in cortical bone and cancellous bone at 3 month after dPTH treatment in RA patients with markedly decreased cancellous bone.

W6-6

Relation between varus alignment and posterior slope of the tibial articular surface in knees with medial osteoarthritis

Ryuji Nagamine¹, Weijia Chen¹, Toru Suguro²

¹Center of Artificial Joint and Rheumatism, Fukuoka Tokushukai Medical Center, ²Research Institute of Rheumatology Medical Treatment

Conflict of interest: None

[Object] Relation between varus angle (VTA) and posterior slope angle (PTS) of the tibial articular surface (TAS) was assessed in 100 case with medial OA and 21 cases with RA. [Methods] In each case, the VTA between the anatomical axis of the tibia and the TAS on the AP view ra-

diograph of the tibia and the PTS between the line along the anterior cortex of the tibial shaft and the TAS on the lateral view radiograph of the knee were measured. The angle AWC between the line along the anterior cortex and the anterior wall of the tibial condyle was also measured. [Results] The mean \pm SD of VTA and PTS was $6.5^\circ \pm 2.5^\circ$ and $9.2^\circ \pm 3.8^\circ$, respectively in OA and was $4.7^\circ \pm 4.0^\circ$ and $10.2^\circ \pm 3.9^\circ$, respectively in RA. The mean \pm SD of AWC in OA was $15.6^\circ \pm 6.7^\circ$. AWC had a significant correlation with PTS. No correlation was found between VTA and PTS. VTA in OA was significantly larger than that in RA. No significant difference was found between PTS in OA and that in RA. The posterior slope of the TAS was created by the posterior rotation of the tibial condyle. We propose a concept of "constitutional posterior rotation". [Conclusions] There was no correlation between the varus angle and the posterior slope angle of the tibial articular surface even in knees with medial osteoarthritis.

W7-1

MMP-3 and bone mineral density in Japanese patients with juvenile idiopathic arthritis from nationwide survey for the core facilities specialized in pediatric rheumatism

Kosuke Shabana¹, Nami Okamoto¹, Hiroaki Umebayashi², Naomi Iwata³, Yuka Okura⁴, Tomohiro Kubota⁵, Masaki Shimizu⁶, Yasuo Nakagishi⁷, Kenichi Nishimura⁸, Mao Mizuta⁶, Masato Yashiro⁹, Takahiro Yasumi¹⁰, Junko Yasumura¹¹, Hiroyuki Wakiguchi¹², Masaaki Mori¹³

¹Department of Pediatrics, Osaka Medical College, ²Department of General Pediatrics, Miyagi Children's Hospital, ³Department of Immunology and Infectious Diseases, Aichi Children's Health and Medical Center, ⁴Department of Pediatrics, KKR Sapporo Medical Center, ⁵Department of Pediatrics, Kagoshima University Graduate School of Medicine, ⁶Department of Pediatrics, Graduate School of Medical Sciences, ⁷Department of Pediatric Rheumatology, Hyogo Prefectural Kobe Children's Hospital, ⁸Department of Pediatrics, Yokohama City University Graduate School of Medicine, ⁹Department of Pediatrics, Okayama University Hospital, ¹⁰Department of Pediatrics, Kyoto University Graduate School of Medicine, ¹¹Department of Pediatrics, Hiroshima University Graduate School of Biomedical & Health Sciences, ¹²Department of Pediatrics, Yamaguchi University Graduate School of Medicine, ¹³Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences

Conflict of interest: None

[Object] We conducted a large-scale survey of MMP-3 and bonemineral density (BMD) for juvenile idiopathic arthritis (JIA) in Japan. [Methods] This first nation-wide epidemiological research on JIA was organized by the study group of Ministry of Health, Labour and Welfare at January 2017. We analyzed MMP-3, BMD (DEXA, L2-4) and administration of treatment. [Results] The data of 726 JIA patients from 15 core facilities were evaluated. MMP-3 was not correlated with JIA disease type but with age. In the cases of non-glucocorticoid (GCs) administration under 12 years old, 76% sensitivity and 64% specificity were indicative of clinical remission if MMP-3 was $<10\text{ng/mL}$. BMD was measured in 250 cases. BMD was low in cases with long cumulative GCs dosing period. Pathological fractures occurred in 11 patients (10 cases are Systemic JIA), and the z-score was less than -3 in 5 of the 8 patients for whom z-score was calculated. There was a significant difference in the cumulative duration of GCs administration between patients with and without a history of pathological fractures (Median 13 months, 157 months, $p < 0.01$). [Conclusions] The BMD and MMP-3 in JIA in Japan were clarified. It was considered that the risk of pathological fracture was high in JIA with long administration period of GCs.

W7-2

Long term illness activity, functional outcomes, and work productivity in juvenile idiopathic arthritis patients

Takayuki Kishi^{1,2}, Yumi Tani^{1,2}, Eiichi Tanaka³, Katsunori Ikari⁴, Toru Igarashi⁵, Tsuyoshi Matsuyama⁶, Satoshi Fujikawa⁷, Eisuke Inoue^{3,8}, Takako Miyamae^{1,2}, Atsuo Taniguchi³, Satoru Nagata¹, Hisashi Yamanaka³

¹Department of Pediatrics, Tokyo Women's Medical University, ²Pediatric Rheumatology, Institute of Rheumatology, Tokyo Women's Medical University, ³Department of Rheumatology, Institute of Rheumatology, Tokyo Women's Medical University, ⁴Department of Orthopaedics, Tokyo

Women's Medical University, ⁵Department of Pediatrics, Nihon Medical University, ⁶Matsuyama Clinic, ⁷Fujikawa Clinic, ⁸Division of Medical Informatics, St. Marianna University

Conflict of interest: None

[Object] We examined juvenile idiopathic arthritis (JIA) patients for long-term illness activity, functional outcomes and work productivity using the Japanese Health Assessment Questionnaire (HAQ), Disease Activity Score (DAS) 28, Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI) and Work Productivity and Activity Impairment (WPAI). [Methods] A retrospective review of these outcomes was performed in 39 patients (Female: 95%) with JIA who were diagnosed before the age of 16. The median follow-up duration was 21 years. [Results] The median age at onset of illness in patients was 14 years, and at evaluation was 34 years. The median JHAQ, DAS28, SDAI, and CDAI scores were 0.1, 2.4, 5.3, and 4.8, respectively. Fifty-four percent of patients received NSAIDs at last follow up and 38% received biologic agents. Eighty-seven percent of patients had a job at time of evaluation and had worked 40 hours in one week. The illness condition was affected work productivity in 47% of patients. Work productivity was significantly associated with JHAQ and CDAI. [Conclusions] The majority of patients were maintained with low disease activity and achieved functional remission during long time follow up. The work productivity was associated with functional outcomes.

W7-3

Experience of using Certolizumab Pegol for patients with intractable juvenile idiopathic arthritis in transition phase

Yuko Akutsu¹, Mariko Mouri², Tomohiro Morio¹, Masaaki Mori²

¹Department of Pediatrics, Tokyo Medical and Dental University, Tokyo, Japan, ²Department of Lifetime Clinical Immunology, Tokyo Medical and Dental University, Tokyo, Japan

Conflict of interest: None

[Background] Biologic agents in Japan for polyarticular juvenile idiopathic arthritis (JIA) are four of tocilizumab, etanercept, adalimumab and abatacept as of October 2018. [Object] We studied whether Certolizumab Pegol (CZP) can be administered effectively and safely to the intractable JIA patients in transition phase. [Methods] The subjects were 8 JIA patients (16-26 years old, median 20.5 years) in a phase of transition 16 years age or older who were ineffective in multiple biologic agents. In all cases, the loading dose was administered and the number of tender and swollen joints, patient VAS, doctor VAS, laboratory findings (CRP, MMP-3, etc.), concomitant medications (prednisolone, methotrexate, other DMARDs) were monitored. [Results] In all cases, the symptoms and laboratory findings were improved by 12 weeks after the administration, and concomitant medications could be reduced by a certain amount. Also, no serious adverse events occurred. In 2 cases, it was tracked from the administration until 202 weeks, but the adverse effect of long-term administration was not observed. [Conclusion] CZP is no application for pediatric use and can not be used for JIA cases under 16 years of age, but it was suggested that it is an effective and safe drug for intractable transitional cases.

W7-4

Chest computed tomography (CT) findings in patients with anti-MDA5 antibody-positive juvenile dermatomyositis (JDM) complicated by interstitial pneumonia (IP)

Asami Oohara¹, Haruna Nakaseko¹, Kazuko Yamazaki², Kenichi Nishimura³, Yutaka Nishida⁴, Yuichi Yamasaki⁵, Shunichiro Takezaki⁶, Satoshi Sato⁷, Norimoto Kobayashi⁸, Takayuki Kishi^{9,12}, Motomu Hashimoto¹⁰, Ichiro Kobayashi¹¹, Shinji Akioka¹², Masaaki Mori¹³

¹Department of Infection and Immunology, Aichi Children's Health and Medical Center, ²Department of Pediatrics, Saitama Medical Center, Saitama Medical University, ³Department of Pediatrics, Yokohama City University School of Medicine, ⁴Department of Pediatrics, Gunma University School of Medicine, ⁵Department of Pediatrics, Kagoshima University Hospital, ⁶Department of Pediatrics, Hokkaido University Hospital, ⁷Division of Infectious Disease and Immunology, Saitama Children's Medical Center, ⁸Department of Pediatrics, Shinshu University Depart-

ment of Medicine, ⁹Department of Pediatrics, Tokyo Women's Medical University, ¹⁰Department of Advanced Medicine for Rheumatic Diseases, Kyoto University, ¹¹Center for Pediatric Allergy and Rheumatology, KKR Sapporo Medical Center, ¹²Department of Pediatrics, Kyoto Prefectural University of Medicine, ¹³Lifetime Clinical Immunology, Tokyo Medical and Dental University

Conflict of interest: None

[Object] To investigate the chest CT findings related to treatment resistance in patients with anti-MDA5 antibody-positive JDM with IP. [Methods] A multicenter collateral retrospective study. The pattern of CT findings before and after corticosteroid + cyclosporine and/or cyclophosphamide (ground-glass opacity [G], consolidation [C], reticulation [R], or nodule [N]) and the changes were investigated. [Results] Eleven CT images from 10 patients at the time of initial onset and relapse were obtained. The outcomes included 2 mortalities and 8 surviving cases. Before treatment, [G] was observed in all cases, [C] in 7 cases, [R] in 10 and [N] in 3. In the mortality cases, diffuse [G] (central lobular distribution (c): 1 case, c+ panicular lobular distribution (p): 1 case) were observed before treatment. In both cases, [G] did not improve even after treatment. In the surviving cases, diffuse p [G]: 2 cases, random c+p [G]: 1 case, upper lobular p [G]: 1 case, lower lobular c [G]: 1 case/p [G]: 4 cases. After treatment, [G] improved/disappeared promptly in 7 cases. Finally, [C][N][R] remained, but [G] disappeared. [Conclusions] Special attention may be needed in patients with diffuse [c] including c [G] before treatment as well as in cases where [G] does not improve even after treatment.

W7-5

Nephrotoxicity after long-term use of calcineurin inhibitors in patients with juvenile lupus nephritis

Masao Ogura¹, Kentaro Nishi¹, Shuichi Ito^{1,2}

¹pediatric Nephrology and Rheumatology, National Center for Child Health and Development, ²Department of Pediatrics, Yokohama City University

Conflict of interest: None

[Object] Efficacy of calcineurin inhibitors (CNI) for lupus nephritis (LN) has been established, but irreversible nephrotoxicity may occur as long-term use. However, there has been few report focusing on CNI nephrotoxicity in patients with LN. [Methods] Among patients with juvenile LN who were treated in our institute between April 2008 and April 2018. We performed renal biopsy after more than two years from initiation of CNI. [Results] Renal biopsy was performed in 6 patients (male 4, female 2). Tacrolimus (Tac) was used in 5 and cyclosporine (CsA) in one. The median age of CNI initiation was 11.1 years old, the median time from CNI initiation to renal biopsy was 2.3 years (2.2-4.8 years). The eGFR at CNI initiation and at renal biopsy was 111.8 and 100.8 ml/min/1.73 m², respectively (p=0.06). The vascular toxicity of CNI was confirmed in 2 cases; arteriovenous meandering (3.9 years Tac use) and arteriolar sclerosis (4.8 years Tac use). No patient developed glomerular sclerosis or interstitial fibrosis. [Conclusions] As our patients were treated with relatively low dose of CNI, CNI nephrotoxicity might be mild and could be reversible. However, our study suggests that renal biopsy for evaluation of CNI nephrotoxicity should be considered if patient use CNI more than 3 years.

W7-6

Cytokine profile of macrophage activation syndrome associated with Kawasaki disease

Naoto Sakumura, Hitoshi Irabu, Maiko Takakuwa, Natsumi Inoue, Mao Mizuta, Masaki Shimizu

Department of Pediatrics, School of Medicine, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University

Conflict of interest: None

[Object] To clarify the kinetics of cytokine release and to compare the accuracy of serum biomarkers for the diagnosis of macrophage activation syndrome (MAS) complicating Kawasaki disease (KD). [Methods] We analysed serum IL-18, neopterin, IL-6, sTNFR-I and II levels in 78 pa-

tients with KD including 5 MAS by enzyme-linked immunosorbent assay. Results were compared with the clinical features of KD and MAS. [Results] Serum IL-18, neopterin, sTNFR-II levels and sTNFR-II/I ratio were significantly elevated in KD patients with MAS compared with those in patients with acute-phase of KD before the administration of intravenous immunoglobulin. Receiver operating characteristic curve analysis revealed area under the curve values and cut off values of IL-18, neopterin, sTNFR-II levels and sTNFR-II/I ratio were 0.9813/1165 ng/ml, 0.9750/30.0 nmol/l, 0.9969/16600 pg/ml, and 0.9875/4.475, respectively. Serum sTNFR-II levels correlated positively with disease activity including serum AST, LDH and ferritin levels. [Conclusions] IFN- γ and TNF- α are closely associated with the pathogenesis of MAS associated with KD as well as MAS associated with other diseases such as systemic juvenile idiopathic arthritis. Serum sTNFR-II might be a useful marker to diagnose the transition to MAS from active-phase KD.

W8-1

Identification of disease related T cell pathways in rheumatoid arthritis

Masaru Takeshita¹, Katsuya Suzuki¹, Yasushi Kondo¹, Yuumi Okuzono², Keiko Koga², Yoshiaki Kassai², Kanae Gamo^{2,3}, Maiko Takiguchi², Rina Kurisu², Hideyuki Mototani², Yukihiko Ebisuno², Tsutomu Takeuchi¹

¹Keio University, ²Takeda Pharmaceutical Company Limited, Research, Immunology Unit, ³FIMECS Inc.

Conflict of interest: Yes

[Object] T cells are considered to be important for the pathogenesis of rheumatoid arthritis (RA). This study aims to identify the features of RA T cells that are most relevant to disease. [Methods] We recruited 10 untreated RA patients, 10 patients receiving MTX monotherapy, 10 patients receiving MTX and IFX, 10 patients receiving TCZ monotherapy, and 10 age- and gender-matched healthy controls. We freshly sorted CD4-Tn, Tem, Tem and CD8-Tn, Tem, Tem, and Temra from their peripheral blood. CD4 and CD8 T cells from 4 synovial fluid of RA were also sorted. In total, 358 samples were prepared and underwent transcriptome analysis. [Results] Samples from peripheral blood clustered according to developmental stage rather than according to the presence of RA or treatment status, whereas synovial fluid T cells seemed to be the most developed. We identified several pathways, such as mTORC1, IL-2-stat5, cell cycle, and interferon-related genes, that were significantly enriched in synovial fluid, in particular, as well as peripheral blood of RA patients, and interestingly, these features reverted after treatment. [Conclusions] We identified several T cell pathways that were enriched in the synovial fluid and were also observed in the peripheral blood associated with disease status.

W8-2

Abatacept modulates phenotype of circulating monocytes in patients with rheumatoid arthritis (RA)

Ryosuke Fukue, Yuka Okazaki, Masataka Kuwana

Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine

Conflict of interest: None

[Object] Abatacept (ABT) inhibits T-cell activation, but recent evidence has indicated that it exerts direct effects on circulating monocytes through CD80/CD86. We investigated effects of ABT on phenotype of circulating monocytes in RA patients. [Methods] We enrolled RA patients with moderate or high disease activity, who were started on ABT or other disease-modifying anti-rheumatic drugs (DMARDs), and whole blood was obtained before, and at 3 months and 6 months after treatment introduction. Whole blood were also obtained from the patients under stable treatment with ABT or other DMARDs for at least 6 months. Multi-color flow cytometry was employed to measure mean fluorescence intensity of CD16, CD32, CD40, CD54, CD62L, CD64, CD80, CD86, CD181, CD182, CD184, CD191, CD192, CD273, CD274, CD275, HLA-DR, and CX3CR1 expressed on CD14+ monocytes. [Results] During ABT treatment, expression levels of CD184, HLA-DR, and CX3CR1 were increased, and those of CD64 and CD273 were decreased. Whereas, patients treated with non-ABT DMARDs exhibited increased expression of

CD64 and CX3CR1, and decreased expression of CD191. There was no phenotypic difference between patients on stable ABT and non-ABT DMARD treatment. [Conclusions] Circulating monocyte phenotype is modulated during treatment with ABT.

W8-3

The evaluation of clinical course of elderly onset rheumatoid arthritis (EORA) for the five-years period in the NinJa registry

Shigeru Yoshizawa¹, Motoki Yoshimura¹, Toshihiro Matsui², Shigeto Tohma³

¹Department of Rheumatology, National Hospital Organization Fukuoka Hospital, ²Department of Rheumatology, National Hospital Organization Sagami Hospital, ³National Hospital Organization Tokyo Hospital

Conflict of interest: None

[Object] To evaluate the disease activity of elderly onset rheumatoid arthritis (EORA) patients in the database of *NinJa* 2012 and 2017 registry. [Methods] The EORA patients of early RA (Disease duration <2 years) registered in both 2012 and 2017 were compared with young onset RA patients. The patients were classified to three groups due to the age of RA onset, group A (G-A) (<65 years old), group B (G-B) (≥65, <75 years old) and group C (G-C) (≥75 years old). [Results] The number of each group were 313 in G-A, 149 in G-B and 59 in G-C. The ratio of Steinbrocker's Stage classification 3+4 in G-A, G-B and G-C were 5.4%, 6.4%, and 11.1% in *NinJa* 2012, and 12.8%, 15.4%, and 24.1% in *NinJa* 2017, respectively. DAS28-ESR in G-A, G-B and G-C were 3.05, 3.42, and 3.16 in *NinJa* 2012, and 2.45, 2.82, and 2.74 in *NinJa* 2017. The ratio of administration of MTX in G-A were 71.6% in 2012 and 69.6% in 2017, and in G-C were 59.3% and 53.4%, respectively. The ratio of administration of Biologics in G-A were 10.9% in 2012 and 23.6% in 2017, and in G-C were 16.9% and 22.4%, respectively. [Conclusions] EORA, especially in the group of the onset age more than 75, may be more progressive disease than young-onset RA in Steinbrocker's Stage classification despite of the equally medication in *NinJa* registry.

W8-4

Central Sensitization in patients with rheumatoid arthritis using the central sensitization inventory

Moe Saitou, Kentaro Noda, Taro Ukichi, Yohsuke Oto, Kazuhiro Otani, Masayuki Yoshiga, Haruyasu Ito, Ken Yoshida, Daitaro Kurosaka
The Jikei University School of Medicine

Conflict of interest: None

[Purpose] The pain of rheumatoid arthritis (RA) is thought to be nociceptive. However, recent studies indicate that RA pain also includes the mechanism of central sensitization (CS). We therefore examined the prevalence of CS among RA patients and the clinical characteristics of these patients. [Methods] The central sensitization inventory (CSI) was used to evaluate 235 outpatients with RA. The disease activity, depression and anxiety, Neuropathic-like pain, Fibromyalgia and health-related quality of life (HRQOL) were evaluated. We compared the clinical parameters between the patients with (CSI≥40) and without (CSI<39) CS. [Results] Eighteen (8.30%) of the RA patients had CS according to the CSI. A multivariate analysis of the clinical parameters associated with CS showed significant differences in EGA (OR 0.597), pain VAS (OR 1.14), FAS-31 (the fibromyalgia activity score 31) (OR 1.89), physical (OR 0.515), mental (OR 0.437), and role-social (OR 0.658) component summary scores on the Short-Form 36-Item Health Survey. [Conclusion] Among RA patients with CS, there was a dissociation between EGA and the pain VAS. The proper treatment of CS in RA patients may improve their HRQOL.

W8-5

Research of risk factors related to progression of upper cervical lesion in patients with rheumatoid arthritis under biologics

Hideo Sakane¹, Yukio Yonemoto¹, Takahito Suto¹, Koichi Okamura¹, Tetsuya Kaneko^{1,2}, Masahiro Tachibana^{1,3}, Chisa Okura^{1,4}, Hirotaka Chikuda¹

¹Department of Orthopaedic Surgery, Gunma University Graduate School

of Medicine, Maebashi, Gunma, Japan, ²Department of Orthopaedic Surgery, Fukaya Red Cross Hospital, Fukaya, Saitama, Japan, ³Department of Orthopaedic Surgery, Kiryu Kosei General Hospital, Kiryu, Gunma, Japan, ⁴Department of Orthopaedic Surgery, Gunma Saiseikai Maebashi Hospital, Maebashi, Gunma, Japan

Conflict of interest: None

[Methods] We studied 21 patients (male; 3, female; 18) with RA that we could evaluate plain X-ray of the cervical spine and joint (shoulder, elbow, hip, knee, ankle) at the baseline and at 3 years. Patients with RA were 67 years old on average and had mean disease duration of 18 years. Eighty six percent of patients used MTX concomitantly, 5.9mg/week on average, 33% of patients used prednisolone. All patients treated with biologics (infliximab; 2, adalimumab; 8, etanercept; 3, tocilizumab; 8). Evaluation of the cervical spine was X-ray lateral image and atlantodental interval (ADI) and Ranawat values were measured, and the joint destruction of the limb was evaluated by ARASHI score. Serum marker (CRP, ESR, MMP-3), disease activity score (DAS28-ESR) at baseline and 6 months were evaluated. [Results] The increase in ADI was 52.4%, the decrease in Ranawat value was 47.6% at 3 years. There was correlation between the change in ADI and DAS28-ESR at 6 months and its change. But there was no correlation between the change in ADI and the progress of joint destruction in ARASHI score. The correlation between the change in Ranawat value and each parameter was not clear. [Conclusions] Early improvement of the disease activity may delay the progression of the cervical spine lesion in RA.

W8-6

Search for genes associated with the onset age of rheumatoid arthritis

Marowa Hashimoto¹, Keiko Funahashi^{1,2}, Kosuke Okuda², Koji Fukuda³, Shinya Hayashi³, Akira Sagawa⁴, Hiroaki Matsuno⁵, Tomomaro Izumihara⁶, Eisuke Shono⁷, Kou Katayama⁸, Toyomitsu Tsuchida⁹, Mitsuhiro Iwahashi¹⁰, Tomomi Tsuru¹¹, Motohiro Oribe¹², Tsukasa Matsubara^{1,2}

¹Research Institute of Joint Diseases, Kobe, Japan, ²Matsubara Mayflower Hospital, Kato, Japan, ³Department of Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan, ⁴Sagawa Akira Rheumatology Clinic, Sapporo, Japan, ⁵Matsuno Clinic for Rheumatic Diseases, Toyama, Japan, ⁶Izumihara Rheumatic and Medical Clinic, Kagoshima, Japan, ⁷Shono Rheumatology Clinic, Fukuoka, Japan, ⁸Katayama Orthopedic Rheumatology Clinic, Asahikawa, Japan, ⁹Tsuchida Clinic, Chiba, Japan, ¹⁰Higashi-hiroshima Memorial Hospital, Higashihiroshima, Japan, ¹¹PS Clinic, Fukuoka, Japan, ¹²Oribe Rheumatism and Internal Medicine Clinic, Oita, Japan

Conflict of interest: None

[Object] Rheumatoid arthritis (RA) increases in incidence and prevalence with age until about 50 years old in Japanese. As the one of causes of difference in the number of onset of RA among generations, it seems that genetic factors affect the difference. In this study, we searched for genes associated with the onset age of RA. [Methods] The subjects were 805 Japanese female patients of RA (≥17 years old). Illumina Human-Hap300K, Human610-Quad or HumanOmniExpress chip were used for genotyping. SNPs used in this study were common among these 3 chips and were 178,753 SNPs. The average age of onset of RA were compared among genotypes using Bonferroni-corrected genome-wide association study (GWAS). [Results] As the result of GWAS, rs843346 ($p = 10^{-4.2}$) on *AP2M1* (Adaptor Related Protein Complex 2 Subunit Mu1) was found among SNPs with comparative lower P value. The average age of onset of RA with rs843346 (G>A) were 42.7 years old (GG carrier), 46.3 years old (GA carrier) and 48.9 years old (AA carrier). [Conclusions] It has been suggested that AP2M1 plays an important role in regulating the intracellular trafficking and function of CTLA-4. Thus, *AP2M1* genotypes may affect the age of onset of RA by regulating CTLA-4 related to suppressing autoimmune disease.

W9-1

Finger joint cartilage evaluated by ultrasound in patients with rheumatoid arthritis

Takehisa Ogura, Ayako Hirata, Norihide Hayashi, Sayaka Takenaka, Hideki Ito, Yuki Inoue, Chihiro Imaizumi, Kennosuke Mizushima, Takaharu Katagiri, Yuto Takakura, Hideto Kameda
Division of Rheumatology, Department of Internal Medicine Toho University Ohashi Medical Center

Conflict of interest: None

[Object] Joint destruction in RA includes both bone and cartilage lesions. Since joint space narrowing (JSN) by X-ray is not a direct evaluation of cartilage, we aimed to examine the validity of ultrasound (US) cartilage evaluation in patients with RA. [Methods] We enrolled 103 RA patients in remission or low disease activity and 42 healthy subjects in this study. The cartilage thickness of bilateral MCP and PIP joints of 2nd to 5th fingers was measured by US, followed by the semiquantitative scoring of the recorded images on a scale of 0-2. In addition, JSN of corresponding joints was scored with a hand X-ray. The relationships among the three methods were assessed by Spearman's rank correlation coefficient. [Results] The total cartilage thickness was significantly thinner in RA patients than those in healthy subjects, and the subsequent semiquantitative sum of 16 joints was significantly greater in RA patients than those in healthy subjects. In RA patients, JSN score showed a significant correlation with cartilage thickness and semiquantitative score ($\rho=0.57$; $p<0.001$, $\rho=0.66$; $p<0.001$, respectively). Furthermore, those scores showed a significant correlation with RA disease duration. [Conclusions] Finger joint cartilage damage by US is valid and useful in patients with RA.

W9-2

Prediction of the recurrence after adalimumab discontinuation by using ultrasound assessment -PROUD study-

Tadashi Okano¹, Kenji Mamoto¹, Tatsuya Koike^{2,3}, Yuko Sugioka², Masahiro Tada⁴, Makoto Wada⁵, Ryota Hara⁶, Takanori Fujimura⁷, Sho Sendo⁸, Takaichi Okano⁸, Yoshihide Ichise⁸, Ikuko Naka⁸, Heiseki Yu⁹, Akihiko Nakabayashi¹⁰, Yoshinobu Matsuura¹⁰, Takahiro Yoshikawa¹¹, Masao Tamura¹¹, Masayasu Kitano¹¹, Yasuhide Kanayama¹²
¹Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan, ²Center for Senile Degenerative Disorders (CSDD), Osaka City University Graduate School of Medicine, Osaka, Japan, ³Shirahama Foundation for Health and Welfare, Wakayama, Japan, ⁴Department of Orthopaedic Surgery, Osaka City General Hospital, Osaka, Japan, ⁵Inflammation and Immunology Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan, ⁶The Center for Rheumatic Diseases, Nara Medical University, Nara, Japan, ⁷Department of Internal Medicine, Takanoara Central Hospital, Nara, Japan, ⁸Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, ⁹Toue Naika Riumachika, ¹⁰Division of Rheumatology and Clinical Immunology, Sakai City Medical Center, Osaka, Japan, ¹¹Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, Hyogo, Japan, ¹²Department of Orthopedic Surgery, Department of Rheumatology, Toyota Kosei Hospital, Toyota, Japan

Conflict of interest: Yes

[Object] We investigated the usefulness of ultrasonography (US) to predict relapse in remission patients with RA after discontinuation of biological DMARDs. [Methods] The patients using adalimumab (ADA) and in remission (DAS28-CRP<2.6) for more than 24 weeks were included in this multicenter prospective study. ADA was stopped and followed up until week 52 and predictive factor for relapse at 24 and 52 weeks was analyzed from baseline clinical data including US examination. ADA was restarted at the time in relapse (DAS28-CRP \geq 3.2). US assessment was performed at 0, 12, 24, 36 and 52 weeks and the time of relapse and modified Total Sharp Score (mTSS) was evaluated at 0, 24, and 52 weeks by conventional X-ray. [Results] Fifty-three cases were included and 10 cases (18.9%) were relapse up to week 24 and 20 cases (37.7%) were up to 52 weeks. The relapse patients tended to have long disease duration, but baseline US findings could not predict relapse. Increases in PD score were seen during follow-up in some relapsed patients. Disease activity

control was good after restarted ADA in relapsed group, and there was no difference in the progression of mTSS in both relapsed and non-relapsed groups. [Conclusions] It was difficult to predict relapse by US after discontinuation of ADA in remission.

W9-3

Ultrasound-guided synovial biopsy is both safe and tolerable technique with enough quality synovial tissue for clinical assessment

Yasushi Kondo^{1,2}, Katsuya Suzuki², Shinji Sato¹, Tsutomu Takeuchi²
¹Division of Rheumatology, Tokai University School of Medicine, ²Division of Rheumatology, Keio University School of Medicine

Conflict of interest: None

[Object] To clarify the safety, tolerability and clinically usefulness of ultrasound (US)-guided synovial biopsy technique. [Methods] Undifferentiated arthritis patients who needed histopathological assessment to determine the cause of arthritis were recruited. All patients were undergone US-guided synovial biopsy and completed a tolerability questionnaire prior to and following biopsy procedures. Synovial tissue was harvested for histopathological analysis and bacterial culture. [Results] Nine patients were included in this analysis and 5 patients were biopsied from wrist and 4 were from knee joint. The mean frequencies of biopsies were 8.1 times per procedure. No significant complications include hematoma, infections and nerve injury were reported following the procedure. We found no significant changes in pain, swelling and stiffness of biopsy sites from before and after procedures. Synovial tissue samples were almost enough quality to assess histopathological analysis and useful for diagnosis of infection or amyloidosis associated arthritis. [Conclusions] US-guided synovial biopsy is a safe and well-tolerated technique for obtaining enough quality of synovial tissue for clinical assessment.

W9-4

Significance of power Doppler ultrasonography for the assessment of response to therapy in peripheral Spondyloarthritis

Keita Fujikawa¹, Tomohisa Uchida¹, Yushiro Endo², Akinari Mizokami¹, Masanobu Mine³, Atsushi Kawakami²

¹Department of Rheumatology, Japan Community Healthcare Organization, Isahaya General Hospital, ²Department of Immunology and Rheumatology, Unit of Advanced Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, ³Department of Rheumatology, Suga Orthopedic Hospital

Conflict of interest: None

[Object] This study investigated the response to therapy of peripheral Spondyloarthritis (pSpA) by power Doppler ultrasonography (PDUS). [Methods] A total 26 patients with active pSpA (24 of uSpA and 2 of PsA) who were treated with csDMARDs or bDMARDs and followed up for more than 6 months were recruited. We assessed the articular synovia, tendons and tendon sheaths, and entheses by PDUS at baseline and follow-up. We evaluated the synovitis score (0-28), tenosynovitis score (0-10), and enthesitis score (0-16) by PDUS and disease activity. [Results] The disease activity decreased from baseline to follow-up; DAPSA from 19.9 to 9.4, ASDAS-CRP from 2.0 to 1.3. 19 patients (73%) fulfilled DAPSA remission criteria. The number of patients with PDUS synovitis decreased from 19 (81%) to 3 (19%), PDUS tenosynovitis 21 (81%) to 5 (19%), and PDUS enthesitis from 26 (100%) to 18 (69%). The synovitis score improved from 1.9 to 0.2, tenosynovitis score from 3.0 to 0.2, enthesitis score from 4.4 to 1.7 ($p<0.001$, respectively). There was no correlation between each PDUS score and DAPSA or ASDAS-CRP at baseline and follow-up. [Conclusions] This study indicated that synovitis, tenosynovitis and enthesitis by PDUS reflected active inflammation of pSpA and were useful for monitoring the disease activity.

W9-5

The high prevalence of sonographic psoriatic arthritis findings in psoriasis patients without musculoskeletal pain and its clinical significance

Yuya Tabuchi¹, Motomu Hashimoto², Shuji Akizuki¹, Ran Nakashima¹,

Kosaku Murakami¹, Hajime Yoshifuji¹, Masao Tanaka², Koichiro Ohmura¹, Kohei Nishitani³, Koichi Murata³, Hiromu Ito³, Tsuneyo Mimori¹

¹Department of Rheumatology and Clinical Immunology, The Graduate School of Medicine, Kyoto University, Kyoto, Japan, ²Department of Advanced Medicine of Rheumatic Diseases, The Graduate School of Medicine, Kyoto University, Kyoto, Japan, ³Department of Orthopedics, The Graduate School of Medicine, Kyoto University, Kyoto, Japan

Conflict of interest: None

[Object] To examine the prevalence of sonographic psoriatic arthritis (PsA) in psoriasis patients without musculoskeletal (MSK) pain, and its significance. [Methods] We evaluated 38 consecutive psoriasis outpatients January 2017 to March 2018, using power Doppler (PD) and color superb microvascular imaging (cSMI). The dorsal side of the hand (tendons and joints of the digits and wrist) and the Leeds Enthesitis Index (LEI) points on the dominant side were scanned. [Results] In the hand, 82 % with MSK pain (n=14 of 17), whose patient's pain VAS or evaluator's pain VAS was not zero, were PD positive and 88% were cSMI positive, while 71% without MSK pain (n=15 of 21) were PD positive and 95% were cSMI positive. At the LEI points, 29% with MSK pain were PD positive and 29% were cSMI positive, while 24% without MSK pain were PD positive and 33% were cSMI positive. The most frequent Doppler positive sites were the extensor tendons around the PIP joints. The cSMI positivity on any LEI point in patients without MSK pain was positively correlated with ESR, not but CRP. [Conclusions] There was a high prevalence of sonographic PsA findings even in patients without MSK pain, and the cSMI positivity at the LEI points positively correlated with ESR in those patients.

W9-6

Indicators for active musculoskeletal ultrasound findings of psoriatic arthritis vary on each body part

Shuji Sumitomo¹, Shoko Tateishi^{1,2}, Harumi Shirai¹, Kumiko Ono⁴, Jun Hirose⁴, Ayumi Yoshizaki³, Yoshihide Asano³, Shinichi Sato³, Sakae Tanaka⁴, Keishi Fujio¹, Kazuhiko Yamamoto¹, Hiroko Kanda^{1,2}

¹Department of Allergy and Rheumatology, The University of Tokyo, Graduate School of Medicine, ²Department of Clinical Laboratory Medicine, The University of Tokyo, Graduate School of Medicine, ³Department of Dermatology, The University of Tokyo, Graduate School of Medicine, ⁴Department of Orthopaedic Surgery, The University of Tokyo, Faculty of Medicine

Conflict of interest: None

[Object] In this study, the musculoskeletal ultrasound (MSUS) findings were divided into seven body parts (fingers, wrist joints, elbows, shoulders, knees, ankle joints, toes), and the relationship between the clinical index of psoriatic arthritis (PsA) and the MSUS findings of each part was examined. [Methods] Total 98 PsA consecutive cases who fulfilled CASPAR criteria were evaluated. PASDAS, DAPSA, PASI, DAS28-CRP, DAS28-ESR, BASDAI, SDAI, CDAI, CPDAI were calculated. MSUS evaluated 60 joints, 16 entheses and 24 tendons. The relationship between the clinica scores and the MSUS findings of 7 body parts was analyzed using the Random forest and the Receiver Operating Characteristic (ROC) curve analysis. [Results] DAS 28 in the fingers, wrist, and ankle, BASDAI in the elbow, shoulder and knee is most predictive of active MSUS findings (PD>= 1 in joints or tendons or positive for inflammation scores of adhesion inflammation). [Conclusions] Composite measures predicting active MSUS findings were different according to body parts. BASDAI is important when considering elbow, shoulder and knee, which is presumably related to the importance of the element of enthesitis in these parts. Careful evaluation according to each part is considered important for prediction of MSUS.

W10-1

Retrospective Analysis of clinical features of Methotrexate related LymphoProliferativeDiseases (MTX-LPD) patients with Rheumatoid Arthritis (RA) diagnosed at our hospital

Ryohei Nagata¹, Hiroshi Takei², Sho Ishigaki¹, Yoshiro Kanayama¹, Yuto Takakura¹, Mayu Nagata¹, Satoshi Kawaai², Megumi Iwasaki¹, Ryo

Hazue², Hiroaki Taguchi², Yasuo Ohson², Yutaka Okano²

¹Department of General Internal Medicine, Kawasaki Municipal Kawasaki Hospital, ²Center for Arthritis and Rheumatic Diseases, Kawasaki Municipal Kawasaki Hospital

Conflict of interest: None

[Object] To clarify the clinical features of poor prognosis MTX-LPD of RA patients in our hospital. [Methods] 26 (22 women, 4 men) of MTX-LPD diagnosed cases from April 2010 to June, 2018 were retrospectively studied by medical record about poor prognosis defined with death or relapse after chemotherapy. [Results] 2 high RA-disease activity and 7 cases with complication of grade 3 or more related to LPD were included. Of 21 biopsies cases, 16 came to malignant lymphoma (ML) diagnosis. There were 10 spontaneous regressions, including a relapse after regression, 15 chemotherapy cases, 2 relapses after chemotherapy and 6 deaths. To compare poor prognosis cases with not, no difference was found about age and MTX dose/duration. B symptoms (85.7 and 22.2%), mean CRP (9.42 and 2.39 mg/dL), LDH (628 and 326 U/mL), and sIL-2R (7667 and 2260 U/mL) were significantly higher in poor prognosis (P<0.05). About Performance Status (P.S) decline (P.S ≥3), difference was not found in the comparison (P=0.07), but the correlation of P.S decline with B symptom, CRP and sIL-2R was found (P<0.05). The diagnosis of ML was not correlated with prognosis. [Conclusions] Clinical findings related to the severity of LPD which lowers P.S, rather than diagnosis of ML, is suggested to be significant prognostic factor for MTX-LPD.

W10-2

Clinicopathological analysis of methotrexate-associated lymphoproliferative disorders in rheumatoid arthritis

Takahiro Okai, Eigo Kikuchi, Naoko Aoki, Taro Yoshioka

Center for Rheumatology and Joint Surgery, Kawakita General Hospital, Tokyo, Japan

Conflict of interest: None

[Object] To analyze of methotrexate-associated lymphoproliferative disorders (MTX-LPD) in rheumatoid arthritis (RA). [Methods] We performed a retrospective analysis of the RA patient characteristics, clinical features and treatment outcomes of cases with MTX-LPD who were treated from 2008 to 2017 in our center. MTX-LPD was diagnosed based on the histological examination and/or the radiographic findings. [Results] There were 21 RA patients with MTX-LPD (mean ages: 77.6 years, mean disease duration of RA: 14.3 years). There were elderly and long RA duration compared with non MTX-LPD RA patients. 14 patients performed histological examination (diffuse large B-cell lymphoma (n=5), immunoblastic T-cell lymphoma (n=2), non-neoplastic tissue (n=4)). Spontaneous regression occurred in 62% (13/21) after MTX discontinuation. 33% (7/21) required additional chemotherapy and/or radiotherapy. Regression was associated with low clinical stage of LPD, low LDH and low soluble IL-2 receptor at the diagnosis of LPD. [Conclusions] The early detection of LPDs and the early cessation of MTX are important for the management of RA patients especially elderly and longstanding history of RA.

W10-3

Clinical features of rheumatoid arthritis complicated by MTX-LPD

Masaru Yoshimura, Hideki Kasahara, Miyuki Bohgaki

NTT-East Sapporo Hospital

Conflict of interest: None

[Objectives] We aim to analyze clinical features of MTX-LPD in our department. [Methods] We examined the clinical pictures of 17 MTX-LPD cases (LPD group), and retrospectively compared LPD group with 326 non MTX-LPD cases (non-LPD group) in 481 RA patients who had visited us as of October, 2018. [Result] In the LPD group, 8 patients had visited us before they developed MTX-LPD. They accounted for about 2.4 % of the total patients who had taken MTX in our department. The mean age at onset of MTX-LPD was 67.3±10.8 years, 12 patients were females and 5 were male. The mean disease duration of RA was 15.3±11.9 years, MTX dose was 9.1±2.6 mg/week, mean period of MTX

administration was 6.1±3.6 years, and total cumulative dose was 2359±1750 mg. Pathological findings included 2 follicular lymphoma, 4 DLBCL, 2 Hodgkin lymphoma, 1 lymphomatoid granulomatosis, and 2 polymorphic LPD. Five of 9 cases were EBER positive. The spontaneous regression after stopping MTX was detected 10 cases (58.8 %). The duration of RA in LPD group vs non-LPD group were 15.4±11.9 years vs 8.3±8.5 years (p<0.003). The Steinbrocker stage 3 or 4 were 58.8 % vs 20.2 % (p<0.0008). [Conclusion] This study has suggested that duration of RA and Stage 3 and 4 might be associated with development of MTX-LPD.

W10-4

Analysis of the predictive factor and mechanism about spontaneous regression of MTX-LPD

Tomohiro Kameda¹, Hiromi Shimada¹, Shusaku Nakashima¹, Yumi Nomura², Risa Wakiya¹, Mikiya Kato¹, Taichi Miyagi¹, Hiroaki Dobashi¹
¹Department of Internal Medicine, Division of Hematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University, Kagawa, Japan, ²Department of Orthopaedic Surgery, Kagawa University, Kagawa, Japan

Conflict of interest: None

[Object] Recently, There are some reports that the Epstein-Barr virus infection or change of peripheral lymphocyte counts (PLC) after MTX discontinuation is related to spontaneous regression of LPD. We investigate the predictive factor for spontaneous regression and the mechanism of MTX-LPD. [Methods] We enrolled RA patients who developed MTX-LPD, and divided into patients who were followed-up after the discontinuation of MTX alone (SR group) and patients who were received chemotherapy (CTx group). The following differences between the two groups were examined: 1) change of PLC after MTX discontinuation, 2) CD8 positive lymphocyte and expression of Granzyme B (GZB) that is the marker of activated T cell of lesion specimen using immunohistochemistry (IHC). [Results] We enrolled 50 MTX-LPD patients, and divided into 34 patients in SR group and 16 patients in CTx group. In SR group, the PLC significantly elevated after MTX discontinuation. In addition, we investigated 12 cases (7 in SR group and 5 in CTx group) that were performed IHC of specimen. CD8 positive lymphocyte counts and the expression of GZB was lower in SR group than CTx group. [Conclusions] We consider that the PLC and the analysis of lymphocyte in biopsy specimen are predictive marker of the spontaneous regression of LPD.

W10-5

Clinicopathological analysis of the influence of calcineurin inhibitors on Lymphoproliferative disorders in patients with Rheumatoid arthritis

Yoshihiko Hoshida¹, Shiro Ohshima², Yukihiko Saeki², Atsushi Kaneko³, Masao Katayama³, Atsushi Hashimoto⁴, Kumiko Akiya⁵, Shigeru Yoshizawa⁶, Akira Okamoto⁷, Norie Yoshikawa⁸, Noriyuki Chiba⁹, Kenji Ichikawa¹⁰, Takao Sugiyama¹¹, Tomoya Miyamura¹², Akiko Mitsu¹³, Atsushi Ihata¹⁴, Koichiro Takahi¹⁵, Yasuo Suenaga¹⁶, Hiroshi Tsutani¹⁷, Fuminori Hirano¹⁸, Shunsuke Mori¹⁹, Shigeto Tohma²⁰

¹Department of Pathology, NHO Osaka Minami Medical Center, ²Department of Rheumatology, NHO Osaka Minami Medical Center, ³Department of Rheumatology, NHO Nagoya Medical Center, ⁴Department of Rheumatology, NHO Sagami National Hospital, ⁵Department of Rheumatology, NHO Tokyo Medical Center, ⁶Department of Rheumatology, NHO Fukuoka Hospital, ⁷Department of Rheumatology, NHO Himeji Medical Center, ⁸Department of Rheumatology, NHO Miyakonojo Medical Center, ⁹Department of Rheumatology, NHO Morioka Hospital, ¹⁰Department of Rheumatology, NHO Hokkaido Medical Center, ¹¹Department of Rheumatology, NHO Shimozu Hospital, ¹²Department of Rheumatology, NHO Kyusyu Medical Center, ¹³Department of Rheumatology, NHO Disaster Medical Center, ¹⁴Department of Rheumatology, NHO Yokohama Medical Center, ¹⁵Department of Rheumatology, NHO Toneyama Hospital, ¹⁶Department of Rheumatology, NHO Beppu Medical Center, ¹⁷Department of Rheumatology, NHO Awara Hospital, ¹⁸Department of Rheumatology, NHO Asahikawa Medical Center, ¹⁹Department of Rheumatology, NHO Kumamoto Saishunso Hospital, ²⁰NHO Tokyo National Hospital

Conflict of interest: None

[Object] Since 1999, TAC has been approved for the medical insurance adapted for patients with RA. Currently, approximately 10% of patients with RA received TAC. TAC administration is regarded as a risk factor of the onset of PT-LPD, especially in pediatric liver transplantation. However, whether TAC is related to LPD development like MTX-LPD among the patients with RA remains unclear. [Methods] Sixty-three patients with RA who had been receiving TAC treatment were enrolled for the study at 33 hospitals belonged to the National Hospital Organization. [Results] TAC-LPD and MTX-LPD showed similar clinicopathological characteristics. About 27% of TAC-LPD had developed LPD within 1 year after initiating TAC. In TAC-LPD, one case showed spontaneous regression with withdrawal of TAC only. The 5-year survival rate in TAC-LPD was significantly worse than that in MTX-LPD. Multivariate analysis revealed that TAC was an independent unfavorable prognostic factor. Among the regression cases that were withdrawn from MTX and/or TAC medication after LPD onset, the frequency of recurrence is higher in the cases of newly TAC administration than that in those of continuous TAC administration. [Conclusion] The RA patients taking calcineurin inhibitors should be taken care for the developing LPD.

W10-6

Clinical characteristics of the rheumatoid arthritis patients who developed lymphoproliferative disorder

Daisuke Kobayashi^{1,2}, Yoko Wada¹, Satoshi Ito², Akira Murasawa², Kiyoshi Nakazono², Hajime Ishikawa², Ichiei Narita¹

¹Division of Clinical Nephrology and Rheumatology, Niigata University, Niigata, Japan, ²Niigata Rheumatic Center, Niigata, Japan

Conflict of interest: None

[Object] To survey the clinical characteristics of patients with rheumatoid arthritis (RA) who developed Lymphoproliferative disorder (LPD). [Methods] Patient data were obtained retrospectively from medical records. Thirty-two patients (15 men, 17 women) developed a LPD (LPD group). We compared them with 96 patients without LPD (control group), who were matched for age, sex, and RA duration among 2,628 patients with RA who attended our outpatient department in 2017. [Results] The median patient age was 71.0 years, and the duration of RA was 15.5 years. Twelve patients were diagnosed with diffuse large B cell lymphoma, 6 with Hodgkin lymphoma, and 5 with T cell lymphoma; 9 patients had other diagnosis. Many patients in LPD group were Stage IV, and Class 3 or 4 (75.0% vs 42.7 %, p<0.01, 71.8% vs 53.1%, p<0.05, respectively). 75 % of patients were treated with MTX in LPD group, and 42.7 % in control (p= 0.0879). Although ESR, CRP, DAS28-ESR, CDAI were not different significantly in both group, MMP-3 is low in LPDs group (80.1 ng/mL vs 102 ng/mL, p<0.05). [Conclusions] Many patients in LPD group were Stage IV, and Class 3/4 compared to the patients without LPD. This might indicate cumulative disease activity were background for the development of LPD but not current disease activity.

W11-1

Early glucocorticoid therapy for the treatment of pneumocystis pneumonia in patients with systemic rheumatic disease with moderate to severe hypoxemia

Shin-ichiro Omura¹, Toshiaki Miyamoto², Daisuke Shichi³, Taio Naniwa¹

¹Department of Rheumatology, Nagoya City University, ²Department of Rheumatology, Seirei Hamamatsu General Hospital, ³Infectious Disease and Rheumatology, Seirei Mikatahara General Hospital

Conflict of interest: None

Objects: Evidence supporting adjunctive corticosteroids during the treatment of Pneumocystis jirovecii pneumonia (PCP) in adults without HIV is not clear. In the current study, we investigate the effectiveness of adjunctive corticosteroids for the treatment of PCP with hypoxemia. Methods: This retrospective cohort study include hospitalized patients with PCP with moderate to severe hypoxemia (A-aDO₂ ≥ 35mmHg, PaO₂ ≤ 70mmHg, SpO₂ < 90%). We compare the patients with or without early glucocorticoid therapy within 48hour after the diagnosis of PCP. Results: Among the 60 included patients, 53 patients received early glu-

cocorticoid therapy (EGT group) and 7 patients did not receive EGT (no EGT group). EGT groups was significantly lower prevalence of 30-day mortality, admission to the ICU, mechanical ventilations than those of no EGT group. Conclusions: The addition of EGT within 48 hour in patients with PCP with systemic rheumatic disease with moderate to severe hypoxemia were associated with improved respiratory outcomes.

W11-2

Prognosis factors associated with *Pneumocystis pneumonia* in systemic rheumatic disease

Shin-ichiro Omura¹, Toshiaki Miyamoto², Daisuke Shichi³, Taio Naniwa¹
¹Department of Rheumatology, Nagoya City University, ²Department of Rheumatology, Seirei Hamamatsu General Hospital, ³Infectious Disease and Rheumatology, Seirei Mikatahara General Hospital

Conflict of interest: None

Objective: To determine the prognostic factors associated with *Pneumocystis pneumonia* (PCP) in systemic rheumatic disease. **Methods:** We reviewed medical records of patients with systemic rheumatoid disease who developed *Pneumocystis pneumonia*. The diagnosis of PCP was based on following the three points, clinical symptoms, GGO on CT scan, and elevated B-D glucan or positive PCR test. The severity of hypoxemia was classified the CDC guideline. The primary outcomes was respiratory failure, including 30 day death, ICU admission, and ventilator support. **Results:** Of the 93 patients with PCP, 3 patients (3.2%) died of PCP. Nine patients developed respiratory failure and there were significantly differences regarding the proportion of severe hypoxemia, A-aDO₂ ≥ 45mmHg, in the diagnosis. A-aDO₂ ≥ 45mmHg in the diagnosis of PCP was independently associated with respiratory failure. **Conclusions:** We must administer anti-PCP drug and prednisolone if A-aDO₂ was ≥ 45mmHg.

W11-3

Long-term prognosis of rheumatoid arthritis patients who survive pneumocystis jirovecii pneumonia: comparison of the recent and old eras

Harunobu Iida¹, Hironari Hanaoka², Yukiko Takakuwa¹, Yoshioki Yamasaki¹, Kimito Kawahata¹

¹Division of Rheumatology and Allergology, St. Marianna University School of Medicine, ²Division of Rheumatology, Keio University School of Medicine

Conflict of interest: None

[Object] To evaluate the long-term survival of patients with rheumatoid arthritis (RA) who survived *Pneumocystis jirovecii* pneumonia (PCP), focusing on the era in which it was diagnosed. **[Methods]** Patients with RA who were diagnosed with PCP at our hospital from 2001 to 2017 were retrospectively evaluated. The patients were divided into 2 groups according to the era in which they were diagnosed: 2001-2008 and 2009-2017. We compared clinical characteristics when PCP was diagnosed and the last visit between groups. We also compared their cumulative survival rates. **[Results]** Eleven-patients were diagnosed with PCP in 2001-2008 and 19 in 2009-2017. Patients diagnosed with PCP in 2001-2008 were significantly younger than those diagnosed in 2009-2017 (p=0.01). On analysis of the last visit, patients diagnosed in 2001-2008 had a higher percentage of glucocorticoid (GC) use, higher dose of GC, and lower percentage of biologics use than those diagnosed in 2009-2017 (p<0.01, p=0.04, and p=0.02, respectively). Cumulative survival rate was significantly higher in 2001-2008 than 2009-2017 (p<0.01). The main cause of death was severe infection. **[Conclusions]** Survival of RA patients who experienced PCP may be improving. Alternative use of biologics for GC may contribute to this better outcome.

W11-4

Examination of availability and adverse events related to the dose of sulfamethoxazole-trimethoprim in rheumatic diseases

Tomoya Harada, Yuriko Sueda, Yoshihiro Funaki, Miki Takata, Ryota Okazaki, Akira Yamasaki

Department of Respiratory Medicine and Rheumatology, Tottori Univer-

sity Hospital, Yonago, Tottori, Japan

Conflict of interest: None

[Object] Infections are the most important prognostic factor in the patients of rheumatic diseases. Especially, *Pneumocystis pneumonia* (PCP) is a life-threatening infection, sulfamethoxazole-trimethoprim (TMP/SMX) is the most common prophylactic drug. Despite the efficacy of TMP/SMX, adverse events (AE) are high frequency and clinician often reduce the dose. **[Methods]** The patients who received TMP/SMX for prophylaxis and immunosuppressive therapy were included in this examination. The rates of AE and discontinuation, management of AE, and the incidence of PCP were retrospectively analyzed. **[Results]** 145 patients were included in normal-dose group (ND), and 75 were included in reduction-dose group (RD). Although AE were significantly high frequency in the ND (24.1% versus 10.7%, p=0.017), the rate of discontinuation of TMP/SMX was not significantly difference in both group (14.5% versus 8%, p=0.165). In ND, 14 patients were required reduction dose of TMP/SMX by AE and no patients developed PCP. The patients who occurred AE were more elderly, affected diabetes mellitus, and had deteriorated renal function. **[Conclusions]** The patients who received reduction dose of TMP/SMX does not occurred PCP. The dose reduction of TMP/SMX for prophylactic is available.

W11-5

Prognostic factors of pneumocystis pneumonia in non-HIV patients

Yohei Koide¹, Kazuko Yamamoto¹, Yushiro Endo², Tomohiro Koga², Atsushi Kawakami², Hiroshi Mukae¹

¹Department of Respiratory Medicine, Nagasaki University Hospital, Nagasaki, Japan, ²Department of Immunology and Rheumatology, Nagasaki University Hospital, Nagasaki, Japan

Conflict of interest: None

[Objectives] Non-HIV related pneumocystis pneumonia (PCP) is increasing with widespread immunosuppressive treatment, with high mortality. The aim of our study was to evaluate the prognostic factors of non-HIV-PCP patients. **[Methods]** This retrospective study evaluated non-HIV patients who were admitted in our hospital and diagnosed with PCP between April 2009 and September 2018. The patients were classified according to their hospital death and respiratory failure (SpO₂/FiO₂ < 300), and their backgrounds, laboratory data, and treatment were compared between groups. A *t* test and χ^2 test were used for statistics. **[Results]** Among 62 non-HIV-PCP patients, the most common underlying conditions were steroids (82.2%), lung diseases (45.1%), diabetes (37.0%), malignancies (32.2%), followed by rheumatoid arthritis (25.8%). Overall hospital mortality was 12.9%, and respiratory failure was detected in 25.8%. Higher performance status (p=0.046), solid cancer (p=0.014), interstitial pneumonia (p=0.002), pulmonary aspergillosis (p=0.033), lower serum albumin (p=0.035), higher CRP (p=0.024) were independently associated with hospital mortality. **[Conclusions]** Poor prognosis of non-HIV-PCP patients are mostly related to host immune status and underlying conditions, rather than the treatment received for PCP.

W11-6

Recurrence rate of PCP after starting immunosuppressive drugs with anti-pneumocystis drugs

Shin-ichiro Omura¹, Toshiaki Miyamoto², Daisuke Shichi³, Taio Naniwa¹

¹Department of Rheumatology, Nagoya City University, ²Department of Rheumatology, Seirei Hamamatsu General Hospital, ³Department of Rheumatology, Seirei Mikatahara General Hospital

Conflict of interest: None

Objectives: *Pneumocystis jirovecii* pneumonia (PCP) is not an uncommon opportunistic infection in systemic rheumatic disease in Japan. However, there have been no evidence of restarting immunosuppressive drugs after developing PCP. In this study, we investigate the recurrence of PCP after starting immunosuppressive drugs with anti-pneumocystis drugs. **Method;** Sixty patients was admitted to the hospital and 37 patients who restarted immunosuppressive drugs with anti-PCP drugs included in this study. **Results:** Twenty three patients received both metho-

trexate (MTX) and biologics (Bio), and 14 patients received MTX. All patients received anti PCP drugs, SMX/TMP;21, pentamidine;11, atovaquone;5. The observation period was 125 weeks. No patients developed PCP recurrence. However 1 patients developed PCP recurrence after the termination of anti-PCP drugs. Conclusion: It is possible that patients may have received immunosuppressive drugs with anti- PCP drugs after the development of PCP.

W11-7

Efficacy and Safety of Weekly One Tablet Sulfamethoxazole-trimethoprim for Chemoprophylaxis of Pneumocystis Pneumonia

Shinji Fukaya¹, Makoto Onobori^{1,2}

¹Department of Rheumatology, Tsukuba Gakuen Hospital, ²Onobori Clinic

Conflict of interest: None

[Object] Sulfamethoxazole-trimethoprim (ST-mix) is effective for prophylaxis of pneumocystis pneumonia (PCP). The decision of prophylaxis varies among rheumatologists due to side effect of ST-mix. In our hospital, chemoprophylaxis is adopted to RA patients who use methotrexate (MTX) with weekly one tablet ST-mix. This study aimed to evaluate the efficacy and safety of this method for chemoprophylaxis of PCP. [Methods] Subjects are RA patients who used MTX from January 2008 to December 2017. Exposure to RA treatments, persistence and side effects of ST-mix, and incidence of PCP were retrospectively analyzed. [Results] Mean age was 71±12 y.o. Overall observation was 3234PY, MTX-use and ST-mix with MTX accounted 2930PY and 2171PY (74.1%), respectively. Mean dosages of corticosteroid and MTX were 0.5mg/day and 6.0mg/week, respectively. Exposure to biologic DMARDs or JAK inhibitor accounted 1646PY (74.1%). Among 511 patients who once used ST-mix, cessation was observed in 26 patients (5.1%). There was no onset of PCP in ST-mix users. One PCP developed after cessation of ST-mix. During the same period, 17 episodes of PCP was observed in 16 patients. All of the case was without ST-mix. [Conclusions] Weekly one tablet ST-mix is effective and persistent methods for chemoprophylaxis of PCP.

W12-1

Clinical features of 8 cases with familial Mediterranean fever as a fever of unknown origin

Rina Watanabe¹, Hirotake Sakuraba¹, Yasuhisa Murai¹, Nahoko Tanaka¹, Keisuke Hasui¹, Hiroto Hiraga^{1,2}, Dai Kishida³, Yoh Ishiguro⁴

¹Department of Gastroenterology and Hematology, Hirosaki University Graduate School of Medicine, ²Department of Community Healthcare Development in Odate and North Akita, Hirosaki University Graduate School of Medicine, ³Division of Nurology and Rheumatology, Department of Internal Medicine, Shinshu University School of Medicine, ⁴Division of Clinical Research, Hirosaki National Hospital Organization

Conflict of interest: None

Introduction: Familial Mediterranean fever (FMF) is a autoinflammatory disease characterized by periodic fever and serositis. Method: Medical records were reviewed during period between January 2008 and December 2017. Clinical features of the patients with Familial Mediterranean fever (FMF), who had first visits to our department due to unidentified fever were assessed. Results: Total 149 cases of unidentified fever were enrolled, and 110 patients fulfilled the criteria of classical fever of unknown origin (FUO). One of 8 cases with FMF diagnosed based on modified Tel Hashomer criteria met the criteria of classical FUO. The mean age of onset was 44.8 years. The mean duration of attacks were 10.1 days. Five patients had atypical disease forms. MEFV gene mutations were observed in 6 patients, exon 2 mutation (n=5) and exon 1 mutation (n=1). Colchicine was effective in 7 patients. Discussion: In our study, the clinical features were late onset, moderate or mild disease activity and longer period of fever attack. These characteristics might be related to MEFV mutations except exon 10. FMF is a major disease characterized by periodic fever, and hard to unite criteria of classical FUO. Periodic fever is important in diagnosis of FUO and we should assume FMF as a cause of FUO.

W12-2

A retrospective observational analysis of idiopathic multicentric Castleman disease-associated lung disease

Shinichiro Tsunoda, Ruriko Kuratani, Satoshi Baba, Rina Okita, Rumiko Miyagi, Kaori Seki, Satoko Nozato

Division of Immunology & Rheumatology, Department of Internal Medicine, Sumitomo Hospital

Conflict of interest: None

[Object] Castleman disease (CD) is a lymphoproliferative disease that causes various clinical symptoms due to overproduction of IL-6. Pulmonary lesions were easily damaged, which was contained in the clinical stratification of CD both overseas and in Japan. Therefore we examined the lung lesions of idiopathic multicentric CD (iMCD). [Methods] We examined lung lesions and clinical data and treatment details of 14 patients (9 men, 5 females, and median age 54 years) confirmed as iMCD retrospectively. [Results] Histological subtype is plasma cell type in all cases. The blood test at the first visit was as follows: CRP 5.42±3.22 mg/dl, Hb 11.3±2.1 g/dl, Alb 3.1±0.8 g/dl, IgG 4222±1367 mg/dl, Elevated KL-6 level was found in 1 case. The CHAP score was 3.5 ± 3.1. In CT image findings, there were 14 lymph node swelling, 14 parenchymal lung lesions (14 thick bronchial vascular thickening, 9 cysts, 9 ground-glass opacities, 9 nodular shadows (6 small, 3 large) Respiratory function test showed a FEV1.0% reduction in 3 out of 8 patients. 10 cases are treated with TCZ, and 1 case with steroid therapy. There are no cases to supply supplemental oxygen. [Conclusions] When diagnosing CD, it is desirable to perform chest CT to evaluate lung involvement and start the appropriate treatment.

W12-3

A 64-year-old woman with multicentric reticulohistiocytosis successfully treated with Etanercept

Masako Utsunomiya^{1,2}, Ayaka Maeda², Akito Takamura²

¹Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, ²Department of Rheumatology, Musashino Red Cross Hospital

Conflict of interest: None

Case: A 64-year-old woman with a history of hypertension and Grave's disease presented with a ten-months history of multiple skin eruptions that had evolved over several months into reddish-brown papules, together with a progressive inflammatory polyarthritis. Physical examination showed tenderness and swelling in the distal interphalangeal (DIP) joints, the proximal interphalangeal (PIP) joints, the metacarpophalangeal (MCP) joints and the bilateral knee joints. Multiple papules around 2mm in diameters were also observed on the dorsal and lateral aspects of fingers, and the forehead, paranasal face and auricle. Rheumatoid factor, anti-nuclear antibody and anti-SSA / Ro antibody were negative, and anti-CCP antibody was weakly positive. Knee synovial fluid analysis showed cell counts of 2380 / μ L, negative crystals and increased histiocytes on cytology. Joint X-ray of hands revealed erosion in DIPs, and MRI of hand showed synovitis in all DIP, PIP and MCP joints. A skin biopsy was performed, and the lesions were diagnosed as multicentric reticulohistiocytosis (MRH). With methotrexate and etanercept her arthritis is in remission. Clinical implication: Because it is uncommon to encounter MRH in Japan, we report this case with literature review.

W12-4

Effect of the biological drug on refractory relapsing polychondritis

Seido Ooka, Kumiko Tonooka, Kanako Suzuki, Hisae Fujimoto, Hiromi Matsushita, Yukiko Takakuwa, Kana Ishimori, Kimito Kawahata

Division of Rheumatology and Allergy, Department of Internal Medicine, St. Marianna University School of Medicine

Conflict of interest: None

[Object] Relapsing polychondritis (RP) is rare disease to result in inflammation to a systemic cartilage tissue, but the cause is unknown. A steroid or an immunosuppressive drug is used for the treatment, but the cases that cannot control condition appear. We examined an effect about a biological drug for refractory RP. [Methods] From January, 2010 to Octo-

ber, 2018, we investigated patients with RP of 56 cases that met classification criteria of Damiani and Michet or MacAdams. We introduced a biological drug for refractory RP14 case and examined effect of treatment backward. [Results] infliximab (INF) was used for nine cases, and tocilizumab (TCZ) was used for five cases. It was necessary until an effect of INF for three months from one week. There were two canceled cases in the TCZ group. There was not INF effect, and the case changed to TCZ was one case. In a case lack in the improvement of RPDAL, there was the decrease in Visual Analogue Scale (VAS) and steroid dose. [Conclusions] It was suggested that there was a constant effect in the biological drug for refractory RP.

W12-5

Clinical manifestations of Adult-onset Still's disease patients

Takahiro Sugiyama¹, Nozomi Nishimura¹, Shunsuke Furuta¹, Kei Ikeda¹, Takao Sugiyama², Hiroshi Nakajima¹

¹Department of Allergy and Clinical Immunology, Chiba University Hospital, Chiba, Japan, ²Department of Rheumatology, National Shimoshizu Hospital, Chiba, Japan

Conflict of interest: None

[Background] Adult-onset Still's disease (AOSD) is a systemic inflammatory disease, but actually it is considered as a heterogeneous disease. Regarding the prognosis, some patients with AOSD experience multiple relapses but others do not. However it is difficult to predict the relapse. [Object] We aimed to reveal the clinical manifestations of AOSD patients. [Methods] A total of 64 AOSD patients (15 men and 48 women) diagnosed between 2000 and 2018 were identified from medical records. Baseline characteristics, treatments, and relapses were evaluated by retrospective chart review. [Results] The median age of disease onset was 38 years old. At the disease onset, 100% of the patients had fever, 88.1% had arthralgia, and 90.1% had eruption. Macrophage activation syndrome was occurred in 20.7%. Corticosteroids were administered in all but one case, and the median starting dose of prednisolone was 50mg/day. During the follow-up period, only one case died of infectious disease. Twenty cases experienced relapse, and the cumulative 5-year relapse-free survival rate was 65.0%. [Conclusions] Although the prognosis of AOSD is relatively good, patients with AOSD often experienced relapses. We discuss the risk factors for the relapse of AOSD with some literature review.

W12-6

Progressive factors associated with achievement of drug-free remission in patients with adult onset still disease

Masashi Suzuki, Shusaku Fukaya, Natsuko Watanabe, Tatsuaki Naganawa, Ai Umeda, Konomi Ashihara, Megumi Kurumizawa, Daisuke Hirano, Takako Hashimoto, Jo Nishino, Shunji Yoshida, Hidekata Yasuoka

Division of Rheumatology, Department of Medicine, Fujita Health University School of Medicine

Conflict of interest: None

[Object] To identify the progressive factors associated with achievement of drug (PSL, immunosuppressant) free remission in patients with adult onset still disease (AOSD) [Methods] 23 patients, who admitted to our department from April 2005 to August 2018 were involved. Patients who achieved drug-free remission (group A) and compared with patients without drug-free remission (group B), whose observation periods were matched. Clinical parameters including labo data, physical findings and treatment were compared. [Results] 6 group A patients and 4 group B patients were extracted. No patients were deceased during follow up period. The number of Plt was higher in group A compared with group B. Initial amount of PSL (group A 26.6±11.7mg/day vs group B 48.8±22.5mg/day, p=0.07), and frequency of additional use of immunosuppressant were lower in group A compared with group B (group A 2cases vs group B 4 cases, p=0.07). as for the other items including Hb, LDH, CRP, Ferritin, there were no difference between 2 groups. [Conclusions] Interestingly, the number of the Plt was higher in patients with AOSD who achieved drug-free remission. Underlying disease process including possible hemophagocytosis feature may associate with the Plt count. Plt might be a novel biomarker for AOSD.

W13-1

Risk factors of pregnancy outcome in patients with Systemic Lupus Erythematosus

Chie Kohno¹, Kayoko Kaneko¹, Chinatsu Takai², Shuko Mishima¹, Misato Kawakami², Mikako Goto³, Michiru Kina³, Satoshi Watanuki³, Yuri Hiramatsu⁴, Yoko Miura⁵, Sakiko Isojima⁵, Mari Yamamoto⁶, Atsushi Ihata⁷, Yoshiro Fujita⁶, Shoji Sugii³, Atsuko Murashima^{1,2}

¹Division of Maternal Medicine, Center of Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development, ²Japan Drug Information Institute in Pregnancy, National Center for Child Health and Development, ³Department of Rheumatology, Tokyo Metropolitan Tama Medical Center, ⁴Department of Rheumatology, Osaka Medical College Hospital, ⁵Department of Rheumatology, Showa University Hospital, ⁶Department of Rheumatology, Chubu Rosai Hospital, ⁷Department of Rheumatology, National Hospital Organization Yokohama Medical Center

Conflict of interest: None

[Object] To identify predictors of pregnancy outcome for preconception care (PCC) of SLE (systemic lupus erythematosus) patients. [Methods] Data were collected about organ lesion, complication, treatment, laboratory data and pregnancy outcome of SLE patients delivered at our and participating hospital between 2002-2017. Cases in which occurred preterm birth or stillbirth or LFD (Light For Date) were defined as APO (Adverse Pregnancy Outcome) group. We statistically compared with APO and non-APO group. [Results] Of 128 pregnancies in 106 patients, preterm birth occurred in 44 cases, stillbirth in 2 cases, LFD in 35 cases. Antiphospholipid antibody syndrome (APS), hypertension, chronic kidney disease (CKD), thrombocytopenia in 2nd trimester, and daily dose of steroid during pregnancy are associated with APO. Lupus nephritis (LN), low complement level and positive anti-DNA antibody were not related to APO. [Conclusions] This study suggests that APS, hypertension, CKD and steroid dose are risk factors for APO as previous reports. LN and serological activity that have been thought to be the risk are not associated in this analysis. Pregnant women with these factors could obtain well outcome. We expect that these findings lead to better PCC for SLE patients.

W13-2

Risk factors associated with adverse events during pregnancy and delivery in women with systematic lupus erythematosus ~LOOPS registry~

Hiroko Yoshinari¹, Kazuhisa Nakano¹, Kazuyoshi Saito², Keisuke Nakatsuka³, Shingo Nakayamada¹, Masao Nawata², Shigeru Iwata¹, Kentaro Hanami¹, Shunsuke Fukuyo¹, Satoshi Kubo¹, Ippei Miyagawa¹, Ayako Yamaguchi¹, Akio Kawabe¹, Yusuke Miyazaki¹, Naoaki Ohkubo¹, Ryuichiro Kanda¹, Yoshiya Tanaka¹

¹The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, ²Department of Rheumatology, Tobata General Hospital, ³Department of Rheumatology, Fukuoka Yutaka Central Hospital

Conflict of interest: None

[Object] SLE affect women of childbearing age, thus they should be managed carefully during pregnancy. We clarified factors of pregnant SLE patients for non-full-term birth, SLE activity and newborn's complication. [Methods] 33 pregnancies of 23 patients in our hospital from 2005 were enrolled. Primary outcome was proportion of full-term birth. [Results] Mean age was 28.9 y.o. and SLEDAI was 1.85. 16 (48.5%) were full-term birth and others were non-full-term birth (4:artificial abortion and 3:spontaneous abortion (SA) in 1st, 3:SA and 2:preterm birth in 2nd, and 4:preterm birth in 3rd trimester) whose risk factors were coexisting APS and low CH50. SLE relapses in past and unplanned pregnancy affected termination in all trimester. SLE became worse in 12 whose WBC and Plt were low, and no immunosuppressant was used. 8/24 (33.3%) were born in preterm and 7 had complications by immaturity which related with coexisting APS, SLE relapses in past, leukocytopenia and anemia in mothers, whereas immunosuppressants use was not. [Conclusions] Proportion of full-term birth was low. Cytopenia and low complement can be risks for perinatal complications and SLE exacerbation. For some immunosuppressants are available during pregnancy, activity of

SLE should be quiescent before the conception with use them.

W13-3

Risk factors for adverse pregnancy outcomes and Apgar score of newborns in pregnancy and delivery complicated with SLE

Hiroshi Shimada, Tomohiro Kameda, Shusaku Nakashima, Risa Wakiya, Mikiya Kato, Taichi Miyagi, Hiroaki Dobashi
Department of Internal Medicine, Division of Hematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University, Kagawa, Japan

Conflict of interest: None

[Object] We investigate the risk factors for adverse pregnancy outcomes (APOs) complicated with SLE and Apgar score of newborns from SLE mothers. [Methods] We extracted 49 SLE patients who were managed from preconception counseling to pregnancy and delivery in our institution. We analyzed the risk factors for APOs and Apgar score of newborns. [Results] In preterm birth, SLEDAI at the first trimester, anti ds-DNA antibody was significantly high. The average dose of corticosteroid during pregnancy and the rate of intensification of treatment was high. In LFD newborns, the serum complement levels were low, and SLEDAI at the third trimester was high. Apgar score at 1 minute was correlated significantly with SLEDAI at 3rd trimester and anti ds-DNA antibody, and at 5 minutes was correlated with anti ds-DNA antibody. Multivariate analysis showed that there was a significant difference between Apgar score and anti ds-DNA antibody. [Conclusions] We revealed that immunological abnormalities, high disease activities, and corticosteroid treatments were demonstrated as the risk factors for preterm birth and LFD. Apgar score of newborns was associated with anti ds-DNA antibody significantly, therefore, we suggest that Apgar score might become a risk factor for neurological development.

W13-4

Is there a difference in pregnancy course and pregnancy outcome among childhood onset systemic lupus erythematosus (SLE) and adult-onset SLE patients?

Yuri Hiramatsu¹, Eri Nakamura¹, Takao Kiboshi¹, Takaaki Ishida¹, Youhei Fujiki¹, Nami Okamoto², Kosuke Shabana², Takuya Kotani¹, Shigeki Makino¹, Tohru Takeuchi¹, Shigeki Arawaka¹
¹Department of Internal Medicine IV, Osaka Medical College, Takatsuki, Osaka, Japan, ²Department of Pediatrics, Osaka Medical College, Takatsuki, Osaka, Japan

Conflict of interest: None

[Object] The onset of SLE is common in young women, and about 20% of the onset develops in less than 18 years of age. Childhood SLE exhibits the same symptoms as adult SLE, but it is reported that there are many cases of nephritis complications compared with adult cases and there are many cases of severe cases. In recent years SLE patient's pregnancy has increased, among them cases where childhood SLE women become pregnant, but differences in pregnancy management with adult SLE are not clear. We examine differences in pregnancy course and pregnancy outcome between both. [Methods] Comparison of pregnancy course and outcome for 23 women with childhood SLE (onset below 18 years of age) and 63 adult SLE women who underwent pregnancy control at our hospital during the period from 2003 to 2018. SLEDAI was used for disease activity assessment. [Results] The median value is shown below. A comparison between childhood SLE and adult SLE is described. SLEDAI values during the pregnancy period, pregnancy period, and postpartum period were significantly lower in childhood SLE during the disease period of 15.7 vs 6.1 years. For pregnancy outcomes, there was no significant difference. [Conclusions] Disease activity during pregnancy was significantly lower in childhood SLE than in adult SLE.

W13-5

Current condition of clinical practice and childbirth of female patients with rheumatoid arthritis who wish to have children in NinJa 2017

Toshihiro Matsui¹, Takao Sugiyama², Shigeto Tohma³

¹Department of Rheumatology, National Hospital Organization Sagami-hara National Hospital, ²Department of Rheumatology, National Hospital Organization Shimoshizu National Hospital, ³National Hospital Organization Tokyo National Hospital

Conflict of interest: Yes

[Object] To clarify the current condition of clinical practice and childbirth of female patients with rheumatoid arthritis (RA) who wish to have children. [Methods] Among 15,185 patients registered in NinJa (National Database of Rheumatic Diseases in Japan) 2017, we extracted female patients under 50 years of age (1,599 cases) and collected information on the presence or absence of childbirth, pregnancy, lactation, and wish to have children. Patients whose information could be collected (916 cases) were classified into group A (under 30 yrs, 76 cases), group B (30-34 yrs, 77 cases), group C (35-39 yrs, 168 cases), and group D (over 40 yrs, 640 cases) and their data were analyzed. [Results] There were 20 births which represent 80.5% [95% CI: 45.2 - 115.8] of the expected number of births calculated from the demographic change survey for the same year. There was no significant difference in CDAI and PSL usage rates between patients with or without wish to have children in all groups, however, usage rate of biologics (54.4% vs 35.4%, p<0.05), and the selection rate of etanercept (94.7% vs 30.7%, p<0.001) were significantly more in patients with wish to have children in group D. [Conclusions] Female RA patients over 40 yrs who wish to have children need more strong treatment for RA.

W13-6

Clinical courses of pregnant women with rheumatoid arthritis who received Etanercept during pregnancy

Chinatsu Takai¹, Mikako Goto¹, Misato Kawakami¹, Chie Kohno², Shuko Mishima², Kayoko Kaneko², Atsuko Murashima^{1,2}

¹The Japan Drug Information Institute in Pregnancy, National Center for Child Health and Development, ²Division of Maternal Medicine, Center for Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development

Conflict of interest: None

[Object] To clarify the clinical courses of pregnant women with rheumatoid arthritis (RA) who received Etanercept (ETN) during pregnancy. [Methods] We detected 25 pregnancies with live birth in patients with RA who had received Etanercept (ETN) at 0th week of pregnancy at our hospital from 2003 to 2017. The disease activity and medication before, during and postpartum were investigated retrospectively. [Results] ETN was discontinued after diagnosis of pregnancy in 16 cases of 25 cases. Of the 16 cases discontinued ETN, 8 cases experienced disease flare during pregnancy and restarted ETN in 7 cases. Of the other 8 cases without disease flare, 7 cases remained discontinued through pregnancy. No significant difference was detected in the disease activity at 3 months before pregnancy among continued group (9 cases), re-started group (8 cases), and discontinued group (8 cases). The disease flare after delivery within 1 month was detected 2 cases in continued group, 4 cases in re-started group and 1 case in discontinued group. No major anomaly was detected in all the 25 cases. [Conclusion] Around half of the cases discontinued ETN during pregnancy experienced disease flare and re-started ETN. It is necessary to clarify which patient can discontinue ETN or not.

W14-1

The Toe Lesion of Patient with Rheumatoid arthritis

Satoko Yokoyama¹, Mami Nakahara², Haruko Ito³, Yoko Nemoto⁴, Mitsuhiro Kawagoe¹, Kazutoshi Aoki¹

¹Aoki Medical Clinic Saitama Japan, ²Juntendo University Koshigaya Hospital, ³Ina Hospital, ⁴Kaneko Clinic

Conflict of interest: None

[Object] Deformity of toe is common in rheumatoid arthritis (RA) patient, and it causes pain and infection. It is important to find and care the toe lesion of RA early. Therefore, we investigated frequency of the toe lesion. [Methods] The subject were 572 RA patients who visited 4 RA clinics from June to July 2018. The questions consists of sex, age, disease

period, sort of toes lesion and treatment. [Results] 572 patients answered the question. M/F ratio was 1:5. 349 patients (61%) had toe lesion, which were callus-calvus 48%, hallux valgus 42%, incurvated nail, deformity 19%, cornification 15%, flat feet 13%, nail hyperplasia 12%, trichophytia 11%, tailor's bunion 6%. Of these, it was 245 non-treatment (70%). [Conclusions] Because foot is weight bearing joint, its destruction and deformity occurs frequently. Foot joint is not included in DAS28 and there is few opportunity to examine it. This study showed joint destruction and deformity were overlooked frequently (70%). ADL of RA patient was improved drastically with evolution RA treatment. Consequently, load to foot became bigger. Nurse must accumulate knowledge for foot care and cooperate with physician in order to find the foot lesion. We will accumulate more data about how foot lesion affect HAQ

W14-2

Usability of Cimzia AutoClicks correlated with hand functions in patients with rheumatoid arthritis

Kaoru Nagai¹, Yasumori Sobue², Tsuyoshi Nishiume², Mochihito Suzuki², Nobunori Takahashi², Takuya Matsumoto², Nobuyuki Asai², Shuji Asai², Toshihisa Kojima², Naoki Ishiguro²

¹Nursing Department, Nagoya University Hospital, ²Department of Orthopedic Surgery, Nagoya University Hospital

Conflict of interest: None

[Conclusions] [Object] We investigated usability of Cimzia AutoClicks for patients with rheumatoid arthritis (RA) and determined factors necessary for the use of this instrument. [Methods] Sixty outpatients with RA at our institution answered usability of Cimzia AutoClicks after they used it. [Results] The average age of the patients was 61.8 years with the average disease duration of 14 years. Ninety-three percent of them were female. The average TJC28, SJC28, CRP, PtGA, Body mass index, grip power, pinch force, and the scores of HAND20 and DAS28 were 1.0, 0.7, 0.3 mg/dL, 24.8 mm, 20.7 kg/m², 17.7 kg, 3.7 kg, 26points and 2.1 respectively. Ninety-three percent of the patients could successfully operate the instrument. Grip power (18.5 kg vs 7 kg), pinch force (3.3 kg vs 0.4 kg), and the score of HAND20 (23 points vs 63 points) were significant factors between patients who could use it and those who could not use it (p<0.05). Cutoff value with "not usable" as the end point was a grip power of 13 kg and a pinch force of 1.2 kg. Disease duration and the score of DAS28 did not affect the usability of Cimzia AutoClicks. Fifty percent of patients preferred buttonless. [Conclusions] Hand functions of patients were important on the usability of Cimzia AutoClicks.

W14-3

Daily living guidance to rheumatism patients using Web videos and their effect on self-efficacy

Yuki Tanaka¹, Naomi Takahashi¹, Ako Ohnishi¹, Noriyoshi Shimahara², Shinji Sato², Makoto Onishi³, Yasuaki Okuda³, Naoya Sawada³

¹Department of Nursing, Center for Rheumatic Diseases, Dohgo Spa Hospital, Ehime, Japan, ²Department of Rehabilitation, Center for Rheumatic Diseases, Dohgo Spa Hospital, Ehime, Japan, ³Department of Internal Medicine, Center for Rheumatic Diseases, Dohgo Spa Hospital, Ehime, Japan

Conflict of interest: None

[Object] Using Web videos, conduct activities of daily living and guidance on joint protection, examine the satisfaction of daily living behavior and the influence on self-efficacy. [Methods] Make movies with doctors / therapists about living behavior, domestic action, bathing behavior. Disease activity · Pain of each joint VAS · PSEQ · Analysis of daily life satisfaction. [Results] There was no significant difference between HAQ-DI, SDAI, and pain VAS before and after video observation. However, the VAS values of wrist and knee joints were improved. Patients who improved PSEQ after observation had significantly higher age and SJC, and VAS and TJC were also higher than those without deterioration / change. Everyday life satisfaction degree is increasing "How to open a bottle cap" and "How to use a frying pan". "I wanted to know when RA was getting worse." There was an opinion that "It became a reference when it hurts." [Conclusions] The fact that patients with high age, joint swelling / pain watching movies of daily living behavior and

guarding of joint protection action reduced pain during everyday activities increased the self-efficacy feeling. At present, it is difficult to continue adequate outpatient rehabilitation, teaching using web animation is effective.

W14-4

How well do rheumatoid arthritis patients recognize the prescribed medications?

Noriko Iwata, Masao Sato, Tomohisa Tani, Toshiro Ohashi
Ohashi-Tani Orthopedics Gihushi Japan

Conflict of interest: None

[Objectives] Drug therapy for rheumatoid arthritis (RA) is classified into 4 types: non-steroidal anti-inflammatory drug (NSAID), disease modifying antirheumatic drug (DMARD), biological drug (BIO), glucocorticoid (GC). We investigated to what extent the RA patients recognize the medicine being used. [Methods] We listened to the types of medicines (NSAID, DMARD, BIO, GC) currently prescribed for RA patient in outpatient clinic and their drug name. Of 267 people examined, 184 subjects using BIO were analyzed. [Results] There were 31 males, 153 females, ages from 14 to 84 years old, average 61.0 years old. The number of usage for each drug was 131 cases for DMARD, 44 cases for GC and 61 cases for NSAID. The numbers of patients accurately grasping the classification of drugs and drug names were 158 cases (85.9%) for BIO, 89 cases (67.9%) for DMARD, 20 cases (45.5%) for GC, 44 cases (72.1%) for NSAID. The average age (years) of drug content graspers and non-graspers is 59.0, 69.5 in BIO, 60.7, 64.2 in DMARD, 59.9, 66.7 in GC, 58.1, 65.0 in NSAID, respectively. [Discussion] As a result of investigating the degree of recognition of prescribed drugs in RA patients using BIO, it became clear that patients who did not grasp the type of medicine or drug name increased with age.

W14-5

Biologic DMARD monotherapy for the treatment of elderly onset rheumatoid arthritis

Megumi Kobayashi¹, Ryoko Koyanagi¹, Yoshioki Yamasaki^{1,3}, Hidehiro Yamada^{1,2}

¹Department of Rheumatology, Yokohama General Hospital, ²Center for Rheumatic Diseases, Seirei Yokohama Hospital, ³Rheumatology and Allergology, St. Marianna University School of Medicine

Conflict of interest: None

[Object] To investigate whether our intensive commitment by medical team to patients with elderly-onset rheumatoid arthritis (EORA) treated with biologics contributed to the safety management. [Methods] Patients with EORA >65 year-old, visited to our clinic from 2015, and treated with biologic (B-) DMARDs alone were retrospectively investigated. [Results] Twenty-three patients were included. The mean age was 78-year-old. The mean follow-up period was 21 months. They had average of 10 swollen joints. HAQ and RAPID3 was 0.9 and 13, respectively. Seven patients had cerebrovascular diseases, each 6 HBV infection / lung diseases, and 5 diabetes mellitus. The patients were treated with subcutaneous abatacept (n= 17), etanercept (n= 3), tocilizumab (n= 2). All except 2 patients received B-DMARDs at the clinic at every 1 or 2 weeks by RA care nurses with careful assessment of the patients. The continuation rate was 80% at 2 year with improvement such as RAPID3 4.9, and HAQ 0.6 (P<0.05). Serious adverse events were included lung cancer (n= 1) and renal cancer (n= 1). No patients experienced serious infections. [Conclusions] No serious infections were seen in our EORA patients. B-DMARDs monotherapy seemed to be safe in this patient population with aggressive commitment of medical staff.

W14-6

Research on the symptoms of depression of elderly patients with rheumatoid arthritis

Mami Nakahara¹, Shigeto Kobayashi², Issei Kida², Kyoko Kubono¹

¹Nursing Department, Juntendo Koshigaya Hospital, ²Department of Rheumatology and Internal Medicine, Juntendo Koshigaya Hospital

Conflict of interest: None

[Object] To investigate psychological symptoms on elderly patients over 65 with rheumatoid arthritis (RA). [Methods] We conducted survey on 55 RA patients, who were treated in our hospital from August to September in 2018. We applied the U test and the rank correlation coefficient of Spearman to The CESD Scale (classified in four items; depression mood, physical symptom, personal relationships and positive feelings). The significance level is set at less than 5%. [Results] Our investigation demonstrated that almost 20% of patients had depression. In Evaluator's Global Assessment, the CESD score of men is 0.7 (0.6) and that of women is 0.3 (0.54). In PGA, men: 1 (1.5), women: 1.5 (1.95). Further, a negative correlation between depression mood and the disease activity is confirmed although positive correlation is found between depression mood and physical symptom. [Conclusions] A paradoxical result was recognized -- the stronger the positive emotion is, the higher score of the physical symptom is. Also, it was revealed that patients with short duration of RA had stronger depressed tendencies, and patients with chronic symptoms were less depressive in contrast. It is suggested that patients with RA need time for disease reception, and the quality and degree of anxiety changes with RA symptoms.

W15-1

A study of music therapy for patients with rheumatoid arthritis on emotional relaxation by using Emotional Relaxation Scale

Yasushi Miura^{1,2}, Ikuko Yamazaki³, Kenya Oga⁴, Koji Fukuda², Ryosuke Kuroda²

¹Department of Rehabilitation Science, Kobe University Graduate School of Health Sciences, ²Department of Orthopaedic Surgery, Kobe University Graduate School of Medicine, ³Department of Healthcare and Welfare, International University of Health and Welfare, ⁴Ibaragi Prefectural University of Health Sciences Hospital

Conflict of interest: None

[Objectives] We previously reported that music therapy improves general health condition, positive emotion and self-efficacy of patients with rheumatoid arthritis (RA) and decreases pain, anxiety and negative emotion. In this study, we investigated the effects of music therapy on relaxation by using Emotional Relaxation Scale (ERS). [Methods] Music therapy was conducted by a music therapist, a pianist, hospital staffs, and students. Eight Japanese songs were sung with a piano accompaniment and 2 were played with chime bars by the participants. General health condition, pain, emotions and emotional relaxation were surveyed by self-rating questionnaire including 10cm general health visual analogue score (VAS), face pain rating scale, TMS, PMS and ERS. [Results] Fourteen female patients were participated. mHAQ was 0.56 ± 0.67 (0-2.50). GH-VAS was significantly improved from 3.4 to 2.4 and FS from 5.7 to 4.3 respectively. The negative emotions evaluated by TMS were decreased and the positive emotions by TMS and PMS were increased. Meanwhile, all four subscales of ERS showed the median score of 4 among 5 indicating positive emotional relaxation effects. [Conclusions] Music therapy increase positive emotions and decrease negative emotions resulting emotional relaxation on patients with RA.

W15-2

Pain accused by RA patients - Relationship between pain intensity, dysfunction, psycho-psychological problems, comparison with disease activity -

Noriyoshi Shimahara¹, Shinji Sato¹, Yuki Tanaka³, Naoya Sawada², Yasuaki Okuda², Makoto Onishi²

¹Department of Rehabilitation, Center for Rheumatic Diseases, Dohgo Spa Hospital, ²Department of Internal Medicine, Center for Rheumatic Diseases, Dohgo Spa Hospital, ³Department of Nursing, Center for Rheumatic Diseases, Dohgo Spa Hospital

Conflict of interest: None

[Introduction] In This Study, we report the relationship between pain intensity, functional impairment and psycho-psychological problems due to disease activity status. [Materials] Of the female RA patients in our hospital visit, 64 subjects agreed to participate in this study were taken.

[Methods] Study was conducted in a prospective study. The evaluation items were SDAI as disease activity, P-VAS as pain intensity, PDAS and HAQ as evaluation of functional impairment, PCS and HADS as psychophysiological states, and the state of SDAI, And analyzed these relationship. [Results] In group comparison, pain intensity and dysfunction did not differ over low disease activity. Patients who showed a catastrophic trend existed outside the remission group. PCS and HADS showed a significant difference depending on the status of disease activity, but helplessness showed a high trend regardless of disease activity. VAS showed moderate correlation with SDAI, PDAS, HAQ, PCS, HADS, and showed a causal relationship with PCS and HADS. [Discussion] Other than the remission group, there was a catastrophic trend, and pain and dysfunction were affected by disease activity. It was suggested that psychological problem was more influential to symptoms of RA patients.

W15-3

The effect of exercise on arthritis in patients rheumatoid arthritis

Satoshi Nakazaki¹, Takashi Murayama¹, Shinichi Kato²

¹Department of Rheumatology, Johoku Hospital, ²Department of Rheumatology, Kamiaraya Clinic

Conflict of interest: None

[Object] Some skeletal muscles communicate with other organ by secreting proteins and peptides called myokine. Some myokines inhibit inflammation of rheumatoid arthritis (RA). To investigate the efficacy of low intensity exercise program on RA. [Methods] Nineteen patients with RA were enrolled. Inclusion criteria were receipt of a stable dose of biologics, JAK inhibitory, and conventional DMARDs more than 3months prior to the first exercise, and corticosteroid and NSAIDs more than one month prior to the first exercise. The exercise circuits consisted of 6 different low extremity exercises intended to improve arthritis. Within the exercise circuits, each exercise was repeated 8-12 times and less than 50% of maximum muscle strength. The exercise circuits were performed 3 times a week. [Results] Mean age was 68y.o., and mean disease duration 17 years. Four patients (21%) used methotrexate and 9 patients (47%) biologics. Mean DAS28 (ESR) was 3.96 at base line and 3.53 at 2 months, mean DAS28 (CRP) 3.45 and 3.07, mean SDAI 15.2 and 11.9, and mean CDAI 14.5 and 11.2, respectively. All index improved significantly at 2 months than baseline. [Conclusions] Low intensity exercise was efficacious against arthritis in patients with RA

W15-4

Secondary sarcopenia due to foot deformities in Rheumatoid Arthritis severely compromise quality of life

Shogo Toyama^{1,2,3,5}, Ryo Oda^{3,5}, Daisaku Tokunaga^{2,3}, Yutaka Kawahito^{4,5}, Yasuo Mikami², Masataka Kohno⁴, Makoto Wada^{4,5}

¹Department of Development of Multidisciplinary Promote for Physical Activity, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ²Department of Rehabilitation Medicine, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ³Department of Orthopaedics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ⁴Department of Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ⁵Center of Rheumatic Diseases, University Hospital, Kyoto Prefectural University of Medicine

Conflict of interest: None

[Introduction] Rheumatoid arthritis is a progressive joint disease, and disorders associated with joint destruction accumulate. We have clarified that QOL of a foot is particularly low in foot suffering cases. In this study, we study sarcopenia and QOL in these patients. [Method] We subjected 33 patients with disorder and chief complaints in foot from our outpatients, with exclusion cases with cognition and data absence, and finally 29 subjects were analyzed. We evaluated ADL and QOL. Diagnosis of sarcopenia was carried out by grip strength, walking speed and body composition analysis. [Results] The average age was 66.8 years (35-84 years) in 1 male and 28 females. The HAQ is 1.14 (0 - 2.75), the physical QOL summary score of SF - 36 is 29.5 (6.8 - 73.0). The grip strength was 11.4 kg (0-23.3), the walking speed was 0.98 m / s (0.48 - 1.7), the body fat percentage was 31.7% (20.3 - 44.2), skeletal muscle mass index was

5.43 (4.4 - 7.6). 79.3% (23/29) was Sarcopenia. [Conclusion] From our study, Sarcopenia was observed at a significantly higher rate than general 65 years or older. Physical QOL decline is related to a decrease in muscle mass and high body fat percentage, therefore appropriate rehabilitation is necessary to obtain “true” remission.

W15-5

Adaptation of shoulder joint rehabilitation in rheumatoid arthritis patients -Examination with ultrasonography-

Akira Inoue¹, Takuro Okari¹, Keio Ayabe²

¹Department of Rehabilitation, Keiyu Orthopedic Hospital, ²Department of Orthopedic Surgery, Keiyu Orthopedic Hospital

Conflict of interest: None

[Object] We compare ultrasound findings due to differences in disease activity, clarify the relationship with local inflammation, and help setting rehabilitation strength. [Methods] The subjects were 21 patients with RA patients 21 shoulder (low, middle and high disease activity 7 each), frozen shoulder 20 cases (20 affected side, 20 healthy side). ultrasonography evaluated inflammation area. The examination site was taken as the total Doppler area in biceps groove, rotator interval, subacromial burse, subdeltoid burse. Disease activity was DAS 28-CRP. Statistics were tested using multiple comparison tests, and group comparisons were performed in 5 groups. [Results] The Doppler area in each group (high / middle / low disease activity / frozen shoulder affected side / healthy side) is 35.8 / 31.7 / 13.3 / 12.9 / 4.5 mm² and frozen shoulder affected side and low disease activity, high disease activity and There was no significant difference in medium disease activity, but there was a significant difference in comparison between other groups ($p < .05$). [Conclusions] The same load is applied as frozen shoulder and low disease activity are the same inflammation. The necessity of proceeding wisely with medium / high disease activity was considered.

W15-6

New RA patient education using Web video

Naoya Sawada¹, Shinji Sato², Noriyoshi Shimahara², Ako Ohnishi³, Makoto Onishi¹, Kiyoshi Takasugi¹

¹Department of Internal Medicine, Dohgo Spa Hospital, ²Department of Rehabilitation, Dohgo Spa Hospital, ³Nursing Department, Dohgo Spa Hospital

Conflict of interest: None

[Object] To improve access to self-care and daily guidance of patients with RA by using Web video. [Methods] We selected the theme based on the needs heard from RA patients, 1. correspond to morning stiffness 2. exercise for deformation prevention (finger/ toe) 3. joint protection method in daily life 4. foot care 5. guide of brace, And so on. As a “rehabilitation / self care of RA” using Web video site, it was released sequentially from September 2017 and urged viewing. (<https://www.youtube.com/channel/UCBemown4OfXIAfRUic9hepA>) [Results] Approximately 17 thousand views were viewed in one year. The preventive exercise for joint deformation was the most frequently viewed and the evaluation was high. It was thought that it reflects the need for fear of deformation progress and countermeasure method. There was also a report of improving deformity of the fingers from the patients used. Sharing skills and knowledge of doctors, nurses and therapists led to medical care smoothing. Although there were no reports of adverse events, there were cases where viewing was difficult for the elderly. [Conclusions] The use of Web video was useful for expanding opportunities for RA patient education.

W16-1

Analysis of the association between aging and circulating follicular T helper (Tfh) cells in patients with rheumatoid arthritis

Yoko Yabe, Shin-ichiro Kagami

Research Center for Allergy and Clinical Immunology, Asahi General Hospital, Chiba, Japan

Conflict of interest: None

[Object] The aim of this study is to analyze the association between aging and circulating Tfh cells in RA. [Methods] We retrospectively reviewed the medical records of 53 patients who were diagnosed as RA and analyzed for peripheral Tfh (CD3+CD4+CD45RA-CXCR5+) cells from July 2014 to May 2018 in our hospital. The Tfh cells were divided into three subsets: Tfh1 (CXCR3+CCR6-), Tfh2 (CXCR3-CCR6-) and Tfh17 (CXCR3-CCR6+). [Results] The median age at diagnosis was 64 years (IQR:50-70 years) and 38 cases were female. The median titers of ACPA and RF at diagnosis were 66.1 U/ml (IQR:3.1-413.8 U/ml) and 57.1 IU/ml (IQR:10.75-191.9 U/ml), respectively. As age increased, the titers of ACPA and RF tended to decrease. The ratio of Tfh2/Tfh cells had a significant positive correlation with age ($p=0.01$, $R=0.33$), and the ratio of CD28+Tfh2/Tfh cells had a significant negative correlation with age ($p=0.01$, $R=-0.31$). Neither the ratio of Tfh1/Tfh cells nor Tfh17/Tfh cells were significant correlation with age. Expression of CD28 on Tfh1 cells and Tfh17 cells were not decreased. [Discussion] Aging was involved in expression of CD28 on Tfh2 cells in RA patients. In elderly RA patients, CD28 negative Tfh2 cells were increased, hence the production of autoimmune antibodies might be impaired.

W16-2

Factors associated with the muscle mass change of patients with rheumatoid arthritis in 7 years

Shinichi Nogi¹, Akito Tominaga¹, Koichiro Horie¹, Takuya Kakutani¹, Kako Kodama¹, Kanako Iwata¹, Hirotaka Tsuno¹, Takahiro Nunokawa¹, Hideki Ogihara¹, Akiko Komiya², Atsushi Hashimoto¹, Toshihiro Matsui¹, Shigetoh Tohma³

¹Department of Rheumatology, National Hospital Organization Sagami-hara National Hospital, ²Department of Clinical Laboratory, National Hospital Organization Sagami-hara National Hospital, ³National Hospital Organization Tokyo National Hospital

Conflict of interest: None

[Objectives] There are few reports about measurement of muscle mass in rheumatoid arthritis (RA) patients. We measured muscle mass of RA patients in 7 year intervals to investigate the relationship between their muscle mass change and backgrounds. [Methods] Muscle masses of 86 RA patients were measured using MC180 Body Composition Analyzer in 2010 and 2017 at our hospital. Patients' backgrounds from NinJa database were associated with muscle mass change (balance (2017-2010) or ratio (2017/2010)). [Results] Their mean age in 2017 was 62.4±9.1 years old. Muscle mass in 2010 showed significant negative correlation with their age or physical function evaluations (mHAQ). Muscle mass change (balance or ratio) showed significant negative correlation with mean DAS28-ESR or -CRP during 7 years and no correlation with initial muscle mass, presence of corticosteroid therapy, age, mHAQ, Steinbrocker Stage or ACR Class in 2010. [Conclusion] RA patients with higher disease activity tended to lose more muscle mass.

W16-3

Serum myostatin in patients with rheumatoid arthritis and its correlation with body composition

Yoko Wada¹, Masanori Sudo¹, Shunsuke Sakai¹, Sayuri Takamura¹, Ayako Wakamatsu¹, Yukiko Nozawa¹, Hiroe Sato², Daisuke Kobayashi¹, Takeshi Nakatsue¹, Takeshi Kuroda², Masaaki Nakano³, Ichiei Narita¹

¹Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan, ²Health Administration Center, Niigata University, Niigata, Japan, ³Medical Technology, School of Health Sciences, Faculty of Medicine, Niigata, Japan

Conflict of interest: None

[Object] To investigate the possible role of myostatin in body composition in patients with rheumatoid arthritis (RA). [Methods] Ninety-eight RA patients who visited Niigata University Hospital between April to June 2017, were recruited in this study. Body composition was measured by bioelectrical impedance analysis with a tetrapolar impedance meter. Serum myostatin level was measured by ELISA. Patients' laboratory findings and disease activities were also measured, and the correlations between the titer of serum myostatin and these factors were analyzed.

[Results] In Spearman's correlation coefficient analysis, serum myostatin level was positively correlated with skeletal muscle mass index and fat-free mass index (FFMI), and negatively correlated with percent body fat (%BF), fat mass index (FMI), swollen joint counts, ESR, and DAS28-ESR (4). In 72 female patients in this study, %BF and FMI/FFMI ratio was significantly higher in patients with low FFMI group (FFMI<13.82, n=22), compared to those with normal FFMI group (n=50). [Conclusions] Serum myostatin level was significantly correlated with body composition and disease activity in RA patients. Patients with lower level of myostatin showed a trend of decreased skeletal muscle and increased body fat, so-called rheumatoid cachexia.

W16-4

Study on bone microstructure of rheumatoid arthritis patients using HR-pQCT

Shigenori Tamaki¹, Takashi Kato², Motokazu Kai³, Kunikazu Ogawa³, Hiroaki Mizuno¹, Hisaji Oshima⁴, Ikuko Tanaka¹

¹Nagoya Rheumatology Clinic, Nagoya, Japan, ²Department of Radiology, National Center for Geriatrics and Gerontology, Obu, Japan, ³Mie Rheumatology Clinic, Suzuka, Japan, ⁴Department of Connective Tissue Disease, Tokyo, Japan, Tokyo Medical Center

Conflict of interest: None

[Object] In this study, we examined the relationship between bone microstructure and joint destruction of RA patients by analysis with HR-pQCT. [Methods] We examined HR-pQCT in the distal radius of 206 female patients with arthritis. Bone microstructure of 80 patients with wrist destruction (A group), 47 patients without wrist destruction (B group), 79 ACPA negative unclassified arthritis patients (C group) was analyzed. [Results] The total volumetric bone mineral density (vBMD) was significantly lower in the A and B groups than in the C group, the cortical vBMD was significantly lower in A group than in the B and C groups, the trabecular vBMD was significantly lower in the A and B groups than in the C group. In the cortical microstructure, the cortical bone porosity are significantly higher in A group than the B and C groups. In the two groups of RA, the trabecular Meta.vBMD, the trabecular Inn.vBMD and the trabecular number are significantly lower than in the C group. [Conclusions] In the group A, cortical porosity was enhanced and the influence of arthritis was considered. On the other hand, trabecular bone loss was observed in group B, suggesting the existence of bone absorption not related to arthritis.

W16-5

High leptin level was related to increased homocysteine for 7 years in patients with rheumatoid arthritis: TOMORROW study

Masato Uematsu¹, Kentaro Inui², Tatsuya Koike³, Yuko Sugioka², Tadashi Okano², Kenji Mamoto², Yutaro Yamada², Koji Mandai⁵, Masahiro Tada⁴, Hiroaki Nakamura²

¹Department of Orthopedics, Higashisumiyoshi Morimoto Hospital, ²Department of Orthopedics, Osaka City Medical University Hospital, ³Department of Orthopedics, Shirahama Hamayu Hospital, ⁴Department of Orthopedics, Osaka City General Hospital, ⁵Department of Orthopedics, Osaka Social Medical Center Hospital

Conflict of interest: None

[Background] Leptin is reported to regulate bone metabolism in negative balance, however the effect on bone quality is not clear. In the patients with rheumatoid arthritis (RA) leptin level is reported high as well as homocysteine (Hcy) level, known as one of the bone quality markers. In this study we evaluate the Hcy level in RA patients for 7 years in comparison with healthy control (Vo), using the data of TOMORROW study. [Method] We analyzed the data from the TOMORROW study (UMIN00003876), which is a 10-years prospective cohort. Questionnaire including clinical and laboratory data were measured at baseline (BL). Changes of Hcy in 7 years (Δ Hcy) were analyzed in comparison with Vo for 7 years, and multivariate analysis of Δ Hcy were conducted with each BL variations as an explanatory factor were performed. [RESULTS] Leptin and Hcy were significantly higher than Vo ($p=0.001$; repeated measure ANOVA). Multivariate analysis revealed Δ Hcy was positively related to leptin at BL ($p=0.0418$). No association of Δ Hcy with

age, disease activity, impaired glucose tolerance, ACPA, NTX, and sex were observed. [Discussion] In RA patients, high level of leptin at BL is related to increase of Hcy. It was suggested leptin was one of the factors lower the bone quality in patients with RA.

W16-6

Rheumatoid arthritis is high risk factor of death from TOMORROW study

Koji Mandai¹, Tatsuya Koike^{2,3}, Yuko Sugioka², Kentaro Inui⁴, Tadashi Okano⁴, Yutaro Yamada^{4,5}, Shohei Anno³, Masahiro Tada⁶, Hiroaki Nakamura⁴

¹Department of Orthopaedics, Osaka Social Medical Center, ²Center for Senile Degenerative Disorders, Osaka City University Graduate School of Medicine, ³Department of Orthopaedic, Search Institute for Bone and Arthritis Disease, ⁴Department of Orthopedics, Osaka City University Graduate School of Medicine, ⁵Department of Orthopaedic, Yodogawa Christian Hospital, ⁶Department of Orthopaedic, Osaka City General Hospital

Conflict of interest: None

[Object] We investigated the risk factor of death in patients with rheumatoid arthritis (RA) from TOMORROW study. [Methods] This study included 413 participants, comprising 208 patients with RA and 205 age- and sex- matched healthy volunteers (Vo) from the prospective "TOMORROW" cohort study that has been ongoing since 2010 were included in this study (women, 84%; mean age, 58 years old). Median disease duration was 10.3 years. [Results] The rate of accomplishment for 8 years was 83.2% in the RA group and 92.7% in the Vo group. There were 14 deaths in the RA group (8.41/1000 person-years) and 2 in the Vo group (0.1/1000 person-years) ($p=0.0035$) for 8 years. Infection was the most common cause of death in the RA group (43%). Cox hazard analysis showed that RA was a significant factor of death (hazard ratio [HR], 7.74; $P=0.007$). In the RA group, steroid use (HR:5.06, $p=0.007$), low platelets (HR:12.9, $p=0.002$) were independent factors of death. Disease activity, duration of disease, use of biological products, use of methotrexate, presence of fall over 8 years was not a significant factor. [Conclusions] RA was significant high risk factor of death. Steroid use and low platelets were independent factors of death in RA patients.

W17-1

Runx2+, Sox9+ positive synovial cells differentiate into hyperplastic chondrocytes; it results in bony ankylosis

Yoko Miura, Satoshi Kanazawa

Department of Molecular and Cellular Biology, Nagoya City University Graduate School of Medical Sciences

Conflict of interest: None

[Object] Rheumatoid arthritis (RA) is a type of chronic inflammation with bone destruction, which leads to bony ankylosis. To confirm ectopic differentiation of synovial fibroblasts (SFs) into osteo-chondrocytes in RA, we studied the fate of SFs with histopathological analyses in mouse model. [Methods] D1BC mice were induced with a low-dose of bovine type II collagen for chronic articular inflammation in the joints. *In situ* hybridization and histopathological examination performed using differentiation markers for SFs and osteochondrogenic lineage. *B7.1* transgene was used as a lineage tracing marker. [Results] D1BC mice shared common features of patients in RA such as chronic inflammation and bony ankylosis. S100A4 and vimentin were expressed in SFs, which expressed *Col2a1* and *Col10a1*. Pannus is composed of three types of SFs, *Runx2*⁺, *Sox9*⁺ positive, *Runx2*⁺ single positive and double negative cells. Ectopic Collagen X positive hypertrophic chondrocytes (HCs) were observed adjacent to pannus. These HCs expressed *Runx2*⁺, *Sox9*⁺ and underwent differentiation into osteoblastic cells, leading to bony ankylosis. [Conclusions] *Runx2*⁺, *Sox9*⁺ positive SFs have a feature of osteo-chondrogenic lineage and differentiate into osteocytes via HCs.

W17-2

IL-17 is expressed on rheumatoid arthritis and Psoriatic arthritis and mediates angiogenesis

Shinichiro Nishimi, Takeo Isozaki, Masahiro Hosonuma, Airi Nishimi, Sho Ishii, Takahiro Tokunaga, Yuzo Ikari, Hidekazu Furuya, Kuninobu Wakabayashi, Tsuyoshi Kasama
Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] IL-17 expression is reported in rheumatoid arthritis (RA) and psoriatic arthritis (PsA). However, the role of IL-17 in angiogenesis is unclear. We have shown the expression of IL-17 in arthritis. [Methods] We measured IL-17 in RA, PsA and osteoarthritis (OA) serum using ELISA. To determine IL-17 expression in synovial tissues, immunohistochemistry was performed. Finally, to determine the regulation of proangiogenic mediators in IL-17 stimulated fibroblasts, ELISA was used. [Results] IL-17 in PsA serum was significantly higher compared with RA and OA. IL-17 is expressed in synovial tissues. VEGF, MCP-1/CCL2 and ENA-78/CXCL5 in IL-17 stimulated fibroblast conditioned medium was significantly higher compared with that in nonstimulated fibroblast conditioned medium. [Conclusions] These data show IL-17 upregulates the production of angiogenic growth factors in synovial fibroblasts.

W17-3

Analysis of the role of ROR γ + Foxp3⁺ regulatory T cells in the regulation of autoimmune arthritis

Kotona Furuyama, Yuya Kondo, Masahiro Yokosawa, Masaru Shimizu, Hiroto Tsuboi, Isao Matsumoto, Takayuki Sumida
Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: None

[Object] To clarify the role of ROR γ ⁺Foxp3⁺ regulatory T (Tr17) cells in the development autoimmune arthritis. [Methods] 1) Lymph node cells were harvested from C57BL/6 mice on 10 days after CII immunization. Cytokine production was analyzed from Tr17 cells by FCM. 2) Lymph node cells were harvested from ROR γ ^{fl/fl}Foxp3^{cre} (cKO) mice on 10 days after first CII immunization. Expression of ROR γ in Foxp3⁺ regulatory T (Treg) cells were analyzed by FCM. 3) Collagen induced arthritis (CIA) was induced in cKO mice and ROR γ ^{fl/fl} (control) mice by CII immunization. Incidence and severity of CIA were evaluated. 4) Lymph node cells were harvested from cKO mice and control mice on 10 days after CII immunization, and cultured with CII in vitro. IL-17 and IFN γ in culture supernatant were measured by ELISA. [Results] 1) IL-10 production was significantly increased in Tr17 cells compared with ROR γ ⁺Treg cells (p<0.001). 2) Frequency of ROR γ ⁺Foxp3⁺Tr17 cell was decreased in cKO mice compared with control mice (p = 0.001). 3) CIA tended to be exacerbated in cKO mice compared with control mice. 4) Production of CII reactive IL-17 production tended to be increased in cKO mice compared with control mice. [Conclusions] Tr17 cells might regulate the pathogenesis of CIA.

W17-4

The role of IL-34 in pathogenesis of rheumatoid arthritis

Hiroko Nagafuchi, Shoichi Ozaki, Kimito Kawahata
Departments of Rheumatology and Allergy, St. Marianna University School of Medicine

Conflict of interest: None

[Object] To treat rheumatoid arthritis (RA), controls of inflammation and bone destruction are important. Interleukin (IL) - 34 is a novel cytokine involved in chronic inflammation and bone resorption, which discovered as a second ligand of colony-stimulating factor-1 receptor (CSF-1 R). There is no data on Japanese patients for IL-34 in RA pathology. The aim of this study is to clarify the role of IL-34 in the pathogenesis of Japanese RA. [Methods] RA and osteoarthritis (OA) patient sera and RA synoviocytes were used. IL-6 and IL-34 were measured by ELISA. [Results] Serum IL-34 was significantly increased in RA compared to OA (p

<0.05). Serum IL-34 was increased in some RA patients with negative inflammatory findings and active synovitis with MRI or echo. IL-34 production was spontaneously observed in the culture supernatant from RA primary synoviocytes. RA fibroblast-like synovial cells (FLS) produced IL-34 upon stimulation with IL-1 and TNF α . IL-6 produced from RA FLS stimulated with IL-1 was suppressed by anti-IL-34 antibody and anti-CSF-1 R antibody. [Conclusions] IL-34 production is elevated in Japanese RA patients, and IL-34 is produced in synovium and revealed that they are involved in the pathogenesis. It was suggested that IL-34 could be a new therapeutic target for RA.

W17-5

Murine Osteoblasts Secrete High Concentration of Osteoprotegerin and Suppress Osteoclastogenesis by Inhibiting Soluble RANKL

Hiroaki Yazawa, Maiko Yanagisawa, Yoshimi Aizaki, Kojiro Sato, Toshihide Mimura
Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University

Conflict of interest: None

Purpose: We once reported that although human M-CSF and human RANKL can induce murine osteoclastogenesis in vitro, human synoviocytes can't induce osteoclasts (OCs) when it was co-cultured with mouse OC precursor cells. Thus, synoviocytes have a character different from osteoblasts. Human synoviocytes stimulated by Vitamin D₃(1,25(OH)₂D₃) and prostaglandinE₂(PGE₂) did not produce RANKL but secreted a high concentration of osteoprotegerin (OPG), a decoy receptor for RANKL. Interestingly, mouse osteoblasts secreted much more OPG than RANKL. Our purpose is to further investigate the results. **Methods:** We obtained osteoblast from neonatal mouse calvaria. They were co-cultured or cultured separately with mouse bone marrow cells (BMCs). We detected OCs by using tartrate-resistant acid phosphatase staining. **Results:** When osteoblasts and BMCs are cultured separately with 1,25(OH)₂D₃ and PGE₂, OCs were not induced. In the presence of M-CSF and a high dose of RANKL (>10ng/ml), BMCs transformed into OCs. **Conclusion:** We propose that membrane-bound RANKL plays a more important role than soluble RANKL in osteoclastogenesis. This may work as a mechanism that prevents ectopic osteoclastogenesis. We also speculate that M-CSF secreted from osteoblasts is insufficient for OC precursor cells to survive.

W17-6

Chronotherapy with Baricitinib attenuates CIA mice arthritis

Arisa Yaekura¹, Ikumi Okumura¹, Kenta Kaneshiro¹, Koto Uchida¹, Yuto Oketani¹, Kanta Morii¹, Kohsuke Yoshida¹, Yoshiko Kawasaki², Nao Shibamura³, Yoshitada Sakai⁴, Akira Hashiramoto¹

¹Department of Biophysics, Division of Clinical of Immunology, Kobe University Graduate School of Health Sciences, Kobe, Japan, ²Department of Rheumatology, Kobe Kaisei Hospital, Kobe, Japan, ³Department of Orthopaedic Surgery, Kobe Kaisei Hospital, Kobe, Japan, ⁴Department of Rehabilitation Science, Kobe University Graduate School of Medicine, Kobe, Japan

Conflict of interest: None

[Object] Diurnal variations are observed in symptoms of rheumatoid arthritis (RA), and serum cytokine concentrations of collagen-induced arthritis (CIA) mice is reported to increase from morning to evening. JAK inhibitor baricitinib (BAR), a wide-ranged cytokine blocker, is oral administrated once a day. In this study, the effect of timing of BAR administration, targeting peaks of cytokine secretion, was examined in CIA mice. [Methods] CIA mice were administered a dose of 3 mg/kg of BAR once a day at zeitgeber time (ZT) 0 or ZT12 for 18 days. On day18, splenic lymphocytes were isolated to measure expressions of IL-1 β , IL-6, IL-17A, TNF and IFN γ by Real-time PCR. [Results] Arthritis score of ZT0 group decreased from day9 as compared to untreated group, and those of ZT12 group was significantly higher than those of ZT0 group from day15. Expressions of IL-6, IL-17A, IFN γ in lymphocytes were significantly decreased by BAR treatment as compared with untreated group. Expressions of IL-1 β in ZT0 treated group were significantly decreased as compared with untreated mice, whereas those in ZT12 group

were not. Expressions of TNF in ZT0 group were lower as compared with ZT12 group. [Conclusions] Effectiveness of chronotherapy targeting cytokine secretions is suggested.

W18-1

HLA-DR sequence variants in idiopathic membranous nephropathy and bucillamine-induced membranous nephropathy

Atsushi Komatsuda, Hideki Wakui

Akita University Graduate School of Medicine

Conflict of interest: None

[Object] Several recent studies in patients with idiopathic membranous nephropathy (i-MN) showed that HLA-DR-B15 genes are significantly associated with i-MN. On the other hand, bucillamine, one of DM-RADs, is known to induce MN (bi-MN). However, there is only 1 report on analysis of HLA regions in Japanese patients with bi-MN, which showed HLA-DR-B8 is associated with bi-MN. [Methods] A total of 31 patients with i-MN and 22 patients with bi-MN were enrolled. All patients were Japanese. We analyzed HLA-DR using genomic DNA prepared from peripheral mononuclear cells from each patient. We then studied differences in HLA-DR among the 2 groups. [Results] Allelic frequency distributions for HLA-DR8 were not different between the i-MN and the bi-MN groups (14.75% and 27.3%, $p=0.18$). Allelic frequency distributions for HLA-DR15 were significantly different between the i-MN and the bi-MN groups (34.4% and 2.27%, $p=0.002$). There are no differences in other HLA-DR. [Conclusions] HLA-DR15 may become a new biomarker indicating the protective factor of bi-MN.

W18-2

Efficacy and safety of biologic agents in elderly patients with rheumatoid arthritis

Akiko Kasahara, Takashi Kida, Takuya Inoue, Shunya Kaneshita, Tomoya Sagawa, Risa Sagawa, Kazuki Fujioka, Hidetake Nagahara, Makoto Wada, Masataka Kohno, Yutaka Kawahito

Department of Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine

Conflict of interest: None

[Object] To evaluate the efficacy and safety of biologic agents in elderly patients with rheumatoid arthritis (RA). [Methods] Retrospective study in a total of 152 elderly patients with rheumatoid arthritis, from April 2008 to March 2017. The study population was divided into two age groups (young-old (109 patients): 65 to 74 years and old-old (43 patients): ≥ 75 years), and the efficacy and safety of biologic agent therapy were assessed. [Results] Overall, 68 (young-old/old-old: 40/28) patients were treated with abatacept; 34 (27/7) with etanercept; 22 (20/2) with tocilizumab; 14 (10/4) with golimumab; 9 (7/2) with certolizumab; 3 (3/0) with adalimumab and 2 (2/0) with infliximab. One-year adherence rates were 77 % in young-old patients and 74 % in old-old patients. Adverse Events were 16.7/100 person-year in young-old patients, and 26.4/100 in old-old patients. Serious infections requiring hospitalization were 1.6/100 person-year in young-old patients, and 6.8/100 person-year in old-old patients. [Conclusions] Abatacept was most used in old-old patients. The rate of serious infection was higher in old-old patients. This study suggests that we have to use biologic agent more carefully in old-old patients.

W18-3

Placental transfer of tocilizumab in a patient with rheumatoid arthritis

Yoshifumi Tada, Mariko Sakai, Yoshinobu Nakao, Akihito Maruyama, Yuri Sadanaga, Nobuyuki Ono, Syuichi Koarada

Department of Rheumatology, Saga University, Faculty of Medicine, Saga, Japan

Conflict of interest: None

Tocilizumab (TCZ) use during pregnancy in patients with rheumatoid arthritis (RA) has not been evaluated in detail. We investigated the pla-

cental transfer of TCZ. A 39-year-old Japanese woman with RA has been treated with TCZ and prednisolone. When she became pregnant after an embryo transfer, we stopped TCZ and increased prednisolone. However, the RA exacerbated and the fetus died. An attempt to control her RA with certolizumab pegol failed, so TCZ was resumed. The patient again became pregnant after the next frozen embryo transfer. We continued TCZ throughout an eventful pregnancy. She gave birth at 38 weeks of gestation by Caesarean section to a girl weighing 3,276 g with no congenital abnormalities. Although the infant was hypoglycemic at birth, she grew normally and continued to thrive. The TCZ concentration of maternal serum at birth was 6.17 mg/mL, and the transfer rate in umbilical cord blood and neonatal sera were 89% and 78%, respectively. We also measured total IgG and IgG1 subclass concentrations. The transfer rates of IgG and IgG1 in cord blood were 152% and 145%, and those in neonatal blood were 159% and 153%, respectively. These results showed that TCZ was transferred to fetus, but its transfer rate seemed to be lower than those of natural IgG and IgG1 antibodies.

W18-4

An attitude survey on RA treatment of clinicians in northeastern Osaka (3rd. report)

Yoshio Ozaki^{1,2,8}, Saki Tsujimoto^{1,2}, Akihiro Tanaka^{1,2,8}, Keiko Shimamoto^{1,2,8}, Tohru Nishizawa^{2,8}, Hideki Amuro^{2,8}, Yonsu Son^{1,2,8}, Hideo Kagawa^{3,8}, Yasuo Kunugiza^{4,8}, Tsuyoshi Teranishi^{5,8}, Shigeo Miyashima^{6,8}, Shinobu Morishita^{7,8}, Tomoki Ito², Shosaku Nomura²

¹Department of Rheumatology and Clinical Immunology, Kansai Medical University Hospital, ²First Department of Internal Medicine, Kansai Medical University, ³Kagawa-Clinic, ⁴Orthopedic Surgery, JCHO Hoshigaoka Medical Center, ⁵Teranishi Naika, ⁶Miyashima RA & Orthopaedic Clinic, ⁷Morishita Orthopaedic and RA Clinic, ⁸Kita-kawachi Rheumatism Network

Conflict of interest: None

[Object/Methods] Kitakawachi region in northeastern Osaka has a population of 1.2 million people. In this region, the majority of examinations and medical treatments for rheumatoid arthritis (RA) are performed in clinics. We conducted 3rd. sentiment survey to build a collaborative system for continuous and effective RA medical examination. Objectives/Method: The survey was distributed to 180 facilities, including internal medicine and orthopedic surgery departments of hospitals and clinics which follow RA patients. [Results/Conclusions] Answers were obtained from 103 facilities (41.2%). 50% of facilities specialized in RA (RA clinic) and 23% of non-specialized facilities (non-RA clinic) diagnosed RA using ACR/EULAR criteria. Doctors in RA clinics made much of physical assessment of joint (TJC: RA clinics 64% vs non-RA clinics 15%, SJC 74% vs 31%). Furthermore, 59% of doctors in non-RA clinics did not use MTX for RA treatment.

W18-5

Circulated cooperation of the hospital and polyclinic for rheumatoid arthritis treatment in Yamagata area (Yamagata Area Rheumatoid Arthritis Neo Noticeable Associated Network; YARANNA network) -for the introduction of two physicians in charge-

Yuya Takakubo^{1,2,4,5,6}, Suran Yang^{1,3,5,6}, Akiko Sasaki^{2,3,4}, Yuta Suzuki^{1,6}, Yasushi Naganuma⁴, Hiroharu Oki¹, Hiroshi Orui¹, Michiaki Takagi¹

¹Department of Rehabilitation & Orthopaedic Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan, ²Department of Orthopaedic Surgery, Yamagata Saisei Hospital, ³Department of Orthopaedic Surgery, Yoshioka Hospital, ⁴Department of Orthopaedic Surgery, Yamagata Prefectural Central Hospital, ⁵Department of Orthopaedic Surgery, Yamagata Prefectural Shinjo Hospital, ⁶Department of Orthopaedic Surgery, Okitama Public General Hospital

Conflict of interest: None

[Object] The patients with RA which make regular visit with our university hospital are increasing annually. We have established the group of the circulated cooperation of the hospital and polyclinic for rheumatoid arthritis treatment in Yamagata area (Yamagata Area Rheumatoid Arthritis Neo Noticeable Associated Network; YARANNA network) since 2013. The aim of this study is to investigate the YARANNA network for

five years. [Methods] We investigate numbers of the patients and polyclinics which has agreed the circulated cooperation as YARANNA network and the drug using for them. [Results] We have one hundred seventy-seven patients (11% in all our patients) with RA which has agreed the YARANNA network. They included fifty-three patients receiving biologics, one hundred three non-biologics, nine for the treatment of osteoarthritis, seven for rehabilitation and two for osteoporosis. [Conclusion] The patients with RA which prefer regular visit with our university hospital may continue to increase, because of the unique right of free-access to any hospital for Japanese patients and increasing elderly people with many complications. It is important to spread this circulated cooperation system of YARANNA network in our area.

W18-6

Factors for delayed treatment intervention in patients with newly diagnosed rheumatoid arthritis

Shohei Nakamura^{1,2}, Yohei Seto^{1,2}, Isao Matsuura¹, Hisashi Yamanaka²
¹Department of Rheumatology, Tokyo Women's Medical University Yachiyo Medical Center, ²Department of Rheumatology, Institute of Rheumatology, Tokyo Women's Medical University

Conflict of interest: None

[Object] To study the proportion and factors which the delayed treatment intervention in patients with newly diagnosed rheumatoid arthritis (RA). [Methods] Patients (clinically suspect arthritis; CSA, undifferentiated arthritis; UA and rheumatoid arthritis; RA fulfilled the ACR/EULAR 2010 classification criteria) were included retrospectively in this study who had newly referred to the clinic from September 2013 to September 2018, and naïve to anti-rheumatic drugs. Patients' background, and the factors for delayed intervention were evaluated. [Results] Total of 4 CSA (Age 59, female 2), 23 UA (Age 68, female 19), 71 RA (Age 56, female 42) were included. Duration from the first visit to treatment intervention was 0, 14 and 0 day, respectively. The reason for delayed intervention were assessment for comorbidity, family planning, differential diagnosis for other rheumatic diseases and/or connective tissue diseases, and planned elective surgeries. [Conclusions] Early treatment intervention is one of the fundamentals for newly diagnosed RA, and management of factors for the intervention delay shall be important.

W19-1

Extending tocilizumab infusion intervals from 4 to 6 weeks in rheumatoid arthritis patients

Osamu Saiki, Hiroshi Uda
Department of Rheumatology, Higashiosaka City Medical Center

Conflict of interest: None

[Object] We showed that the interval between successive IV TCZ can be extended from 4w to 6w in 60% of patients with low diseases activity (LDA) at 4w intervals (Clin Exp Rheum, 2017). We investigated the efficacy and safety of extending the interval from 4w to 6w. [Methods] A retrospective observational study was conducted by enrolling patients in whom the intervals of TCZ infusions could be extended from 4w to 6w with an LDA for more than 2 years. We compared the efficacy and safety of TCZ infusions at 4w and 6w in a cohort of patients. We also examined serum lipid, platelet, IL-6 and trough TCZ levels. [Results] A total of 125 patients with an LDA at 4w intervals were enrolled, of which 78 patients maintained LDA at 6w intervals. After extending the intervals, the efficacy was maintained, and the side effects decreased significantly. In addition, the levels of total cholesterol and triglyceride were returned to normal, and the serum trough levels of TCZ became undetectable at 6w intervals. [Conclusions] We proved that intervals between TCZ infusions can be extended from 4w to 6w in more than 60% of RA patients along with a decrease in the side effects, thus suggesting the need to change the infusion intervals in suitable patients.

W19-2

Comparative effectiveness of switching to TNF inhibitors, abatacept or JAK inhibitors after inadequate response to tocilizumab in patients with rheumatoid arthritis

Hiroshi Kanazawa, Hiromitsu Takemori
Department of Rheumatology, Aomori Prefectural Central Hospital

Conflict of interest: None

Objective: In EULAR recommendation for management of RA (2016 update), if a bDMARD or tsDMARD failed, treatment with another bDMARD or a tsDMARD should be considered. The aim of study is to compare the effectiveness of TNF inhibitors (TNFi), abatacept (ABT) or JAK inhibitors (JAKi) after inadequate response to tocilizumab (TCZ-IR) in patients with RA. Method: In this retrospective study, we evaluated 27 RA patients (85.2% of women, average age 59.8 years old, and average disease duration 8.2 years), switched to TNFi (9, IFX (1), ETN (3), GLM (2) and CZP (3)), ABT (11), or JAKi (7, tofacitinib (6), baricitinib (1)) after TCZ discontinuation by the clinical effectiveness and background at week 24. Result: The drug retention rate at week 24 was 55.6% (TNFi), 63.6% (ABT) and 57.1% (JAKi). The proportion rate of patients achieving CDAI \leq 2.8 (remission) at week 24 was 22.2% (TNFi), 36.3% (ABT) and 14.3% (JAKi). The mean value of CDAI at week 24 was 8.38 (TNFi), 6.16 (ABT) and 7.93 (JAKi). In this analysis, significant difference was not provided statistically. Serious adverse event was not observed in any groups. Conclusion: Our findings showed no significant difference of switching to TNFi, ABT or JAKi after TCZ-IR. Further clinical trial is expected for RA patients with TCZ-IR.

W19-3

Switching to Abatacept from Other Biological Agents due to Adverse Event in Patients with Rheumatoid Arthritis

Yuji Hirano, Daisuke Kihira
Department of Rheumatology, Toyohashi Municipal Hospital

Conflict of interest: Yes

[Object] Main reasons for stopping biological agents (BIO) in RA patients are lack of efficacy (LOE) and adverse event (AE). Information on next choice after stopping BIO due to AE are lacking. We have chosen abatacept (ABT) after BIO which is stopped due to AE and investigated the results. [Methods] Toyohashi RA Database was used. 21 RA patients treated with ABT after BIO failed due to AE were used in this retrospective study. Patients' characteristics, drug retention rates of both ABT and former BIO (Kaplan-Meier) and efficacy of ABT were investigated. [Results] Patients characteristics at ABT initiation (n=21): 17 female and 4 male. Average age was 66.9 years. RA duration was 14.5 years. 33.3% was concomitant with MTX. 66.7% was concomitant with PSL. If all reasons for stopping drugs were assigned as outcome, mean drug retention periods was 1037 days and 808 days in ABT and former BIO, respectively and there were no significant difference (p=0.198). If only AE was assigned as outcome, there was significant differences (ABT: 1428 days, former BIO: 808 days, p=0.023). Reasons for stopping ABT were LOE in 5 cases and AE in 4 cases. DAS28-CRP and SDAI were significantly improved after ABT initiation. [Conclusions] It was suggested that ABT after BIO failed due to AE was acceptable.

W19-4

Stopping methotrexate in combination with abatacept for rheumatoid arthritis-multicenter analysis using FIT-RA registry-

Hiraku Motomura¹, Isao Matsushita¹, Toshihito Hiraiwa¹, Takashi Murayama², Satoshi Nakazaki^{2,3}, Shinichi Kato^{2,3}, Hiroshi Fujinaga⁴, Tetsuo Watanabe⁴, Haruki Takagi⁵, Toshiyuki Kitaori⁵, Hirofumi Taki⁶, Koichiro Shinoda⁶, Tomoatsu Kimura¹

¹Department of Orthopedic Surgery, University of Toyama, ²Department of Rheumatology, Juhoku Hospital, ³Department of Rheumatology, Kamiaraya Hospital, ⁴Japanese Oriental Medicine and Rheumatology, Toyama Prefectural Central Hospital, ⁵Department of Orthopedic Surgery, Fukui Red Cross Hospital, ⁶Department of First Medicine, University of Toyama

Conflict of interest: None

[Object] To assess the clinical results of stopping methotrexate (MTX) in combination with abatacept (ABT) for patients with rheumatoid arthritis (RA). [Methods] We enrolled 66 patients with RA who were administered MTX in combination with ABT and observed for more than 1 year in FIT-RA (Fukui, Ishikawa, Toyama-rheumatoid arthritis) registry. Twenty-two patients were stopped MTX in combination with ABT (4 patients discontinued due to adverse events). We examined 18 patients without adverse events for the clinical variables at baseline, at the time of stopping MTX and at final follow-up. [Results] The mean age was 58.9 years old and the mean disease duration of RA was 10.1 years. ACPA or RF positive rate was 94.4%. The mean dose of concomitant MTX was 7.0 mg/week at baseline and biological naïve were 6 patients (33.3%). The mean time to stopping of concomitant MTX with ABT was 1.8 years. No patient resumed MTX to final follow up. The mean DAS28-ESR was 4.65 at baseline, decreased to 2.67 at the time of stopping MTX and furthermore decreased to 2.40 at final follow-up. [Conclusions] MTX in combination with ABT was stopped in one-third of patients. The clinical efficacy after stopping MTX maintained during ABT therapy.

W19-5

Does the dose reduction strategy of MTX following remission with biologics in rheumatoid arthritis maintain the remission status?

Mikio Nakajima, Tsuyoshi Jotoku, Norio Morimoto
Katsuragi Hospital

Conflict of interest: None

[Object] The aim of this study was to assess whether the dose reduction of MTX after sustained remission combined with biologics is useful for rheumatoid arthritis patients. [Methods] Disease activity score (DAS-28CRP) were researched in 13 rheumatoid arthritis patients (average age 60yo, morbidity duration 7.7 years) who were treated by biologic agents (ETN 7, ADA4, TCZ 2) and MTX (mean initial dose 10.8mg/w) at the start of treatment (DAS28CRP 3.32). [Results] DAS28CRP score of before and after first dose reduction of MTX were 1.36/1.42, in second reduction 1.54/1.54. Aggravation of scores were recognized in five cases, none of these patients fail there remission. [Conclusions] The treatment strategy of MTX dose reduction after sustained remission was useful for prevention of adverse effects of MTX.

W19-6

Decreasing methotrexate dose after remission in case of rheumatoid arthritis patients who had MTX plus BIO: a clinical course observation

Toshiaki Miyamoto, Kenji Yamazaki, Ryuhei Ishihara
Internal Medicine and Rheumatology, Seirei Hamamatsu General Hospital

Conflict of interest: Yes

Objective: MTX is important as a first-line in treating RA. On the other hand, it is also important to reduce MTX to reduce side effect of MTX, especially lymphoproliferative disorder (LPD), but the timing to decrease of MTX is not known in present. In patients with rheumatoid arthritis (RA) that maintained remission by MTX plus Biologic DMARD (BIO) and got their consent, the clinical course after decreasing MTX was evaluated respectively. **Methods:** Subjects were 52 patients who had MTX plus BIO from March 2014 to July 2016. Baseline characteristics were Mean age 55.8 years, mean duration of illness 64.9months, mean use period of BIO 35.0 months. The course of DAS28, SDAI, CDAI and remission rates were analyzed. **Results** Mean DAS28-ESR, SDAI, CDAI were no significant rise at 52 weeks after decreasing MTX (1.73→1.85, 0.42→0.76, 0.32→0.69). Remission rates of DAS28-ESR, SDAI, CDAI were 87.8%,93.9%,93.9% at 52 weeks. **Conclusion:** This study shows the possibility that decreasing methotrexate dose after remission in case of rheumatoid arthritis patients who had MTX plus BIO might be a useful option after REM.

W20-1

The efficacy and safety of remission induction therapy in patients with giant cell arteritis (GCA)

Mana Taniguchi, Kenichiro Tokunaga, Hideto Oshikawa
Department of Rheumatology, Japanese Red Cross Kumamoto Hospital

Conflict of interest: None

[Object] To assess the efficacy and safety of remission induction therapy in patients with giant cell arteritis (GCA). [Methods] We reviewed clinical data of patients with GCA diagnosed between Nov 2014 and Aug 2018. [Results] Fourteen patients with GCA (average age 73.5 years (y) (60-86), disease duration 30 months (mts) (3-90), 4 women (28.6%)) participated and were observed for 21.3 mts (2-48.5). Twelve patients underwent temporal artery biopsy, which confirmed arteritis in 57.1%. Initial treatment was prednisolone (PSL; 1 mg/kg/d); the initial remission induction rate was 92.9%, and time to remission was 0.6 mts (0.25-4). Seven patients were observed for more than 12 mts. At 12 mts, the average PSL dose was 6.0 mg/d, cumulative PSL dose was 6068.4 mg, and remission rate was 87.5%. No patients received tocilizumab, and 14.3% received methotrexate and PSL. The relapse rate was 35.7%, and mean time to relapse was 13.2 (2-48.5) mts. Adverse events were diabetes mellitus (21.4%), infection (14.3%), and others. [Conclusions] Almost all patients achieved initial remission, which was maintained for 12 mts. Meanwhile, high infection and diabetes incidences were observed. The relapse rate after 12 mts was relatively high despite sufficient steroids. Further research will help determine appropriate PSL doses.

W20-2

Tocilizumab as remission induction and steroid-sparing therapy for giant cell arteritis

Hiroshi Ito, Hidehiro Yamada, Hironari Hanaoka
Medical Center for Rheumatic Diseases, Seirei Yokohama Hospital

Conflict of interest: None

[Purpose] The clinical question on the treatment of giant cell arteritis (GCA) with tocilizumab (TCZ) is how to reduce the cumulative dose of steroids because of multiple comorbidity. Here we describe 5 GCA cases in whom we attempted a rapid tapering of steroid after methylprednisolone (mPSL) pulse plus TCZ therapy. [Cases] Five patients (mean age 68.4) with GCA were treated with mPSL pulse and TCZ without other immunosuppressants. The clinical manifestations included headache, jaw claudication, double vision in 2 cranial-GCA, and fever, abdominal pain in 3 large vessel-GCA. Two patients had polymyalgia rheumatica (PMR). Mean initial dose of PSL was 22.5 mg. The median observation periods was 11 months. All patients responded well to the induction therapy, resulting in remission. PSL was tapered down to the mean 6 mg/day after 3 months. Three patients discontinued PSL within 10 months. One patient showed a flare of PMR after 10 months, which was treated with increasing dose of PSL, because the patient experienced leukocytopenia which improved after extending the interval of TCZ. There was no other serious adverse events. [Conclusion] Induction therapy with mPSL pulse and TCZ may facilitate the tapering and cessation of steroid without adding serious adverse events in GCA.

W20-3

Usefulness of tocilizumab for patients with Takayasu's arteritis

Shota Okamoto, Hiroto Tsuboi, Taihei Nishiyama, Hirofumi Toko, Masaru Shimizu, Fumika Honda, Mizuki Yagishita, Ayako Ohyama, Izumi Kurata, Saori Abe, Hiroyuki Takahashi, Atsumu Osada, Masahiro Yokosawa, Yuya Kondo, Isao Matsumoto, Takayuki Sumida
Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: None

[Object] To investigate usefulness of tocilizumab (TCZ) for patients with Takayasu's arteritis (TKA). [Methods] We examined 1) background, 2) concomitant drugs, 3) CRP, 4) prednisolone (PSL) dose, 5) relapse and adverse events, in patients with TKA who started TCZ between Aug 2017 and Sep 2018 in our hospital, retrospectively. [Results] 1) 6 patients (all

female, 25.0±8.1 years old, 5.2±4.8 years of disease duration, 3 cases of type II a and 3 of type V) were investigated. TCZ was used for the first induction therapy (Tx) in 2 cases and the maintenance Tx in 4 cases. All 6 cases received TCZ subcutaneously. 2) In 2 cases of induction Tx, 45 and 30 mg/d of PSL was concomitantly used. In 4 cases of maintenance Tx, 9.0±4.3 mg/d of PSL was used, and all 4 cases received concomitant immunosuppressants (MTX in 2 cases, azathioprine 2, CsA 1, and MMF 1). 3) CRP significantly decreased from 1.9±2.6 (0W) to 0.03±0.0 (8W) mg/dl (P<0.05). 4) In 2 cases of induction Tx, PSL doses were tapered from 1.1 and 0.5 mg/kg/d (0W) to 0.5 and 0.3 mg/kg/d (8W), respectively. In 4 cases of maintenance Tx, PSL doses (0.2±0.1 mg/kg/d) did not change for 8W. 5) No relapse and adverse events occurred for 32.0±19.4W of observational period. [Conclusions] TCZ might serve as both induction and maintenance Tx for TKA.

W20-4

Efficacy and safety of tocilizumab in patients with recurred Takayasu arteritis in our hospital

Mikiya Kato, Taichi Miyagi, Risa Wakiya, Shusaku Nakashima, Hiromi Shimada, Tomohiro Kameda, Hiroaki Dobashi
Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Kagawa University School of Medicine

Conflict of interest: None

[Object] To investigate the efficacy and safety of TCZ for the treatment of TAK patients who recurred during tapering GC. [Methods] Six subjects of TAK treated with TCZ were analyzed. Baseline characteristics, remission rate, adverse events, GC dose, were examined retrospectively. The structural changes of LV were evaluated using enhanced-CT, MRI, and FDG-PETCT. [Results] All 6 cases (one male and 5 female) were initiated by TCZ treatment. The average age was 38.0 ± 14.2 years old. The disease duration at the administration of TCZ was 157 ± 131 months. The mean dosage of PSL was 7.42 ± 4.09 mg/day, and the immunosuppressants combined with GC were prescribed in 3 cases. The dose escalation of GC was conducted in only one patient at TCZ administration. Within 6 months after initiating TCZ treatment all patients achieved remission, and the PSL dose was reduced to 4.33 ± 2.49 mg/day. Immunosuppressants could be discontinued in 2 out of 3 cases. No serious adverse events were observed. [Conclusions] TCZ was a safe and effective option of treatment for TAK. In addition, the treatment strategy for the recurred TAK patients without dose escalation of GC could be conducted using TCZ. Furthermore, we will discuss the structural changes of LV treated with TCZ using imaging findings.

W20-5

Consideration on the persistence rate and therapeutic effect of tocilizumab for large vasculitis

Atsuhiko Yamamoto, Kaori Ishimura, Hiroki Akazawa, Chisato Ashida, Fusayo Ikeda, Akinori Okada, Daisuke Tomita, Tetsu Itami, Kenji Sakai, Shinkai Ri, Asuka Inoue, Toshihiko Shiga, Kazuya Kishimoto, Yasuaki Hirooka, Yuji Nozaki, Koji Kinoshita, Masanori Funouchi, Itaru Matsumura
Kinki University School of Medicine Affiliated Hospital College of Collagen Disease

Conflict of interest: None

Objective: Tocilizumab (TCZ) efficacy has been reported as a treatment for Takayasu arteritis and giant cell arteritis. In this study, we investigated continuation rate, inflammatory marker and relapse rate of TCZ treatment group (P+T group) combined with steroid and steroid monotherapy group (P group) in large vasculitis. METHODS: As of October, 2018, the baseline of P group (11 cases), P + T group (9 cases), continuation rate after 6 months for inflammatory large-scale vasculitis in 20 cases at our homospital, inflammation Markers, and whether or not relapse was present were examined. Results: the six-month continuation rate in the P+T group was 1case but 100% was found in the diverticulitis. Baseline and ΔWBC and ΔCRP after 6 months were significantly lower in the P+T group than in the P group. There was no significant difference in Plt and blood sediment. in relapse within 6months of treatment, 3 of 11 patients showed back pain, general malaise and CRP elevation, but

no relapse was observed in groups. TCZ therapy for large-scale vasculitis has good continuation rate, good inflammatory response reduction and no recurrence, so it was shown to be useful for Large vessel vasculitis.

W20-6

The use of biologics in large vessel vasculitis

Tsuyoshi Shirai¹, Tomoyuki Mutoh¹, Yoko Fujita¹, Hiroshi Fujii¹, Tomonori Ishii¹, Yasuhiko Hirabayashi², Hideo Harigae¹

¹Hematology & Rheumatology, Tohoku University Graduate School of Medicine, ²Department of Rheumatology, Hikarigaoka Spellman Hospital

Conflict of interest: None

[Object] Large vessel vasculitis (LVV) contains Takayasu arteritis (TAK) and giant cell arteritis (GCA). Although biologics are approved for LVV, little information exist. This study analyzed LVV patients treated with biologics. [Methods] 101 LVV patients (GCA, 6) who visited our hospital in 2018 were retrospectively evaluated. Details of biologics, dosing of prednisolone (PSL) and immunosuppressants, efficacy, and adverse events were evaluated. [Results] 26 patients (TAK, 25) were treated with biologics including tocilizumab (TCZ, n=20), infliximab (n=2), adalimumab (n=2), golimumab (GLM, n=2), abatacept (n=2), and rituximab (n=1). Mean-follow up duration was 27 months. In TAK, 23 cases received biologics upon relapse, and two cases for extravascular manifestations. The mean dose of PSL was reduced from 10.6 to 6.4 mg/day (P=0.001). PSL was stopped in one patient under TCZ. Immunosuppressants were used in 12 cases, and stopped in 6 cases. Biologics were switched in 3 cases. Two patients receiving TCZ experienced relapse, and they were treated with GLM or high dose of PSL. [Conclusions] The use of biologics showed significant steroid-sparing effect in TAK. Meanwhile, some cases relapsed without the elevation of inflammatory markers, indicating needs to monitor symptoms and imaging.

W21-1

Current state of the health care costs of patients with ANCA-associated vasculitis in Japan using a large insurance database

Hirokazu Nishina, Eiichi Tanaka, Ryoko Sakai, Masayoshi Harigai, Hisashi Yamanaka

Department of Rheumatology, Tokyo Women's Medical University Hospital

Conflict of interest: None

[Objective] The aim of this study is to investigate the current medical cost by treatment in Japanese ANCA associated vasculitis (AAV) patients. We use a large insurance database. [METHODS] We selected 8,402 cases from 24,673 cases of hospitalized AAV (microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) and eosinophilic granulomatosis with polyangiitis (EGPA) patients from April 2008 to April 2017. Prednisolone (PSL) over 30 mg or steroid pulse therapy or immunosuppressive drugs (rituximab, cyclophosphamide, methotrexate, mycophenolate mofetil and hospitalization days over 7 days) were defined as induction therapy group and we analyzed these (2,299 cases). [Results] AAV (821 cases), MPA (1,055 cases), GPA (261 cases), EGPA (404 cases). Median of hospitalization cost was 1,382,524 yen, 1,413,041 yen, 1,359,152 yen, 1,454,047 yen. In the case of IVCY, they were slightly increased (1,762,436 yen, 1,839,252 yen, 1,486,644 yen, and 1,938,735 yen). In the case of rituximab, It were doubled (2,699,665 yen, 2,778,315 yen, 2,770,317 yen, 3,104,470 yen). In the case of plasma exchange, it were tripled (3,978,383 yen, 3,663,162 yen, 4,404,019 yen, 4,032,512 yen). [Conclusion] In Japanese AAV patients, medical costs become expensive due to rituximab and plasma exchange.

W21-2

QOL of elderly ANCA-associated vasculitis

Yoko Miura, Ryo Yanai, Nobuyuki Yajima

Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] As advances in the treatment of anca-associated vasculitis, acute phase deaths have decreased. So, it is important to treat with keeping Quality of life. In this study, we determined the factors related to re-hospitalization of elderly ANCA-associated vasculitis people. [Methods] 68 ANCA-associated vasculitis patients who diagnoses at Showa university hospital department of Rheumatology were targeted. They were hospitalized among January 2006 and July 2017. The main outcome is re-hospitalization which was unexpected. The type of vasculitis, damaged organ, age, underlying disease, BMI, steroid pulse, the use of immunosuppressant, and infection during first hospitalization, rehabilitation and ADL were considered as risk factors. [Results] 68 patients with anca-associated vasculitis were examined. Of the 68 people, 50 MPA, 10 GPA, 8 EGPA, age 77.7 ± 7 , female 73.4%. The prevalence of the unscheduled hospitalization within one year was 31.8%. Infections were the most common reasons for hospitalization. There are no remarkable factors of the unscheduled hospitalization within one year. [Conclusions] The prevalence of the unscheduled hospitalization within one year was 31.8%. There are no remarkable factors of the unscheduled hospitalization within one year.

W21-3

The clinical features of otitis media with ANCA-associated vasculitis in Ehime university hospital

Koichiro Suemori¹, Jun Ishizaki¹, Takuya Matsumoto¹, Eiji Sada², Katsuto Takenaka¹, Hitoshi Hasegawa¹

¹Hematology, Clinical Immunology and Infectious Diseases, Ehime University Graduate School of Medicine, ²Ehime Prefectural University of Health Sciences

Conflict of interest: None

[Object] To investigate clinical characteristics, efficacy, and safety of treatment in patients with otitis media with ANCA-associated vasculitis (OMAAV) in our hospital. [Methods] 30 patients (8 males, 13 females) who were diagnosed with OMAAV between March 2010 and February 2018 were retrospectively evaluated. [Results] Mean age was 67.8-year-old. The durations from the onset to the diagnosis were 3 months (median value). The clinical symptoms were impaired hearing, congested feeling, tinnitus, headache and fever. MPO- and PR3-ANCA were positive in 23 and 4 cases, respectively. Hypertrophic pachymeningitis, facial palsy, pulmonary disorders and renal lesions were observed in 4, 5, 14 and 8 cases, respectively. Otitis media was involved in bilateral ears in 19 cases. All patients were treated with prednisolone (mean 0.71mg/kg/day), 22 with methylprednisolone pulse therapy, 21 with azathioprine, 9 with intravenous cyclophosphamide, and 8 with rituximab. In 29 of 49 ears, audibility test was improved one month after initial treatments. Overall, 24 patients survived, 10 re-exacerbated and 6 (4 with infection and 2 with other disease) died. [Conclusions] Although immunosuppressive therapy was effective against OMAAV, infection should be remarkable as treatment related-death.

W21-4

Predictor for otitis media in patients with ANCA associated vasculitis

Seiji Kobayashi, Hiroko Kadota, Shinji Watanabe, Yuichiro Shirai, Takahisa Gono, Mitsuhiro Takeno, Masataka Kuwana
Nippon Medical School Graduate School of Medicine

Conflict of interest: None

[Objective] Diagnosis and treatment at the early stage in OMAAV is important in view of prognosis of hearing in patients with AAV. In addition, it is necessary to choose effective immunosuppressive therapy in terms of organ disorders associated with systemic vasculitis. Therefore, we examined predictors for OMAAV complications in patients with AAV. [Methods] This is a single-center, retrospective study involving 22 patients with AAV between January 2016 and September 2018. All patients underwent otolaryngologic evaluation of otitis media. Demographic and clinical information was obtained by review of medical charts. [Results] Eight patients (36.4%) were diagnosed with OMAAV. Of all ears, one ear was sensorineural hearing loss, four ears were conductive hearing loss, and seven ears were mixed hearing loss. All AAV patients complicated with OMAAV had mastoiditis, compared with those without OMAAV

(100% vs 21.4%, $p < 0.001$). In OMAAV patients, responsiveness to induction therapy with steroid or immunosuppressive agents was poor, and recovery of hearing was poor. [Conclusions] Mastoiditis is one of the predictors for otitis media in patients with ANCA associated vasculitis.

W21-5

Association of Otitis Media with ANCA Associated Vasculitis and Hypertrophic Pachymeningitis

Takeshi Nakatsue¹, Shunsuke Sakai¹, Sayuri Takamura¹, Ayako Wakamatsu¹, Hiroe Sato², Daisuke Kobayashi¹, Yoko Wada¹, Takeshi Kuroda², Masaaki Nakano³, Ichiei Narita¹

¹Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan, ²Health Administration Center, Niigata University, Niigata, Japan, ³Department of Medical Technology, School of Health Sciences, Faculty of Medicine, Niigata University, Niigata, Japan

Conflict of interest: None

[Object] We clarify an association of otitis media with ANCA associated vasculitis (AAV) and hypertrophic pachymeningitis (HP). [Methods] Two hundred and eight patients with ANCA associated vasculitis (107 microscopic polyangiitis, 71 granulomatosis with polyangiitis and 30 eosinophilic granulomatosis with polyangiitis) were admitted to Niigata University Hospital from 1989 through 2018. An association of AAV and HP was analyzed in 36 patients with otitis media and 172 patients without otitis media. [Results] 10 cases (28 %) of HP were observed in otitis media group and five cases (2.9 %) of HP in non-otitis media group ($P < 0.01$). Three cases (8 %) of facial palsy were seen in otitis media group and no cases were observed in non-otitis media group ($P < 0.01$). In all 15 cases of HP, 10 cases of otitis media or mastoiditis, six cases of sinusitis, two cases of orbital or cavernous inflammation, and one case of nasopharyngeal inflammation were seen. No eye, ear, nose, or throat manifestations were observed in one case. [Conclusion] Since HP is often complicated with otitis media with AAV, brain MRI should be considered to search HP in otitis media with AAV.

W21-6

Incidence and risk factors of new-onset hypertrophic pachymeningitis in patients with anti-neutrophil antibody-associated vasculitis

Aya Imafuku, Naoki Sawa, Akinari Sekine, Masahiro Kawada, Eiko Hasegawa, Junichi Hoshino, Yoshifumi Ubara, Kenmei Takaichi
Nephrology Center, Toranomon Hospital

Conflict of interest: None

[Object] Hypertrophic pachymeningitis (HP) is a rare complication in patients with anti-neutrophil antibody-associated vasculitis (AAV). The incidence and risk factors associated with new-onset HP remains unknown. [Methods] We retrospectively studied 93 AAV patients, comparing HP incidence between patients with granulomatosis with polyangiitis (GPA) and to those with microscopic polyangiitis (MPA). We further analyzed the risk factors for HP. [Results] Among 93 patients (MPA; 76, GPA; 17), 6 developed HP (MPA; 1, GPA; 5) over an average observation period of 4 years. All patients who developed HP were positive for MPO-ANCA. HP incidence was significantly higher in patients with GPA than in those with MPA (60.2 vs 3.3 persons per 1000 person-years, $P = 0.002$). Univariate classification and regression tree (CART) analysis grouped the patients into patients with HP who have otitis media (33%) and patients with HP who have sinusitis (21%), and both conditions were associated new-onset HP ($P < 0.001$ and $P = 0.014$, respectively). Adjusted odds ratio for otitis media was 38.1 ($P = 0.004$). [Conclusions] HP incidence was higher in patients with GPA than in those with MPA. Otitis media was the most discriminating factor to predict new-onset HP in patients with AAV.

W22-1

Efficacy and Safety of Ixekizumab in Patients with Active Psoriatic Arthritis and Previous Inadequate Response to TNF Inhibitors: SPIRIT-P2 (2-years data from Phase 3 Study)

Masato Okada¹, Akimichi Morita², Ko Nakajo³, Hitoe Torisu-Itakura³, Amanda M Gellert⁴, Lisa Kerr⁴

¹Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan, ²Department of Geriatric and Environmental Dermatology, Nagoya City University Graduate School of Medicine, Nagoya, Japan, ³Eli Lilly Japan K.K., Kobe, Japan, ⁴Eli Lilly and Company, Indianapolis, IN, USA

Conflict of interest: Yes

[Object] Evaluate efficacy and safety of ixekizumab (IXE) in patients (pts) with active psoriatic arthritis (PsA) who have had an inadequate response (IR) or intolerance to 1 or 2 TNF inhibitors (TNFi). [Methods] Pts were randomised to placebo (PBO) or, after a 160 mg initial dose, to IXE 80 mg every 4 weeks (Q4W) or 2 weeks (Q2W). Pts in PBO were re-randomised to IXE Q4W or Q2W at Week (Wk) 16 if IRs or Wk24. From Wk32, pts were discontinued if TJC and SJC improvement <20%. ACR20/50/70, PASI75, LEI, LDI-B, MDA, DAS28-CRP, HAQ-DI were evaluated. Ad-hoc analysis for Wk0-108 included pts randomised to IXE at Wk0. [Results] 186 of 363 pts completed Wk108. Wk108 efficacy [ACR/20/50/70: Q4W=59.6/46.2/23.2%, Q2W=47.9/32.5/22.6%; PASI75: Q4W=65.1%, Q2W=48.3%; LEI=0: Q4W=45.5%, Q2W=37.5%; LDI-B=0: Q4W=63.0%, Q2W=60.0%; MDA: Q4W=30.7%, Q2W=25.9%; DAS28-CRP change from baseline (CFB): Q4W=-2.1, Q2W=-1.8; HAQ-DI CFB: Q4W=-0.39, Q2W=-0.35]. Most Adverse Event (AE) were mild/moderate in severity. 3 deaths occurred, and incidence of Serious AE in Q4W and Q2W were 5.8 and 7.7/100 pt-yr. [Conclusions] 2-years IXE treatment showed clinically meaningful and sustained improvement in PsA signs and symptoms among pts who have IR or intolerance to TNFi. No unexpected safety outcomes were reported.

W22-2

Efficacy and Safety of Risankizumab in Japanese Patients with Active Psoriatic Arthritis: Results From a Phase 2 Trial

Masato Okada¹, Graham Heap², Ann Eldred², Andrew Topp², Susumu Kitamura³, Akimichi Morita⁴

¹St. Luke's International Hospital, Tokyo, Japan, ²AbbVie Inc., North Chicago, IL, USA, ³AbbVie GK, Tokyo, Japan, ⁴Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Conflict of interest: Yes

[Object] Risankizumab (RZB), a humanized IgG1 mAb, binds to the p19 subunit of interleukin-23, a key cytokine in the pathogenesis of psoriatic arthritis (PsA). We report results from a Japanese subset from a RZB study in patients (pts) with PsA. [Methods] In this double-blind, dose-ranging phase 2 study, pts with active PsA were randomized 2:2:1:2 (stratified by prior TNF inhibitor and concurrent methotrexate use) to RZB (150 mg at Wk 0, 4, 8, 12, and 16 [Arm 1], 150 mg at Wk 0, 4, and 16 [Arm 2], 150 mg at Wk 0 and 12 [Arm 3], 75 mg at Wk 0 [Arm 4]) or matching placebo (PBO, Arm 5). The primary efficacy endpoint was ACR20 response at Wk 16. [Results] Of 185 pts enrolled, 14 were from Japan. At Wk 16, 100% of Japanese pts in RZB arms 1, 2, and 4 and 33% in arm 3 achieved ACR20 responses (82% all RZB vs 0% PBO, $P<0.05$); global Wk 16 ACR20 responses were 57%-65% across all RZB arms (36% PBO). Wk 24 RZB ACR20 responses were 73% (0% PBO, Japan) and 48% (31% PBO, global). RZB was well tolerated in Japanese RZB-treated pts; there were no serious adverse events (AE), deaths, or tuberculosis cases; infection was the most common AE (36% all RZB vs 33% PBO). [Conclusions] In Japanese pts with PsA, ACR20 responses were significantly greater in pts receiving RZB, and RZB was well tolerated.

W22-3

SPiRiT-P1, a phase 3 study of ixekizumab (IXE): 3-year efficacy and safety results in patients (pts) with active psoriatic arthritis (PsA)

Hideto Kameda¹, Suchitrita Rathmann², Kohei Hagimori³, Ko Nakajo³

¹Department of Internal Medicine, Toho University, Tokyo, Japan, ²Eli Lilly and Company, Indianapolis, IN, USA, ³Eli Lilly Japan K.K., Kobe, Japan

Conflict of interest: Yes

[Object] To assess efficacy and safety of IXE up to 3 years in PsA pts. [Methods] Biologic DMARD-naive PsA pts (N=417 [ITT], 12 Jp) were randomized to placebo (N=106), adalimumab (N=101) 40 mg once every 2 wks (Q2W), or IXE 80 mg (starting dose 160 mg) Q2W (N=103) or Q4W (N=107) in the Double-Blind Treatment Period (Wk 0-24). Pts who completed the period entered the Extension Period (Wk 24-52) and the Long-term Extension Period (LTEP: Wk 52-156), and were given 80 mg IXEQ4W or IXEQ2W. [Results] Of 210 pts (IXE-ITT, 6 Jp) randomized at Wk 0, 125 (60%) pts completed LTEP. ACR20/50/70 response rates (mNRI) at Wk 156 for IXEQ2W (62/56/44%) and IXEQ4W (70/52/33%) were consistent with those at Wk 52 (mNRI) for IXEQ2W (76/61/45%) and IXEQ4W (76/60/40%). In IXE-ITT Jp pts, 2 out of 4 (IXEQ2W) and 1 out of 2 (IXEQ4W) completed LTEP and were ACR20/50/70 responders. In the majority of pts, radiographic progression was not found or minimal through Wk 156. Frequencies of TEAEs were similar between IXEQ2W and IXEQ4W. The majority of TEAEs were mild or moderate in severity. [Conclusion] In IXE-treated pts, improvements in PsA symptoms persisted up to 3 years. No unexpected safety signals were observed, and the safety profile was consistent with previous IXE studies.

W22-4

Early diagnosis of psoriatic arthritis: How to diagnose arthritis preceding-psoriatic arthritis earlier

Syuichi Koarada¹, Mariko Sakai¹, Yoshinobu Nakao¹, Yuri Sadanaga¹, Akihito Maruyama¹, Nobuyuki Ono¹, Mitsunori Komine², Yoshifumi Tada¹

¹Division of Rheumatology, Saga University, ²Department of Orthopedics, Tsuruta Rehabilitation Clinic

Conflict of interest: None

[Object] In psoriatic arthritis (PsA), joint destruction is progressive and early diagnosis is required. However, early diagnosis of arthritis preceding-PsA (AP-PsA) is difficult. Clinical features of AP-PsA are analyzed and extract factors contributing to early diagnosis. [Methods] Of 107 patients with PsA, we examined clinical features and images. In early PsA, sensitivity of CASPER and Fournie classification were analyzed. [Results] Among PsA, AP-PsA is 21%, skin preceding- 38%, simultaneous- 16%, and sine syndrome 25%. Although it was difficult to classify early AP-PsA by CASPAR criteria (sensitivity 37.5%), sensitivity of Fournie criteria was higher (81.3%). Laboratory findings did not show any specificity for AP-PsA. Findings of conventional radiography that contributed to diagnosis were DIP lesion, bone proliferation, axial joint lesion, and dactylitis. Although sensitivity of the shape of erosions, pencil in cup deformity, ivory formation, ankylosis was lower, they were specific for PsA. Sensitivity of MRI, sonography, bone scintigraphy, and PET-CT are higher and was a reference for diagnosis. [Conclusions] In PsA, making an early diagnosis of AP-PsA is difficult before appearance of rash. A novel classification with comprehensive and including a new modality is required.

W22-5

Is there any tissue that exists in all organs involved in spondyloarthritis?

Ryuji Nagamine¹, Weijia Chen¹, Toru Suguro²

¹Center of Artificial Joint and Rheumatism, Fukuoka Tokushukai Medical Center, ²Research Institute of Rheumatology Medical Treatment

Conflict of interest: None

[Object] Spondyloarthritis (SpA) is a type of arthritis that attacks the spine and the joints. SpA can also involve the skin, intestines, eyes and genital organs. Diagnosis of SpA is based mainly on the results of a medical history and physical exam. It has not been reported why so many different organs are involved. Our hypothesis was that there is any tissue that exists in all organs involved in SpA. Literature review was performed to detect such tissue in SpA. [Methods] The lesion locates in enthesitis, eye, skin, colon, lung and genital organ in SpA. The tissue that exists in all lesions and is related with MHC class I was searched by literature review. [Results] The tissue that locates in all lesion was the lymph tissue. Mucosa associated lymph tissue (MALT) is located in lung

(BALT), colon (GALT), skin (SALT) and eye. The MALT is the immune system that produces IgA. CD8 positive T cell exists in the MALT. The dendritic cell mainly works as the antigen presenting cell. Bursa and lymph tissue exist in the entheses. Therefore, the lymph tissue exists in all lesions of SpA. Further study is necessary to clarify the pathology of SpA in each lesion. However, the lymph tissue can connect all organs involved in SpA. [Conclusions] The lymph tissue exists in all lesions in SpA.

W22-6

On the usefulness of MASEI (Madrid Sonographic Enthesitis Index) score in spondyloarthropathy for psoriasis differential diagnosis

Hiroki Akazawa, Chisato Ashida, Yuji Nozaki, Kaori Ishimura, Fusayo Ikeda, Atsuhiko Yamamoto, Akinori Okada, Daisuke Tomita, Tetsu Itami, Kenji Sakai, Asuka Inoue, Shinkai Ri, Toshihiko Shiga, Kazuya Kishimoto, Shoichi Hino, Yasuaki Hirooka, Koji Kinoshita, Masanori Funachi, Itaru Matsumura

Department of Hematology and Rheumatology, Kindai University Faculty of Medicine

Conflict of interest: None

(Objects) To evaluate of the efficacy of MASEI (MAdrid Sonographic Enthesitis Index) score, we evaluated the grade and site of tendon attachment flame in PsA and non-PsA cases by that. (Methods) This study analyzed retrospectively thirteen PsA cases and twenty four non-PsA cases (peripheral SpA 8 cases, palmoplantar pustulosis 2 cases, SAPHO syndrome 1 case, JIA 1 case, inflammatory bowel disease 7 cases, ankylosing spondylitis 3 cases) diagnosed SpA and evaluated by the MASEI score during November 2017 to September 2018. MASEI score was also classified into inflammatory abnormality (MSAEI-inflammatory) and chronic injury (MASEI-damage). (Results) The diameter of thickening (right upper arm tendon ·left distal patellar tendon) ·total score (right distal patellar tendon bone erosion ·bilateral Achilles tendon osteophyte formation) significantly differed between the 2 groups, but MSAEI-inflammatory, MASEI-damage did not significantly differ. (Conclusion) It was shown that MASEI of distal patella, upper arm, and Achilles tendon attachment part in SpA cases may be useful for differential diagnosis for PsA. It is necessary to study the usefulness of ultrasonic examination for prediction of onset of arthritis preceding type PsA and therapeutic reactivity for each case.

W23-1

Clinical value of measuring KL-6 in RA patients at one time point; detection of interstitial lung disease

Yuta Takamura, Kazuhiro Kurasawa, Tomoyuki Miyao, Ayae Tanaka, Ryutaro Yamazaki, Satoko Arai, Takayoshi Owada, Reika Maezawa, Masafumi Arima

Rheumatology, Dokkyo Medical University

Conflict of interest: None

Purpose: To clarify the clinical value of measuring KL-6 in RA patients at one time point, particularly detection ability for interstitial lung disease (ILD). **Methods:** Subjects were 208 RA patients who received HR-CT scans before and after starting biologics. We examined the sensitivity and specificity of chest radiograph and serum KL-6 detect ILD that was defined by HR-CT findings. Clinical features of patients with KL-6 elevation were also examined. **The results:** Subjects were 66 male and 59.2 years old (average) with 7.9 years of disease duration. Pulmonary abnormalities were found in 146 cases (70%) with 81 of ILD by CT. Chest radiography was conducted in 173 cases, including 74 of ILD. Sensitivity and specificity of chest radiography were 0.36 and 0.87, respectively. KL-6 was measured in 129 patients, including 48 ILD. When the cutoff level was 400U/ml, patients with elevated KL-6 was found in 24 of 48 patients with ILD and 10 of 81 patients without ILD; the sensitivity and specificity of KL-6 for ILD were 0.5 and 0.87, respectively. New ILD was developed similarly in non-ILD patients with and those without KL-6 elevation. **Conclusion:** Measuring KL-6 at one point has a similar clinical value to chest radiography in detecting ILD in RA patients. When suspect ILD, HR-CT should be conducted.

W23-2

Effect of biologics on pulmonary events in rheumatoid arthritis patients with existing lung disease

Shinji Watanabe, Takahisa Gono, Yuichiro Shirai, Seiji Kobayashi, Mitsuhiro Takeno, Masataka Kuwana

Department of Allergy and Rheumatology, Nippon Medical School, Tokyo, Japan

Conflict of interest: None

[Object] To investigate whether administration of biologics newly cause pulmonary events in rheumatoid arthritis (RA) patients with existing lung disease. [Methods] 90 RA patients with existing lung disease, including interstitial lung disease [ILD] in 37 patients, airway disease [AD] in 52, and emphysema in 21, were enrolled in this study. The patients were divided into biologics group (n=38: TNF inhibitors in 16, abatacept in 19, tocilizumab in 10) and non-biologics group (n=52) to compare pulmonary events, including pulmonary infection, exacerbation of ILD or AD, and development of organized pneumonia, by using the Propensity score (PS) matching method. [Results] The pulmonary events occurred in 31 cases. The levels of KL-6 and steroid use were identified as factors significantly related to administration of biologics by multiple logistic regression analysis. We adjust these two factors to match clinical background between the two groups by using the PS matching. There was no significant difference in the pulmonary events between the two groups (P = 0.37). [Conclusions] In RA patients with existing pulmonary disease, the administration of biologics was not significantly associated with the development of pulmonary events.

W23-3

Studies on the factors contributing to the development of usual interstitial pneumonia (UIP) and non-specific interstitial pneumonia (NSIP) in patients with rheumatoid arthritis (RA)

Shinji Motojima, Tamao Nakashita, Akira Yoshida, Akira Jibatake

Rheumatology and Allergy, Kameda Medical Center, Kamogawa, Japan

Conflict of interest: None

[Object] Interstitial lung diseases (ILD) are important complications in patients with RA. However, different from ILD in other CTDs, approximately 1/3 of ILD are UIP in RA. We tried to find factors that contribute to the development of UIP and NSIP in patients with RA. [Methods] Subjects are 567 patients with RA who performed chest CT during treatment. The relations of the pattern of ILD to clinical factors were analyzed. [Results] Analysis of chest CT findings revealed that the prevalence of ILD was 39 %, that is; 29.1 %, 7.2 %, and 2.6 % in NSIP, UIP and OP, respectively. When the durations from the onset of RA and chest CT were divided into 3, namely less than 3 years, less than 7 years and more than 7 years, the prevalence of ILD were 33 %, 42 % and 42 %, respectively, with significant difference. The prevalence of UIP were 7 %, 11 %, and 7 %, respectively, and those of NSIP were 24 %, 28 %, and 29 %, respectively. NSIP tended to increase. Logistic analysis revealed that age of RA development, smoking Hx, and RF titer contribute to the development of UIP, on the other hand, age of RA development and the duration from RA development to CT performance in NSIP. [Conclusions] Smoking Hx relates strongly to UIP, however RA duration relates to NSIP.

W23-4

Treatment of interstitial lung disease associated with rheumatoid arthritis

Takeshi Shoda, Tohru Takeuchi, Koji Nagai, Kenichiro Hata, Yoko Matsumura, Ayaka Yoshikawa, Takuya Kotani, Shigeaki Makino, Shigeaki Arawaka

Department of Internal Medicine IV, Osaka Medical College

Conflict of interest: None

[Object] To study the treatment of interstitial lung disease (ILD) associated with Rheumatoid arthritis (RA). [Methods] Of patients with RA-ILD who were attend to our hospital between January 2015 to September 2017, targeting consecutive cases after more than 1 year had passed. The

subjects examined treatment, images, and prognosis using the clinical data. [Results] RA-ILD was 95 cases (36 males, 59 females, average age of 69 ± 9.9 years). The using MTX was 37 cases (38%), the amount of MTX was 6.9 ± 2.4 mg, the using PSL 35 cases (36%), the amount 5.6 ± 3.1 mg, the using TAC 36 cases (37%), the amount 2.1 ± 0.8 mg, the using IGU 2 patients (0.02%), the using SASP 33 cases (34%), and the using BUC 6 cases (0.06%). The total of Bio + TOF use was 61 cases (64%), INF 3 cases (3%), ETN 6 cases (6%), ADA 5 cases (5%), GLM 5 cases (5%), CTZ 0 cases (0%), ABT 29 cases (30%), TCZ 5 cases (5%), TOF 3 cases (3%), and many cases of using ABT. [Conclusions] In the treatment of RA-ILD, bio was used at a high frequency of 64%, and treatment was relatively safe.

W23-5

Poor prognostic factors in RA patients with acute lung injury

Tomoyuki Miyao, Kazuhiro Kurasawa, Yuta Takamura, Ayae Tanaka, Ryutaro Yamazaki, Satoko Arai, Takayoshi Owada, Reika Maezawa, Masafumi Arima

Department of Rheumatology, Dokkyo Medical University

Conflict of interest: None

[Object] To identify poor prognostic factors in RA patients with acute lung injury, a critical situation in RA-ILD. [Methods] We retrospectively reviewed 26 consecutive RA patients (8 male, 18 female) with acute lung injury that was diagnosed by respiratory failure and CT findings. To find prognostic factors, we compared clinical features of dead patients with survivors. [Results] No differences were found in backgrounds (gender, age, disease duration, and treatment for RA) between dead patients and survivors. Preexisting ILD and UIP were not identified as poor prognostic factors. Fever and respiratory symptoms were similarly found in both groups. Respiratory condition on admission was a factor to distinguish the dead and the live. GGO/ consolidation was equally found in both groups, however, newly developing traction ectasia was frequently found in dead patients. Serum LDH and KL-6 levels were significantly high in dead group, but not CRP levels. Positivity of b-D glucan test was similar in both groups. Treatment for lung injury was similar in both groups. [Conclusions] Only severity of lung injury on the admission, which was suggested by respiratory condition, traction ectasia and elevated KL-6 and LH levels, was a poor prognostic factor in RA patients with acute lung injury.

W23-6

We evaluated the risk factor of clinical fractures in patients with rheumatoid arthritis -TOMORROW study-

Shohei Anno¹, Kentaro Inui², Yuko Sugioka³, Kenji Mamoto², Tadashi Okano², Masahiro Tada⁴, Tatsuya Koike^{3,5}, Hiroaki Nakamura²

¹Department of Orthopedic Surgery, Yodogawa Christian Hospital, ²Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine, ³Center for Senile Degenerative Disorders (CSDD), Osaka City University Graduate School of Medicine, ⁴Department of Orthopedic Surgery, Osaka City General Hospital, ⁵Search Institute for Bone and Arthritis Disease (SINBAD)

Conflict of interest: None

[Object] We investigated the risk factor of the incidence of clinical fractures in patients with RA based on the TOMORROW study. [Methods] We evaluated lifestyle habit, bone mineral density and muscle mass, disease activity, and the incidence of clinical fractures over a period of 7 years in 208 patients with RA and in 204 age- and sex-matched controls (Co). [Results] The number of clinical fractures were no differences between RA and Co (RA:47, Co:38, $p=0.37$). Comparing RA patients with and without the incidence of clinical fractures, age ($p=0.01$), disease duration ($p=0.01$), glucocorticoid dose ($p<0.001$), the number of falls ($p<0.001$), and average DAS28 ($p=0.03$) were higher in patients with the incidence of clinical fractures. Multivariate logistic regression analysis revealed that RA was not a risk factor (OR:0.66, 95%CI:0.30-1.45, $p=0.30$), and the lack of exercise (OR:2.22, 95%CI:1.21-4.08, $p=0.001$) and glucocorticoid use (OR:2.28, 95%CI:1.04-5.02, $p=0.04$) were the risk factor for clinical fractures. In RA, the lack of exercise represented an independent risk factor for the incidence of clinical fractures (OR:4.47,

95%CI: 1.21-16.45, $p=0.03$). [Conclusions] In RA patients, the lack of exercise was a risk factor for the incidence of clinical fractures.

W24-1

Outcome of the Sauvé-Kapandji procedure in patients with rheumatoid arthritis

Ayako Kubota¹, Masayuki Sekiguchi¹, Arata Nakajima², Masato Sonobe², Toru Suguro¹, Hiroshi Takahashi¹

¹Toho University Omori Medicine Center, Tokyo, Japan, ²Departments of Orthopaedics and Rheumatology, Toho University Sakura Medical Center, Chiba, Japan

Conflict of interest: None

[Object] To investigate the clinical and radiological results of the SK procedure in RA wrists. [Methods] 43 joints were subjected to a follow-up for one year or more after operation. The average age of the patients was 60.3 years old at surgery, and the average disease duration was 15.7 years. Biologics were used in 36 joints at surgery and in 37 joints at the operation. The evaluation item was the excursion of the wrist and the forearm at surgery and at the time of the study. Radiographic evaluation was CHR and CTI. The presence or absence of joint surface remodeling between the radio carpal joint in lateral views was also examined. [Results] A significant difference was observed in pronation, but no significant difference was observed in supination and wrist excursion. No significant difference was observed in CHR and CTI. In the lateral views, remodeling was observed for 11 joints (25.6%) at surgery and 24 (53.5%) joints at follow up. It increased significantly. [Conclusions] The S-K procedure maintained excursion, and no carpal collapse or progression of ulnar deviation was observed. Remodeling in radio carpal joint was observed with a significant difference. The effectiveness of the SK procedure was suggested in cases of progressed bone destruction.

W24-2

Investigation after RA enforcement of Sauve-Kapandji against RA hand abnormalities

Nozomi Kaga¹, Toshiaki Aizawa¹, Tetsuya Kawano¹, Hiroki Ito², Takeshi Kashiwagura³, Yoichi Kataoka⁴, Natsuo Konishi⁵, Masakazu Urayama⁶, Hiroshi Aonuma⁶, Tsutomu Sakuraba⁷, Moto Kobayashi⁷, Keiji Kamo⁸, Norio Suzuki⁹, Takayuki Tani¹⁰, Hidekazu Abe¹¹, Yusuke Sugimura¹², Naohisa Miyakoshi¹³, Yoichi Shimada¹³

¹Department of Orthopedic Surgery, Kita Akita Municipal Hospital, Akita, Japan, ²Department of Orthopedic Surgery, Noshiro Kousei Medical Center, Akita, Japan, ³Department of Orthopedic Surgery, Akita City Hospital, Akita, Japan, ⁴Joto Orthopedic Clinic, Akita, Japan, ⁵Department of Orthopedic Surgery, Akita Kousei Medical Center, Akita, Japan, ⁶Department of Orthopedic Surgery, Ogachi Central Hospi, Akita, Japan, ⁷Department of Orthopedic Surgery, Hiraka General Hospital, Akita, Japan, ⁸Department of Orthopedic Surgery, Akita Rosai Hospital, Akita, Japan, ⁹Department of Orthopedic Surgery, Yuri Kumiai General Hospital, Akita, Japan, ¹⁰Department of Orthopedic Surgery, Akita Red Cross Hospital, Akita, Japan, ¹¹Department of Orthopedic Surgery, Ugo Municipal Hospital, Akita, Japan, ¹²Department of Orthopedic Surgery, Nakadori General Hospital, Akita, Japan, ¹³Department of Orthopedic Surgery, Akita University Graduate School of Medicine, Akita, Japan

Conflict of interest: None

[Object] To investigate the postoperative results of Sauvé-Kapandji (hereinafter referred to as SK method) which was enforced against RA hand abnormalities in Akita prefecture. [Methods] Since 1991, we performed Sauvé-Kapandji procedure on 38 wrists (34 patients). The mean age at the time of the operation was 58.2 years. The biologics (Bio) was administered to 16 patients. Radiographic evaluation was performed in terms of CHR, RCDR and RRA. [Results] The mean total range of motion of supination / pronation increased postoperation. The mean CHR decreased significantly 0.42 to 0.40 at the time of the recent follow-up. The mean RCDR and the RRA did not change significantly. There was an ankylosis in 19 cases (50.0%) at the time of the final observation, but 3 cases / 16 cases (18.8%) combined with Bio. preparation and 16 cases / 22 cases (72.7%), There was significantly less ankylosis in the case of combined use of Bio. [Conclusions] Although X-ray findings showed

carpal bone collapse change, improvement of forearm rotation range was obtained, and the SK method is considered to be an effective method. There is a tendency to suppress radial carp joint destruction under the combined use, there is a possibility of expansion of the SK appended case in the future.

W24-3

Long Term Results of Unlinked type Total Elbow Arthroplasty for Rheumatoid Arthritis

Yoshio Uchida^{1,2}, Takuji Nishikawa¹, Kenichi Shimane¹, Kenta Makabe¹
¹Department of Rheumatology, Bokutoh Metropolitan Hospital, Tokyo, Japan, ²Department of Rheumatology, Uchida Clinic

Conflict of interest: None

[Object] To evaluate a long-term outcome of unlinked type total elbow arthroplasty (TEA) in rheumatoid arthritis. [Methods] Primary TEAs from January 2007 to December 2008 were reviewed. Radiographic images, clinical results and complications were evaluated. Survival rate was calculated using TEA revision as the endpoint. [Results] We evaluated 35 elbows. Revision TEA was four elbows. In all revision TEA cases there was no cement filling above the proximal edge of the humeral component. Two elbows perforated to extra cortically ulnar component. Two elbows ulnar neuropathy, One elbow posterior interosseous nerve paralysis. One elbow delay of wound healing and two elbows intraoperative fracture. The loosening of compartments were 3 elbows on the humerus side and 4 elbows on the ulnar side. One elbow of ulnar neuropathy did not improve. The range of motion, MEPS was significantly improved at the time of the last observation than before the operation. The survival rate was 84.1% at 100 months postoperatively. [Conclusions] The results of the unlinked TEA were as good as the past reports.

W24-4

The relationship between the joint line and postoperative range of motion after K-elbow total elbow arthroplasty

Kota Shimomura^{1,2}, Mitsuyasu Iwasawa¹, Takeomi Nakamura¹, Satoru Ohashi¹

¹Department of Orthopedic Surgery, Sagamihara National Hospital, Sagami-hara, Kanagawa, Japan, ²Department of Orthopaedic Surgery, Sapporo Medical University, Sapporo, Japan

Conflict of interest: None

[Object] To investigate the correlation between the joint line after implantation, osteotomy and postoperative range of motion (ROM) following the use of K-elbow. [Methods] 12 elbows were operated on - 8 cases of Painful Instability (PI), and 4 of Painful Stiffness (PS). The joint line of humeral implant setting was measured at the base of the olecranon fossa, and the ulnar joint line at the olecranon dorsum cortex. [Results] For PI, preoperative mean ROM was Extension-27°, Flexion134° and postoperative was -32°, 132°. Preoperative mean ROM was -31°, 80° and postoperative was -41°, 120° for PS. The Mayo Elbow Performance Scores were PI: 93, PS: 90, improved significantly. The mean displacements on the humeral side were PI: 3.2mm, PS: 1.1mm (p=0.05), and in the ulnar side were PI: 1.7mm, PS: 3.1mm (p=0.01). No correlation was apparent between displacement and postoperative ROM. Postoperative ROM is greater in PI cases, so more bone was left intact to promote stability. PS cases tend to be more stable, so more bone was cut to achieve greater postoperative ROM. Postoperative ROM was limited in PS cases, but showed significant improvement. [Conclusions] Good postoperative outcomes were obtained, although the course of action required is different for PI and PS.

W24-5

Complication after Total Elbow Arthroplasty for Rheumatoid Arthritis

Kenji Kishimoto, Toshihisa Kojima, Nobunori Takahashi, Shuji Asai, Nobuyuki Asai, Takuya Matsumoto, Yasumori Sobue, Tsuyoshi Nishiume, Mochihito Suzuki, Yutaka Yokota, Kyosuke Hattori, Naoki Ishiguro
Orthopaedic Surgery and Rheumatology, Nagoya University Hospital

Conflict of interest: None

Object Total elbow arthroplasty (TEA) which relieves elbow pain and improves range of motion is accepted as the treatment for severely destroyed elbow joints in patients with rheumatoid arthritis (RA). But the rate of infection after TEA is higher than THA and TKA, and TEA has various complications such as fracture and nerve injury. This study attempted to examine complication after TEA. Methods We performed primary TEA for 39 elbows in 36 patients with RA between 2004 and 2018. We examine the complication after TEA. Results Mean age of patients was 64 years. There were 6 males and 30 females. Mean disease duration of RA was 22 years. 25 elbows were treated with unlinked TEA and 14 elbows were treated with semiconstrained TEA. We identified complications in 14 elbows. There were infection in 2 cases, fracture in 7 cases, nerve injury in 3 cases, wound trouble in 1 case and aseptic loosening in 2 cases. 3 patients required reoperation and 2 patients required revision. Mutilating changes of elbow joints and semiconstrained type are relatively high risk of fracture (P<0.05). Conclusions The rate of fracture and nerve injury after TEA is relatively high. We must particularly take care of cases with mutilating changes of RA.

W25-1

10-year longitudinal changes of rheumatoid thumb deformity

Ryo Oda^{1,3}, Shogo Toyama^{1,3}, Masato Ohara¹, Daigo Taniguchi¹, Daisaku Tokunaga^{1,3}, Hiroyoshi Fujiwara¹, Makoto Wada², Masataka Kohno², Yutaka Kawahito^{2,3}, Toshikazu Kubo^{1,3}

¹Department of Orthopaedics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ²Department of Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ³Center for Rheumatology, University Hospital Kyoto Prefectural University of Medicine

Conflict of interest: None

[Object] Rheumatoid thumb deformity that is functionally important occurs frequently, and it interferes with the pinch and grip. In this study, we investigated the time course of the new occurrence and progression of rheumatoid thumb deformity in the long term. [Methods] 37 cases 63 fingers who completed follow-up investigation in 5 years and 10 years were targeted. The thumb deformities were classified into Nalebuff classification and type CM and type MP with only thumb CM joint or MP joint destruction. The thumb deformities at each evaluation time point were recorded and the change with time were investigated. [Results] The thumbs without deformation at each evaluation time point were 10/5/3 thumbs at the time of start / 5 years / 10 years respectively. Type I were the most frequent through the course, 35/34/34 thumbs. type CM for 6/6/1 thumbs, type MP for 3/3/1 thumbs, and these many cases advanced to type III. In 4 type I 4 thumbs advanced to type IV. [Conclusions] In this study, it became clear that the rheumatoid thumb deformities increased and progressed over time. In addition to appropriate medication therapy, it is important to intervention such as orthosis and surgery at appropriate timing according to the progress of deformation, in order to maintain daily living activities.

W25-2

Swan-neck and Boutonniere deformity in rheumatoid hand - 10-year cohort of rheumatoid hand -

Masato Ohara¹, Shogo Toyama^{1,3,4}, Ryo Oda^{1,3}, Daigo Taniguchi¹, Daisaku Tokunaga¹, Hiroyoshi Fujiwara¹, Makoto Wada², Masataka Kohno², Yutaka Kawahito^{2,3}, Toshikazu Kubo¹

¹Department of Orthopaedics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ²Department of Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ³Rheumatism Center, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ⁴Department of Development of Multidisciplinary Promote for Physical Activity, Graduate School of Medical Science, Kyoto Prefectural University of Medicine

Conflict of interest: None

[Object] In rheumatoid arthritis, fingers are hindered and daily activity disorders are caused. Even now medication has advanced, some cases

show the progression of deformation and new incidence. In this study, we investigated long-term changes in the occurrence and progression of Swan-neck and boutonniere deformities. [Methods] 37 cases 63 fingers completed follow-up in 5 years and 10 years were targeted. Swan-neck and boutonniere deformities were classified into Nalebuff classification, functions were assessed with MKI, and ADL with DASH. [Results] 9 deformities newly occurred in 14 hands no deformation initially. Swan-neck deformities increased from 65.1% to 81.0%, boutonniere deformities from 19.0% to 33.3%, finally the deformities are mixed in 14 hands. MKI worsened from 32.1 to 29.1 and DASH from 51.3 to 53.4. In swan-neck deformities, MKI and DASH were poor even in mild cases, boutonniere deformities progressed and MKI and DASH worsened. [Conclusions] In this study, dysfunction has also progressed with increase of finger deformity. Although appropriate medication is important to prevent new deformation, it is also important to apply treatment such as orthosis and surgery at appropriate timing in accordance with the progress of deformity for maintaining daily living activities.

W25-3

Deformity progression pattern analysis from a cumulative evaluation of each finger deformity in rheumatoid hand

Shogo Toyama^{1,2,3,5}, Ryo Oda^{3,5}, Daisaku Tokunaga^{2,3}, Yutaka Kawahito^{4,5}, Yasuo Mikami², Masataka Kohno⁴, Makoto Wada^{4,5}

¹Department of Development of Multidisciplinary Promote for Physical Activity, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ²Department of Rehabilitation Medicine, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ³Department of Orthopaedics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ⁴Department of Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ⁵Center of Rheumatic Diseases, University Hospital, Kyoto Prefectural University of Medicine

Conflict of interest: None

[Introduction] Rheumatoid hands are highly complexed and involved some typical deformities, then require us rheumatologist well-experienced. Additionally, there is almost no evidence showing a natural history from a long-term viewpoint, so it is difficult for us to show a clear treatment strategy. We have performed an original hand cohort and shown some trials for comprehensive evaluation. [Methods] We assessed overall 156 cases 297 hands cross-sectionally at the three endpoints (2004, 2009 and 2015). A cluster analysis was done using each parameter of each deformity, and classified subjects into 7 groups. We interested in the cases with any changes in groups between endpoints and analyzed them mainly. [Results] The most typical transient pattern was following; starts from thumb type I deformity, next observe a worsening of ulnar drift or swan-neck deformity. In these cases, if thumb joints affection continued, a severe functional impairment developed irrespective of the status of the other fingers. [Conclusions] It is more desirable that rheumatologists could intervene before disability develops than after disability become apparent. We believe all rheumatologist should keep in mind of the natural history of deformity progression to avoid any irreversible functional impairments.

W25-4

Patient's satisfaction of Swanson metacarpophalangeal arthroplasty for the rheumatoid hand

Shinji Taniguchi^{1,2}, Hajime Ishikawa¹, Asami Abe¹, Tomonori Sakamoto¹, Hiroshi Otani¹, Kiyoshi Nakazono¹, Yoichi Kurosawa¹, Eriko Hasegawa¹, Satoshi Ito¹, Koichi Nakagawa², Akira Murasawa¹

¹Department of Rheumatology, Department of Rheumatology, Niigata Rheumatic Center, Shibata, Japan, ²Department of Orthopaedic Surgery, Toho University Sakura Medical Center, Sakura, Japan

Conflict of interest: None

[Objective] To clarify the patient's satisfaction level of Swanson Metacarpophalangeal Joint Arthroplasty (SMPA) for the rheumatoid hand and to investigate the factors, which associate with its level. [Methods] A prospective study was performed on 145 metacarpophalangeal joints in 49 hands of rheumatoid arthritis patients, who underwent SMPA at our

hospital from March 2013 to March 2015. A follow up period was three years. Subjective measurements included visual analogue scale (VAS) of Pain, Appearance, Motion, Power, Usability and Overall satisfaction (0:dissatisfied,100:highly satisfied). Objective measurements included arc of motion, grip power and prehensile pattern. For the hand in which SMPA was performed in the thumb or the index finger, tip and side pinch power were also measured. [Results] The average VAS of each satisfaction level at three years after surgery were Pain:78.0, Appearance:68.7, Motion:59.4, Power:53.1, Usability:62.8, Overall:71.0. The factor which affected Overall satisfaction was Usability (P<0.01). There was a positive correlation between Usability and change in prehensile pattern (r=0.297) and between Usability and change in side pinch power (r=0.350). [Conclusions] Usability of the hand was associated with prehensile pattern and side pinch power.

W25-5

Investigation of reoperative cases with fracture of hand finger silicone implant in RA patients

Toshiharu Okuda

Okuda Orthopedic Clinic

Conflict of interest: None

Objective: Silicon implants are often used mainly for MP joints for the reconstruction of deformed fingers of RA patients, but, there are problems such as sinking and breakage as a change. The use of silicone implant in RA finger reconstructive surgery at our hospital was 326 joints. We report cases where recursive surgery has been performed due to the patient's wishes due to the failure of the silicone implant breakage this time. Methods: The subjects were 5 cases (all women), 58.3 years of age, the MP joints were 2 cases with 5 joints, and the PIP joints were 3 cases 3 joints. The period from initial surgery to re-replacement was 10.8 years on average (6 - 20 years), the damaged implants were Swanson 5 joints for MP joints, 2 Avanta joints for PIP joints, and 1 Swanson joints. Results: There were no postoperative complications such as infection. Although the elapsed time is as short as 1.8 years on average, there is no pain / deformation, instability and range of motion are improved, patient satisfaction is high, no ADL disorder is present at present. Conclusion: Finger joint arthroplasty using silicone implant is relatively easy to re-replace when the implant is broken, and it seems to be useful as a method for reconstructing deformed RA fingers.

W26-1

Transcription factors regulating pathogenic mechanisms of Tph cells

Hiroyuki Yoshitomi^{1,2,3}, Aya Miyagawa-Hayashino⁴, Akinori Okahata³, Kohei Doi³, Kohei Nishitani⁵, Koichi Murata⁵, Hiromu Ito³, Tatsuki Tsuruyama⁶, Hironori Haga⁴, Shuichi Matsuda³, Junya Toguchida^{1,2,3}

¹Institute for Frontier Life and Medical Sciences, Kyoto University, ²Center for iPS Cell Research and Application, Kyoto University, ³Department of Orthopaedic Surgery, Kyoto University Graduate School of Medicine, ⁴Department of Diagnostic Pathology, Kyoto University Hospital, ⁵Department of Advanced Medicine for Rheumatic Diseases, Kyoto University Graduate School of Medicine, ⁶Department of Drug Discovery Medicine, Kyoto University Graduate School of Medicine

Conflict of interest: Yes

[Object] PD-1 (high) CXCR5 (-) helper T (Tph) cells are a distinct CD4⁺ subset that is involved in the pathogenesis of rheumatoid arthritis (RA). However, transcription factors that regulate Tph cells have been unclear. [Methods] We comprehensively analyzed gene expression in human CD4⁺ T cells under conditions above followed by identification of upregulated transcription factors. Additionally, we analyzed function of Maf and Blimp1 reportedly regulated transcription factors in Tph cells. [Results] Sox4 was identified as the transcription factor upregulated under inflammatory conditions above. Lentiviral overexpression into human naïve CD4⁺ T cells showed the involvement of Sox4 in upregulation of PD-1 and CXCL13, and in downregulation of CXCR5. On the other hand, Maf was involved in the upregulation of genes related to B-help activities; transcription repressor Blimp1 generally downregulated genes above. Interestingly, while TGF- β upregulated both Sox4 and Maf, IL-2 downregulated Sox4 but upregulated Maf. [Conclusions] Collectively,

these findings imply that pathogenic functions of Tph cells are regulated finely by several transcription factors depending on surrounding inflammatory environments.

W26-2

Functions and TCR repertoire of PD-1high CD4 T cells in rheumatoid arthritis

Takahide Sakuragi¹, Hisakata Yamada^{1,2}, Akihisa Haraguchi¹, Junichi Fukushi¹, Satoshi Ikemura¹, Yukio Akasaki¹, Toshifumi Fujiwara¹, Tomoko Tsutsui¹, Masakazu Kondo², Yasuharu Nakashima¹

¹Department of Orthopaedic Surgery, Kyushu University, ²Kondo Clinic of Rheumatology and Orthopaedic Surgery

Conflict of interest: None

[Object] Autoreactive CD4 T cells are implicated in the pathogenesis of rheumatoid arthritis (RA). Because bystander CD4 T cells might also infiltrate in the synovium, identifying autoreactive CD4 T cells is important for the development of disease-specific therapies. A CD4 T cell subset expressing high levels of PD-1 and producing IL-21, but different from follicular helper T cells, was recently discovered in RA joint. Since PD-1 is expressed on T cells chronically stimulated with the antigens, these could be the pathogenic autoreactive CD4 T cells in RA. In this study, we analyzed the functions and TCR repertoire of PD-1high CD4 T cells in RA joint. [Methods] Mononuclear cells were isolated from the synovial fluid and peripheral blood of RA patients. The expression levels of PD-1, activation markers, chemokine receptors, cytokines and TCR repertoire of CD4 T cells were examined by a flow cytometer. [Results] PD-1high CD4 T cells expressed high levels of activation markers and produced IL-21, IFN- γ , GM-CSF and CXCL13. The pattern of chemokine receptor expression was mostly Th1 type. PD-1high CD4 T cells showed different pattern of TCR repertoire distribution compared to other subsets. [Conclusions] PD-1high CD4 T cells might be the pathogenic autoreactive CD4 T cells in RA.

W26-3

MAIT cells as a new therapeutic target of systemic lupus erythematosus

Go Murayama^{1,2}, Asako Chiba², Hirofumi Amano¹, Ken Yamaji¹, Naoto Tamura¹, Sachiko Miyake²

¹Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan, ²Department of Immunology, Juntendo University School of Medicine, Tokyo, Japan

Conflict of interest: None

<Background>Mucosal-associated invariant T (MAIT) cells are a subset of innate-like lymphocytes. In this study, we investigated whether MAIT cells could be a therapeutic target for lupus. <Methods>Infiltration of MAIT cells was assessed in kidney biopsy specimens from lupus patients using a confocal microscope. Disease progression and lymphocytes in the spleen and kidneys were compared between MR1^{-/-} and MR1^{+/+} Fc γ RIIB^{-/-}Yaa mice. Fc γ RIIB^{-/-}Yaa mice were treated with a suppressive MR1 ligand orally and we investigated whether inhibition of MAIT cell activation by i6-FP suppressed lupus in Fc γ RIIB^{-/-}Yaa mice. <Result>MAIT cells were accumulated in the nephritic kidneys of lupus patients. The frequency of MAIT cells and CD69⁺MAIT cells were higher in the kidneys than those in the spleen. MAIT cell deficiency reduced the germinal center responses, innate T and T cell responses in Fc γ RIIB^{-/-}Yaa mice. Administration of MR1 ligand decreased the serum levels of anti-dsDNA antibody and the severity of lupus nephritis. <Discussion>Using two approaches of MAIT cell deficiency, MR1 knockout animals and the inhibitory MR1 ligand, our findings suggested that MAIT cells may serve as attractive targets for the development of new strategies to treat lupus.

W26-4

The effect of ribavirin on improving IFN signature of SLE patients is obtained by correcting multiple histone modification abnormalities

Qiaolei Wang¹, Daisuke Oryoji¹, Yasutaka Kimoto¹, Tetsushin Murakami¹, Masahiro Ayano², Hiroki Mitoma², Mitsuteru Akahoshi²,

Yojiro Arinobu², Koichi Akashi², Hiroaki Niuro³, Takahiko Horiuchi¹

¹Department of Internal Medicine, Kyushu University Beppu Hospital,

²Department of Clinical Immunology, Rheumatology and Infectious Diseases, Kyushu University Hospital, ³Faculty of Medical Sciences Medical Education, Kyushu University School of Medicine

Conflict of interest: None

[Object] Interferon stimulated gene (ISG) is involved in the pathogenesis of SLE. We have reported the antiviral drug, ribavirin, can increase the H3K9me2 level in the ISG region and decrease expression of ISG in CD4 naive T cells of SLE patients. In order to elucidate the more detailed mechanism of action of ribavirin, we performed the analysis of multiple histone modifications and histone modifying enzyme. [Methods] Expression of ISG in CD4 naive and memory T cells obtained from SLE patients and healthy subjects was compared by qPCR and microarray analysis. Histone modification levels in the ISG region were compared by ChIP-qPCR. Furthermore, histone modification levels in the ISG region were compared in those cells under ribavirin treatment. [Results] In SLE, high expression of ISG was observed compared to healthy individuals, and multiple histone modification abnormally levels were observed in *MX1* and others. Inhibition of the expression of ISG was observed by administration of ribavirin, inhibition of ISG expression was canceled by inhibiting of G9a. [Conclusions] Ribavirin can be a candidate drug for treatment SLE by improving IFN signature by correcting H3K9me2 level in the ISG region and changing the others of histone modification level which cooperatively affect with H3K9me2.

W26-5

The expression and pathogenesis of citrullinated Inter alpha trypsin inhibitor heavy chain 4 (ITIH4) in inflamed joints

Atsumu Osada, Isao Matsumoto, Izumi Kurata, Ayako Ohyama, Yuya Kondo, Hiroto Tsuboi, Takayuki Sumida

Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: None

Background/Purpose: ITIH4 is one of the citrullinated proteins in blood, which is associated with disease activity in pGIA and RA. The aim of this study was to clarify the expression of native or citrullinated ITIH4 in inflamed joints and to investigate the involvement of PAD enzymes. **Methods:** 1) Immunohistochemistry (IHC) of ITIH4 was performed in pGIA joints. 2) Citrullinated ITIH4 in pGIA joints was assessed by immunoprecipitation and Western blot. 3) Expression of PADI2 and PADI4-mRNA and PADI4 protein in pGIA joints were measured by qPCR and IHC. 4) The concentration of ITIH4 in synovial fluid (SF) from untreated RA and osteoarthritis (OA) patients were examined by ELISA. 5) Citrullinated ITIH4 in SF from untreated RA and OA patients were assessed by immunoprecipitation and Western blot. **Results:** 1) and 2) The increased amount of ITIH4 and its citrullination was observed in pGIA joints of Day14. 3) PADI4 mRNA and protein increased in pGIA joints of Day14. 4) ITIH4 concentration in SF was significantly higher in RA patients. 5) Citrullinated ITIH4 was detected in SF from RA. The intensity of citrullinated ITIH4 was higher in SF than plasma in each RA patients. **Conclusion:** The citrullinated ITIH4 was generated in inflamed joints via PADI4.

W26-6

Investigation of pain-related microRNAs contained in synovial fluid-derived exosomes in Rheumatoid Arthritis and Osteoarthritis

Hirota Tsuno¹, Nobuho Tanaka², Satoru Ohashi³, Mitsuyasu Iwasawa³, Toshihiro Matsui¹, Naoshi Fukui^{2,4}

¹Department of Rheumatology, National Hospital Organization Sagami-hara National Hospital, ²Clinical Research Center for Allergy and Rheumatology, National Hospital Organization Sagami-hara National Hospital, ³Department of Orthopedic Surgery, National Hospital Organization Sagami-hara National Hospital, ⁴Department of Life Sciences, Graduate School of Arts and Sciences, The University of Tokyo

Conflict of interest: None

[Object] To elucidate factors involved in joint pain, we semi-comprehensively investigated pain-related miRNAs of synovial fluid-derived exosomes in the patients with OA and RA. [Methods] Exosomes were isolated from synovial fluid samples obtained from 8 patients (4 with OA and 4 with RA). From these 4 patients with OA, synovial fluid was obtained two times, at painful period (Painful OA:P-OA group) and at pain-free period (Non-painful OA:NP-OA group). The miRNAs extracted from the exosomes were subjected to miScript miRNA PCR Array™ (Qiagen). The miRNAs whose expression levels were significantly different between the NP-OA and the P-OA groups were considered to be the candidates involved in knee OA related pain. Furthermore, we compared the expressions of these exosomal miRNAs between the OA and the RA groups. [Results] MicroRNAs which showed significantly different expression levels between the NP-OA and the P-OA groups were miR-21-5p, miR-25-3p, miR-204-3p, miR-199a-3p/miR-199b-3p, miR-30d-5p, miR-495-3p, miR-92a-3p, and miR146b-5p (paired-T test, $p < 0.05$). Out of these miRNAs, the expression level of miR-92a-3p was significantly lower in the RA group, compared to the P-OA group. [Conclusions] Exosomal miRNAs involved in joint pain could be different between OA and RA.

W27-1

Clinical result of IVCY therapy in patients with interstitial pneumonia associated with connective tissue disease

Rumiko Miyagi, Satoshi Baba, Rina Okita, Ruriko Kuratani, Shinichiro Tsunoda

Division of Immunology and Rheumatology, Sumitomo Hospital

Conflict of interest: None

[Object] To evaluate the efficacy and side effect rate of IVCY in patients with interstitial pneumonia associated with connective tissue disease in our hospital. [Methods] We investigated the medical records of 11 patients with interstitial pneumonia had admitted to our hospital from March 2017 until October 2018. [Results] 11 patients (5 rheumatoid arthritis, 1 scleroderma with anti-centromere antibody-positive, 1 scleroderma with anti-RNA polymerase III antibody-positive, 1 scleroderma with anti-RNP antibody-positive, 1 polymyositis and 2 dermatomyositis) were treated with IVCY therapy. The age median was 76 years old. Observation mean period was 13 months. IVCY therapy of 500mg/2-4week was administered from 3 to 8 times. Before and after IVCY therapy, PSL dose was $16.8 \pm 12.3 \text{ mg} \rightarrow 7.5 \pm 4.4 \text{ mg}$, KL-6 levels was $1684 \pm 1955 \text{ U/ml} \rightarrow 1580 \pm 1505 \text{ U/ml}$ and respiratory function (%VC) was $62.8 \pm 12.2\% \rightarrow 66.9 \pm 11.3\%$. [Conclusions] Although there was not the clear improvement of KL-6 levels and respiratory function (%VC) before and after IVCY therapy, we were able to reduce a dose of PSL and no fatal cases were observed. IVCY therapy could be effective in elderly patients with interstitial pneumonia.

W27-2

Association between Autoantibodies and Long-term Clinical Outcomes in Pulmonary Arterial Hypertension (PAH) related with Connective Tissue Diseases

Yuko Shirota^{1,2}, Tsuyoshi Shirai², Hiroshi Fujii², Takao Kodera¹, Junichi Kameoka¹, Tomonori Ishii², Hideo Harigae²

¹Department of Hematology and Rheumatology, Tohoku Medical and Pharmaceutical University Hospital, ²Department of Hematology and Rheumatology, Tohoku University Hospital

Conflict of interest: Yes

[Object] We assessed the detailed autoantibodies and discriminative long-term clinical symptoms and followed up their outcomes. [Methods] This retrospective study included 50 CTD-PAH associated with SSc (n=17), SLE (n=18), primary SS (n=8), and MCTD (n=7) referred to our hospital between 2000 and 2018. We obtained their serum and determined autoantibodies against centromere, Scl-70, RNA-polymerase III, centriole, NuMA1, RNP, Sm, SSA/Ro, SSA/Ro52, SSB, PM-Scl, fibrillarin, Th/To, Ku, dsDNA, nucleosomes, histones, ribosomal P. We treated all patients with pulmonary vasodilators, and additionally treated with immunosuppressants, including IVCY and steroid for the patients with inflammatory symptoms. [Results] In terms of SSc, we divided into three

groups, which were (1) overlapping SS (n=7), (2) with centriole antibodies (n=3), or (3) others (n=7). We treated some SSc-PAH with SS and centriole- by immunosuppressants. there was a trend towards a better survival rate in centriole or SS-SSc-PAH than in other SSc. One of anti-Th/To Ab positive SSc-PAH relapsed. Ribosomal P antibody existed in 5 patients and 3 were severe PAH. [Conclusions] We suggested that detailed auto-antibody investigation are useful to estimate long-term clinical outcome, and expect the effect of immunosuppressants.

W27-3

Three cases of exacerbated rheumatoid arthritis-associated interstitial lung disease treated with two immunosuppressive drugs

Kayoko Hase¹, Kyoko Kojima¹, Jun Kishi¹, Ryosuke Sato², Shinji Yoshioka²

¹Department of Medicine, Division of Rheumatology, Tokushima Municipal Hospital, Tokushima, Japan, ²Orthopedic Surgery, Tokushima Municipal Hospital, Tokushima, Japan

Conflict of interest: None

[Background] Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is poor prognosis; however, there is no established evidence to cure disease in acute exacerbation. [Case] Three all men in the RA-ILD had RA treatment. Case1 was 71-year-old, appeared cough, fever and dyspnea, was admitted. From the sputum MRCNS was detected, we tried VCM drip with no improvement. As exacerbated RA-ILD, he was treated with mPSL0.5g pulse at the 2nd day and mPSL1.0g pulse at the 10th day. On PSL30mg/day, his condition became more exacerbated so he was treated with cyclosporine (CsA) 200mg/day at the 15th day and cyclophosphamide (CY) intravenous infusion at the 17th day; however died at the 30th day. Case2 was 74-year-old, and Case3 was 69-year-old, after the PSL dosage was reduced to 5or 4mg/day, and RA-ILD were exacerbated. These patients were treated with mPSL1.0g pulse at 1st day, CsA200mg/day + CY100mg/day by oral were started early until the 6th day. Case2, mPSL1.0g pulse was added at the 8th day and both patients on PSL60mg/day after pulse therapy. PSL are gradually reduced and CsA200mg/day + CY50mg/day are continued. [Discussion] RA-ILD should be considered also in addition to the steroids from an early stage with multiple immunosuppressive drugs for acute exacerbation.

W27-4

Comparison of prognosis and causes of deaths of 4 rheumatic diseases (RA, SSc, PM/DM, MPA) with interstitial pneumonia

Shigeki Makino¹, Takuya Kotani², Takeshi Shoda³, Hidehiko Makino², Koji Nagai², Tohru Takeuchi², Shigeki Arawaka²

¹Division of Internal Medicine, Osaka Medical College Mishima-Minami Hospital, Takatsuki, Osaka, Japan, ²Department of Internal Medicine IV, Osaka Medical College, Takatsuki, Osaka, Japan, ³Division of Rheumatology, Yodogawa Christian Hospital, Osaka, Japan

Conflict of interest: Yes

[Background] We aim to compare between the influences of interstitial pneumonia (IP) involvement on prognosis of 4 connective tissue diseases (RA, SSc, PM/DM, MPA). [Methods] We reviewed clinical data concerning about prognosis and causes of deaths of each connective tissue diseases with IP patients of our institute from August 2008 to July 2018. [Results] RA-IP patients are 255 (114 males, average 74 years). Dead cases were 40 (22 males). 5-year survival rate was 84%, 10-year survival rate was 60%. IP related death were 14 (35%), lung cancer related death were 7. SSc-IP patients are 212 (34 males, average 70 years). Dead cases were 25 (7males). 5-year survival rate was 91%, 10-year survival rate was 80%. IP related death were 7 (28%). PM/DM-IP patients are 197 (57 males, average 64 years). Dead cases were 39 (18males). 5-year survival rate was 74%, 10-year survival rate was 52%. IP related death were 28 (72%). MPA-IP patients are 70 (31 males, average 76 years). Dead cases were 20 (8males). 5-year survival rate was 81%, 10-year survival rate was 50%. IP related death were 6 (30%). [Conclusions] Between 4 diseases-IP patients, SSc-IP patients had better prognosis. In 4 diseases-IP patients, many IP related deaths were observed. So IP of 4 diseases influence on prognosis.

W27-5

The efficacy of OP treatment for BMD and lean mass in patients with rheumatoid arthritis

Tsuyoshi Watanabe

Department of Orthopedics, National Center for Geriatrics and Gerontology

Conflict of interest: None

[Background] Rheumatoid arthritis (RA) causes secondary Osteoporosis (OP) and low lean mass (LM). OP pharmacological treatment should improve bone mineral density (BMD) and LM. [Object] To assess the efficacy of OP treatment in RA patients during the prospective observational study for 1 year. [Methods] 72 patients (53 female and 19 males; mean age 74.6) with RA were enrolled in the study in 2016-2017. They completed risk factors questionnaire, Health Assessment Questionnaire (HAQ). Disease activity were assessed with SDAI. BMD, SMI, total body composition, LM and fat mass, and fat free mass index were measured by dual energy X-ray absorptiometry (Hologic Discovery). Patients were followed up in 12 months. [Results] Average SDAI was decreased from 8.13 to 5.3. OP and low LM patients were found out in 34% and 52%. Osteo-Sarcopenia patients are 39%. Average change rate of BMD and LM were +5.1% in Lumbar Spine (LS), +1.6% in Femoral neck and -1.2% in SMI. OP group was treated by some medicine. In OP group (n=42), change rate was higher than non-OP group (n=32). (OP: non-OP; LS +10.2%: +3.2%, Femoral neck +6.5%: +0.3%, SMI +5.8%: -3.6%). No statistical difference was found with using bDMARDs, Glucocorticoid use and SDAI. [Conclusions] OP treatment may maintain not only BMD but also LM.

W27-6

The analysis of 16 cases of osteonecrosis of the femoral head in autoimmune disease

Aki Sakashita¹, Aiko Hirano¹, Yu Isoda¹, Kazuki Fujioka^{1,3}, Hidetake Nagahara¹, Shogo Toyama^{2,3}, Ryo Oda^{2,3}, Toshikazu Kubo^{2,3}, Makoto Wada¹, Masataka Kohno¹, Yutaka Kawahito^{1,3}

¹Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ²Department of Orthopaedics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ³Rheumatic Center, University Hospital, Kyoto Prefectural University of Medicine

Conflict of interest: None

[Objective] The use of glucocorticoid is the risk factor for osteonecrosis of the femoral head (ONFH) in autoimmune disease. We examined 16 cases of ONFH to clarify its clinical features. [Method] We retrospectively analyzed clinical data of 16 ONFH cases with autoimmune diseases treated with glucocorticoids from January 2008 to October 2018. [Results] The average age at the diagnosis of ONFH was 47.5 years and the male-to-female ratio was 4:12. Six cases were patients with SLE, 2 were MPA, 2 were dermatomyositis, and the others were MCTD, GPA, EGPA, PN, adult onset Still's disease. Five patients took steroid pulse therapy and average of the maximum dose of prednisolone was 46mg/day. The median duration from the starting of the steroid therapy to diagnosis of ONFH was 14.6 months. Eleven patients had bilateral necrosis, but only 2 patients of them had bilateral pain, 8 had unilateral pain, and 1 had no pain. All 16 cases underwent X-ray at diagnosis, however only 3 cases of them had abnormal findings in it, and all of them needed surgical treatment. In total 5 patients needed surgical treatment, 4 of which was total hip arthroplasty, and 1 of which was osteotomy. [Conclusion] ONFH with autoimmune disease was often asymptomatic, and one third patients needed surgical treatment.

W28-1

Is flare after administration of Certolizumab pegol a specific phenomenon to Certolizumab pegol? - Comparative study with adalimumab therapy from multicenter registry study (TBCR)

Yasuhide Kanayama¹, Atsushi Kaneko², Nobunori Takahashi³, Takefumi Kato⁴, Yuji Hirano⁵, Yosuke Hattori², Nobuyuki Asai², Takayoshi Fujibayashi⁶, Tomone Shioura⁷, Masatoshi Hayashi⁸, Naoki Ishiguro², Toshihisa Kojima³

¹Department of Orthopaedic Surgery and Rheumatology, Toyota Kosei Hospital, Toyota, Japan, ²Department of Orthopaedic Surgery and Rheumatology, Nagoya Medical Center, Nagoya, Japan, ³Department of Orthopedic Surgery, Nagoya University School of Medicine, Nagoya, Japan, ⁴Department of Orthopaedic Surgery, Kato Clinic, Okazaki, Japan, ⁵Department of Rheumatology, Toyohashi Municipal Hospital, Toyohashi, Japan, ⁶Department of Orthopaedic Surgery, Konan Kosei Hospital, Konan, Japan, ⁷Department of Rheumatology, Shizuoka Welfare Hospital, Shizuoka, Japan, ⁸Department of Orthopaedic Surgery and Rheumatology, Nagano Red Cross Hospital, Nagano, Japan

Conflict of interest: None

[Object] To clarify and analyze whether Flare caused after completion of Loading of Certolizumab Pegol (CZP) against RA is unique to CZP compared with adalimumab (ADA) therapy. [Methods] In 70 cases of CZP and 77 cases of ADA were improved in which the DAS 28-ESR at 4 weeks from the start improved by 0.6 or more. Comparative study was conducted on the deterioration rate of DAS 28 - ESR between 4 and 12 weeks. [Results] CZP vs. ADA had an average age of 57.8 vs 56.2 years (p = 0.485), a disease duration of 9.3 vs 14.0 years (p = 0.001), a BIO-naive patients rate of 79% vs 77% (p = 0.777) and DAS28 - ESR 5.09 vs 5.68 (p = 0.002). The case rates were 35.7% vs 37.7% (p=0.807), 14.3% vs 23.4% (p = 0.161), 5.7 (p = 0.807), DAS 28-ESR deteriorated at 4 to 12 weeks (0 to 0.6, 0.6 to 1.2, The aggravation rate is 34.5% vs 39.0% (p = 0.624), 14.5% vs 25.4% (p = 0.148), 5.5% vs 11.9% (p = 0.203) in the BIO-naive patients (CZP 55, ADA 59) The deterioration rate in 34.5% vs 34.9% (p = 0.956), 17.2% vs 22.2% (p = 0.492), 6.9% vs 11.1% (p = 0.421) in the case of MTX combination patients (CZP 58, ADA 63) It was almost the similar. [Conclusions] It is suggested that flare generated after CZP loading is not a specific phenomenon to CZP.

W28-2

Methotrexate dose on the efficacy and safety of certolizumab pegol in patients with rheumatoid arthritis

Shinkai Ri, Yuji Nozaki, Hiroki Akazawa, Chisato Ashida, Fusayo Ikeda, Atsuhiko Yamamoto, Tetsu Itami, Kenji Sakai, Asuka Inoue, Toshihiko Shiga, Kazuya Kishimoto, Koji Kinoshita, Masanori Funauchi, Itaru Matsumura

Department of Hematology and Rheumatology, Kindai University Faculty of Medicine

Conflict of interest: None

[Object] With the aging of rheumatoid arthritis (RA) patients, there are cases in which methotrexate (MTX) increase and selection of TNF inhibitors therapy are difficult. Currently, there are few reports comparing therapeutic effects by certolizumab pegol (CZP) by MTX dose, and we examined the therapeutic effect by MTX dose in CZP therapy. [Methods] From August 2013, RA cases treated with CZP (N=28) were retrospectively studied. The continuation rate, the clinical treatment effect (DAS28-CRP), the disease activity and EULAR treatment response by DAS28-CRP in high (≥ 8 mg/week) and medium to low (<8mg/week) MTX dose were the main outcome measure. They were compared for RA cases treated with adalimumab (ADA) (N=40) as control group. [Results] With respect to the continuation rate one year after CZP and ADA treatment, ADA group significantly higher in the H group, and there was no significant difference in the L group. DAS remission rate, one year after treatment DAS 28-CRP did not show any significant difference in both groups, but the group with good therapeutic response (Good + Moderate response) significantly increased with L group's CZP treatment. [Conclusions] They was shown that ADA treatment is higher effect in high MTX dose, CZP in medium to low MTX dose.

W28-3

The Comparative Observational Study about Efficacy, Safety and Continuation Rate between Abatacept and Tocilizumab in Patients with Rheumatoid Arthritis

Mayumi Matsuda¹, Yu Funakubo¹, Takuma Wada¹, Norisune Kozu², Kojiro Sato¹, Toshihide Mimura¹

¹Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University Hospital, ²Kouzu Orthopedic

Conflict of interest: None

[Object] Biologic agents used in patients with rheumatoid arthritis (RA) have increased in recent years. We investigated the efficacy, safety, and continuation rate of abatacept (ABT) or tocilizumab (TCZ) in our RA patients. [Methods] 155 patients treated with ABT or TCZ retrospectively were observed for one year. We compared the baseline characteristics, disease activity, physical disability, continuation rate, and safety. [Results] In ABT group (n=76) compared with TCZ group (n=79), we found older at initiation (ABT vs. TCZ:63 vs. 57years), higher HAQ-DI (1.4 vs. 1.0), and fewer MTX-users (46.1 vs. 65.8%). Age of onset, disease duration, rate of female, naïve rate of biologics, body weight, DAS28-ESR4, MMP-3, ACPA positive rate, dose of MTX, and dose of PSL were similar. CDAI and HAQ-DI significantly decreased in one year in both groups. There were fewer patients who achieved remission or low disease activity in ABT group than in TCZ group (63.3 vs. 84.4%). There was no significant difference in the continuation rate (81.6 vs. 84.8%), adverse events (10.5 vs. 10.1%), and inefficacy rate (7.9 vs. 3.8%). [Conclusions] Smaller efficacy was obtained in ABT group, who had disadvantageous conditions, compared to TCZ group, but continuation rate and safety were equivalent between two groups.

W28-4

In adalimumab treatment, Remission induction and treatment continuation at 208 weeks in 186 patients

Toshiaki Miyamoto, Kenji Yamazaki, Ryuhei Ishihara
Internal Medicine and Rheumatology, Seirei Hamamatsu General Hospital

Conflict of interest: Yes

Objective Clinical usefulness and treatment continuation following 256 weeks of adalimumab (ADA) in rheumatoid arthritis (RA) patients were investigated. **Methods** Subjects were 186 analyzable patients introduced to ADA at the author's institution from May 2009 to Oct. 2014. Mean age was 54 years, mean duration of illness 6.8 years. 151 received MTX ≥ 10 mg/week (≥ 10 group) and 29 MTX < 10 mg/week (< 10 group). The course of DAS28 (ESR), HAQ and remission rate were analyzed. **Results** Overall DAS28 (ESR) remission rate showed clinical remission in 48% of patients from 12 weeks, and achieved 66% from 52 weeks, after that this condition continued. Changes in DAS 28 (ESR) remission rates of 4, 12, 24, 52, 80, 104, 152, 208, 256 weeks for the < 2 and ≥ 2 groups were similar to those seen in the N and S groups. Overall HAQ remission rate at 256 weeks was 82%; treatment continuation rate was 63.3%, and those of ≥ 10 group was 65.2%. **Conclusion** Remission was induced early with ADA in about 48% of patients, and achieved 66% of patients at 256 weeks. ADA plus an adequate dose of MTX with early escalation in early-stage RA and Bio Naïve patients is the best approach to maximally exploit the ADA potential.

W28-5

Long-term efficacy and safety of treatment with tocilizumab (TCZ) in elderly rheumatoid arthritis patients (RA)

Shiro Ohshima¹, Kentaro Isoda¹, Yuji Yoshida¹, Maiko Yoshimura¹, Yoshinori Harada¹, Satoru Teshigawara¹, Hidetoshi Matsuoka¹, Kentaro Kuzuya¹, Yasutaka Okita¹, Eri Oguro¹, Takaaki Noguchi², Shosuke Akita², Shigeyoshi Tsuji¹, Jun Hashimoto¹, Yukihiko Saeki³

¹Department of Clinical Research/Rheumatology & Allergology, Osaka Minami Medical Center, ²Department of Orthopaedics, Osaka Minami Medical Center, ³Department of Clinical Research, Osaka Minami Medical Center

Conflict of interest: None

[Objective] Long-term efficacy and safety of treatment with tocilizumab (TCZ) in elderly rheumatoid arthritis patients (RA) were examined. [Methods] We extracted elderly RA patients over 75 years old who received TCZ at Osaka Minami Medical Center using clinical data accumulated in our real world database (MiRAi). We examined background and disease activity, continuation rate, and adverse events were compared

with patients under 75 years of age. [Results] There were seven elderly RA patients aged over 75 who received TCZ at our hospital from April 2008 to April 2016, 6% of all patients with TCZ therapy were extracted. There were 6 cases continuing for over 3 years after introduction, 5 of which were monotherapy. In 7 cases, steroids were used at baseline, but all cases were weighed and stopped in 5 cases. Low disease activity of CDAI was maintained, with no cessation or death due to serious side effects. [Conclusion] Tocilizumab (TCZ) is considered to be a possible medical option for elderly RA. Both social and economic problems should be considered in the future.

W28-6

Patient Reported Outcome survey on syringe formulation and auto-injector formulation of adalimumab

Tomohiko Yoshida^{1,2}, Naooki Katsuyama^{1,2}, Yoichiro Akiyama^{1,2}, Yasuhiro Otaki^{1,3}

¹Department of Rheumatology, Setagaya Rheumatology Clinic, ²Department of Rheumatology, Toshin Yoshida Internal Medicine Rheumatology, ³General Medical Education and Research Center, Teikyo University

Conflict of interest: None

[Object] Adalimumab (ADA) auto injector formulation (AI) was additionally released in June 2018. Changes from syringe formulation (SY) to AI were expected to cause changes in patient's self-injection operability, storage and management, psychological state such as tension, psychiatric pain, and the like. We conducted questionnaires on RA patients and investigated Patient Reported Outcome in adding AI. [Methods] We targeted 30 RA patients administering SY of ADA visiting our hospital from August to October 2018. 1 Procedure 2 Device 3 Storage and management 4 feeling 5 pain upon injection We conducted a questionnaire using VAS. [Results] [Pain upon Injection] There was no difference between SY and AI VAS 12:12. [Management] VAS 26:32 of SY and AI. [Technique] SY and AI were VAS 27:6. [Device] VAS 27:9 with SY and AI. [Feeling] SY and AI were VAS 40:12. [Conclusions] ADA has SY and AI forms. AI was easier in injection procedure and the feeling of tension and anxiety to injection were alleviated. AI, which is easy to grasp for RA patients and invisible injection needles, was supported.

W29-1

Deep remission in 12 months after the initiation of treatment for early rheumatoid arthritis determines good prognosis for radiographic progression

Tomoko Sugiura
Sugiura Clinic

Conflict of interest: None

[Object] To compare the impact of poor prognostic factors of radiographic damage between untreated early rheumatoid arthritis (RA) and early RA after 12, 24, and 36 months of treatment. [Methods] This study included 130 outpatients with a disease duration of < 1 year (median, 3 months; 74% women). The outcome was assessed on the basis of the presence or absence of radiological progression of RA in the hand, wrist, and foot. [Results] At baseline, 30% of the patients already had a bone erosion, and the following were the associated risk factors: presence of anti-cyclic citrullinated peptide (CCP) antibody (odds ratio [OR], 6.6), high disease activity (OR, 1.66), and delayed treatment initiation (OR, 1.36). By contrast, only high disease activity at 12 months (OR, 2.03; 95% confidence interval [CI], 1.11-3.73) was associated with new bone lesion at 12 months. Furthermore, a new bone lesion at the following months was associated with the most recently developed bone lesion (OR, 20.5 for 24 months and 10.9 for 36 months). The cutoff SDAI score for preventing new bone lesion at 12 months was estimated to be 2.25 (sensitivity, 72%; specificity, 55%; area under the curve [AUC], 0.72). [Conclusions] To prevent structural damage, induction to deep remission in 12 months is most important.

W29-2

Examination of the factor to give residual symptoms among patients with rheumatoid arthritis in SDAI-remission or low disease activity.~Analysis of joint ultrasonography, PRO, patient background and the serologic characteristics ~

Masao Nawata^{1,2}, Yuya Fujita^{1,2}, Kazuki Someya^{1,2}, Kazuyoshi Saito^{1,2}, Yoshiya Tanaka²

¹Tobata General Hospital, ²University of Occupational and Environmental Health, Japan

Conflict of interest: None

[Object] I identify factors contributing residual symptoms of RA patients in SDAI-remission. [Methods] 127 patients were enrolled. The synovitis evaluated gray scale (GS) and power doppler (PD) with 26 both hands joints. I evaluated age, sex, the number of tender and swelling joints (TJ and SJ), the serologic characteristics (CRP, ESR, CCP, RF, MMP-3), PRO (morning stiffness, pain-VAS, fatigue-VAS). [Results] The 127 patients background the sex 17.3%/82.7% (M/F), TJ 2.7±4.6, SJ 1.4±3.2, CRP 1.0±2.0, RF 111.2±187.6, CCP 270.3±491.1, MMP-3 153.6±296.2, SDAI 10.5±12.4, morning stiffness 199.2±472.9, pain-VAS 3.4±3.0, fatigue-VAS 3.7±3.1, GS 1.3±1.0, PD 0.8±0.9 (mean±SD). I made a stratified analysis in SDAI-remission group and SDAI-low disease activity group. As a result of single variable analysis, TJ, SJ, CRP, pain-VAS, fatigue-VAS, GS≥2, PD1 and PD2 were extracted for significant difference. For the multivariate analysis by the step Wise method, TJ, fatigue-VAS and GS≥2 were extracted with a dominant difference. After performing a stratified analysis more in fatigue-VAS, TJ and GS≥2 were extracted for significant difference. [Conclusions] Association was shown in the residual symptoms (fatigue-VAS) with the residual inflammation (TJ and GS≥2) and significant difference.

W29-3

The optimal timing of administration of TNF inhibitors to lead to drug-free remission in early RA is the “time corresponding to phase 1 of the EULAR recommendation”

Eiji Matsui

Medical Corporation Matsui Orthopedic Clinic, Uji, Kyoto, Japan

Conflict of interest: None

In 2014, the presenter was developed the “Matsui method” of drug-free remission in early RA patients. The purpose of the study was to demonstrate the mechanism that drug-free remission is achieved when the Matsui method is performed. (Theory of the Matsui method) Drug-free remission is achieved when all of the activated TNF-producing cells are lead to apoptosis. Among TNF-producing cells, membranous TNF-producing cells can be killed by administration of IFX, ADA, and GLM. By contrast, non-membranous TNF-producing cells cannot be killed. To kill non-membranous cells, wait until they change to membranous cells and administer bio. After TNF-producing cells finish producing TNF- α , they enter a resting phase. The resting cells subsequently divide and exponentially increase in number. It takes approximately six months for this cell group to be activated again and change to membranous cells. “Deep remission” is “a state in which TNF- α is not present in the blood and only unused bio that has been administered is present in the body”. When membranous cells appear in this environment, a large amount of unused bio will immediately kill the membranous cells. That is, if deep remission can be achieved quickly and maintained for nine months, it is possible to kill all TNF-producing cells.

W29-4

Trends in methotrexate dose and disease activity in patients with rheumatoid arthritis who had achieved remission by adalimumab plus methotrexate treatment

Toshihiko Hidaka, Kazuyoshi Kubo, Yayoi Hashiba, Hiroshi Kuroda
Insititution of Rheumatology, Zenjinkai Shimin-no-Mori Hospital, Miyazaki, Japan

Conflict of interest: Yes

[Objectives] We assessed the trends in methotrexate (MTX) dose in

patients with rheumatoid arthritis (RA) who achieved remission by adalimumab (ADA) plus MTX treatment. [Methods] In 77 RA patients who had been treated with ADA, 31 RA patients who had achieved within one year and maintained remission more than 3 months by ADA plus MTX treatment were evaluated. These patients were divided into 3 groups; group R (G-R, n=8): patients who reduced MTX dosage, group M (G-M, n=19): maintained MTX dosage, group I (G-I, n=4): increased MTX dosage. We assessed DAS28ESR, SDAI and the trends in MTX dose in 3 groups at the point of 0, 3, 6, 9 and 12 months after remission. [Results] Mean age, mean disease duration (months), DAS28ESR, SDAI, MTX dosage at the start of ADA were as follows; G-R: 56.3, 56.6, 4.72, 20.14, 10.5mg/W, D-M: 54.1, 41.9, 3.80, 13.48, 10.4mg/W and G-I: 55.0, 10.0, 3.78, 11.16, 9.0mg/W, respectively. DAS28, SDAI and MTX dosage at the point of remission/12 months after remission were as follows; G-R: 2.12/1.88, 3.38/1.14, 10.5/6.9, G-M: 2.01/1.77, 3.29/1.74, 10.5/10.5, and G-I: 2.05/1.88, 1.92/1.80, 9.0/11.3, respectively. [Conclusions] Regardless of MTX dosage, patients with RA who had achieved remission by ADA plus MTX treatment in early phase can maintain remission.

W29-5

Predictors of sustained remission in rheumatoid arthritis patients using gradual de-escalation of abatacept

Masaomi Yamasaki

Shin-Yokohama Rheumatology Clinic, Yokohama, Japan

Conflict of interest: None

[Object] To study prognostic factors for achievement of sustained remission in rheumatoid arthritis patients receiving gradual de-escalation of abatacept. [Methods] Efficacy was evaluated by CDAI and Boolean remission criteria. Abatacept were gradual de-escalation with patient who had sustained remission (susREM) for 3months. [Results] 237 of RA patients were treated with abatacept and enrolled in this study. Overall susREM rate was 38.0% (90 cases). 88 out of 90 cases were achieved drug reduced remission (DRR) and 6 out of 88 patients were achieved drug free remission (DFR). Although there were no significant differences in duration of RA, age and initial CDAI, ACPA positive, combination of csDMARDs and reduction of CDAI at first 3months of treatment were predictors for susREM. DFR patients showed lower number of swelling joints compared with DRR patients. All patient achieved to DFR fulfill Boolean remission criteria. [Conclusions] ANCA positivity, combination of csDMARDs and more rapid initial response are the predictor of successful tapering and maintaining remission. Using gradual de-escalation of abatacept also useful for susREM.

W29-6

Comparative Analysis of bDMARDs retention rates from National Database in Japan

Katsuhiko Takabayashi^{1,2,4}, Fumihiko Ando², Takahiro Suzuki^{2,4}, Kei Ikeda⁴, Hiroshi Nakajima⁴, Hideki Hanaoka^{3,4}

¹Sanwa Hospital, ²Department of Management and Medical Informatics, Chiba University Hospital, ³Department of Clinical Research, Chiba University Hospital, ⁴Department of Allergy and Collagen Diseases, Chiba University School of Medicine

Conflict of interest: None

[Objectives] To analyze the effectiveness of bDMARDs from NDB data. [Method] By using NDB (National DataBase which includes all Japanese claims data) the retention rates of 166,987 patients who were treated by bDMARDs and Jak inhibitor at least once in 7 years were analyzed by Kaplan Meier Method. [Result] Tofacitinib has the longest retention months (median 34 months) and highest retention rate (0.56 at two years), following by TCZ, ABT, GLM, ETN, IFX, CPZ and ADA. [Conclusion] The retention rate is the highest in Jak inhibitor followed by non TNF inhibitor and TNF inhibitors.

W30-1

Factors Affecting Differences between Responders and Non-responders on Work Productivity in RA Patients Treated with Tocilizumab-SC: 104-week-Results in the FIRST ACT-SC Study

Yoshiya Tanaka¹, Hideto Kameda², Kazuyoshi Saito³, Yuko Kaneko⁴, Eiichi Tanaka⁵, Shinsuke Yasuda⁶, Naoto Tamura⁷, Keishi Fujio⁸, Takao Fujii⁹, Toshihisa Kojima¹⁰, Hitoshi Kohsaka¹¹

¹The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, ²Toho University, ³Tobata General Hospital, ⁴Division of Rheumatology Department of Internal Medicine, Keio University School of Medicine, ⁵Institute of Rheumatology, Tokyo Women's Medical University, ⁶Department of Rheumatology, Endocrinology and Nephrology, Hokkaido University Faculty of Medicine and Graduate School of Medicine, ⁷Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, ⁸Department of Allergy and Rheumatology, The University of Tokyo, ⁹Department of Rheumatology and Clinical Immunology, Wakayama Medical University, ¹⁰Department of Orthopaedic Surgery and Rheumatology, Nagoya University Graduate School of Medicine, ¹¹Department of Rheumatology, Tokyo Medical and Dental University

Conflict of interest: Yes

[Object] In a study conducted on patients with rheumatoid arthritis (RA) receiving subcutaneous injections of tocilizumab (TCZ-SC), the effect on labor productivity was evaluated, and the factors contributing to improvement were determined. [Methods] FIRST ACT-SC Study (UMIN000012306) was a cohort study assessing the 2-year treatment outcome of TCZ-SC in biologics-naïve Japanese patients with RA. Logistic regression was performed to determine the factors that contributed to responses in terms of activity impairment (AI) of WPAL. In addition, the association of these responses with the withdrawal rate and the quality of life (QOL) was also evaluated. [Results] Of the 295 patients were included in the analysis. The results showed an association between the results of subjective assessments, such as the utility value of EQ-5D ($p < 0.001$) and HAQ-DI ($p = 0.02$). Findings also suggested that subjects in a better condition were more likely to be AI responders. A significant difference in withdrawal rate was found between responders and non-responders (27.0% vs. 46.9%; $p < 0.001$). [Conclusions] Starting TCZ-SC treatment at an early stage may contribute to an improvement in labor productivity, a long-term continuation of treatment, and an improvement of the QOL.

W30-2

Onset of action of sarilumab plus methotrexate (MTX) in patients (pts) with active rheumatoid arthritis (RA) and inadequate response to MTX in 2 phase 3 studies (KAKEHASI and MOBILITY)

Yoshiya Tanaka¹, Kazuteru Wada², Yoshinori Takahashi², Owen Hagino³, Hubert Van Hoogstraten⁴, Neil Graham⁵, Hideto Kameda⁶

¹The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, ²Sanofi K.K., ³Sanofi, ⁴Sanofi Genzyme, ⁵Regeneron Pharmaceuticals, Inc., ⁶Division of Rheumatology, Department of Internal Medicine, School of Medicine, Toho University

Conflict of interest: Yes

[Object] This post-hoc analysis assessed the time to onset of clinical efficacy and durability of response of sarilumab at Weeks (wks) 2, 4, 8, 12 and 24 in the phase 3 MOBILITY and KAKEHASI studies. [Methods] In MOBILITY (global centres) and KAKEHASI (Japan), pts with a prior inadequate response to MTX (MTX-IR), received subcutaneous sarilumab 150 mg q2w + MTX (S150), 200 mg q2w + MTX (S200), or placebo + MTX (P) for up to 52wks. [Results] Baseline characteristics were well balanced in both studies. Sarilumab showed improvements (vs P) in efficacy at all timepoints. Improvements in ACR20 response were seen as early as 2wks in both studies: MOBILITY (20.5% S150; 20.8% S200; both nominal $p < 0.01$ vs P); KAKEHASI (18.5% S150; 15.0% S200; nominal $p < 0.05$ vs P); and, from around wk4 for ACR50/70. In both studies, greater reductions in DAS28-CRP from baseline were observed with both doses of sarilumab vs P at wk2 (nominal $p < 0.0001$ vs P). Numerical improvements of both doses in CDAI (nominal $p < 0.05$ vs P) and HAQ-DI were observed from wk2. TEAEs were consistent with the

class. Infection was the most common TEAE ($\geq 10\%$ of patients) in all groups at wk12 TEAEs. [Conclusions] Sarilumab rapidly improved signs and symptoms and physical function in MTX-IR RA pts both in Japan and overseas.

W30-3

Long-Term Effect of Sarilumab Plus Methotrexate on Disease Activity, Physical Function and Radiographic Progression: A 5-Year Analysis

Yoshiya Tanaka¹, Gerd R Burmester², Yong Lin³, Gregory St John⁴, Sheldon Wang³, Juan José Gómez-reino Carnota⁵, José Antonio Maldonado-cocco⁶, Juan Carlos Salazar-buitrago⁷, Désirée Van Der Heijde⁸, Mark C Genovese⁹, Hideto Kameda¹⁰

¹The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, ²Charité - University Medicine Berlin, ³Sanofi Genzyme, ⁴Regeneron Pharmaceuticals, Inc., ⁵Complejo Hospitalario Universitario de Santiago de Compostela, ⁶School of Medicine, Buenos Aires University, ⁷Riesgo de Fractura S.A - CAYRE, ⁸Leiden University Medical Centre, Leiden, The Netherlands, ⁹Stanford University Medical Center, ¹⁰Division of Rheumatology, Department of Internal Medicine, School of Medicine, Toho University

Conflict of interest: Yes

[Object] To examine 5-year safety, efficacy and radiographic outcomes of sarilumab in adults with RA and inadequate response to methotrexate (MTX-IR). [Methods] In MOBILITY (NCT01061736) Part B Cohort 2 1197 patients with moderately to severely active RA and MTX-IR were randomized to placebo, sarilumab 150 or 200mg SC q2w+MTX for 52 weeks. 897/901 completers received sarilumab 200mg q2w+MTX in the open-label extension EXTEND (NCT01146652). [Results] Initial treatment with sarilumab 200mg+MTX was associated with reduced radiographic progression at Year 5 vs sarilumab 150mg+MTX or placebo+MTX (no progression in mTSS: 52% vs 47% and 40%, respectively). Efficacy (DAS28-CRP, CDAI and HAQ-DI) was sustained. The safety profile was stable over 5-year follow-up and consistent with IL-6R blockade. Absolute neutrophil count $< 1000/\text{mm}^3$ was observed but not associated with increased rate of infection. [Conclusions] Clinical efficacy, including reduction in disease activity, improvement in physical function, and inhibition of radiographic progression with sarilumab+MTX was sustained over 5-years. No new safety signals emerged. [Acknowledgments] Study funding and editorial support (Natalie Roberts, Adelphi Communications Ltd) was provided by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

W30-4

Sustained Clinical Remission after Discontinuation of Infliximab with a Raising Dose Strategy or a Standard Dose Treatment in Patients with Rheumatoid Arthritis (RRRR study): A Randomized Controlled Trial

Yoshiya Tanaka¹, Takao Koike^{2,3}, Nobuyuki Miyasaka⁴, Tsuneyo Mimori⁵, Tsutomu Takeuchi⁶, Shintaro Hirata⁷, Eiichi Tanaka⁸, Hidekata Yasuoka⁶, Yuko Kaneko⁶, Kosaku Murakami⁵, Tomohiro Koga⁹, Kazuhisa Nakano¹, Koichi Amano¹⁰, Kazuyasu Ushio¹¹, Tatsuya Atsumi¹², Masayuki Inoo¹³, Kazuhiro Hatta¹⁴, Shinichi Mizuki¹⁵, Shohei Nagaoka^{3,16}, Shinichiro Tsunoda^{4,17}, Hiroaki Dobashi¹⁸

¹The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, ²Hokkaido Medical Center for Rheumatic Diseases, ³Department of Medicine II, Hokkaido University Graduate School of Medicine, ⁴Department of Rheumatology, Tokyo Medical and Dental University, ⁵Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, ⁶Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, ⁷Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, ⁸Department of Rheumatology, School of Medicine, Tokyo Women's Medical University, ⁹Center for Bioinformatics and Molecular Medicine, Nagasaki University, Graduate School of Biomedical Sciences, ¹⁰Department of Rheumatology & Clinical Immunology, Saitama Medical Center, ¹¹Ushio Clinic, ¹²Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, ¹³Utatsu Hospital, ¹⁴Department of General Medicine, Tenri Hospital, ¹⁵Depart-

ment of Rheumatology, Matsuyama Red Cross Hospital, ¹⁶Department of Rheumatology, Yokohama Minami Kyosai Hospital, ¹⁷Division of Rheumatology Department of Internal Medicine, Hyogo College of Medicine, ¹⁸Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University

Conflict of interest: Yes

Object: The Remission induction by Raising the dose of Remicade in RA study (RRRR Study) (UMIN000005113) was designed to evaluate the clinical remission after 54 weeks of “programmed” treatment, whose dose of IFX for each patient was determined by the baseline serum TNF- α . **Methods:** RRRR study was a randomized, active controlled, multicenter phase4 study. IFX-naïve RA patients who showed MTX-IR were randomized to the programmed treatment group, a dose of IFX was kept or raised based on baseline levels of serum TNF the standard treatment group, 3mg/kg of IFX was kept. If patients showed a SDAI \leq 3.3 at week 54, they discontinued IFX. **Results:** 405 patients were enrolled in the study. At week 54, 39.4% in the programmed group and 32.3% in the standard group could attain the remission defined by SDAI and withdrew IFX treatment. At week 106, the 1-year sustained discontinuation rate, the primary endpoint, of the programmed group and standard group was 23.5% and 21.6%, respectively. **Conclusions:** Programmed treatment strategy using different dose of IFX based on the baseline levels of serum TNF- α tended to increase the remission rate at week 54, but did not increase the sustained remission rate after 1-year discontinuation of IFX treatment at week 106.

W31-1-1

Frequency and related factors of pancytopenia in patients with systemic lupus erythematosus (SLE)

Daijirou Soda^{1,2}, Susumu Nishiyama¹, Tetsushi Aita¹, Yasuhiko Yoshinaga¹, Shoji Miyawaki¹, Akio Morinobu²

¹Rheumatic Disease Center, Kurashiki Medical Center, ²Division of Rheumatology, Kobe University Hospital

Conflict of interest: None

[Object] To examine the frequency and related factors of pancytopenia in SLE patients. **[Methods]** Of 224 patients with SLE (visited our hospital 2005-2017), 25 (24 females) developed pancytopenia. Age at the SLE onset was 29.0 \pm 14.6 and the disease duration was 20.2 \pm 13.5 years. **[Results]** Pancytopenia occurred 37 times. Age at the first occurrence of pancytopenia was 49.4 \pm 13.5. Median duration (IQR) of the 37 times pancytopenia was 7 (3-16.5) days. Patients were classified as A) 11 patients due to SLE, B) 5 due to SLE and drugs, C) 5 due to SLE and other diseases, D) 1 due to drugs, and E) 3 due to other diseases. Patients with SLE-related pancytopenia (A + B + C) had significant high SLEDAI and short period from the SLE onset to the pancytopenia occurrence compared to others (D + E). Abnormal findings except for hypocellularity of bone marrow or reticulocyte index were 0/6 in SLE-related pancytopenia and 3/3 in SLE-unrelated. The cumulative survival rates of 10, 20, and 30 years in patients with pancytopenia were 95.5, 68.4, and 35.9%, respectively. **[Conclusions]** High disease activity and short duration until the pancytopenia occurrence was observed in patients with SLE-related pancytopenia. Prognosis of SLE patients accompanied by pancytopenia was poor.

W31-1-2

Effectiveness of hydroxychloroquine (HCQ) on thrombocytopenia associated with systemic lupus erythematosus (SLE)

Sayaka Takatori, Kensaku Okamoto, Yuta Ikechi, Tomoki Kawahata, Kitaru Tanaka, Kyohei Takatori, Ryota Yoshimoto, Kouhei Eguchi, Daisuke Fujishiro, Satoru Kodama, Atsushi Kobayashi, Yuichi Makino, Tsuguhito Ota

Division of Metabolism and Biosystemic Science, Department of Medicine, Asahikawa Medical University, Asahikawa, Japan

Conflict of interest: None

[Object] To analyze an effect of HCQ on thrombocytopenia associated with SLE **[Methods]** Among the 58 SLE patients administered with

HCQ at our hospital, 4 cases showed an increase in platelet (Plt) count from thrombocytopenia of less than 100,000 (μ L) at the time of diagnosis or during their clinical course. We reviewed the clinical course of the 4 cases. **[Results]** <Case 1> A 57-year-old female. Prednisolone (PSL) was administered against immune thrombocytopenic purpura (ITP), but low Plt counts persisted. Then she was diagnosed as SLE and HCQ was introduced. Plt count was increased from 19,000 to 90,000. <Case 2> A 16-year-old female. Diagnosis of SLE was made and treated with PSL and HCQ. Plt increased from 73,000 to 227,000. <Case 3> A 37-year-old female. She was diagnosed as SLE and lupus nephritis class IV +V (WHO). Since decrease in Plt count was persistent, splenectomy was performed. Plt increased to 70,000 temporally, but her Plt decreased to 15,000. After introduction of HCQ, Plt increased to 56,000. <Case 4> A 38-year-old female. She was diagnosed as SLE and treated with PSL. Her Plt count was decreased to 80,000 but after introduction of HCQ it was increased to 110,000. **[Conclusions]** Treatment with HCQ may potentially therapeutic for thrombocytopenia in SLE.

W31-1-3

Investigation of the Risk for Clinical Macrophage Activation Syndrome in Patients with Systemic Lupus Erythematosus

Yasuhiro Hasegawa, Yoshiyuki Arinuma, Kazuma Ino, Junichi Kondo, Takumi Muramatsu, Yu Matsueda, Takayuki Hoshiyama, Toshihiro Tono, Tatsuhiro Wada, Tatsuo Nagai, Sumiaki Tanaka, Kunihiro Yamaoka
Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine

Conflict of interest: None

[Object] Macrophage activation syndromes (MAS) clinically involved in SLE patients (CMAS) is prevalent but refractory complication in patients with SLE. The aim of this study is to investigate the risk for MAS. **[Methods]** SLE patients who had admitted for induction therapy in Kitasato University hospital since January in 2010 to September in 2018 were enrolled. Patients having CMAS were defined as those who fulfilled ACR/EULAR 2016 classification criteria for MAS in sJIA. Risk factors for CMAS were investigated based on medical histories. **[Results]** 71 patients were enrolled. Of 71 patients, 13 patients (17.6%) were complicated with CMAS. CRP level was not a risk for CMAS. Among immunological tests, higher C1q was a risk for CMAS (odds ratio (OR), 7.36, $p=0.21$), unlike higher IgG or lower complement. Among antibodies, positive for anti-Sm antibody independently increased a risk for CMAS (OR 4.31, $p=0.12$) in multivariate analysis. Steroid pulse therapy and calcineurin inhibitors were used for treatment. There was no fatal patient during observation period. **[Conclusions]** CMAS is one of the complications by high disease activity of SLE. An appropriate clinical diagnosis of MAS and use of calcineurin inhibitor could improve prognosis.

W31-1-4

Retrospective study of combination therapy including continuous hemodiafiltration with a cytokine-adsorbing hemofilter (AN69ST) for hemophagocytic lymphohistiocytosis complicated with systemic lupus erythematosus

Koto Hattori¹, Yuichi Ishikawa¹, Yasuhiko Koizumi², Orié Chinone³, Michio Fujiwara¹, Yasuhiko Kita^{1,2}

¹Department of Rheumatology, Yokohama Rosai Hospital, ²Immunorheumatology Center, Yokohama Rosai Hospital, ³Department of Nursing, Yokohama Rosai Hospital

Conflict of interest: None

[Object] To examine the clinical course and safety of continuous hemodiafiltration with a cytokine-adsorbing hemofilter (AN69ST-CHDF) for hemophagocytic lymphohistiocytosis complicated with systemic lupus erythematosus (SLE-HPS). **[Methods]** We retrospectively examined four SLE-HPS patients who received combination therapy including AN69ST-CHDF at our department from 2016 to 2018. **[Results]** The study subjects were four SLE-HPS patients. The median age was 42. Three patients had neuropsychiatric SLE, and one had HPS from onset of SLE. When AN69ST-CHDF was initiated, glucocorticoid pulse therapy and plasma exchange were given in all patients. The median duration of the stay in the ICU and oxygen therapy were 17 days and 15 days, respec-

tively. The median SLEDAI, platelet count, ferritin were $20,4.9 \times 10^3/\mu\text{l}$, 14054 ng/ml before initiation of treatment and $8, 8.7 \times 10^3/\mu\text{l}$, 2297 ng/ml on the day of ICU discharge. Although cyclosporine was administered in two cases and rituximab was administered in one case before the initiation of AN69ST-CHDF, there were no patients who need another immunosuppressant after the initiation of AN69ST-CHDF. No adverse event associated with the use of AN69ST-CHDF was observed. [Conclusions] AN69ST-CHDF might be a safe adjuvant therapy for SLE-HPS.

W31-1-5

Analysis of pulmonary manifestations in systemic lupus erythematosus

Kaoru Mizukawa, Keisuke Nishimura, Keiichiro Kadoba, Hiroki Mukoyama, Tomohiro Yoshida, Daisuke Waki, Toshihiko Yokota
Department of Endocrinology and Rheumatology, Kurashiki Central Hospital, Kurashiki, Okayama, Japan

Conflict of interest: None

[Object] Pulmonary involvement in systemic lupus erythematosus (SLE) are rarely reported. We analyzed the clinical features of patients with pulmonary involvement in SLE. [Methods] To analyze the clinical features of 138 patients with SLE who were treated in our hospital from January 2006 to July 2018. And to analyze 23 patients with mixed connective tissue disease (MCTD) involving lung treated in the same period. [Results] Patients with SLE were diagnosed with ACR or SLICC criteria. Of 138 patients, 21 patients had pulmonary manifestation. Sixteen patients had interstitial lung disease (ILD), two had diffuse alveolar hemorrhage (DAH), two had pulmonary hypertension (PH) and one had both DAH and PH. Pulmonary involvements were found to be significantly more frequent in older ($p=0.0011$), men ($p=0.0098$), and negative of anti-Ro/SSA antibody ($p=0.0002$). In MCTD patients, 14 patients had ILD, four had PH, three had both ILD and PH, one had lipid pneumonia, and one had hilar lymphadenopathy. Two-year survival rate of SLE patients with pulmonary involvement is 85.2%, equivalent to MCTD patients. [Conclusions] Pulmonary involvements in SLE are maybe more common than conventional reports.

W31-1-6

Comorbidity of malignancies in systemic lupus erythematosus patients in the cohort of LUNA registry

Kunihiro Ichinose¹, Takashi Igawa¹, Momoko Okamoto¹, Nobuyuki Yajima², Ken-ei Sada³, Ryusuke Yoshimi⁴, Shigeru Ohno⁵, Mizuna Otsuka¹, Yushiro Endo¹, Sosuke Tsuji¹, Ayuko Takatani¹, Toshimasa Shimizu¹, Remi Sumiyoshi¹, Tomohiro Koga¹, Shin-ya Kawashiri¹, Naoki Iwamoto¹, Mami Tamai¹, Hideki Nakamura¹, Tomoki Origuchi⁶, Atsushi Kawakami¹

¹Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, ²Division of Rheumatology, Department of Medicine, Showa University School of Medicine, ³Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ⁴Department of Hematology and Clinical Immunology, Yokohama City University School of Medicine, ⁵Center for Rheumatic Disease, Yokohama City University Medical Center, ⁶School of Health Sciences, Division of Physical Therapy, Nagasaki University

Conflict of interest: None

[Object] It is known that the incidence of malignancies is higher in systemic lupus erythematosus (SLE) patients compared to healthy subjects. We examined the malignancy complication of patients with SLE in the cohort of LUNA registry. [Methods] We evaluated 234 cases diagnosed as SLE and could detect the presence or absence of malignancy. The life history such as drinking and smoking, treatment including steroid pulse, intravenous cyclophosphamide pulse therapy (IVCY) and hydroxychloroquine (HCQ), vaccination history, and comorbid complications were retrospectively analyzed. [Results] Comorbidity of malignancy was observed in 23 cases (9.8%). No association was found between age, the treatment history of steroid pulse, IVCY, HCQ and ma-

lignancy. Fourteen of 23 (60.9%) cases had gynecological malignancies such as uterus and ovarian cancer. Comorbidity of malignancy associated with higher SDI (SLICC Damage index) ($p=0.0229$), history of osteoporosis ($p=0.0049$), non-inoculation of pneumococcal vaccination ($p=0.0169$), history of pyelonephritis ($p=0.0095$) and ovarian insufficiency ($p=0.0032$). [Conclusions] Further large scales of cohort and longitudinal studies are needed to examine the relationship between SLE complications and the incidence of malignancy.

W31-1-7

Baricitinib (Bari) in Systemic Lupus Erythematosus (SLE): Results from a Global Phase 2, Double-Blind, Placebo-Controlled Study

Yoshiya Tanaka¹, Daniel Wallace², Richard Furie³, Kenneth Kalunian⁴, Marta Mosca⁵, Michelle Petri⁶, Thomas Dörner⁷, Mario Cardiel⁸, Ian Bruce⁹, Ayako Konomi¹⁰, Taeko Ishii¹⁰, Yasushi Takita¹⁰, Elisa Gomez¹¹, Maria Silk¹¹, Robert Hoffman¹¹

¹The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, ²David Geffen School of Medicine, University of California, Los Angeles, USA, ³Zucker School of Medicine at Hofstra/Northwell, New York, USA, ⁴Univ of California at San Diego School of Medicine, La Jolla, USA, ⁵Univ of Pisa, Pisa, Italy, ⁶Johns Hopkins Univ School of Medicine, Baltimore, USA, ⁷Charite Universitätsmedizin Berlin, Berlin, Germany, ⁸Centro de Investigación Clínica de Morelia SC, Morelia, México, ⁹The Univ of Manchester, Manchester, UK, ¹⁰Eli Lilly Japan K.K., Kobe, Japan, ¹¹Eli Lilly and Company, Indianapolis, USA

Conflict of interest: Yes

[Object] To report results from a Global Phase 2, double-blind, placebo (PBO)-controlled study of Bari in SLE patients (pts). [Methods] Of 314 SLE pts (positive ANA or anti-dsDNA, clinical SLEDAI-2K ≥ 4 with arthritis and/or rash and background therapy required), 57 were Asian and 33 were Japanese (JP). Randomization was 1:1 to PBO, Bari 2 or 4mg groups. The primary endpoint was resolution of SLEDAI-2K arthritis and/or rash at wk 24. [Results] At wk 24, a significantly greater proportion of pts receiving 4mg compared to PBO achieved resolution of SLEDAI-2K arthritis and/or rash (67% vs 53%; $p<0.05$); and SRI-4 response (64% vs 48%; $p<0.05$). Fewer flares (SELENA-SLEDAI Flare Index) occurred in 4mg than PBO. Greater proportion of pts achieved LL-DAS, and reductions in tender joint count from baseline with 4mg compared to PBO. Rates of adverse events (AEs) led to discontinuation (PBO: 3.8%; 2mg: 9.5%; 4mg: 10.6%) and serious AEs (PBO: 4.8%; 2mg: 10.5%; 4mg: 9.6%) were higher for Bari compared to PBO. There were no deaths, malignancies, major adverse cardiovascular events, tuberculosis, or serious herpes zoster infections. Consistent results were observed in pts from Asia/JP. [Conclusions] Bari 4mg was associated with clinical improvements compared to PBO and an acceptable benefit/risk profile.

W31-2-1

The analysis of Lupus Low Disease Activity State after induction treatments in patients with SLE

Jun Kikuchi, Hironari Hanaoka, Shuntaro Saito, Naoshi Nishina, Kotaro Otomo, Yuko Kaneko, Katsuya Suzuki, Tsutomu Takeuchi
Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] Lupus Low Disease Activity State (LLDAS) defined by Franklyn et al has been reported to be associated with the organ damage and relapse in SLE. The purpose of this study is to clarify the factors related to the attainment of LLDAS after induction therapy. [Methods] Active SLE patients with BILAG 1A or 2B or more who started induction therapy from April 2015 to October 2018 in our hospital and were followed for more than 12 months were selected. [Results] We enrolled 63 patients with a mean age of 42 years, a disease duration of 86 months, the first-onset 37%, average SLEDAI 16 and nephritis 68%. Eighty-six percent experienced LLDAS during the average observation period of 28 months. The median percentage to attainment of LLDAS was 53% at 12 months. LLDAS attainment within 12 months was significantly greater in

patients with first-onset, exhibited fever at baseline, low SLEDAI and low urinary protein creatinine ratio in patients with lupus nephritis after treatment for 3 months. [Conclusions] LLDAS attainment in 12 months after the induction therapy remained about half in SLE patients. First-onset, presenting fever, low SLEDAI and urinary protein after treatment for 3 months were advantageous to LLDAS attainment.

W31-2-2

The predictive factors for LLDAS attainment in systemic lupus erythematosus: A cross-sectional study of LUNA registry

Daiga Kishimoto¹, Ryusuke Yoshimi¹, Yosuke Kunishita¹, Chiharu Hidekawa¹, Natsuki Sakurai¹, Masaki Mitsuhashi¹, Yumiko Sugiyama², Yuki Iizuka¹, Takaaki Komiyama¹, Hideto Nagai¹, Naoki Hamada¹, Naomi Tsuchida¹, Yutaro Soejima¹, Reikou Kamiyama¹, Kouji Kobayashi², Yukiko Asami¹, Yohei Kirino¹, Nobuyuki Yajima³, Ken-ei Sada⁴, Kunihiro Ichinose⁵, Shigeru Ohno², Hideaki Nakajima¹

¹Department of Hematology and Clinical Immunology, Yokohama City University School of Medicine, ²Center for Rheumatic Disease, Yokohama City University Medical Center, ³Division of Rheumatology, Department of Internal Medicine, Showa University School of Medicine, ⁴Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ⁵Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: None

[Object] To search for factors which affect the achievement of lupus low disease activity state (LLDAS) using a multicenter SLE registry. [Methods] We cross-sectionally analyzed the relationship between the LLDAS achievement and various parameters related to the patients' background by using the data of SLE patients registered in the LUNA registry. [Results] Among 165 cases, 60 (36%) achieved LLDAS. Fever and anti-SS-A antibody seropositivity at onset were observed more frequently in the non-LLDAS achievement group as compared with the achievement group (52% vs 33%, $p = 0.034$, and 67% vs 48%, $p = 0.019$, respectively). Although proliferative nephritis was observed less frequently in the non-LLDAS (87% vs 51%, $p = 0.017$), there was no difference in the frequency of membranous nephropathy. In the non-achievement group, tacrolimus (28% vs 13%, $p = 0.034$), hydroxychloroquine (49% vs 25%, $p = 0.002$), bisphosphonate (64% vs 47%, $p = 0.036$), and sulfamethoxazole-trimethoprim (13% vs 1.7%, $p = 0.017$) were administered more frequently, and azathioprine were administered less frequently (8.6% vs 23%, $p = 0.008$) than in the achievement group [Conclusions] Fever at onset and serum anti-SS-A antibody seropositivity may be risk factors for not achieving LLDAS.

W31-2-3

Serologically Active Clinically Quiescent Disease in Systemic Lupus Erythematosus: a 5-year Follow-up Study

Naoko Konda, Yasuhiro Katsumata, Yuko Okamoto, Rina Moriyama, Sayumi Baba, Mari Tochihara, Shinya Hirahara, Akira Nishino, Yasushi Kawaguchi, Masayoshi Harigai, Hisashi Yamanaka
Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] We studied the clinical features of serologically active clinically quiescent (SACQ) SLE in prospectively followed Japanese SLE patients. [Methods] Japanese patients with SLE were enrolled and assessed by SLEDAI-2K and SDI. SACQ was defined as the state without clinical activity (clinical SLEDAI-2K ≤ 0), with persistent serologic activity (increased anti-ds DNA and/or hypocomplementemia), and PSL ≤ 7.5 mg. The Clinical features of SACQ and 5-year outcome of the patients with SACQ were analyzed. In addition, patients with SACQ were compared with those who were both clinically and serologically quiescent (CQSQ; SLEDAI-2K ≤ 0). [Results] Ultimately, 148 patients enrolled (at baseline, mean age 45.0, 134 female, mean disease duration 12 years, mean SDI 1.1), 16 patients satisfied SACQ (mean age 13.0, 16 female,

mean disease duration 12 years, mean SDI 1.2), 22 patients satisfied SQQC. Among the original SACQ group, 7 patients remained SACQ, 2 patients became SQQC, and 7 patients were in clinical flare in 2016. There were no significant differences between the SACQ and SQQC groups in the ratio of SACQ or SQQC, SDI, score or rate increase of SDI, dosages of PSL, decrease dosage or rate of PSL. [Conclusions] This study showed some clinical features of SACQ in Japanese patients with SLE.

W31-2-4

Remission and flare in patients with systemic lupus erythematosus (SLE) according to the definition "DORIS" -Durable remission off steroid is rare-

Shoji Miyawaki, Susumu Nishiyama, Tetsushi Aita, Yasuhiko Yoshinaga
Rheumatic Disease Center, Kurashiki Medical Center

Conflict of interest: None

[Object] Retrospective assessment of remission and flare in 83 SLE patients according to DORIS (Definitions Of Remission In SLE, 2015). [Methods] 83 SLE patients were divided into 1) clinical remission (ClinR), 2) clinical remission on treatment (ClinROT), 3) complete remission (CompR), 4) complete remission on treatment (CompROT), and non-remission (NonR). [Results] Disease duration of SLE was 24.7 \pm 8.6 years. One hundred-eleven ClinROT, 35 CompROT, 65 NonR and 2 off steroid ClinR were observed; no CompR. Seventy-nine (69.9%) flares occurred in ClinR +ClinROT were significantly higher than 16 (45.7%) flares in CompROT. Thirty-one patients with cumulative remission of more than 50% of disease duration were significantly older, had shorter duration until first remission, more ClinROT or CompROT, lower nephropathy, lower maximum SLEDAI and SLICC damage index (SDI) than 52 patients with remission of less than 50% of duration. Twenty-one patients with prednisolone (PSL) 2.5 mg daily had significantly longer cumulative remission, more CompROT, and less flares and increase of SDI than patients maintaining more than PSL 5mg daily. [Conclusions] Prolonged remission off steroid is rare in Japanese SLE compared to Caucasian SLE. Maintenance of PSL 2.5 mg daily might be useful to prolong remission.

W31-2-5

A Prospective cohort study on the short and long-term prognosis, including pregnancy outcomes, of young patients with systemic lupus erythematosus in Japan. (Pleasure-J study): progress report

Kayoko Kaneko¹, Nobuyuki Yajima², Yoko Miura², Yasunori Iwata³, Kae Onishi⁴, Naoshi Nishina⁵, Takuya Nemoto⁶, Toru Hirano⁷, Nobuya Abe⁸, Takako Miyamae⁹, Hideyuki Iwai¹⁰, Kenji Oku⁸, Tsutomu Takeuchi⁵, Naoto Tamura⁶, Masaaki Mori¹¹, Takashi Wada³, Atsuko Murashima¹²

¹Division of Maternal Medicine, Center of Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development, ²Division of Rheumatology, Department of Medicine, Showa University, ³Division of Nephrology, Kanazawa University Hospital, ⁴Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical, ⁵Department of Lifetime Clinical Immunology Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, ⁶Department of Internal Medicine and Rheumatology, Juntendo University, ⁷Department of Respiratory Medicine, Allergy and Rheumatic Disease, Osaka University, ⁸Division of Rheumatology, Endocrinology, Graduate School of Medicine, Hokkaido University, ⁹Institute of Rheumatology, Tokyo Women's Medical University, ¹⁰Department of Medicine and Rheumatology, Tokyo Medical and Dental University, ¹¹Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, ¹²National Center for Child Health, Center for Maternal-Fetal, Neonatal and Reproductive Medicine

Conflict of interest: None

[Objective] Systemic lupus erythematosus (SLE) is more prevalent in young people. While the life prognosis has got to be improved, the accumulated physical and mental damage and the decline in QOL due to long-term morbidity are remained to be unsolved problem. We started multicenter prospective cohort study from November 2017 to clarify the

physical and mental prognosis of young SLE patients in Japan. [Method] Six to 40 years old SLE patients diagnosed within one year were registered. Disease activity (SLEDAI-2K), physical function disorder (SLICC/ACR Damage Index) and comprehensive/disease specific quality of life (SF12v2, Lupus PRO) were evaluated. [RESULTS] Thirty-three patients were enrolled. 4 males, 29 females, median age at the time of registration was 24 (19.5, 28.5) years old. SLEDAI-2K at diagnosis is 16 (10, 21). In QOL evaluation, the disease-specific health related and non-health related score were 60.4 (44.2, 81.7) and 57.7 (50, 69.7). The comprehensive QOL summary score in the physical, mental and role/social aspect were 50.0 (39.1, 60.8), 48.2 (42.0, 55.88) and 39.72 (26.8, 48.1), respectively. [Conclusion] The prospective cohort study of the young SLE has been started. It is expected that we could report high-quality evidence on the prognosis of Japanese young SLE.

W31-2-6

Long-term renal outcome in systemic lupus erythematosus without lupus nephritis

Hironari Hanaoka, Shuntaro Saito, Hiroshi Takei, Tatsuhiro Ohshige, Kazuoto Hiramoto, Yuko Kaneko, Tsutomu Takeuchi
Division of Rheumatology, Keio University School of Medicine

Conflict of interest: None

[Object] To investigate long-term renal outcome in systemic lupus erythematosus without lupus nephritis. [Methods] We retrospectively evaluated newly diagnosed SLE patients from 2000 to 2018 in our hospital. All the patients were divided them into 2 groups according to the presence of lupus nephritis. Lupus nephritis was defined as pathologically proven or persistent proteinuria (more than 50 mg/dL or 0.5 g/gCr for more than 3 months). Deterioration of renal function (more than 40% eGFR decline from baseline) was compared between them. [Results] Seventy-six patients with lupus nephritis and 62 without lupus nephritis were evaluated. Patients with lupus nephritis had a higher dose of prednisolone ($p=0.04$) and immunosuppressive agent use ($p=0.04$) than those without. Observational period (10.1 vs 11.6 years, $p=0.43$) and cumulative deterioration rate of renal function (19.7 vs 16.1%, $p=0.31$) were not differed between them. For patients without lupus nephritis, a higher percentage of patients had both anti-Sm antibody and anti-Ro antibody at baseline (70.0% vs 7.6%, $p<0.01$). [Conclusions] Long-term renal outcome was not significantly different between patients with and without lupus nephritis for about 10 years observation.

W32-1

Comprehensive analysis of correlation between each clinical symptom, laboratory finding, and organ involvement in systemic lupus erythematosus patients

Takeshi Iwasaki¹, Hiroshi Doi¹, Yuya Tabuchi¹, Motomu Hashimoto², Shuji Akizuki¹, Kosaku Murakami¹, Ran Nakashima¹, Hajime Yoshifuji¹, Wataru Yamamoto³, Masao Tanaka², Koichiro Ohmura¹, Tsuneyo Mimori¹

¹Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ²Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ³Kurashiki Sweet Hospital

Conflict of interest: None

[Object] To clarify the pathological mechanisms of systemic lupus erythematosus (SLE) by analyzing correlation between each clinical symptom, laboratory finding, and organ involvement. [Methods] 362 SLE patients in Kyoto University Hospital were surveyed for 15 organ involvements, each item of new ACR/EULAR classification criteria, sex, anti-U1RNP, and anti-SS-A/Ro antibodies. We conducted comprehensive univariate (Fisher's exact test) and multivariate (lasso regression) correlation analysis. [Results] By univariate analysis, correlation between fever and arthritis as well as low complement and Class III/IV lupus nephritis, etc. were identified. By multivariate analysis, correlations between pleural/pericardial effusion and fever; lupus colitis and low complement / anti-Sm; alopecia or acute cutaneous lupus and anti-U1RNP; pulmonary hypertension and anti-U1RNP / anti-dsDNA; etc. were identified. [Discussion] By comprehensive analysis, novel correlations between organ in-

volvement and serological tests were identified. These results may facilitate prediction of future organ involvement and patient education as well as understanding pathological mechanisms. [Conclusion] Comprehensive correlation analysis was useful to identify new biomarkers to predict certain organ involvements.

W32-2

Evaluation of relapse rate and life prognosis after therapy induction in proliferative and membranous lupus nephritis

Momoko Okamoto¹, Kunihiro Ichinose¹, Keita Fujikawa², Yoshiro Horai³, Naoki Matsuoka⁴, Masahiko Tsuboi⁴, Fumiaki Nonaka⁵, Yukitaka Ueki⁶, Yushiro Endo¹, Sosuke Tsuji¹, Ayuko Takatani¹, Toshimasa Shimizu¹, Remi Sumiyoshi¹, Tomohiro Koga¹, Shin-ya Kawashiri¹, Naoki Iwamoto¹, Mami Tamai¹, Tomoki Origuchi⁷, Atsushi Kawakami¹

¹Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, ²Department of Rheumatology, JCHO Isahaya General Hospital, ³Department of Rheumatology, NHO Nagasaki Medical Center, ⁴Nagasaki Medical Hospital of Rheumatology, ⁵Department of Island and Rural Medical Research, Nagasaki University Graduate School of Biomedical Sciences, ⁶Sasebo Chuo Hospital, ⁷Department of Rehabilitation Sciences, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: None

[Object] To evaluate the relapse rate and life prognosis after therapy induction in proliferative and membranous lupus nephritis (LN). [Methods]: One hundred fifty one cases who underwent renal biopsy at our hospital and community hospitals from 1993 to 2016 were enrolled in this study. We retrospectively analyzed the complete response (CR) rate at 12 months after therapy induction and evaluated the predictive factors for CR, relapse rate and life prognosis. [Results]: In 140 cases, we were able to examine the therapeutic response, relapse rate and life prognosis at 12 months after therapy was introduced. Multivariate analysis showed that lower index of chronicity as assessed by the NIH histological scoring system in proliferative LN, and neutrophil infiltration and CH50 in membranous LN were predictive factors for achieving CR at 12 months. Kaplan-Meier analysis showed that relapse rate and life prognosis were not different in proliferative and membranous LN. [Conclusions]: In general, proliferative LN is more immunologically active than membrane LN, however there were no influence on the achieving CR at 6 months and 12 months after therapy induction, the relapse free period and life prognosis.

W32-3

Influence of prior treatment on pathology and prognosis in 54 patients with lupus nephritis

Kazuya Matsumoto, Shoichi Nawachi, Reika Hayashi, Ryutaro Yamanaka, Hidetoshi Kagawa
Japanese Red Cross Society Himeji Hospital

Conflict of interest: None

[Object] ISN / RPS classification type IV is the most common in many lupus nephritis reports, but we experience relatively large number of type III patients. We examined the effect of treatment preceding renal biopsy on histology and remission rate. [Methods] We include 54 lupus nephritis patients underwent initial renal biopsy from October 2007 to March 2018. We treated them for more than 6 months. We divided them into two groups, pre-biopsy treatment group that was treated prior to renal biopsy and post-biopsy treatment group that started treatment after renal biopsy. We conducted cross-sectional study. [Results] 35 patients were in pre-biopsy treatment group and 19 patients were in post-biopsy treatment group. The numbers of patients in each category were as follows: class II, 4; class III, 17; class IV, 29; class V, 4. The proportion of type III in the proliferative type tended to be high in the former. In addition, the longer the preceding treatment period, the more the proportion of type III tended to increase. The complete remission rate at 6 months was significantly higher in the former group than the latter (71% vs. 42%, $p=0.04$). [Conclusions] Present study suggest that early treatment may improve the histology and prognosis in lupus nephritis patients.

W32-4

Analysis of 21 cases of lupus nephritis who underwent both the first and second biopsy at our department

Yoshinori Takei, Hidekazu Ikeuchi, Masato Kinoshita, Junya Suwa, Shunsuke Takahashi, Yuko Oishi, Mithuharu Watanabe, Hiroko Hamatani, Masao Nakasatomi, Toru Sakairi, Yoriaki Kaneko, Keiju Hiromura

Department of Nephrology and Rheumatology, Gunma University Graduate School of Medicine

Conflict of interest: None

[Object] In the present study, we sought to determine the histological changes of LN in the repeat biopsy. [Methods] We retrospectively analyzed LN patients who underwent a repeat renal biopsy, among 165 biopsy-proven Japanese LN patients (14 males and 151 females) at our department between 1976 and 2017. Renal histology was categorized by ISN/RPS 2003 classification. Class III+V and IV+V were classified as mixed type. Data were expressed as median (IQR). [Results] Twenty-one patients (3 males and 18 females) received a repeat renal biopsy. Median age at the 1st biopsy was 30 years old (23.3, 36.2). The interval between the 1st and the repeat biopsy was 15.7 years (12.4, 19.4). All patients received renal biopsy due to flare. Histological analysis was as follows: II, 2 pts; III, 1 pt; IV, 11 pts; V, 1 pt; mixed, 6 pts; at the first biopsy and III, 1 pt; IV, 8 pts; V, 1 pt; mixed, 10 pts; not determined, 1 pt; at the repeat biopsy. Class transformation was observed in 7 pts. Chronic lesions (A/C or C) were increased from 5 pts to 17 pts at the repeat biopsy ($p < 0.001$). [Conclusions] Repeat biopsy was performed a long time after the first biopsy due to flare. More than 30% patients showed class transformation and chronic lesions were increased in the repeat biopsy.

W32-5

Risk of thrombosis in patients with lupus nephritis with steroid pulse therapy

Suguru Honda¹, Ryoko Sakai¹, Sho Suzuki^{1,2}, Masayoshi Harigai¹, Hisashi Yamanaka¹

¹Department of Rheumatology, School of Medicine, Tokyo Women's Medical University, ²Department of Public Health, School of Medicine, Tokyo Women's Medical University

Conflict of interest: None

[Objective] To compare risk of thrombosis between patients with and without steroid pulse (SP) in lupus nephritis (LN). [Methods] Using claims data provided by Medical Data Vision Co., Ltd (Tokyo, Japan), we defined individuals as LN cases if they had at least one LN diagnostic code, started daily prednisolone ≥ 30 mg, and were 16 years old or over between April 2009 and January 2018 ($n=1217$). LN cases were divided into 2 groups; receiving SP (SP group: $n=692$) or not receiving SP (non-SP group: $n=525$). After propensity-score matching ($n=434$), incidence of thrombosis at Month 1, 2, 3, 4, and 12, and mortality at Month 3 were calculated. [Results] The mean age was 47 years old and proportion of female was 76%. There were no statistically significant differences in baseline variables between the two groups. The incidences of thrombosis were not significantly different (SP vs non-SP at Month 1, 2, 3, 4, and 12 months; 3.0% vs 4.4% ($p=0.28$), 3.5% vs 5.1% ($p=0.24$), 3.9% vs 5.3% ($p=0.331$), 4.6% vs 5.5% ($p=0.536$), and 4.6% vs 6.0% ($p=0.536$), respectively). However, mortality of the SP group at Month 3 were significantly elevated (SP vs non-SP; 4.6% vs 0.7% ($p < 0.0001$)). [Conclusion] This study revealed that SP did not increase the risk of thrombosis in patients with LN.

W32-6

Identification of Predictive factors of cardiovascular events in patients with systemic lupus erythematosus from the LUNA registry : A cross-sectional study

Takashi Igawa¹, Kunihiro Ichinose¹, Momoko Okamoto¹, Nobuyuki Yajima², Ken-ei Sada³, Ryusuke Yoshimi⁴, Shigeru Ohno⁵, Mizuna Otsuka¹, Yushiro Endo¹, Sosuke Tsuji¹, Ayuko Takatani¹, Toshimasa Shimizu¹, Remi Sumiyoshi¹, Tomohiro Koga¹, Shin-ya Kawashiri¹, Naoki Iwamoto¹, Mami Tamai¹, Hideki Nakamura¹, Tomoki Origuchi⁶, Atsushi Kawakami¹

¹Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ²Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan, ³Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, ⁴Department of Hematology and Clinical Immunology, Yokohama City University School of Medicine, Japan, ⁵Center for Rheumatic Diseases, Yokohama City University Medical Center, Yokohama, Japan, ⁶Nagasaki University School of Health Sciences, Division of Physical Therapy

Conflict of interest: None

[Objective] The risk of developing cardiovascular events (CVD) in systemic lupus erythematosus (SLE) was evaluated using a multicenter registration study [Lupus registry of nationwide institution (LUNA)] in Japan. [Methods]: We analyzed the presence or absence of CVD about 532 SLE patients. The relationship between cardiovascular event, blood test data, life history, medications and complications was retrospectively evaluated. [Results] We found 93 cases (17.5%) accompanied with CVD. Among the disease-related features the group of patients who had CVD showed significantly higher maximum dose of prednisolone in past ($p=0.0095$), lower hemoglobin level ($p=0.0267$), higher CRP value ($p=0.0194$), lower estimated glomerular filtration amount (eGFR) ($p=0.0002$), comorbidity of idiopathic necrosis of femoral head ($p=0.0040$), ovarian dysfunction ($p=0.0175$), comorbidity of diabetes ($p < 0.0001$), fewer event of new skin rash ($p=0.0087$) and fewer event of hair loss ($p=0.0074$) compared to the group that had not CVD. The multivariate analysis revealed that the predictive factors for CVD was eGFR (OR: 0.985, 95% CI: 0.974-0.997, $p=0.0120$) and diabetes [OR: 2.453, 95% CI: 1.112-5.409, $p = 0.0319$]. [Conclusions] The risk of developing CVD in SLE of LUNA registry was consistent with the results reported in other countries.

W33-1

The flare and damage of patient with systemic lupus erythematosus in long term maintenance therapy

Ryutaro Matsumura, Kazuyuki Ishijima, Keiko Umemiya, Yoshihiro Oya, Hidekazu Futami, Takuya Nakazawa
Center of Rheumatology, Allergy and Clinical Immunology, National Hospital Organization Chiba East Natinal Hospital

Conflict of interest: Yes

[Object] Results of long term conventional maintenance therapy in patients with SLE are not clear. [Methods] The flare and damage of 22 patients with SLE who had history of maintenance treatment more than 20 years were examined retrospectively. [Results] The onset of SLE was an average of 28.7 years old and a duration of treatment period was 21-or 46 years, an average of 27 years. At the time of onset strong activity including lupus nephritis, alveolar hemorrhage and CNS lupus was seen. Large dose steroid treatment, steroid pulse therapy and cyclophosphamid IV therapy were carried in more than 80 percent. Less than 5 mg of steroid was done in the majority an average of 27 years later. At the onset of SLE, the DNA antibody was positive and became negative by 80 percent, and positiveness of a ANF and anti SS-A antibody continued. Flare was observed in a case of 3/4, and there was serious flare in a case of 1/4, and significant correlation was observed in accumulation of damage and the number of times of flare. 2 patients of more than 7 damage score were dead by cardiovascular disease. [Conclusions] For the more improving of vital prognosis and QOL, the restrain accumulation of damage by prevention of flare should be need in long treatment of a SLE patient.

W33-2

Corticosteroid-sparing effect of hydroxychloroquine versus tacrolimus in patients with systemic lupus erythematosus

Masahiro Ayano^{1,2}, Mitsuteru Akahoshi¹, Yasutaka Kimoto³, Hiroki Mitoma¹, Yojiro Arinobu¹, Koichi Akashi¹, Takahiko Horiuchi³, Hiroaki Niuro⁴

¹Department of Medicine and Biosystemic Science, Kyushu University

Graduate School of Medical Sciences, Fukuoka, Japan, ²Department of Stem Cell Biology and Medicine, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan, ³Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, ⁴Department of Medical Education, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan

Conflict of interest: None

[Object] This study aimed to compare the corticosteroid-sparing effect of hydroxychloroquine (HCQ) with tacrolimus (TAC) in patients with systemic lupus erythematosus (SLE). [Methods] The subjects of this study were 66 SLE patients who received HCQ or TAC from September 2015 to March 2018. We assessed changes in doses of prednisolone, SLEDAI score and serum C3 and anti-dsDNA levels, and examined continuation rates and adverse effects. [Results] 42 and 23 SLE patients received HCQ and TAC, respectively. At baseline, SLEDAI score and use of other immunosuppressive agents in HCQ groups were significantly higher than those in TAC groups. The median daily dose of prednisolone was reduced from 9 mg at baseline to 8.25 mg at 6 months and 8 mg at 12 months in HCQ group ($p < 0.001$), whereas the dose was reduced from 10 mg at baseline to 9 mg at 6 months and 9 mg at 12 months in TAC group ($p = 0.10$). The SLEDAI score and serological markers remarkably improved similarly in the both groups. The continuation rate at 12 months was 82.3 and 78.6%, respectively. Adverse events with discontinuation of treatment were almost the same between the groups. [Conclusions] The both HCQ and TAC showed high efficacy in mild active SLE patients. Corticosteroid-sparing effect of HCQ might be superior to TAC.

W33-3

Investigation of 71 patients received hydroxychloroquine ofr systemic lupus erythematosus

Makoto Wada, Akiko Kasahara, Tomoya Sagawa, Shunya Kaneshita, Takuya Inoue, Takashi Kida, Kazuki Fujioka, Hidetake Nagahara, Masataka Kohno, Yutaka Kawahito
Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

Conflict of interest: None

[Object] To examine the details of cases in which hydroxychloroquine (HCQ) was administered to with systemic lupus erythematosus (SLE). [Methods] Among the patients diagnosed as SLE in 1997 ACR classification criteria, 71 patients who received HCQ were analyzed. They were added during maintenance therapy for SLE. [Results] The average dose of prednisolone in the maintenance therapy was reduced (-1.25 ± 4.56 mg at 54 week (48 cases), and 7.5 mg ± 12.6 mg at 104 week (21 cases). The serum complement C3 and C4 were increased (C3: 25.4 ± 18.1 mg/dL at 54 week, 8.95 ± 32.3 mg/dL at 104 week, C4: 8.0 ± 5.0 mg/dL at 54 week, 0.75 ± 7.37 mg/dL at 104 week). Seven cases withdrew HCQ for drug rash, 1 case withdrew for general malarise, and 1 case withdrew for patient's decision. [Conclusions] Additional administration of hydroxychloroquine is expected to reduce prednisolone without flare of the disease activity of SLE. Conflict of interest: No

W33-4

Efficacy of hydroxychloroquine (HCQ) and experience of HCQ monotherapy in our hospital

Masanobu Horikoshi¹, Akari Kato¹, Teppei Kamikawa¹, Yuichi Handa¹, Teruchika Yamada²
¹Department of Rheumatology, Japanese Red Cross Saitama Hospital, ²Ohmiya Clinic

Conflict of interest: None

[Object] To clarify the background of SLE patients treated with HCQ and its efficacy on serological activities and the dose of PSL. [Methods] Electronic medical records of 81 patients treated with HCQ were retrospectively reviewed and analyzed. [Results] 78 (96%) of the patients were female. The median age of the patients was 42, disease duration was 9 years, and the dose of PSL was 8mg. In 10 patients, HCQ was started as a remission induction therapy with other immunosuppressive agents

(IMs) including 4 patients at their first diagnosis. In 3 of the 4 patients, PSL has been successfully tapered to 2mg/day over a year. In the patients HCQ was added to the maintenance therapy, the median dose of PSL was significantly tapered from 7.8mg before to 6.3mg 6 months after the initiation of HCQ ($p = 0.033$). In 12 patients with hypocomplementemia, CH50 was significantly elevated from 22.2 before to 28.5 6 months after the initiation of HCQ ($p = 0.04$). HCQ was used as a monotherapy in 5 patients without severe organ involvement. In 3 of the 5 cases, HCQ was effective and continued as monotherapy for more than a year. [Conclusions] HCQ significantly reduced the dose of PSL and improved hypocomplementemia. In mild SLE patients, HCQ monotherapy is an effective therapeutic option.

W33-5

Evaluation of adverse events and relapse risk of systemic lupus erythematosus during treatment with hydroxychloroquine

Kunihiro Ichinose¹, Keita Fujikawa², Akinari Mizokami², Toshiyuki Aramaki³, Yukitaka Ueki³, Mizuna Otsuka¹, Momoko Okamoto¹, Yushiro Endo¹, Sosuke Tsuji¹, Ayuko Takatani¹, Toshimasa Shimizu¹, Remi Sumiyoshi¹, Tomohiro Koga¹, Shin-ya Kawashiri¹, Naoki Iwamoto¹, Takashi Igawa¹, Mami Tamai¹, Hideki Nakamura¹, Tomoki Origuchi⁴, Atsushi Kawakami¹

¹Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, ²Department of Rheumatology, JCHO Isahaya General Hospital, ³Rheumatic and Collagen Disease Center, Sasebo Chuo Hospital, ⁴Division of Physical Therapy, Nagasaki University School of Health Sciences

Conflict of interest: None

[Object] To evaluate adverse events and relapse risk of systemic lupus erythematosus (SLE) during treatment with hydroxychloroquine (HCQ). [Methods] One hundred nine cases who were diagnosed as SLE treated with HCQ at least 12 months were analyzed. The primary endpoint was identification of relapse risk at 12 months after introduction of HCQ. [Results] The mean observation period after HCQ introduction was 12 months. The SELENA-SLEDAI decreased significantly after 3 months of introduction. The amount of oral prednisolone also decreased significantly after 6 months of introduction. Eighty six cases (78.9%) continued HCQ at 12 months after introduction. The adverse events appeared in 27 cases (24.8%), including 11 cases of skin rashes (10.1%). Predictive factor for adverse event was anti-SSB/La antibodies positive (odds ratio: 6.886, 95% CI: 1.150-41.22, $p = 0.0243$). The relapse rate after HCQ introduction was 14.0% and C4 value at the time of introduction was the predictive factor of relapse (odds ratio: 0.841, 95% CI: 0.718 - 0.984, $p = 0.0097$). [Conclusions] The lower value of C4 at HCQ introduction was a predictive factor for relapse and anti-SSB/La antibodies positive was a predictive factor for adverse event.

W33-6

Successful Desensitization for Hydroxychloroquine: a single center experience

Kakeru Yamamoto¹, Hironari Hanaoka², Kana Ishimori³, Yukiko Takakuwa³, Kimito Kawahata³

¹Department of Pharmacy, St. Marianna University School of Medicine Hospital, Kawasaki, Japan, ²Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, ³Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan

Conflict of interest: None

[Object] Hydroxychloroquine (HCQ) is a cornerstone in the treatment of systemic lupus erythematosus (SLE). About 10% of patients treated with HCQ develop skin eruptions due to hypersensitivity. Since no other available option was comparable to HCQ in terms of efficacy, desensitization to HCQ has been challenged in especially other countries. Here we conducted desensitization of HCQ and evaluated its efficacy and safety in Japanese population. [Methods] We selected SLE patients who discontinued HCQ due to skin eruption in our hospital from 2015 to 2018. Desensitization protocol was consisted with starting dose of 0.1mg/

day and 37 days observation. We collected patients reported safety outcome including eruption, itching sensation, fever, vomiting, nausea, diarrhea, cough every 2 weeks. [Results] Two patients (1 female and 1 male) were enrolled. Average age was 37.0 ± 21.2 years. At baseline, prednisolone dose was 2.5 ± 3.5 mg/day, 1 patient was additionally treated with mycophenolate mofetil 2000 mg/day and systemic lupus disease activity index was 1.0 ± 1.4 . Over 75.5 ± 57.3 days observation, recurrence of skin eruption was not reported in all the patients. [Conclusions] Desensitization of HCQ might be safe and future work should be performed to further verify our results.

W34-1

Reactivation of hepatitis B virus (HBV) in patients with HBV carrier-rheumatoid arthritis

Atsushi Hashimoto¹, Toshihiro Matsui¹, Fuminori Hirano², Kenji Ichikawa³, Noriyuki Chiba⁴, Takao Sugiyama⁵, Ryutarō Matsumura⁶, Hiroshi Tsutani⁷, Atsushi Kaneko⁸, Masao Katayama⁸, Yukihiko Saeki⁹, Akira Okamoto¹⁰, Eiichi Suematsu¹¹, Shigeru Yoshizawa¹², Yasuo Suenaga¹³, Koichiro Saisho¹⁴, Yukitomo Urata¹⁵, Shigeto Tohma¹⁶

¹Department of Rheumatology, National Hospital Organization Sagami-hara National Hospital, Sagami-hara, Japan, ²National Hospital Organization Asahikawa Medical Center, Asahikawa, Japan, ³National Hospital Organization Hokkaido Medical Center, Sapporo, Japan, ⁴National Hospital Organization Morioka National Hospital, Morioka, Japan, ⁵National Hospital Organization Shimoshizu National Hospital, Yotsukaido, Japan, ⁶National Hospital Organization Chiba Higashi National Hospital, Chiba, Japan, ⁷National Hospital Organization Arawa National Hospital, Arawa, Japan, ⁸National Hospital Organization Nagoya Medical Center, Nagoya, Japan, ⁹National Hospital Organization Osaka Minami Medical Center, Kawachinagano, Japan, ¹⁰National Hospital Organization Himeji National Hospital, Himeji, Japan, ¹¹National Hospital Organization Kyushu Medical Center, Fukuoka, Japan, ¹²National Hospital Organization Fukuoka National Hospital, Fukuoka, Japan, ¹³National Hospital Organization Beppu Medical Center, Beppu, Japan, ¹⁴National Hospital Organization Miyakonojo Medical Center, Miyakonojo, Japan, ¹⁵Tsugaru General Hospital, Goshogawara, Japan, ¹⁶National Hospital Organization Tokyo National Hospital, Tokyo, Japan

Conflict of interest: Yes

[Object] Rheumatoid arthritis (RA) patients with hepatitis B virus (HBV) infection have higher risk for HBV reactivation. We investigated frequency of HBV reactivation in HBV carrier-RA patients and their usage of nucleoside analogues (NA). [Methods] We retrospectively analyzed HBV carrier (HBs antigen positive)-RA patients in 14 hospitals from April 2012 to December 2017 as a National Hospital Organization network group multi-center study. HBV reactivation was decided as serum HBV-DNA increase of more than tenfold or positive change in serum HBe antigen or HBV-DNA. [Results] In a total of 119 patients, women were 71%, mean age was 69.9 years old and mean observation period was 3.9 year. Estimated HBV reactivation rate was approximately 1%. Forty patients (33.6%) had received no NA. HBV reactivation was found in 10 patients who all had taken no NA. Their RA therapies before reactivation were methotrexate (n=7), corticosteroids (n=5), tacrolimus (n=3) and so on. A patient with biologic therapy and a patient with salazosulfapyridine and iguratimod involved in reactivation. No patients died of hepatitis. [Conclusions] HBV carrier-RA patients without NA have higher risk for HBV reactivation on the setting.

W34-2

Clinical features and human T-cell leukemia virus type -1 (HTLV-1) proviral load in HTLV-1-seropositive rheumatoid arthritis (RA) patients

Katsumi Eguchi¹, Kaoru Terada¹, Toshiyuki Aramaki¹, Yoshika Tsuji¹, Shota Kurushima¹, Kanako Kojima¹, Natsumi Kawachi¹, Kazuhiko Arima², Naoki Iwamoto³, Kunihiro Ichinose³, Atsushi Kawakami³, Yukitaka Ueki¹

¹Rheumatic Collagen Disease Center, Sasebo Chuo Hospital, Sasebo, Japan, ²Department of Public Health, Nagasaki University Graduate School of Biomedical Sciences, ³Department of Rheumatic and Collagen Disease, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: None

[Object] HTLV-1 proviral load (VL) was quantified in HTLV-1-seropositive RA patients. [Methods] HTLV-1 VL in 83 patients were measured by real-time PCR. [Results] The median VL was 8.6 copies/1000PBMCs (range, 0-256.6). The median VL were significantly correlated with the titers of anti-HTLV-1 antibodies and counts of circulating lymphocytes. As compared with the group in the absence of comorbidities, the median VL were significantly higher in RA groups with bronchiectasis, malignancies, autoimmune diseases, and opportunistic infection including PCP, NTM. The VL in who had uveitis and family history of ATLL were preferentially distributed in higher quartile (Q 3 or 4). There were no differences in the VL among the kinds of biological DMARDs. Median VL in the patients treated with JAK inhibitor were preferentially distributed in the highest quartile. [Conclusions] These results indicated that seropositive RA patients comorbid for pulmonary diseases, autoimmune diseases, malignancies and opportunistic infections might have a higher HTLV-1 proviral loads. It seems likely that these comorbidities, and elevated anti-HTLV-1 antibody titer and circulating lymphocyte count might be clinically useful surrogate markers of HTLV-1 VL, resulting in a significantly high risk for ATLL.

W34-3

The time-sequential changes of human T-cell leukemia virus type 1 (HTLV-1) markers in HTLV-1-positive patients with rheumatoid arthritis during anti-rheumatic therapies; a retrospective cohort study

Kunihiko Umekita¹, Yayoi Hashiba², Yumi Kariya¹, Ayako Aizawa¹, Chihiro Iwao¹, Kosho Iwao¹, Mao Rikitake¹, Takeshi Kawaguchi¹, Motohiro Matsuda¹, Kazuyoshi Kubo², Shunichi Miyauchi¹, Katoko Takajo¹, Ichiro Takajo¹, Toshihiko Hidaka², Akihiko Okayama¹

¹Department of Rheumatology, Infectious Diseases and Laboratory Medicine, Internal Medicine, University of Miyazaki, ²Zenjinkai Shimin-nomori Hospital

Conflict of interest: None

[Object] To investigate the time-sequential changes of human T-cell leukemia virus type 1 (HTLV-1) markers, which are risk factors for ATL development, in HTLV-1-positive rheumatoid arthritis (RA) patients. [Methods] HTLV-1 infection was screened and confirmed in 365 RA patients. Twenty-three HTLV-1-positive RA patients were included in the study cohort. Blood samples were obtained from these patients at each observation time point. The values of HTLV-1 proviral load (PVL) and serum soluble IL-2 receptor (sIL2-R) were measured. [Results] The median age of HTLV-1-positive RA patients was greater than those of HTLV-1-negative patients with RA ($p=0.02$). Three HTLV-1-positive RA patients showed a high PVL value which is known as one of risk factors of ATL development. No remarkable changes were observed in the PVL and sIL2-R values during the observation period. The PVL values in two patients who had a high PVLs were more likely to decrease after withdrawal from MTX. [Conclusions] Although it remains unclear whether anti-rheumatic therapies affect HTLV-1 infection, a through clinical assessment of developing ATL may be necessary in daily clinical practice for RA patients in HTLV-1-endemic areas in Japan.

W34-4

Effectiveness of prophylactic administration of nucleic acid analogs for hepatitis B virus reactivation under immunosuppressive treatment in rheumatoid arthritis patients with persistent infection

Wataru Fukuda¹, Tadamasa Hanyu², Masaki Katayama³, Shinichi Mizuki⁵, Toshiyuki Kitaori⁴, Akitomo Okada⁶, Masatoshi Hayashi⁷, Masayuki Miyata⁸, Yuichi Handa⁹, Hiroyuki Hagiya¹⁰, Yoshinobu Koyama¹⁷, Kaoru Arai¹¹, Yoshinori Urushitani¹², Yoshihiko Ikeno¹⁴, Takeshi Suzuki¹⁵, Masatoshi Kadoya¹, Atsushi Omoto¹, Shigeko Inokuma^{6,16}, Daigo Taniguchi¹³

¹Center for Rheumatic Disease, Japanese Red Cross Kyoto Daiichi Hospital, ²Department of Rheumatology, Nagaoka Red Cross Hospital, ³Department of Rheumatology, Osaka Red Cross Hospital, ⁴Department of Orthopedics, Fukui Red Cross Hospital, ⁵Department of Rheumatology, Matsuyama Red Cross Hospital, ⁶Department of Rheumatology, Japanese Red Cross Nagasaki Genbaku Hospital, ⁷Department of Orthopedics, Naganano Red Cross Hospital, ⁸Department of Internal Medicine, Fukushima

Red Cross Hospital, ⁹Department of Rheumatology, Saitama Red Cross Hospital, ¹⁰Department of Rheumatology, Yokohama-City Bay Red Cross Hospital, ¹¹Department of Internal Medicine, Japanese Red Cross Kochi Hospital, ¹²Department of Rheumatology, Matsue Red Cross Hospital, ¹³Department of Orthopedics, Japanese Red Cross Kyoto Daini Hospital, ¹⁴Department of Rheumatology, Nasu Red Cross Hospital, ¹⁵Department of Allergy and Rheumatic Diseases, Japanese Red Cross Medical Center, ¹⁶Department of Allergy and Rheumatology, Chiba Central Medical Center, ¹⁷Department of Rheumatology, Okayama Red Cross Hospital

Conflict of interest: None

[Object] Immunosuppressive therapy (IST) should be avoided in hepatitis B virus (HBV) persistently infected patients with RA, and prophylactic nucleic acid analogue (NA) administration is recommended when the therapy is inevitable. We investigate the effectiveness of NA by following the course of HBV persistent infection patients during IST for RA. [Methods] HBV-DNA and ALT highest values were prospectively observed once a year for patients with HBs antigen or HBV-DNA positive at the initial registration. [Results] We observed 3.2 years for 57 patients, none of them showed serious hepatitis. 42 patients were administered NA at the enrollment (group A), 10 started NA during the observation (group B), 5 finished observation without receiving NA (group C). There was no difference in the frequency of ALT elevation among the 3 groups, but the frequency of HBV-DNA positivity >1.3 Log IU/ml during the observation in 15 patients of B and C group was higher than 42 in group A (31.0 vs 66.7, $p=0.016$). [Conclusions] Although the effect of decreasing the viral load of NA was observed, the effect of suppressing liver enzyme elevation was not clear. It was suggested that prophylactic administration of NA is effective and HBV-DNA positivity are not directly related to the onset of hepatitis.

W34-5

A case of intracranial varicella zoster virus vasculopathy difficult to distinguish from neuropsychiatric systemic lupus erythematosus

Tomofumi Tatsutani¹, Shoichiro Inokuchi¹, Yojiro Arinobu¹, Koji Mishima¹, Masahiro Ayano¹, Yasutaka Kimoto², Hiroki Mitoma¹, Mitsuteru Akahoshi¹, Koichi Akashi¹, Takahiko Horiuchi², Hiroaki Niino³
¹Department of Clinical Immunology and Rheumatology/Infectious Disease, Kyushu University, ²Department of Internal Medicine, Kyushu University Beppu Hospital, ³Department of Medical Education, Faculty of Medical Sciences, Kyushu University

Conflict of interest: None

[Case] The patient was an 18-year-old female diagnosed with SLE at 6-year-old and has been treated with combination of immunosuppressive drugs. Two months before she visited our hospital, she presented headache, vomiting and symptoms of cranial nervous disorder. Head MRI showed multiple white matter hyperintensities on T2WI/FLAIR and interleukin-6 levels in cerebrospinal fluid (CSF) were elevated. She was diagnosed as neuropsychiatric SLE (NPSLE), and treated with corticosteroid pulse therapy and intravenous cyclophosphamide pulse therapy. However, she developed hydrocephalus and disturbance of consciousness. She was transferred to our hospital. The next day, she presented generalized tonic-clonic seizure. Intraventricular hemorrhage and exacerbation of the hydrocephalus was identified in head CT. Angiography showed multiple cerebral aneurysms. As VZV-DNA was detected in the CSF, she was diagnosed as VZV vasculopathy and treated with anti-herpes virus agents for seven weeks. [Discussion] Intracranial VZV vasculopathy is caused by reactivation of latent VZV within cranial nerves and characterized by vessel wall damage and aneurysm. As the clinical manifestations of intracranial VZV vasculopathy may be resemble with that of NPSLE, careful diagnosis should be warranted.

W34-6

A case of Mycoplasma haemohominis infection, which is the second case in the world that exhibits the pathology of SLE and has been diagnosed with the next generation sequencer

Takahiro Tokunaga, Sho Ishii, Ryo Yanai, Yoko Miura, Tsuyoshi Kasama
Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan

Conflict of interest: None

A 56-year-old woman. Spotted or patchy erythema appeared one week after traveling to Australia, and it extinguished in 5 days. After that, intermittent fever lasted for 2 months. Physical findings were cheek erythema, lymph node, hepatosplenomegaly. Progressive pancytopenia, liver injury, ANA40 times (SPECKLED, cytoplasmic) Anti-dsDNA antibody 93.4U/ml Anti-Sm antibody 24.3U/ml Anti-cardiolipin antibody 22U/ml Anti mitochondrial M2 antibody 19.2U/ml SMA80 times, urinary showed 0.62g/Cr granular cylinder. Five were met in SLE (1997 ACR) and seven in SLICC (2012). Bone marrow revealed HPS and plasma cell, and liver biopsy showed AIH. We started steroid therapy for HPS by SLE, but it was poor. Despite having no hemorrhagic diathesis, it became a hemorrhagic shock after liver biopsy and died. Fever and skin rash were observed in a needle sticking at the time of liver biopsy, infection was suspected and metagenom analysis of serum by the next generation sequencer revealed 16S rRNA of Mycoplasma haemohominis in both patients. It is an infectious cause hemolytic anemia in cats, but the pathology in humans is unclear. There has been one report from the UK, this example is the second report in the world. We report a case of Mycoplasma haemohominis infection with pathology of SLE.

W35-1

Prevention of osteoporosis in patients with rheumatic diseases using steroids

Hideshi Yamazaki, Tetsuo Takanashi
Center for Rheumatic Disease, Marunouchi Hospital

Conflict of interest: None

[Object] We examined osteoporosis status in steroid-treated patients to investigate preventive effects of steroids on osteoporosis and their effects in rheumatic disease patients. [Methods] Patients with rheumatic diseases using steroids in 2017 were investigated with regard to steroid dosage, osteoporosis treatment, treatment contents, bone mineral density (BMD), fracture occurrence, and preventive effect on osteoporosis. [Results] The study population consisted of 391 steroid-treated patients, 27-94 years old (mean 71 years), 309 with rheumatoid arthritis, 43 with polymyalgia rheumatica, and 29 other cases. Steroid dosage was 1-30 mg (average 4.9 mg) in terms of prednisolone. There were 262 cases of osteoporosis treatment, 47 with steroid withdrawal, and 82 untreated cases. Osteoporosis treatment consisted of bisphosphonate in 169 cases, active vitamin D3 in 47, denosumab in 23, and other drugs in 33. Average BMD was 92.6% for lumbar YAM and 74.9% for the femur. Bone fractures occurred in 91 cases (23.2%). [Conclusions] Preventive measures against osteoporosis for rheumatic diseases during steroid therapy in daily clinical practice are insufficient. It is necessary to reduce steroids and review osteoporosis drugs for interventional patients.

W35-2

Protective efficacy for glucocorticoid induced osteoporosis of bisphosphonate

Takao Sugiyama, Toyohiko Sugimoto, Chisaki Ajima, Yusuke Yokoyama, Mieko Yamagata, Ayako Norimoto, Yoshie Sanayama, Masaaki Furukawa
Department of Rheumatology, National Hospital Organization Shimoshizu National Hospital

Conflict of interest: None

[Object] The glucocorticoid induced osteoporosis (GIO) cause vertebral fracture (VF) and is a serious problem on glucocorticoid (GC) therapy. Lately, aggressive prophylaxis of the bisphosphonate (BP) is recommended. We confirm effect of BP on GIO and adverse reaction of BP in a long term. [Methods] We observed 127 patients who started GC therapy (\geq PSL20mg/day) and BP at the same time, and whose bone density (BD) was inspected before and during therapy. 19 patients were men, and 108 were women. The age of them was 58.1 y.o. and, they started PSL 34.3mg and was observed for 83.1 months after treatment, in average. We examined a change of YAM (young adult mean of BD) before and during the treatment, and observed the appearance of the clinical VF, the atypical bone fracture (AF), the osteonecrosis of the jaw (ONJ). [Results]

The mean YAM% was 86.3 at the start of therapy and was 84.2 one year later and was 86.3 three years later and was 90.1 five years later and was 87.9 ten years later. Clinical VF developed in 13 patients (at start an average of the age is 65.5 y.o.) 41.7 months after in average. There was no appearance of AF and ONJ. [Conclusions] We can maintain the bone density of the patients using BP together during GC therapy, and can reduce the vertebral fractures of the patients.

W35-3

Efficacy and safety of sodium RISedronate for glucocorticoid induced Osteoporosis with rheumatoid arthritis (RISOTTO study): a multi-center, double-blind, randomized, placebo-controlled trial

Yuichiro Fujieda¹, Tetsuya Horita², Kazuhide Tanimura³, Yoshiharu Amasaki⁴, Hideki Kasahara⁵, Shin Furukawa⁶, Tsuyoshi Takeda⁷, Shinji Fukaya⁸, Kazuo Matsui⁹, Akira Sagawa¹⁰, Kou Katayama¹¹, Kaoru Takeuchi¹², Kazuaki Katsumata¹³, Takashi Kurita¹⁴, Masaru Kato¹, Kenji Oku¹, Shinsuke Yasuda¹, Norimasa Iwasaki¹⁵, Tatsuya Atsumi¹

¹Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine Hokkaido University, ²Internal Medicine, Tomakomai City Hospital, ³Hokkaido Medical Center for Rheumatic Diseases, ⁴Department of Rheumatology, Tonan Hospital, ⁵Department of Rheumatology, NTT Sapporo Medical Center, ⁶Internal Medicine, Kushiro Red Cross Hospital, ⁷Internal Medicine, Hokkaido Spinal Cord Injury Center, ⁸3rd Department of Internal Medicine, Obihiro Kosei Hospital, ⁹Internal Medicine, Takikawa City Hospital, ¹⁰Sagawa Akira Rheumatology Clinic, ¹¹Katayama Orthopedic Rheumatology Clinic, ¹²Aozora Takeuchi Internal Medicine Clinic, ¹³Department of Rheumatology, Teine Keijinkai Hospital, ¹⁴Internal Medicine, Kitami Red Cross Hospital, ¹⁵Department of Orthopaedic Surgery, Graduate School of Medicine and Faculty of Medicine, Hokkaido University

Conflict of interest: Yes

Object: Sodium Risedronate (RIS) is effective in the treatment of glucocorticoid induced osteoporosis (GIO). However, the efficacy and safety of RIS for GIO with rheumatoid arthritis (RA) remains unclear. **Methods:** This 6 months randomized study of 19 centers tested the efficacy and safety of 75mg once-monthly oral RIS for treatment of GIO with RA patients. Ninety-nine patients were randomized to 2:1 and the results of 95 patients (RIS (n=61), placebo-control (PB) (n=34) were analyzed. The primary endpoint was the change from baseline in lumbar spine bone mineral density (L-BMD). The secondary endpoint was the change from baseline in femoral neck BMD (F-BMD) and the occurrence of vertebral fractures. The incidence of adverse events was evaluated. **Results:** The change of L-BMD in RIS group was significantly higher compared with PB group (RIS: 3.49% (95% CI: 1.92-5.05) vs PB: 0.12% (95% CI: -2.07-2.30), p <0.0001). There was no significant difference in F-BMD. Adverse events were observed in 28 patients (RIS: 19 (30.2%), PB: 9 (26.5%)) without serious adverse events. In addition, non-traumatic vertebral fractures were identified in 10 patients (RIS: 6, PB: 4). **Conclusion:** RIS is effective for bone mineral augmentation and acceptable to patients for treatment of GIO with RA.

W35-4

A prospective, single-center, open-label, randomized-controlled study on drug therapy for the prevention of glucocorticoid-induced osteoporosis following teriparatide therapy in patients with collagen vascular diseases. Denosumab or Bisphosphonates?

Hirofumi Takei, Yusuke Okada, Akiko Shibata, Kentaro Chino, Takahiko Kurasawa, Ayumi Okuyama, Tsuneo Kondo, Koichi Amano
Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan

Conflict of interest: None

[Object] To compare the usefulness of denosumab (DSM) and bisphosphonates (BIS) for glucocorticoid-induced osteoporosis (GIO) in patients with collagen vascular diseases (CVD) who had finished 2-year teriparatide (TPTD) therapy. **[Methods]** Fifteen patients had received or would be treated with glucocorticoid (GC) following TPTD therapy were enrolled in this study (IRB: 1034, UMIN: 000014570) with a written informed consent from Jan 2015 to Jun 2017. **[Methods]** Patients were ran-

domized to receive DSM or BIS and were followed up for one year. Primary endpoint was the rate of vertebral fracture (VFX) and secondary endpoint was increase of bone mineral density in lumbar spine and hip (LSBMD, HBMD). **[Results]** Eight patients were prescribed DSM and 7 received BIS. Baseline patients' profiles of each group were not significantly different. Although there was no significant difference in VFX rate, new VFX developed in one patient in the BIS-group. Median LSBMD during one year in the DSM-group increased significantly from the baseline (+3.71%; P=0.023). However the rates of increase of both LSBMD and HBMD was not significantly different between 2 groups. **[Conclusions]** In CVD patients with GIO who had completed 2-year TPTD therapy, DSM might be more useful for the prevention of VFX than BIS.

W35-5

Effects of alendronate and denosumab on glucocorticoid-induced osteoporosis by a randomized, open-labeled study

Takahide Ikeda, Hideki Tani, Ayaka Kato, Motochika Asano, Koichiro Taguchi, Yoshihiko Kitada, Hiroyuki Morita
Department of General Internal Medicine, Gifu University Graduate School of Medicine

Conflict of interest: None

[Object] We compared with safety and efficacy of denosumab and alendronate on glucocorticoid-induced osteoporosis by a randomized, open-labeled study. **[Methods]** A prospective, single-center study of 23 patients who satisfied Guideline on the management and treatment of glucocorticoid-induced osteoporosis of the Japanese Society (2014). Participants were randomized to either alendronate (35mg orally once a week) or denosumab (60mg subcutaneously once every 6 months) and all participants received alfacalcidol. The primary endpoint was Percent change in bone mineral density (BMD) of the lumbar spine and femoral neck and incident vertebral fracture and non-vertebral fracture at 12 months of treatment. **[Results]** New vertebral fracture and non-vertebral fracture did not have both groups. Both groups decreased BMD of the lumbar spine and femoral neck from 12 months to baseline. Alendronate and denosumab treatment decreased serum level of TRACP-5b and BAP at 12 months. **[Conclusions]** In patients treated with high-dose prednisolone, alendronate and denosumab suppressed bone turnover. But both treatment decreased BMD.

W35-6

Comparison of the effect of denosumab and teriparatide in patients with steroid-induced osteoporosis resistant to bisphosphonates

Yasuaki Hirooka¹, Tetsu Itami², Kenji Sakai², Asuka Inoue², Shinkai Ri², Toshihiko Shiga², Kazuya Kishimoto², Yuji Nozaki², Masafumi Sugiyama¹, Koji Kinoshita², Masanori Funauchi², Itaru Matsumura²

¹Department of Rheumatology, Nara Hospital Kindai University School Of Medicine, ²Division of Hematology and Rheumatology, Kindai University Faculty of Medicine

Conflict of interest: None

[Object] Although bisphosphonates (BP) has been used for steroid-induced osteoporosis, there are some cases with insufficient response. Denosumab (DMAB) or teriparatide (TRPD) can be alternatives to BP. We prospectively compared the effects of DMAB and TPTD on bone mineral density (BMD) in patients who had been resistant to BP. **[Methods]** Thirty six patients taking BP for steroid-induced osteoporosis whose YAM in lumbar spine or femoral neck less than 70% were examined. BP was switched to DMAB (18 cases) or TRPD (18 cases), and the changes of the BMD before and after 104 weeks were determined. **[Results]** There was no significant difference in age, BMI, total steroid dose, and baseline BMD between the two groups. The rate of change of BMD after 104 weeks in lumbar spine were 4.1% vs. 7.4%, and in femoral neck were 1.2% vs. 3.8%, respectively (DMAB vs. TPTD). In lumbar spine, the rate of change of BMD were significantly increased at both groups, whereas in femoral neck, increased at only TPTD group. There was no significant difference in comparison between the two groups. **[Conclusions]** Since TPTD group had a tendency of higher increase rate of BMD than DMAB group, it was suggested that TPTD could be a better alternative in patients with steroid-induced osteoporosis resistant to BP.

W36-1

Trajectories of EQ-5D in RA patients treated with biologics using the IORRA cohort

Kumiko Saka¹, Eiichi Tanaka¹, Eisuke Inoue^{1,2}, Mai Abe¹, Mika Kawano¹, Eri Sugano¹, Naohiro Sugitani^{1,3}, Yoko Higuchi¹, Moeko Ochiai¹, Rei Yamaguchi¹, Naoki Sugimoto¹, Katsunori Ikari¹, Ayako Nakajima^{1,3}, Atsuo Taniguchi¹, Hisashi Yamanaka¹

¹Department of Rheumatology, School of Medicine, Tokyo Women's Medical University, ²St Marianna University, ³Mie University

Conflict of interest: None

[Objective] To identify subclasses with distinct trajectories of EQ-5D in RA patients who initiated biologics (BIO) and examine clinical features whose QOL improved after initiation of BIO use in daily practice. [Methods] The subjects were 785 RA patients who initiated BIO. We estimated the latent classes for the time trend of EQ-5D score for 3 years after initiation of BIO use. We estimated each patients' latent class based on posterior probability. We compared clinical characteristics of each latent class. [Result] Clustering the 785 patients based on the time trend of the EQ-5D score, they were classified into four classes; Class1 (N=160): patients with persistent low EQ-5D score (EQ-5D stayed under 0.6), Class2 (N=314): patients with persistent moderate EQ-5D score (EQ-5D around 0.7), Class3 (N=229): patients whose EQ-5D score improved after Bio use (EQ-5D improved from 0.7 to 0.9), and Class4 (N=82): patients with persistent high EQ-5D score (EQ-5D stayed around 0.9). The patients in Class3 were younger ($p < 0.001$), shorter disease duration ($p < 0.001$), higher DAS28 ($p < 0.001$), lower J-HAQ ($p = 0.038$), and more frequent in non-steroid use ($p = 0.002$) than those in Class2. [Conclusion] We elucidated clinical features of RA patients whose QOL improved after Bio use in daily practice.

W36-2

Using treat-to-target strategy by determining physical disability and glucocorticoid reduction strongly influence functional remission in rheumatoid arthritis

Takafumi Hagiwara, Kazuya Kamada, Noriyuki Namura
Department of Rheumatology, Takarazuka City Hospital

Conflict of interest: None

[Objects] We aimed to determine the factors that inhibit the achievement of functional remission (FcR) in terms of HRQoL. [Methods] A total of 227 patients with RA who had underwent first treatment between October 2014 and December 2017 and had not changed/added another DMARDs for 12 weeks before the observation day were examined. We evaluated the HAQDI and EQ5D5L. FcR was defined in this study as $HAQDI \leq 0.5$ and $EQ5D \geq 0.867$. We investigated their some factors at the first interview and the last observational day. The odds ratio for FcR was examined. [Results] Odds ratios were 1.034 ($p = .202$) for disease duration (per 1 year), 1.576 ($p < .001$) for HAQ-DI at first interview (per 0.5), 0.615 ($p = .232$) and 4.943 ($p < .01$) for GCs state, and 1.164 ($p < .05$) for age at last observational day. [Conclusions] Our results indicated the importance of functional assessment at first interview and demonstrated how to use GCs for the treatment of RA. To achieve FcR, functional assessment should be performed during the first interview and short-term use of GC is useful for prompt functional recovery, in consideration of aging.

W36-3

Elderly in patients with rheumatoid arthritis affects aging of modified health assessment questionnaire independently of disease activity: TOMORROW study

Kazuki Orita¹, Kentaro Inui², Tadashi Okano², Tatsuya Koike^{4,5}, Masahiro Tada³, Yuko Sugioka⁵, Hiroaki Nakamura²

¹Department of Orthopedics, Daito Chuou Hospital, ²Department of Orthopedics, Osaka City University, ³Department of Orthopedics, Osaka City General Hospital, ⁴Search Institute for Bone and Arthritis Disease (SINBAD), ⁵Center for Senile Degenerative Disorders (CSDD), Osaka City University Medical School

Conflict of interest: None

[Object] HAQ depends on disease activity in patients with RA. We investigated the change of mHAQ in RA patients and examined the relationship with disease activity. [Methods] We used RA patient data from 2010 (BL) to 2017 for TOMORROW study (a prospective cohort study of 208 patients with RA and 202 volunteers matching age and sex). DAS-CRP in BL was divided into three groups of low (< 2.7), middle (2.7-4.1), high (4.1 $<$) and related to the change of mHAQ. Changes in mHAQ after 7 years (Δ mHAQ), correlation between Δ mHAQ and each BL factor and multivariate analysis with Δ mHAQ as the objective factor and each BL factor and variations as an explanatory factor were performed. [Results] mHAQ tended to increase over time. There was no significant correlation between Δ mHAQ and each BL factor. In the three group comparison, the mHAQ was significantly higher in the high group than in the other groups ($p < 0.001$). In multivariate analysis using Δ mHAQ as a objective factor, age and BL-DAS using each BL factor as an explanatory factor were extracted and the change of BMI and DAS-CRP using each variation as an explanatory factor were extracted as independent factors. [Conclusions] The aging of mHAQ in patients with RA was independently associated with the aging as the disease activity fluctuated.

W36-4

Influence of the age of patients with rheumatoid arthritis on clinical joint assessments

Ayako Hirata, Takehisa Ogura, Norihide Hayashi, Takaharu Katagiri, Chihiro Imaizumi, Yuki Inoue, Kennosuke Mizushina, Munetsugu Imamura, Sayaka Takenaka, Hideki Ito, Rie Kujime, Hideto Kameda
Toho University Ohashi Medical Center, Tokyo, Japan

Conflict of interest: None

[Objective] To validate the clinical assessments of rheumatoid arthritis (RA) by using ultrasonography (US) as the gold standard in the current super-aged society. [Methods] Fifty RA patients (68 y/o in average) who underwent US examination for IP/PIP, MCP, hand, elbow, shoulder, knee and foot joints in addition to the questionnaire for the presence of subjective joint symptoms (spontaneous pain or stiffness) and the joint examination for the presence of tenderness and swelling were enrolled in this study. Each clinical assessment was evaluated for its sensitivity and specificity referring to the presence of US synovitis. [Results] The number of patients was as follows: 15 for the age < 65 , 20 for 65-75 and 15 for ≥ 75 , respectively. Among a total of 1492 joints, the sensitivity and specificity were 49% and 90% for subjective symptoms, 32% and 93% for tenderness, and 44% and 93% for swelling, respectively. Joint swelling showed the best accuracy without the influence of patient age. By contrast, the specificity of subjective symptoms decreased to 82% in the age ≥ 75 group, and the sensitivity of tenderness was $< 30\%$ except for the age ≥ 75 group (40%). [Conclusion] RA clinical assessments other than joint swelling were affected by the age of patients.

W36-5

Prediction for individual prognosis using big data in patients with rheumatoid arthritis

Susumu Nishiyama¹, Tetsuji Sawada², Tetsushi Aita¹, Yasuhiko Yoshinaga¹, Shigeto Tohma³

¹Rheumatic Disease Center, Kurashiki Medical Center, ²Department of Rheumatology, Tokyo Medical University Hospital, ³Department of Rheumatology, National Hospital Organization Tokyo National Hospital

Conflict of interest: None

[Object] To predict individual prognosis of patients with rheumatoid arthritis (RA) using big data. [Methods] Joint index vector $V(x, y, z)$: x (upper limb index), y (lower limb index), z (large or small dominance) was calculated in each patients with RA registered in the National Database of Rheumatic Diseases in Japan (*NinJa*). Large joint dominant (LAR) group was defined as square root of $(x^2 + y^2) \leq 0.1$ & $z > 0.2$. Transformation matrix was computed from mean vector and its translation vector. [Results] Patients in the LAR group had high disease activity and poor physical function. (Positive Predictive Value, Negative Predictive Value, Likelihood Ratio) in predicting LAR group with estimated vector were (0.59, 0.85, 5.9) for all subjects, (0.61, 0.86, 7.2) for MTX users, (0.68, 0.82, 7.4) for bDMARDs users, and (0.68, 0.84, 8.6) for

both users. Of female patients with disease duration ≤ 10 years who were predicted in the LAR group with MTX therapy but in the non-LAR group with MTX and bDMARDs, 75% were actually entered in the non-LAR group with MTX and bDMARDs, while 53% with MTX therapy. [Conclusions] Joint index vector was useful tool for precision medicine using big data.

W36-6

Significance of body mass index as a prediction factor for treatment effect of biological disease modifying anti-rheumatic drugs in rheumatoid arthritis - Results from Kansai Consortium for Well-Being of Rheumatic Disease Patients

Kosaku Murakami¹, Motomu Hashimoto², Takashi Matsuo¹, Koichi Murata³, Wataru Yamamoto^{2,3}, Ryota Hara⁴, Masaki Katayama⁵, Akira Onishi⁶, Sadao Jinno⁶, Tohru Takeuchi⁷, Takuya Kotani⁷, Yonsu Son⁸, Hideki Amuro⁸, Toru Hirano⁹, Kosuke Ebina¹⁰, Kohei Nishitani², Masao Tanaka², Hiromu Ito¹¹, Koichiro Ohmura¹, Tsuneyo Mimori¹

¹Department of Rheumatology and Clinical Immunology, Kyoto University Graduate School of Medicine, ²Department of Advanced Medicine for Rheumatic Diseases, Kyoto University Graduate School of Medicine, ³Department of Health Information Management, Kurashiki Sweet Hospital, ⁴The Center for Rheumatic Diseases, Nara Medical University, ⁵Department of Rheumatology, Osaka Red Cross Hospital, ⁶Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, ⁷Department of Internal Medicine IV, Osaka Medical College, ⁸First Department of Internal Medicine, Kansai Medical University, ⁹Department of Respiratory Medicine, Allergy and Rheumatic Disease, Osaka University Graduate School of Medicine, ¹⁰Department of Orthopedic Surgery, Osaka University Graduate School of Medicine, ¹¹Department of Orthopedic Surgery, Kyoto University Graduate School of Medicine

Conflict of interest: None

[Object] To assess whether body mass index (BMI) affects clinical outcomes in rheumatoid arthritis (RA) patients starting a molecular-targeted agent. [Methods] From Kansai consortium for well-being of rheumatic disease patients (ANSWER) cohort, we analyzed RA patients who continued a bDMARD more than 6 months. Dividing these patients between BMI more than 24 (high BMI) or not (low BMI), we compared the achievement rate of Simplified Disease Activity Index Remission (SDAI-REM) defined as lower than 3.3. [Results] In each drug, patients number and SDAI-REM rate (low BMI, high BMI, p-value by Chi-square test) after 6 months was as follows; Infliximab (IFX, 73): 46%, 19%, $p=0.0311$; Etanercept (ETN, 93): 45%, 55%, not significant (NS); Adalimumab (ADA, 51): 33%, 47%, NS; Golimumab (GLM, 99): 36%, 35%, NS; Certolizumab pegol (CZP, 34): 17%, 60%, $p=0.0115$; Tocilizumab (TCZ, 147): 32%, 15%, $p=0.042$; Abatacept (ABT, 125): 26%, 21%, NS. [Conclusions] A contribution of BMI for therapeutic outcome seems to vary with each bDMARD in real world observation.

W37-1

Can the leucine-rich alpha-2-glycoprotein (LRG) detect ultrasound subclinical synovitis in patients with rheumatoid arthritis?

Yutaro Yamada^{1,2}, Kentaro Inui¹, Tadashi Okano¹, Koji Mandai^{1,3}, Kenji Mamoto¹, Yuko Sugioka⁴, Tatsuya Koike⁴, Hiroaki Nakamura¹

¹Department of Orthopedics, Osaka City University Graduate School of Medicine, ²Department of Orthopedics, Yodogawa Christian Hospital, ³Department of Orthopedics, Osaka Social Care Center, ⁴Center for Senile Degenerative Disorders (CSDD), Osaka City University Graduate School of Medicine

Conflict of interest: None

[Background] The subclinical synovitis (SS) can be detected by ultrasound (US) in CRP-negative patients with rheumatoid arthritis (RA). The new biomarker 'leucine-rich alpha-2-glycoprotein' (LRG) is known to be more sensitive to inflammation. [Objective] We investigated the utility of LRG in detecting SS. [Methods] We examined laboratory data in 34 patients with RA (27 female, average age 65.0). Their LRG level was also measured by ELISA method. They had US at bilateral MCP, PIP, wrist and MTP joints and are semi-quantitatively assessed by Grey

Scale and Power Doppler score (GSUS, PDUS). We investigated the relationships between LRG and conventional inflammatory marker, disease activity, GSUS and PDUS. [Results] LRG was significantly correlated with CRP ($r=0.69$, $p<0.001$) and ESR ($r=0.54$, $p=0.001$), but not with DAS28-ESR ($r=-0.15$, $p=0.38$) and PDUS ($r=0.06$, $p=0.73$). 12 patients had SS. Among those with or without SS, CRP was 0.21 ± 0.22 , 0.53 ± 1.04 mg/dl ($p=0.29$), ESR was 21.9 ± 25.8 , 17.3 ± 12.7 mm/1h ($p=0.49$), LRG was 64.7 ± 17.6 , 68.4 ± 19.4 ng/ml ($p=0.58$), respectively. The cut-off value of LRG for predicting SS, defined as $PDUS>1$, was 63.5 ng/ml (AUC 0.564) by ROC analysis, however kappa value of this was -0.15 . [Conclusion] LRG cannot detect SS. This indicates the importance of US.

W37-2

Prognostic factors toward Health Assessment Questionnaire disability progression in rheumatoid arthritis patients in clinical practice: A post hoc analysis of a nationwide longitudinal cohort in Japan

Remi Sumiyoshi¹, Toshihiko Hidaka², Tomohiro Koga^{1,3}, Akitomo Okada⁴, Takaaki Fukuda⁵, Tomonori Ishii⁶, Yukioka Ueki⁷, Takao Kodera⁸, Munetoshi Nakashima⁹, Yuichi Takahashi¹⁰, Yoshiro Horai¹¹, Ryu Watanabe⁶, Hiroshi Okuno¹², Toshiyuki Aramaki^{4,7}, Tomomasa Izumiyama¹³, Osamu Takai¹⁴, Taiichiro Miyashita^{11,15}, Shin-ya Kawashiri^{1,16}, Naoki Iwamoto¹, Kunihiro Ichinose¹, Mami Tamai¹, Hideki Nakamura¹, Tomoki Origuchi^{1,17}, Kiyoshi Aoyagi¹⁸, Katsumi Eguchi^{1,19}, Atsushi Kawakami¹

¹Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ²Institution of Rheumatology, Zenjinkai Shimin-no-Mori Hospital, Miyazaki, Japan, ³Center for Bioinformatics and Molecular Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ⁴Department of Rheumatology, Japanese Red Cross Nagasaki Genbaku Hospital, Nagasaki, Japan, ⁵Department of Rheumatology, Tenjinkai Koga Hospital 21, Kurume, Japan, ⁶Department of Hematology and Rheumatology, Tohoku University Hospital, Sendai, Japan, ⁷Rheumatic and Collagen Disease Center, Sasebo Chuo Hospital, Sasebo, Japan, ⁸Department of Hematology and Rheumatology, Tohoku Medical and Pharmaceutical University Hospital, Sendai, Japan, ⁹Department of Rheumatology, Kurume University Medical Center, Kurume, Japan, ¹⁰Yu Family Clinic, Miyagi, Japan, ¹¹Department of General and Internal Medicine, Rheumatology, Clinical Research Center, National Hospital Organization, Nagasaki Medical Center, Omura, Japan, ¹²Department of Orthopaedic Surgery, Tohoku Rosai Hospital, Sendai, Japan, ¹³East Sendai Rheumatism and Internal Medicine Clinic, Sendai, Japan, ¹⁴Department Of Rheumatology, Osaki Citizen Hospital, Osaki, Japan, ¹⁵Miyashita Rheumatology Clinic, Omura, Japan, ¹⁶Department of Community Medicine, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ¹⁷Department of Rehabilitation Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ¹⁸Department of Public Health, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ¹⁹Sasebo City General Hospital, Sasebo, Japan

Conflict of interest: None

[Object] To determine prognostic factors of progression of the Health Assessment Questionnaire (HAQ) scores in patients with rheumatoid arthritis (RA) in clinical practice. [Methods] Using data from a nationwide, multicenter, prospective study in Japan, we evaluated 408 RA patients with moderate to high disease activity at study entry after being treated with conventional synthetic DMARDs. These patients were treated according to a treat-to-target (T2T) strategy for 1 year. We performed a multiple logistic regression analysis to explore the factors to predict the progression of HAQ score at 1 year. [Results] During the observation, although the DAS28-ESR improved from 4.27 to 3.16, the progression of HAQ score was observed in 24.7% of the patients. The multiple logistic regression analysis revealed that the independent variables to predict the HAQ progression were: time-integrated DAS28-ESR during the 1 year post-baseline >4.2 (OR=2.94, 95%CI 1.65-5.22), and HAQ score at baseline >0.5 (OR=13.9, 95%CI 7.88-24.4). [Conclusions] Our data suggests that maintaining clinical improvement according to T2T and initiating the treatment at the early stage before ADL impairment are important for functional improvement after 1 year.

W37-3

Infliximab concentration can be estimated using the infliximab detection kit

Masao Sato¹, Masao Takemura², Tomohisa Tani¹, Toshiro Ohashi¹
¹Ohashi-Tani Orthopedics, Gifu, Japan, ²Advanced Diagnostic System Laboratory, Fujita Health University

Conflict of interest: Yes

[Objective] To determine whether the concentration (conc) detection kit could be used to estimate IFX conc. [Methods] As a preliminary test, the time for the colored line to appear was measured for serum samples diluted by a factor of 2, 4, 5, 6.7, and 16.7 of a patient with an IFX conc of 19.89 µg/mL. Next, the IFX concs of 19 patients and the time required for the colored line to appear in the kit were measured to determine. [Results] The time required for the colored line to appear for patients in the preliminary test was 16 s for 1-fold dilution, 36 s for 2-fold dilution, 61 s for 4-fold dilution, 82 s for 5-fold dilution, 109 s for 6.7-fold dilution, and 268 s for 16.7-fold dilution. Subsequently, for the 19 patients, a graph was prepared with the actual measured IFX conc on the Y-axis and the time required for the colored line to appear on the X-axis. The graph showed that the IFX conc and the time required for the colored line to appear were 3 µg/mL and 100 s, 5 µg/mL and 70 s, 10 µg/mL and 30 s, and 20 µg/mL and 20 s, indicating that the approximate IFX conc could be estimated by the time required for the colored line to appear. [Conclusion] Estimation of the IFX conc to a certain extent was thought to be possible using the qualitative kit.

W37-4

Discrepancy between the efficacy of biological RCT and the effectiveness in daily practice based on the IORRA cohort

Eri Sugano¹, Eiichi Tanaka¹, Eisuke Inoue^{1,2}, Mai Abe¹, Mika Kawano¹, Kumiko Saka¹, Naohiro Sugitani^{1,3}, Yoko Higuchi¹, Moeko Ochiai¹, Rei Yamaguchi¹, Naoki Sugimoto¹, Katsunori Ikari¹, Ayako Nakajima^{1,3}, Atsuo Taniguchi¹, Hisashi Yamanaka¹

¹Institute of Rheumatology, Tokyo Women's Medical University Hospital, Tokyo, Japan, ²St. Marianna University School of Medicine Department of Medical Information, ³Mie University Hospital Center for Rheumatic Disease

Conflict of interest: None

[Purpose] To investigate discrepancy between the efficacy of biologics in RCTs and the effectiveness of biologics in RA patients in routine clinical practice based on the IORRA. [Method] The effectiveness of biologics (etanercept (n=33), golimumab (n=20), certolizumab (n=17), abatacept (n=14), and tocilizumab (TCZ, n=24)) in RA patients who initiated in 2016 was compared with the efficacy based on each RCT (total 8 trials). The effectiveness was evaluated by ACR achievement rates and remission rate at half or 1 year after initiation of biologics. [Results] According to the MATSURI study (TCZ) whose inclusion criteria were not strict, eligible patients (n=13) indicated better effectiveness than those in non-eligible patients (n=11). In other 7 RCTs, there were almost no patients who fulfilled inclusion criteria in the IORRA. When compared under that condition, ACR achievement rate was higher in patients with RCTs, while remission rate was higher in patients in the IORRA. Average DAS28 at baseline in the RCTs group was significantly higher than that in the IORRA. [Conclusion] Although RA patients in RCT indicated better ACR achievement rate than those in routine practice, clinical remission was difficult to achieve. This might be due to the difference in disease activity at baseline.

W37-5

The clinical significance of patient reported outcomes (PROs) in patients with rheumatoid arthritis (RA) under a treat-to-target (T2T) strategy

Masako Majima¹, Ryoko Sakai¹, Fumio Hirano², Masayoshi Harigai¹, Hisashi Yamanaka¹

¹Department of Rheumatology, School of Medicine, Tokyo Women's Medical University, Tokyo, Japan, ²Department of Pharmacovigilance; Department of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Bunkyo, Japan

Conflict of interest: None

[Object] To investigate the clinical significance of PRO in patients with RA under a T2T strategy. [Methods] We analyzed 271 RA patients with moderate-to-high disease activity under a T2T strategy in the multi-center prospective cohort study. We compared PRO measures between two groups using Mann-Whitney U tests and identified associated factors using multivariate analysis [Results] In 271 patients (mean age, 61 years old; female, 77%; mean disease duration, 55 months), visual analogue scale (VAS) for fatigue at all weeks were significantly lower in the patients with Health Assessment Questionnaire (HAQ) ≤ 0.5 at week 72 (n=164) than those without (n=64). We identified age, HAQ score, and modified Total Sharp Score (mTSS) at week 0, and VAS for fatigue at week 24 as factors significantly associated with HAQ ≤ 0.5 at week 72. In 93 RA patients with SDAI ≤ 3.3 at week 24 (mean age, 60.3 years old; female, 78.5%; mean disease duration, 45 months), HAQ scores at week 24 was significantly associated with duration of sustaining SDAI remission. Factors associated with HAQ scores at week 24 were age, VAS for fatigue at week 24, and patient's VAS at week 24. [Conclusions] These results indicate that fatigue was associated with functional remission and sustaining SDAI remission.

W37-6

Expressions of clock genes were varied by treatments of biological DMARDs in patients' leukocytes

Kanta Morii¹, Yuto Oketani¹, Kenta Kaneshiro¹, Koto Uchida¹, Ikumi Okumura¹, Arisa Yaekura¹, Kohsuke Yoshida¹, Yoshiko Kawasaki², Nao Shibamura³, Yoshitada Sakai⁴, Akira Hashiramoto¹

¹Department of Biophysics, Division of Clinical of Immunology, Kobe University Graduate School of Health Sciences, Kobe, Japan, ²Department of Rheumatology, Kobe Kaisei Hospital, Kobe, Japan, ³Department of Orthopedics, Kobe Kaisei Hospital, Kobe, Japan, ⁴Department of Rehabilitation Science, Kobe University Graduate School of Medicine

Conflict of interest: None

Object: Patients with RA demonstrate circadian variations of symptom such as morning stiffness or increased cytokine's production around mid-night, and we have reported influences of clock genes on the pathogenesis of RA. In this study, we compared the variation of clock genes' expressions in leukocytes by treatments with biological DMARDs (bDMARDs), and evaluated the relationship with the disease activity. Methods: Total RNA was extracted from leukocytes to examine expressions of clock genes (*Bmal1*, *Clock*, *Per1/2*, *Cry1/2*) and clock controlled genes (*Dbp*, *Hlf*, *Tef*, *E4bp4*, *Rora*, *Rorγ*, *Rev-erba*) by Real-time PCR. Blood samples was collected before and the study end-point; DAS28-ESR < 3.2. 15 RA patients treated with bDMARDs were enrolled in this study; TNF inhibitor (TNFi: 5), Tocilizumab (TCZ: 5), Abatacept (ABT: 5). Results: At the end points, expressions of *Clock* were increased (TNFi; $p=0.064$, TCZ; $p=0.076$, ABT; $p<0.01$), expressions of *Per2* were increased (TNFi; $p=0.055$, TCZ; $p<0.05$, ABT; $p<0.01$), and expressions of *Rora* were increased (TNFi; $p=0.075$, TCZ; $p=0.098$, ABT; $p<0.05$), as compared with those before treatments. Conclusions: Results indicated that *Clock*, *Per2* and *Rora* could be useful as a biomarker to represent the therapeutic response for bDMARDs or the disease activity in RA.

W38-1

Long term Efficacy and Safety Results from the Phase 2b/3 Randomized, Placebo-controlled, Double-blind trial of Upadacitinib, a JAK-1 Selective inhibitor in Japanese Patients with Active Rheumatoid Arthritis and Inadequate Response to Conventional Synthetic DMARDs

Hideto Kameda¹, Tsutomu Takeuchi², Kunihiko Yamaoka³, Motohiro Oribe⁴, Mitsuhiro Kawano⁵, Yijie Zhou⁶, Ahmed A Othman⁶, Aileen L Pangan⁶, Shinichi Asabe⁷, Susumu Kitamura⁷, Sebastian Meerwein⁸, Yoshiya Tanaka⁹

¹Division of Rheumatology, Department of Internal Medicine, Toho University Ohashi Medical Center, ²Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, ³Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine, ⁴Department of Rheumatology, Oribe Clinic of Rheumatism and Medicine, ⁵Department of Rheumatology, Honjo Rheumatism Clinic, ⁶AbbVie Inc., North Chicago, IL, USA, ⁷AbbVie GK, Tokyo, Japan, ⁸Ab-

bVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany, ⁹The First Department of Internal Medicine, University of Occupational and Environmental Health

Conflict of interest: Yes

[Object] Long-term efficacy and safety of upadacitinib (UPA) in Japanese patients (pts) with active RA and inadequate response to conventional synthetic DMARDs (csDMARDs-IR). [Methods] Pts on stable csDMARDs were randomized to receive UPA 7.5, 15 or 30 mg once daily or PBO (upto Wk12, UPA thereafter) in a blinded manner. Reported here are safety and efficacy outcomes (ACR, DAS28 [CRP] responses) at Wk60 (as observed analysis). [Results] Of 197 pts treated, 156 (79.2%) completed Wk60. Proportion of pts (15mg, Wk60, as observed) - ACR20 and DAS28-CRP \leq 3.2, both 88%; ACR50: 67%; ACR70: 51%; DAS28-CRP $<$ 2.6: 72%. Responses with all doses were improved or maintained through Wk60. Frequencies of TEAEs, serious/opportunistic infections, herpes zoster, lymphopenia, neutropenia and CPK elevation were highest in the 30mg arm. Upto Wk60, 2 deaths (30mg, 1 TEAE respiratory failure), 2 malignancies (15 mg, ALL; 30mg, Hodgkins disease: 1 each), 2 MACE events (7.5mg, cerebral infarction; 30mg, respiratory failure: 1 each), 1 DVT event (30mg) and no cases of tuberculosis were recorded. [Conclusions] Through Wk60, all 3 doses of UPA were effective in treating signs and symptoms of RA. The overall safety was consistent with global UPA trials in RA.

W38-2

A Phase 3, Randomized Controlled Trial Comparing Upadacitinib Monotherapy to MTX Monotherapy in MTX-Naïve Patients with Active Rheumatoid Arthritis

Tsutomu Takeuchi¹, Ronald Van Vollenhoven², Aileen L Pangan³, Alan Friedman³, Mohamed Eslam Mohamed³, Su Chen³, Maureen Rischmueller⁴, Ricardo Blanco⁵, Ricardo M Xavier⁶, Vibeke Strand⁷

¹Division of Rheumatology, Department of Internal Medicine, Keio University of Medicine, Tokyo, Japan, ²Amsterdam Rheumatology and Immunology Center ARC, Amsterdam, the Netherlands, ³AbbVie Inc., North Chicago, IL, USA, ⁴The Queen Elizabeth Hospital and University of Adelaide, Adelaide, Australia, ⁵Hospital Universitario Marques de Valdecilla, Cantabria, Spain, ⁶Universidade Federal do Rio Grande do Sul Porto Alegre, Rio Grande do Sul, Brazil, ⁷Stanford University, Palo Alto, CA, USA

Conflict of interest: Yes

[Object] Compare safety/efficacy and inhibition of structural damage with upadacitinib (UPA) monotherapy vs methotrexate (MTX) in MTX-naïve patients (pts). [Methods] Pts received (1:1:1) once-daily UPA 15mg, 30mg monotherapy, or weekly MTX. Primary endpoints were ACR50 at Wk12, or DAS28CRP $<$ 2.6 at Wk24. [Results] 945/947 pts, including 83 Japanese, were treated; 88.7% completed Wk24. Primary and secondary endpoints were met. More pts on UPA15 and 30mg vs MTX achieved Wk12 ACR50 (52.1% and 56.4% vs 28.3%) and Wk24 DAS28CRP $<$ 2.6 (48.3% and 50.0% vs 18.5%). At Wk24, Δ mTSS were 0.14 and 0.07 vs 0.67 and more pts had no radiographic progression on UPA15 and 30mg vs MTX. More pts on UPA vs MTX achieved LDA and remission. Rate of AEs and serious AEs were similar on UPA15 and MTX, and higher on UPA30. AEs leading to discontinuation were similar across arms. More pts on UPA30 had serious infections. Herpes Zoster was higher on UPA vs MTX. 4 malignancies, and 6 deaths were reported (MTX: 1 sudden CV; UPA15, 1 CV, 1 metastatic malignant melanoma; UPA30, 1CV,1 pneumonia and sepsis,1 peritonitis). 2 VTE were reported (MTX:1 PE, UPA30:1 DVT). [Conclusions] UPA monotherapy showed significant clinical improvements and less radiographic progression vs MTX. Safety was consistent with other UPA studies.

W38-3

Upadacitinib as Monotherapy: A Phase 3 Randomized Controlled Double-Blind Study in Patients with Active Rheumatoid Arthritis and Inadequate Response to Methotrexate

Yoshiya Tanaka¹, Josef S Smolen², Stanley Cohen³, Paul Emery⁴, William Rigby⁵, Ying Zhang⁶, Alan Friedman⁶, Ahmed A Othman⁶, Heidi S Camp⁶, Aileen L Pangan⁶

¹The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, ²Medical University of Vienna, Austria, ³Metroplex Clinical Research Center, TX, USA, ⁴Leeds Inst of Rheumatic & Musculoskeletal Medicine, Leeds NIHR BRC, UK, ⁵Dartmouth College, NH, USA, ⁶AbbVie Inc., North Chicago, IL, USA

Conflict of interest: Yes

[Object] To assess safety and efficacy of switching to UPA monotherapy vs continuing methotrexate (MTX) as a blinded study drug in MTX inadequate responders. [Methods] Pts received (1:1:1) once-daily UPA 15 or 30mg monotherapy or continued MTX (cMTX) at prior stable dose. Primary endpoints at Wk 14 were pts achieving ACR20 or DAS28-CRP \leq 3.2. [Results] All 648 randomized pts, including 65 Japanese pts, were treated; 92.3% completed 14 wks. Primary and key secondary endpoints were met ($p<.001$); At Wk 14, significantly more pts on UPA 15 and 30 vs cMTX achieved ACR20 (67.7% and 71.2% vs 41.2%), and DAS28-CRP \leq 3.2 (44.7% and 53.0% vs 19.4%). AEs were reported at similar rates across arms; serious AEs were higher on UPA15 but similar between cMTX and UPA 30. More infections were reported in cMTX and UPA30 vs UPA15. Herpes zoster was highest on UPA 30. 3 malignancies (cMTX: 1; UPA15: 2), 3 adjudicated MACE (UPA15: 1; UPA 30: 2), 1 adjudicated PE (UPA 15), 1 death (UPA15: stroke due to ruptured aneurysm) were reported. Lab abnormalities were consistent with prior UPA studies. [Conclusions] In MTX-IR pts, switching to UPA monotherapy showed significant improvements vs continuing MTX. Safety was similar to prior UPA studies.

W38-4

RAJ3: Efficacy and safety of peficitinib (ASP015K), a novel oral JAK inhibitor, in patients with RA who had an inadequate response to DMARDs

Yoshiya Tanaka¹, Tsutomu Takeuchi², Sakae Tanaka³, Atsushi Kawakami⁴, Yeong-Wook Song⁵, Yi-Hsing Chen⁶, Hiroyuki Izutsu⁷, Yuichiro Kaneko⁷

¹University of Occupational and Environmental Health, ²Keio University School of Medicine, ³University of Tokyo, ⁴Nagasaki University, ⁵Seoul National University, Korea, ⁶Taichung Veterans General Hospital, Taiwan, ⁷Astellas Pharma, Inc.

Conflict of interest: Yes

[Object] To evaluate the efficacy and safety of peficitinib (PEF) when used alone or in combination with DMARDs for RA in patients who had an inadequate response (IR) to DMARDs. [Methods] This was a multicenter, randomized, placebo (PBO)-controlled, double-blinded study conducted in Japan, Korea and Taiwan. Patients with RA and an IR to DMARDs were randomized to either PBO (n=102), PEF 100 mg/day (PEF 100, n=104), PEF 150 mg/day (PEF 150, n=102), or etanercept 50 mg/wk (Open-label, n=201). At wk12, patients in the PBO were switched to PEF 100 or 150 under blinded condition. A stable dose of DMARDs throughout the 52-wk study were permitted to be taken for patients with DMARDs concomitantly. [Results] ACR20 response rate at wk12 or early termination was higher in the PEF 100 and 150 than in the PBO ($p<.001$). The 12-wk safety outcome was similar among all groups, but serious adverse events were more common in the PBO. The incidence of serious infection and herpes zoster were higher in the PEF groups, with no clear dose-dependency. No deaths were reported during the study. [Conclusions] In patients with RA who had an IR to DMARDs, PEF 100 and 150 are effective in reducing symptoms. Compared with safety profile of PEF in previous studies, no additional safety concerns were identified.

W38-5

RAJ4: Efficacy and safety of peficitinib (ASP015K), a novel oral JAK inhibitor, in patients with RA who had an inadequate response to methotrexate (MTX)

Tsutomu Takeuchi¹, Yoshiya Tanaka², Sakae Tanaka³, Atsushi Kawakami⁴, Hiroyuki Izutsu⁵, Yuichiro Kaneko⁵

¹Keio University School of Medicine, ²University of Occupational and Environmental Health, ³University of Tokyo, ⁴Nagasaki University, ⁵Astellas Pharma, Inc.

Conflict of interest: Yes

[Object] To evaluate the efficacy and safety of peficitinib (PEF) when used in combination with MTX for RA in patients who had an inadequate response to MTX. [Methods] Patients with RA in Japan who had an inadequate response to MTX were randomized to either PBO (n=170), PEF 100 mg/day (PEF 100, n=175) or PEF 150 mg/day (PEF 150, n=174) concurrently with MTX at a stable dose (≤ 16 mg/wk) during the 52-wk study. At wk12, patients who showed an inadequate response in the PBO group were switched to PEF 100 or 150, and those remaining were switched to PEF 100 or 150 at wk28 under blinded condition. [Results] ACR20 response rate at wk12/early termination (ET) was higher in the PEF 100 and 150 groups than in the PBO group ($p < 0.001$). At wk28/ET, the mean change in modified Total Sharp Score was smaller in the PEF groups than in the PBO group ($p < 0.001$). The incidence of serious infection and herpes zoster were higher in the PEF groups during the study, with no clear dose-dependency. [Conclusions] In patients with RA who had an inadequate response to MTX, PEF 100 or 150 taken concurrently with MTX reduced RA symptoms and prevented joint destruction. Compared with safety profile of PEF in previous studies, no additional safety concerns were identified.

W38-6

Characterization and changes of lymphocyte subsets in Baricitinib-treated patients with rheumatoid arthritis: an integrated analysis

Yoshiya Tanaka¹, Tsutomu Takeuchi², Iain McInnes³, Masaru Tanaka⁴, Yasushi Takita⁴, Nicole Byers⁵, Lei Chen⁵, Stephanie Bono⁵, Maher Issa⁵, William Macias⁵, Veronica Rogai⁵, Terence Rooney⁵, Douglas Schlichting⁵, Masayoshi Harigai⁶, Paul Emery⁷

¹The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, ²Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, ³University of Glasgow, Glasgow, UK, ⁴Eli Lilly Japan K.K., Kobe, Japan, ⁵Eli Lilly and Company, Indianapolis, USA, ⁶Department of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, ⁷Leeds MSK Biomed / Chapel Allerton Hospital, Leeds, UK

Conflict of interest: Yes

[Object] To evaluate changes in lymphocyte subsets during Baricitinib (Bari) treatment and association with infections. [Methods] An analysis was conducted by pooling data from 3 completed Phase 3 trials comparing placebo and Bari and 1 ongoing long-term extension study in 2186 patients (including 227 Japanese) with RA. [Results] Bari was associated with an early transient increase in total lymphocyte count at week 4, which returned to baseline by week 12. Up to week 104, transient changes within normal reference ranges in T cells and subsets were observed. B cells and subsets increased after 4 weeks with no further increases noted through 104 weeks. Natural killer (NK) cells transiently increased after 4 weeks, before decreasing below baseline levels and then stabilizing over time. A modest potential association was observed for Bari 4-mg between low NK cells and treatment emergent infections but not for serious infections or herpes zoster. No notable difference was observed for Japanese and overall. [Conclusions] Changes in lymphocyte subsets were largely within normal reference ranges, and were not associated with serious infections.

W39-1

Long-term Safety (up to 6 years) of Baricitinib (Bari) in Patients (pts) including Japanese (JP) with Moderate to Severe Active Rheumatoid Arthritis (RA): an Integrated Analysis

Masayoshi Harigai¹, Tsutomu Takeuchi², Josef S Smolen³, Kevin Winthrop⁴, Mark C Genovese⁵, Taeko Ishii⁶, Minako Sato⁶, Atsushi Nishikawa⁶, Yasushi Takita⁶, Terence Rooney⁷, Chris Dickson⁷, Yoshiya Tanaka⁸

¹Department of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, ²Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, ³Medical University of Vienna, Vienna, Austria, ⁴Oregon Health Sciences University, Portland, USA, ⁵Stanford University Medical Center, Palo Alto, USA, ⁶Eli Lilly Japan K.K., Kobe, Japan, ⁷Eli Lilly and Company, Indianapolis,

USA, ⁸The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan

Conflict of interest: Yes

[Object] To evaluate long-term safety of Bari in pts with moderate to severe active RA including JP. [Methods] Incidence rates (IR per 100 patient-year [PY]) of adverse events (AEs) were calculated using data in the ALL BARI RA analysis set which included pts exposed to any Bari dose, and from completed phase 1-3 studies and an ongoing long-term extension study. [Results] 3492 pts (514 JP) were exposed to Bari for 7860 total PY (maximum exposure: 6 years) as of Apr 2017. Compared with previously reported (cut off Sep 2016), similar trend was observed in IRs of deaths (0.35), AEs leading to discontinuation (5.4), malignancies excluding non-melanoma skin cancer (0.8), major adverse cardiovascular events (0.5), serious infections (3.0), Herpes zoster (HZ) (3.3), lymphoma (0.08), GI perforation (0.04), tuberculosis (0.14), and pulmonary embolism and deep vein thrombosis (0.53). In JP, HZ (6.9) were more frequent than overall, but the HZ IR was similar to previously reported and stable with longer exposure and events were considered manageable. IRs of AEs except for HZ were not notably different from those of overall. [Conclusions] With longer exposure, Bari had an acceptable safety profile in pts with active RA as described in the previous report.

W39-2

Dose reduction of baricitinib for rheumatoid arthritis patients who achieved remission or low disease activity in real world data

Eiji Torikai, Daisuke Suzuki

Department of Rheumatology, Iwata City Hospital

Conflict of interest: None

[Object] To investigate the effects of baricitinib (Bari) dose step down in patients who achieved remission (RMS) or low disease activity (LDA) with 4mg/day of Bari treatment. [Methods] We included 12 RA patients in RMS or LDA who received 4mg/day of Bari dose for >3months. They stepped down to 2mg/day and could rescue to 4mg/day if in flare-up. We evaluated the changes of disease activity and HAQ. [Results] At the start of Bari treatment, mean ages, disease duration, MTX dose, PSL dose, CDAI and HAQ were 62.0years, 3.03years, 7.64mg/week (91.7%) and 3.70mg/day (41.7%), 26.5 and 0.74 respectively. At the step-down of Bari, mean score of CDAI and HAQ were 4.63 and 0.21. Nine of 12 patients sustained RMS or LDA after the step down. Three patients who flared up could re-capture RMS or LDA after rescue. Although HAQ of them also deteriorate at flare-up (mean score: 0.50), they were improved after rescue (mean score: 0.29). No patient discontinued Bari due to adverse events. Three patients discontinued Bari because of sustained RMS. [Conclusions] Most patients could sustain RMS or LDA with step down therapy to Bari dose of 2mg/day in real world clinic. All patients who flared up could capture their previous status of the disease activity and HAQ.

W39-3

The Efficacy of baricitinib for patients with rheumatoid arthritis resistant to several other biologic agents

Tomofumi Kiyokawa, Yukiko Takakuwa, Yoshioki Yamasaki, Takayasu Ando, Harunobu Iida, Yutaka Goto, Kanako Suzuki, Yusa Asari, Marina Uchida, Hisae Fujimoto, Kana Ishimori, Keiichi Sakurai, Hiromi Matsushita, Kumiko Tonooka, Mitsuru Imamura, Takeshi Suzuki, Hiroko Nagafuchi, Seido Ooka, Kimito Kawahata

Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Kanagawa, Japan

Conflict of interest: None

[Object] To investigate the efficacy of baricitinib (BAR) for patients with rheumatoid arthritis (RA) resistant to several other biologic anti-rheumatic drugs (bDMARDs). [Methods] We retrospectively analyzed 6 patients with RA who were previously treated with several bDMARDs and showed resistance to those drugs and then switched to BAR from January to September 2018. Efficacy of BAR was evaluated at 12 weeks

from the initiation of BAR. [Results] All 6 patients were female. Anti-CCP antibodies and rheumatoid factor were positive in all patients. The mean age of the patients was 64.7 year-old with mean disease duration of 13.9 years. The DAS28-CRP at the baseline was 4.83. Methotrexate (average dose of 6 mg/week) was used in 2 patients and prednisolone (average dose 2.7 mg/day) in 3. All six patients had previously treated with one or more tumor necrosis factor (TNF) and interleukin-6 (IL-6) inhibitors and therefore received three or more bDMARDs. DAS28-CRP at 12 weeks was 3.20, which was significantly lower than the baseline with a change of -1.63 ($P = 0.046$). [Conclusions] The significant improvement of DAS28-CRP was seen by BAR. BAR can be the candidate for RA patients who showed resistance to several other bDMARDs such as IL-6-IR and TNF-IR.

W39-4

Does the Efficacy of Tofacitinib depend on previous DMARDs?

Tsuneo Kondo, Yusuke Okada, Akiko Shibata, Kentaro Chino, Takahiko Kurasawa, Hirofumi Takei, Koichi Amano
Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University

Conflict of interest: None

[Object] To elucidate whether the efficacy of tofacitinib (Tofa) is different among previous DMARDs in RA patients. [Methods] The medical records of 91 RA patients who had received Tofa and been followed up for more than 24 weeks were retrospectively evaluated. [Results] Female was 90.1%. Average age was 63.4 years, mean disease duration were 15.6 years, average DAS28 at start of Tofa was 5.2. Previous DMARDs included csDMARDs (33.0%), TNF inhibitors (29.7%), tocilizumab (TCZ) (27.5%) and abatacept (ABT) (9.8%). LOCF analysis revealed that DAS28-ESR decreased significantly from 5.2 ± 1.0 to 3.4 ± 0.9 in switching to Tofa from csDMARDs, 5.7 ± 1.1 to 3.7 ± 0.9 from TNF inhibitors, 4.6 ± 1.7 to 3.6 ± 1.1 from TCZ and 5.5 ± 1.4 to 3.6 ± 1.0 from ABT in 24 weeks (respectively, $P < 0.01$). The average rates of change of DAS28-ESR with Tofa during 24 weeks were $-33.7 \pm 17\%$ from csDMARDs, $-31 \pm 20\%$ from TNF inhibitors, $-12 \pm 32\%$ from TCZ and $-34 \pm 17\%$ from ABT. [Conclusions] Tofa was effective after switching from all kinds of DMARDs including biological agents. Lower reduction rate of DAS28-ESR in patients treated with TCZ seems to be due to lower baseline DAS28-ESR at the start of Tofa.

W39-5

7 RA patients passed more than one year after discontinuation of concomitant MTX by the treatment with tofacitinib (TOF)

Keio Ayabe, Akira Inoue, Takuro Okari
Keiyu Orthopedic Hospital Gunma Japan

Conflict of interest: None

[Objectives] We performed reducing and discontinuation of MTX for RA patients good in progress out of the concern such as decline in age of the renal function, pulmonary obstacles, other many complications or lymphoproliferative disorders in Keiyu Orthopedic hospital from several years ago. We reduced and discontinued concomitant MTX for the patients under treatment with biologics and JAK inhibitor equally in progress if good. This study aims to evaluate the effect of tofacitinib (following TOF) for RA patients after discontinuation of concomitant MTX. [Methods] Seven of 34 RA patients passed more than three years after the initiation of the treatment with TOF by August, 2015 from December, 2013 apply in Keiyu Orthopedic Hospital. The seven patients (3 males 4 females; mean age: 68.7 years old) passed more than one year after discontinuation of concomitant MTX by the treatment with TOF. We examined the progress such as changes of the disease activity and laboratory data for them. [Results] Mean DAS28CRP was improved (baseline/3 years after dosage: 3.3/2.1) in spite of discontinuation concomitant MTX. [Conclusions] Tofacitinib is the drug which can reduce and discontinue concomitant MTX.

W40-1

Chronic damage in elderly-onset ANCA associated vasculitis

Keiji Ohashi, Ken-ei Sada, Yosuke Asano, Keigo Hayashi, Yuriko Yamamura, Sumie Asano Hiramatsu, Michiko Morishita, Haruki Watanabe, Mariko Narazaki, Yoshinori Matsumoto, Tomoko Kawabata, Jun Wada

Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Conflict of interest: None

Background: Characteristics of chronic damage in patients with elderly onset antineutrophil cytoplasmic antibody-associated vasculitis (AAV) are not fully elucidated. Method: Thirty-two patients with microscopic polyangiitis or granulomatosis with polyangiitis, diagnosed and treated at Okayama University Hospital from 2009 to 2013, were enrolled. The patients were divided into two groups based on age of onset: elderly onset group, onset ≥ 70 years; control group, onset < 70 years. We compared the Vasculitis Damage Index (VDI) at 18-24 months after the initiation of treatment between two groups. Result: Mean age of elderly onset and control group were 77 and 61 years, respectively. There was no significant difference in sex, type of vasculitis, disease activity at baseline and total VDI. As for each organ damage, elderly onset group had significant higher score in musculoskeletal (0.35 vs 0 , $p = 0.013$) and neuropsychiatric involvement (0.65 vs 0.20 , $p = 0.05$) than control group. 'Significant muscle atrophy or weakness' in musculoskeletal and 'peripheral neuropathy' in neuropsychiatric damage were the most frequent items. Conclusion: More rapid tapering of glucocorticoids and earlier initiation of rehabilitation might be required for patients with elderly onset AAV highly.

W40-2

Clinical significance of podocyte foot process effacement in ANCA-associated vasculitis

Yoshinobu Fuke¹, Yusuke Murata¹, Seiichiro Hemmi¹, Takamasa Nozaki², Noboru Kitamura², Takayuki Fujita³, Masami Takei², Masanori Abe¹

¹Division of Nephrology, Hypertension and Endocrinology, Nihon University, School of Medicine, Tokyo, Japan, ²Division of Hematology and Collagen Disease, Nihon University, School of Medicine, Tokyo, Japan, ³Department of Nephrology and Blood Purification, Yokohama Chuo Hospital

Conflict of interest: None

[Object] ANCA-associated vasculitis (AAV) is characterized by necrotizing lesions and crescent formations in kidney, frequently leading to rapidly progressive glomerulonephritis. Podocyte injury is well known to involve in the pathogenesis of urinary protein (UP) and glomerulosclerosis in various glomerular diseases, however few studies have been assessed in AAV. This study aims to provide clinical significance of podocyte foot process effacement (FPE) in AAV. [Methods] 27 adults with AAV were studied. FPE rates were calculated by $FPE \text{ length} / GBM \text{ length} \times 100$ (%) on electron micrograph. We analysed relationships between FPE rate and, laboratory and renal pathological findings. [Results] Mean FPE rate was $42.2 \pm 13.4\%$. FPE rate was correlated with UP ($r = 0.615$, $p < 0.001$), and negatively with Ccr ($r = -0.496$, $p < 0.005$). There was strong correlation between FPE rate and global sclerotic glomeruli+crescentic glomeruli/all glomeruli rate ($r = 0.750$, $p < 0.001$). In Histopathologic classification of ANCA-associated glomerulonephritis, FPE rate of focal class ($n = 12$: 33.8 ± 10.8) was significantly lower than, crescentic class ($n = 4$: 53.4 ± 11.1) and mixed class ($n = 10$: 45.2 ± 10.0) ($p < 0.05$). [Conclusions] Expanded FPE suggesting podocyte injury might involve progression of the renal injury and the prognosis in AAV.

W40-3

Evaluation of clinical and pathohistological features of renal biopsy proven ANCA associated vasculitis: single center study

Taro Horino, Satoshi Inotani, Tatsuki Matsumoto, Yoshiko Shimamura, Kosuke Inoue, Yoshio Terada

Department of Endocrinology, Metabolism and Nephrology, Kochi Medical School, Kochi University

Conflict of interest: None

[Object] Our goal is to assess the clinical and pathohistological features of ANCA associated vasculitis with glomerulonephritis. [Methods] 28 patients with MPO-ANCA associated vasculitis who had been admitted to our hospital and undergone renal biopsy from 2007 to 2018 were enrolled. [Results] Female were 13 (46.4%). Mean age was 70.7±1.9 years old. According to Watt's algorithm, EGPA, GPA and MPA patients were 5 (17.8%), 5 (17.8%), and 18 (64.2%), respectively. Pathohistological classification of renal biopsy were as follows; sclerotic 5 (17.8%), focal 18 (64.2%), crescentic 4 (14.2%), and mixed 1 (3.5%). 19 patients had good prognosis, while 9 patients (3 need RRT) had poor. Duration of hospitalization was positively related to Hb and negatively related to initial dosage of PSL. UPE was positively related to Cr levels and negatively related to Mg levels. Sclerotic change of renal histology, but cellular crescent, was positively associated with renal prognosis. [Conclusions] Our data suggests that chronic lesions such as global sclerosis in kidneys could cause poor renal prognosis, while active lesions cellular crescent might have good response for therapies.

W40-4

Urinary inflammatory cell analysis reflects the renal histopathology in ANCA-associated vasculitis

Masanori Sudo¹, Yoko Wada¹, Ayako Wakamatsu¹, Yukiko Nozawa¹, Hiroe Sato², Daisuke Kobayashi¹, Takeshi Nakatsue¹, Takeshi Kuroda², Masaaki Nakano³, Ichiei Narita¹

¹Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan, ²Niigata University Health Administration Center, Niigata, Japan, ³School of Health Sciences, Faculty of Medicine, Niigata University Division of Medical Technology, Niigata, Japan

Conflict of interest: None

[Object] To investigate the utility of urinary inflammatory cell analysis for accessing renal pathological injury in ANCA-associated vasculitis (AAV). [Methods] Thirty-six AAV patients who had been referred to Niigata University Hospital between 2002 and 2018, and performed percutaneous kidney biopsy and urinary inflammatory cell analysis, were participated in this study. The pathological findings were classified into Berden's classification (a method to categorize glomerular lesions into four classes) and Neumann's classification (a method to evaluate glomerular, tubulointerstitial, and vascular lesions by using activity index (AI) and chronicity index (CI)). The correlations between the results of both methods and the number of urinary inflammatory cells were examined. [Results] The number of urinary inflammatory cells showed a trend of increase in Crescentic category without statistical significance in Berden's classification. Meanwhile, AI had significant correlation with the number of urinary CD3 positive cells ($r = 0.541$, $p < 0.001$), CD14 positive cells ($r = 0.354$, $p = 0.034$), and total inflammatory cells ($r = 0.449$, $p = 0.006$) in Neumann's classification. [Conclusions] Urinary inflammatory cell analysis may be useful measure to infer the active lesions of kidney in AAV.

W40-5

Clinical study of rituximab maintenance therapy according to demand for patients with refractory granulomatosis with polyangiitis with renal dysfunction

Miho Karube, Yuko Ozawa, Noriko Ikegaya, Soko Kawashima, Takahisa Kawakami, Kazuhito Fukuoka, Yoshinori Komagata, Shinya Kaname
First Department of Internal Medicine, Nephrology and Rheumatology, Kyorin University School of Medicine

Conflict of interest: None

[Objective] RTX treatment of refractory GPA patients compared B cell suppression and onset of vasculitis in On Demand and periodic treatment. [Methods] The subjects were 2 patients who underwent RTX treatment irregularly in response to elevated B cells due to impaired renal function. Six patients on routine treatment had normal renal function and infused with RTX approximately every 6 months. Both groups were observed for 24 weeks to 36 weeks. [Results] Renal function of on-demand

patients was less than eGFR 45 ml/min/1.73 m². Both RTX doses were 375 mg/m² once. Serum IgG decreased from 799.5 mg/dl to 458.5 mg/dl after 6 months. CD19 positive change averages 8.5 months. One patient had relapse of vasculitis. The patient's interval of administration was 20 months. On the other hand, 6 patients who had normal renal function and regularly administered RTX did not show decrease in serum IgG or B cell positivity and did not show recurrence of vasculitis. [Conclusions] Refractory GPA with impaired renal function sustains low serum IgG values even on-demand treatment. However, because there is fear of relapse of vasculitis due to prolonged administration interval, prompt RTX treatment is desired after elevating at least CD 19 while paying attention to infectious diseases.

W40-6

Responsiveness to immunosuppressive treatment of lung abnormalities on chest computed tomography and the relevance of initial therapy for remission induction in patients with microscopic polyangiitis

Mieko Yamagata^{1,2}, Kei Ikeda², Takashi Itoh^{2,3}, Hirotohi Kawashima^{3,5}, Daisuke Kashiwakuma³, Shin-ichiro Kagami³, Itsuo Iwamoto³, Daiki Nakagomi^{1,4}, Takao Sugiyama¹, Shunsuke Furuta^{2,6}, David Jayne⁶, Hiroshi Nakajima²

¹Department of Rheumatology, National Hospital Organization Shimoshizu Hospital, Yotsukaido, Chiba, Japan, ²Department of Allergy and Clinical Immunology, Graduate School of Medicine, Chiba University, Chiba, Japan, ³Research Center for Allergy and Clinical Immunology, Asahi General Hospital, Asahi, Chiba, Japan, ⁴Department of Internal Medicine 3 Faculty of Medicine, University of Yamanashi, Chuo, Yamanashi, Japan, ⁵Department of Rheumatology and Allergy, Japanese Red Cross Narita Hospital, Narita, Chiba, Japan, ⁶Lupus and Vasculitis Clinic, Addenbrooke's Hospital, Cambridge University Hospitals, Cambridge, UK

Conflict of interest: None

[Object] A wide variety of lung abnormalities on the chest computed tomography (CT) can be identified in patients with microscopic polyangiitis (MPA). We aimed to determine the responsiveness of lung lesions to immunosuppressive therapy and investigated the responsiveness to treatment and what kind of treatment. [Methods] We retrospectively identified 76 MPA patients whose chest CT images before and within 3 months after treatment were available. We determined the presence and the responsiveness to treatment (improved/unchanged/worsened) of a total of 22 CT imaging components. We examined the relevance between responsiveness and treatment. [Results] For interstitial lung lesions were responsive, grand glass opacity (GGO) improved in 22 patients, interlobular septal thickening in 21, consolidation in 21. For airway and pleural lesions, bronchiolitis improved in 32, bronchial wall thickening in 21, pleural thickening in 10. We treated by prednisolone 40mg/day (median dosage). The 50 patients received intravenous cyclophosphamide pulse therapy (IVCY), and 16 methylprednisolone pulse therapy. Most of the them whose GGO was improved were received IVCY. (improved: 20 of 22, unchanged/worsened: 30 of 54, $P = 0.0061$) [Conclusions] The improvement of GGO was relevant to use of IVCY.

W41-1

Two distinct subsets of low density granulocytes in ANCA associated vasculitis

Akiko Endo, Yoshinori Komagata, Soko Kawashima, Noriko Ikegaya, Takahisa Kawakami, Kazuhito Fukuoka, Miho Karube, Shinya Kaname
Division of Nephrology & Rheumatology, First Department of Internal Medicine, Kyorin University School of Medicine

Conflict of interest: None

[Object] Low density granulocyte (LDG), a proinflammatory population of neutrophils, has been shown to contribute to lupus pathogenesis. We investigated the characteristics of LDG in ANCA associated vasculitis (AAV) patients. [Methods] LDGs were assessed using cell surface expression of CD14 low~intermediate and CD15 high and isolated by CD66b positive selection. We examined the ability of NETs formation of AAV-LDGs, AAV Normal density granulocytes (NDGs) and healthy controls NDGs and performed comparative proteomic analysis among those

cells. [Results] LDG frequencies were higher in AAV patients. AAV-LDG showed higher ability of NETs formation relative to NDG. We identified two subsets of AAV-LDG, CD10 positive LDG showing mature neutrophil characteristics and CD10 negative LDG showing immature granulocyte characteristics. Although the frequency of CD10 positive LDG decreased along with disease activity, the frequency of CD10 negative LDG increased. Comparative proteomic analysis revealed common protein were upregulated in both populations of LDGs. The expression of protein in granules of CD10 negative LDGs revealed they are immature granulocytes. [Conclusions] CD10 positive LDG and CD10 negative LDG were distinct subset each other and they may have different roles in AAV.

W41-2

Serum TIMP1 level as a disease activity marker in ANCA-associated vasculitis patients during induction and maintenance therapy

Jun Ishizaki¹, Takuya Matsumoto¹, Koichiro Suemori¹, Eiji Sada², Katsuto Takenaka¹, Hitoshi Hasegawa¹

¹Department of Hematology, Clinical Immunology, and Infectious Diseases, Ehime University Graduate School of Medicine, Toon, Ehime, Japan, ²Department of Medical Technology, Ehime Prefectural University of Health Sciences

Conflict of interest: None

[Object] We have reported that TIMP1 was the best-performing biomarker of disease activity before treatment and at 6 months after treatment in ANCA-associated vasculitis (AAV). We examine whether the levels of serum TIMP1 are useful as a disease activity marker during induction and maintenance therapy. [Methods] The subjects were 24 AAV patients. Serum TIMP1 levels were measured by ELISA using serum samples collected serially from December 2017 to October 2018. Remission was defined as BVAS (ver.3) of 0, and relapse was defined as the newly present or worse of one or more symptoms of BVAS. [Results] Of the 5 new-onset patients, the TIMP1 levels in 3 remission patients rapidly decreased at 2 to 3 months after induction therapy, but those in 2 non-remission patients remained high. The TIMP1 levels of 16 patients who kept in remission had a median value of 138 ng/mL, which is almost same to healthy subjects. In the 3 relapsed cases, TIMP1 levels were elevated and were significantly higher than the remission group. Moreover, TIMP1 levels at 3 or 6 months before relapse were high. [Conclusions] Serum TIMP1 level was suggested to be a useful marker for judgment of the remission and prediction of relapse in AAV.

W41-3

the research of circulating cell free DNA in anca associated vasculitis as a bio-marker

Tepei Hashimoto¹, Yuichi Yokoyama², Mai Morimoto¹, Naoto Azuma¹, Kohsuke Yoshida³, Akira Hashiramoto³, Kiyoshi Matsui¹

¹Department of Rheumatology, Hyogo College of Medicine, ²Department of Rheumatology, Hyogo Prefectural Nishinomiya Hospital, ³Department of Biophysics, Kobe University Graduate School of Health Sciences

Conflict of interest: None

[Objective] ANCA associated vasculitis (AAV) patients may be fatal course at a few weeks and required the bio-markers or prognostic factors. Fragmented cell-free DNA (ccf-DNA) is released into blood circulation as results of damage or death of cells, and it is significantly increased in those of cancer patients and inflammatory disease to be used in monitoring disease activities. In AAV, it is not clear whether the concentration of ccf-DNA is useful bio-maker, however it is possible to be increased associated with vascular endothelial cells injury and neutrophil extracellular traps. [Method] The study group includes 8 patients with EGPA, 7 MPA and 8 GPA. The concentration of ccf-DNA in serum was measured by quantitative real-time PCR before and after therapy, and 10 healthy individuals. We also evaluated the correlation between ccfDNA and the clinical activity. [Result] The concentration of ccf-DNA before therapy in EGPA patients was higher than healthy individuals ($p < 0.001$) MPA ($p < 0.001$) and GPA ($p < 0.001$). After therapy, it was decreased in EGPA patients, not changed in MPA and GPA. It was also correlated with BVAS in EGPA patients. [Conclusion] Considering to the result, ccf-DNA may be associated with eosinophils released. Ccf DNA is useful biomarkers in

EGPA patients.

W41-4

Low serum complement C3 is a risk factor for relapse of antineutrophil cytoplasmic antibody-associated vasculitis

Sotaro Nakajima

National Center for Global Health and Medicine

Conflict of interest: None

[Object] This study aimed to reveal the value of low serum complement C3 in predicting the risk of relapse with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). [Methods] We conducted a retrospective analysis of 83 consecutive patients who were diagnosed with AAV at our hospital from 1999 to 2018. The association between C3 level and relapse-free time was analyzed. [Results] Ten cases (13%) had a low C3 level (< 90 mg/dL), and there were no significant differences in onset age, sex, disease type, and ANCA subtype. A low C3 level was significantly associated with the percentage of patients who achieved remission (70% vs. 94%; $p = 0.03$). Among them, the median relapse-free time was significantly shorter in the low C3 group [8 months; 95% confidence interval (CI) 3-NA] than the control group (64 months; 95%CI 46-123, $p = 0.008$). The data were corrected by multiple logistic regression analysis with age, sex, disease type, ANCA subtype, Five Factor Score, lung involvement, and cardiac involvement reported as risks of relapse in the past. Low complement was still related to relapse ($p = 0.02$, hazard ratio 5.26, 95%CI 1.37-20.28). [Conclusion] We found that a low C3 level at diagnosis was significantly associated with the relapse ratio in AAV patients.

W41-5

Effectiveness and safety of concomitant cyclophosphamide as remission induction therapy for antineutrophil cytoplasmic antibody-associated vasculitis; a propensity score-matched analysis of RemIT-JAV and RemIT-JAV-RPGN

Haruki Watanabe¹, Ken-ei Sada¹, Masayoshi Harigai², Hirofumi Makino³

¹Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, ²Department of Rheumatology, School of Medicine, Tokyo Women's Medical University, Tokyo, Japan, ³Okayama University, Okayama, Japan

Conflict of interest: Yes

[Object] To evaluate effectiveness and safety of concomitant cyclophosphamide (CY) for patients with microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA). [Methods] Newly diagnosed MPA and GPA patients were enrolled from two prospective cohort studies. A propensity score (PS) for the use of CY was calculated using age, types of vasculitis, renal function, disease activity, disease severity and glucocorticoids (GC) dosage. After PS-matching, outcomes were compared between 94 patients with CY (CY group) and 94 without CY (non-CY group). [Results] Baseline characteristics were balanced except for MPO-ANCA positivity (87% in CY vs. 97% in non-CY, $p = 0.028$). Six-month-remission rates were comparable while the proportion of the remission with prednisolone dose of ≤ 10 mg/day tended to be more frequent in CY group than non-CY group (47% vs. 32%, $p = 0.052$). Overall, relapse-free, and end-stage renal disease-free survival rates, Vasculitis Damage Index, and serious infections were comparable between the two groups. GC doses at each time points were lower in CY group than non-CY group (0.19 vs. 0.27 mg/kg/day at Month 6, $p < 0.0001$; 0.14 vs. 0.18 at Month 12, $p = 0.0047$; and 0.09 vs. 0.14 at Month 24, $p = 0.0024$). [Conclusions] GC sparing effect of concomitant CY was demonstrated.

W41-6

Association study of MUC5B and TERT polymorphisms with interstitial lung disease in ANCA-associated vasculitis

Aya Kawasaki¹, Ken-ei Sada², Fumio Hirano^{3,4}, Shigeto Kobayashi⁵, Hidehiro Yamada⁶, Hiroshi Furukawa^{1,7}, Kenji Nagasaka⁸, Takahiko Sugihara⁹, Aika Suzuki¹⁰, Kunihiro Yamagata¹¹, Takayuki Sumida¹², Shigeto Tohma^{7,13}, Sakae Honma¹⁰, Shoichi Ozaki¹⁴, Hiroshi Hashimoto¹⁵,

Hirofumi Makino¹⁶, Yoshihiro Arimura¹⁷, Masayoshi Harigai¹⁸, Naoyuki Tsuchiya¹

¹Molecular and Genetic Epidemiology, University of Tsukuba, Tsukuba, Japan, ²Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Okayama, Japan, ³Department of Rheumatology, Tokyo Medical and Dental University, Tokyo, Japan, ⁴Department of Lifetime Clinical Immunology, Tokyo Medical and Dental University, Tokyo, Japan, ⁵Department of Internal Medicine, Juntendo University Koshigaya Hospital, Koshigaya, Japan, ⁶Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan, ⁷Clinical Research Center for Allergy and Rheumatology, Sagami Hospital, Sagami, Japan, ⁸Department of Rheumatology, Ome Municipal General Hospital, Tokyo, Japan, ⁹Department of Medicine and Rheumatology, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan, ¹⁰Department of Respiratory Medicine, Toho University, Tokyo, Japan, ¹¹Department of Nephrology, University of Tsukuba, Tsukuba, Japan, ¹²Department of Internal Medicine, University of Tsukuba, Tsukuba, Japan, ¹³National Hospital Organization Tokyo National Hospital, Tokyo, Japan, ¹⁴St. Marianna University School of Medicine, Kawasaki, Japan, ¹⁵Juntendo University School of Medicine, Tokyo, Japan, ¹⁶Okayama University, Okayama, Japan, ¹⁷Department of Nephrology and Rheumatology, Kyorin University, Tokyo, Japan, ¹⁸Department of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

Conflict of interest: None

[Object] Interstitial lung disease (ILD) is associated with poor prognosis in ANCA-associated vasculitis (AAV). A proportion of patients with idiopathic pulmonary fibrosis (IPF) are positive for MPO-ANCA and develop microscopic polyangiitis, suggesting that ILD in AAV and IPF may share some pathogenic processes. Recently, in an international collaboration study, we reported that *MUC5B*, an IPF susceptibility gene, was associated with presence of ILD in the patients with rheumatoid arthritis. In this study, we examined whether *MUC5B* and another IPF susceptibility gene *TERT* are associated with ILD in AAV. [Methods] Association of *MUC5B* rs35705950 and *TERT* rs2736100 was tested in 477 AAV, including 150 MPO-ANCA positive AAV (MPO-AAV) with ILD and 198 MPO-AAV without ILD, and 4366 controls. [Results] *MUC5B* rs35705950T was increased in MPO-AAV with ILD compared with controls ($P=0.0013$, odds ratio [OR] 4.44) and MPO-AAV without ILD ($P=0.024$, OR 9.44). No significant association of *TERT* rs2736100 with ILD was observed when only ILD positive MPO-AAV was tested. However, association was observed when all MPO-AAV was compared with controls ($P=2.7 \times 10^{-4}$, OR 1.34). [Conclusions] *MUC5B* was associated with ILD in AAV. In addition, *TERT* was associated with MPO-AAV, regardless of the presence of ILD.

W42-1

Predictors of Deterioration of IgG4-Related Disease in Untreated Patients with IgG4-Related Disease

Ichiro Mizushima¹, Masahiro Konishi¹, Hajime Sanada¹, Kazuyuki Suzuki¹, Akari Takeji¹, Satoshi Hara¹, Kiyoaki Ito¹, Takashi Kawane², Hiroshi Fujii¹, Kazunori Yamada¹, Mitsuhiro Kawano¹
¹Department of Rheumatology, Kanazawa University Hospital, Kanazawa, Japan, ²Department of Nephrology, Rheumatology, and Infectious Diseases, Toyama Red Cross Hospital

Conflict of interest: None

[Object] This study aimed to clarify the outcomes of untreated patients (Pts) with IgG4-RD and the factors related to the outcomes. [Methods] We retrospectively evaluated clinical features including laboratory data and involved organs at diagnosis in 107 Pts with IgG4-RD. Among them, 27 Pts were followed up without treatment after the initial diagnosis. Age- and sex-adjusted logistic regression analysis was performed to assess factors related to deterioration of IgG4-RD. [Results] The Pts comprised 73 men and 34 women (mean age 65.7 years). The 27 untreated Pts had significantly lower IgG4-RD responder index (10.8 vs 13.8, $P=0.048$) and fewer affected organs (1.9 vs 3.0, $P=0.001$) than did the 80 Pts who underwent treatment. Of these 27 Pts, 8 experienced deterioration of IgG4-RD. In logistic regression analysis, serum IgG4 elevation (per 100 mg/dL, odds ratio 1.194, 95% confidence interval 1.017-1.402) was the only significant factor related to deterioration of disease in un-

treated Pts, whereas serum IgG4 levels did not relate to deterioration in Pts who underwent treatment. [Conclusions] The present study suggests that serum IgG4 levels may be useful to predict the outcomes of untreated Pts with IgG4-RD, who tend to have fewer affected organs and lower IgG4-RD responder index.

W42-2

Relationship between therapeutic response of IgG4-related disease by cluster analysis and pretreatment serum cytokine levels

Motohisa Yamamoto¹, Satsuki Aochi², Chisako Suzuki¹, Satoko Nakamura³, Saho Honda⁴, Rieko Murakami⁴, Hiroki Takahashi¹

¹Department of Rheumatology and Clinical Immunology, Sapporo Medical University School of Medicine, ²Department of Internal Medicine, Japan Self Defense Force Sapporo Hospital, ³Department of Rheumatology, Hokkaido Orthopedic Memorial Hospital, ⁴Department of Rheumatology, JR Sapporo Hospital

Conflict of interest: None

[Object] With regard to prediction of therapeutic response, we could previously divide the cases with IgG4-related disease (IgG4-RD) into four groups by the cluster analysis based on the clinical data at the first visit. The two groups (cluster 1/3) presented with high frequency of the relapse and necessity of higher dose of glucocorticoid as maintenance treatment. On the other hand, the maintenance dose of glucocorticoid was lower and the rate of drug-free remission was higher in the patients with cluster 4. Therefore, we aimed to measure the pretreatment serum cytokine levels in each group and to extract the cytokines related to this disease. [Methods] The objects were 52 IgG4-RD cases, who visited to our hospital. They were already divided into four clusters by previous cluster analysis. We analyzed the levels of pretreatment serum cytokines in each group. [Results] There was significant difference in the serum IL-5 concentrations between cluster 1/3 and 4. [Conclusions] It is considered that several cytokines are involved in the pathogenesis and regulate the therapeutic responses in IgG4-RD. It is especially suggested that elevated levels of serum IL-5 lead to increase the maintenance dose of glucocorticoid and occur the relapse.

W42-3

Validation of the diagnostic criteria for IgG4-related kidney disease 2011: a single center experience

Takako Saeki¹, Tomoyuki Ito¹, Maasa Tamura², Hajime Yamazaki¹, Ichiei Narita³

¹Department of Internal Medicine, Nagaoka Red Cross Hospital, ²Department of General Medicine, Nagaoka Red Cross Hospital, ³Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences

Conflict of interest: None

[Object] To validate the diagnostic criteria for IgG4-related kidney disease (IgG4-RKD) 2011. [Methods] Seventeenth patients with renal abnormalities, in whom the serum levels of IgG4 and/or IgG4-positive plasma cells were evaluated histopathologically between 2012 and 2018 at Nagaoka Red Cross Hospital, were classified according to the diagnostic criteria for IgG4-RKD 2011. The final clinical diagnosis for each patient was based on the attending physician's opinion. [Results] Among 17 patients, the final diagnosis was IgG4-RKD in 8 and non-IgG4-RKD in 9. Of the 8 patients with IgG4-RKD, 7 were classified as definite IgG4-RKD. However, one patient who had tubulointerstitial nephritis with abundant IgG4-plasma cell infiltration with fibrosis, but without storiform fibrosis in the renal pathology was classified as possible IgG4-RKD. Of the 9 non-IgG4-RKD patients, 6 were classified as possible IgG4-RKD and 3 as unlikely IgG4-RKD. [Conclusions] The IgG4-RKD criteria 2011 are useful for diagnosis of IgG4-RKD and their specificity is high. However, "storiform fibrosis" as a requirement for diagnosis of definite or probable IgG4-RKD might decrease the sensitivity.

W42-4

Consideration concerning similarities and differences between ANCA-associated vasculitis and IgG-4 related diseases: case series and review of literature

Junichi Ishikawa, Shunjiro Kurihara, Kazuma Iida, Norihiro Mimura, Hirotohi Kawashima, Takao Yanagisawa, Masaki Hiraguri
Internal Medicine (Rheumatology, Allergy), Japanese Red Cross Narita Hospital

Conflict of interest: None

[Introduction] Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and immunoglobulin G4-related diseases (IgG4-RD) are regarded as entirely different disease types with different etiological mechanisms. However, we experienced two cases that had clinical features of both AAV and IgG4-RD. [Case presentations] The first case is an 81-year-old woman who showed periaortitis and retroperitoneal fibrosis with elevation of myeloperoxidase-ANCA and IgG4 levels. The second case is a 63-year-old woman who had dura mater, ear, nose, lung, and kidney involvement with serum negative for ANCA and elevated IgG4. Renal biopsy revealed tubulointerstitial nephritis involving IgG4+ plasma cells. On the other hand, lung biopsy showed features of AAV. These two cases suggested that AAV and IgG4-RD might overlap. To investigate the similarities and differences between AAV and IgG4-RD, we retrospectively analyzed 13 cases of AAV, and 13 cases of IgG4-RD at our hospital, and found some differences that can be useful in the differential diagnosis. [Conclusions] Although AAV and IgG4-RD are distinguishable based on characteristic findings in many cases, the diagnosis can be unclear in rare cases, in which clinicians should consider possible coexistence of AAV and IgG4-RD.

W42-5

A case of IgG4-related disease with pancytopenia due to hypophysitis and bone marrow involvement

Masahiro Sekiguchi, Yuichi Yokoyama
Division of Rheumatology, Department of Internal Medicine, Hyogo Prefectural Nishinomiya Hospital, Hishinomiya, Japan

Conflict of interest: None

[Case] An 82-year-old woman with malaise was referred because of anemia. Workup showed pancytopenia (white blood cells: 2,000/ μ l, hemoglobin: 8.5 g/dl, platelets: 14.7 \times 10⁴/ μ l), hyponatremia, hyperkalemia, hypocomplementemia, and β 2-microglobulin in urine, and markedly elevated IgG (6,538 mg/dl) and IgG4 (2,410 mg/dl) levels. Renal biopsy revealed interstitial nephritis and infiltration of IgG4-positive plasma cell (20/high-power field [HPF]). She was diagnosed with IgG4-related disease (IgG4-RD). MRI suggested hypophysitis, showing thickening of the hypophyseal stalk and pituitary enlargement. Moreover, infiltration of IgG4-positive plasma cells (20/HPF) was observed in myeloid tissue on bone marrow biopsy. Although resting serum cortisol and ACTH were within normal range, levels were relatively low. In this case, pancytopenia was thought to be influenced by secondary hypoadrenocorticism and/or bone marrow involvement due to IgG4-RD. Treatment with prednisolone (25 mg/day) resulted in rapid improvement in malaise. Pancytopenia and other laboratory findings were also improved with prednisolone. (Conclusion) Although IgG4-RD with pancytopenia is rare, it is possible that hypophysitis or bone marrow involvement due to IgG4-RD induced aberrant hematopoiesis.

W42-6

Is dyslipidemia a complication of IgG4RD ?

Kazuhiro Hatta, Hiroyuki Akebo, Hirofumi Miyake, Ryuichi Sada, Hiroyasu Ishimaru
Department of General Internal Medicine, Tenri Hospital

Conflict of interest: None

A 79-year-old female came to hematological department of our hospital, because of further exam of systemic lympho-adenopathy. Because FDG-PET scan showed pancreatic mass and aortic wall uptake. Laboratory data revealed ANA and RF positivity, she transferred to our depart-

ment. From pancreatic lesion and elevation of IgG4 value (900), she was diagnosed to have IgG4RD. In addition, high triglyceride value (900) and low HDL-cholesterol (20) were noted, and triglyceride increased to maximum to 263 mg/dl, which went down to 1200 mg/dl with anti-TG drug. Soon after corticosteroid started both values reached to within normal range. [Conclusions] This clinical course showed us that dyslipidemia might be a complication of IgG4RD.

W43-1

A case of IgG4 related disease diagnosed by pathological findings of ruptured subclavian aneurysm

Hyeryong Lee, Soko Kawashima, Hikaru Kukimoto, Takayuki Takahashi, Yoshinori Komagata, Shinya Kaname
First Department of Internal Medicine, Nephrology and Rheumatology, Kyorin University School of Medicine

Conflict of interest: None

Background: IgG4-related disease (IgG4-RD) is a disease of unknown showing swelling and nodular lesions of whole body organs by infiltration of IgG4-positive plasma cells. Arterial lesions arising from IgG4-RD are often reported in abdominal aorta. However, it is rare that the branch of aorta is involved and there are not any other involved organs than the artery. Case: A 70-year-old male who had a history of endovascular repair for abdominal aortic aneurysm 5 years ago was admitted into our emergency department because of hemoptysis. CT scanning showed a ruptured right subclavian artery aneurysm, and it perforated the trachea. The pathological findings of ruptured aneurysm from the cardiovascular operation revealed significant infiltration of IgG4 positive plasma cells into the vessel wall. We confirmed the diagnosis of IgG4-RD, in spite of no other organ involvements. He responded well to steroid therapy and the remission have been maintained after the dose reduction of steroid. Discussion: In our case, ruptured subclavian aneurysm was associated with IgG4-related aortitis. IgG4-related vascular lesions were observed the subclavian artery without multiple organs phenomenon. To our knowledge, this is the first report of a patient with ruptured subclavian aneurysm.

W43-2

Antibodies to IgG4 may participate the complement activation in patients with IgG4-related disease

Hiroshi Watanabe, Jumpei Temmoku, Yuya Fujita, Naoki Matsuoka, Makiko Furuya Yashiro, Tomoyuki Asano, Shuzo Sato, Hiroko Kobayashi, Kiyoshi Migita
Department of Rheumatology, Fukushima Medical University

Conflict of interest: None

[Object] To investigate the possibility that antibodies to IgG4 contribute to the activation of the complement pathway in IgG4-related disease (IgG4RD) with hypocomplementemia. [Methods] To determine which complement pathway was activated in patients with IgG4RD, we measured the ability of the complement capacity of all three pathways using WELISA method. Then, we measured the titer of antibodies to IgG4 in sera of IgG4RD patients. Complement-activating ability of antibodies to IgG4 in sera was determined with C4 deposition assay. [Results] We observed reduced complement activity in all complement pathways of sera of IgG4RD with hypocomplementemia. We also observed elevated levels of antibodies to IgG4 as well as C4 deposition in sera of IgG4RD patients with hypocomplementemia. [Conclusions] Antibodies to IgG4 may participate the complement activation in patients with IgG4RD by forming immune complex.

W43-3

The pathogenic roles of CCL18-CCR8 axis in patients with IgG4-related disease

Hiroto Tsuboi, Fumika Honda, Hanae Kudo, Yuko Ono, Saori Abe, Hiroyuki Takahashi, Yuya Kondo, Isao Matsumoto, Takayuki Sumida
Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: Yes

[Object] To clarify the protein expression and expressing cells, and the pathogenic roles of CCL18 and its receptor CCR8 in patients with IgG4-related disease (IgG4-RD). [Methods] 1) The protein expression and expressing cells of CCL18 in labial salivary glands (LSGs) were compared between IgG4-RD (N=3), Sjögren's syndrome (SS) (N=4), and healthy controls (HC) (N=5) by immunofluorescence (IF) staining. 2) The expression and expressing cells of CCR8 in LSGs were compared between 3 groups by IF. 3) The effects of the CCL18-CCR8 axis on total IgG, IgG2, and IgG4 production by PBMCs of HC stimulated with CD40L, IL-4, IL-10, and IL-21 were examined by in vitro assays. [Results] 1) In LSGs of IgG4-RD, CCL18⁺macrophages, DCs, and plasmacytes significantly increased than in SS and HC, and CCL18⁺B cells significantly increased than in HC (P<0.05). 2) CCR8 was similarly expressed in LSGs of IgG4-RD and SS, and CCR8⁺T, B cells, and plasmacytes were comparable between two groups. 3) CCL18 specifically and significantly enhanced IgG4 production by PBMCs stimulated with CD40L+IL-4+IL-10+IL-21 (P<0.05), while no effects on total IgG and IgG2. [Conclusions] CCL18-CCR8 axis was up-regulated in LSGs of IgG4-RD and enhanced IgG4 production, suggesting the pathogenic roles of this axis in IgG4-RD.

W43-4

Usefulness of PET/CT in IgG4 related diseases

Sosuke Tsuji¹, Yuya Fujita², Ayuko Takatani¹, Takashi Igawa¹, Toshimasa Shimizu¹, Remi Sumiyoshi¹, Tomohiro Koga¹, Shin-ya Kawashiri¹, Naoki Iwamoto¹, Kunihiro Ichinose¹, Hideki Nakamura¹, Tomoki Origuchi³, Atsushi Kawakami¹

¹Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ²Department of Rheumatology, Fukushima Medical University School of Medicine, Fukushima, Japan, ³Department of Rehabilitation Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: None

[Object] We analyzed cases of IgG4 related disease (IgG4-RD) who underwent PET/CT in our hospital and examined the usefulness of PET/CT in IgG4-RD. [Methods] This study included 20 IgG4-RD patients. We compared the findings of PET-CT with those of plain CT which was diagnosed as IgG4-RD from July 2005 to August 2017. [Results] The median age of the case was 58.4 ± 13.4 years. There were 13 males and 7 females. The median IgG4 was 690.2 ± 597.3 mg/dl. The median of initial dose of PSL was 30 mg. In the pathological tissues, 16 cases had IgG4 / IgG ≥ 40%. There were 16 cases in which PET/CT was performed before treatment and 4 cases were after treatment. The organs in which abnormal findings were pointed out by PET-CT, but not pointed out by CT was 5 in 13 submandibular glands, 3 out of 5 parotid glands, 1 out of 13 lymph node, 2 out of 2 thyroid glands, 2 out of 5 pancreases, 1 out of 4 aorta, and 1 out of 3 prostatic glands. [Conclusions] This study suggested that PET/CT was useful for detection of organs involvements, in particularly the parotid gland, submandibular gland and thyroid gland as compared with plain CT.

W43-5

Diffuse large B cell lymphoma of the prostatic gland arising from a patient with clinically and laboratory Castleman disease and pathologically IgG4 related disease

Keigo Setoguchi, Fangyi Chin, Hideyuki Takahashi, Sayaka Tsuzuki
Department of Systemic Immunological Diseases, Tokyo Metropolitan Komagome Hospital

Conflict of interest: None

A 66 year-old man presented with urinary retention due to prostatic gland swelling. Though, he had had lymphadenopathy (neck, axilla, inguinal, mediastinum and pelvic) and lymph node biopsy consisted with IgG4 related disease, his laboratory data showed anemia, hypergammaglobulinemia and serum high level of CRP. He had been clinically ob-

served as a Castleman disease without specific treatment. His serum level of PAS was within normal range. His prostatic hypertrophy was suspected of IgG4 related disease. His prostatic biopsy showed diffuse large B cell lymphoma. He was treated with chemotherapy (R-CHOP) and his urinary retention was improved. His laboratory findings suggesting Castleman disease were also improved.

W43-6

A case of IgG4-related disease (IgG4-RD) with ureteropelvic junction mass and tubulointerstitial nephritis (TIN) without imaging abnormality of the renal parenchyma

Tatsuhito Miyana^{1,2}, Ichiro Mizushima², Masahiro Konishi², Hajime Sanada², Kazuyuki Suzuki², Ryoko Hamano¹, Susumu Kitajima¹, Hiroaki Muramoto¹, Akari Takeji², Satoshi Hara², Kiyooki Ito², Takashi Kawane³, Hiroshi Fujii², Kazunori Yamada², Mitsuhiro Kawano²

¹Internal Medicine, JCHO Kanazawa Hospital, Kanazawa, Japan, ²Department of Rheumatology, Kanazawa University Hospital, Kanazawa, Japan, ³Department of Nephrology, Rheumatology, and Infectious Diseases, Toyama Red Cross Hospital

Conflict of interest: None

A 72 years-old man was admitted to our hospital because of progressive renal failure. He had been followed up for 18 years after surgical removal of bladder tumor. Six months before the present admission, periodic computed tomography (CT) revealed his right ureteropelvic junction mass. He was clinically diagnosed as right ureter cancer and received neoadjuvant therapy and right nephroureterectomy. Pathological study revealed IgG4-positive cell infiltration, obliterative phlebitis and storiform fibrosis in the removed mass, leading to the diagnosis of IgG4-RD. Moreover, there was IgG4-positive plasma cell infiltration in the right kidney although no imaging abnormality was detected by preoperative CT. Because renal function gradually worsened and IgG4-related tubulointerstitial nephritis (IgG4-TIN) in the left kidney was suspected, he was admitted. Close examinations suggested no IgG4-related extra-renal organ involvement neither imaging abnormality of the left kidney. However, glucocorticoid trial to treat suspected microscopic TIN resulted in an improvement of his renal function, suggesting that he had IgG4-TIN. The possibility of IgG4-TIN should be considered in IgG4-RD patients with renal dysfunction even if no imaging abnormality is observed.

W44-1

Efficacy and safety of secukinumab in Japanese patients with active ankylosing spondylitis: Results from an open-label, phase 3 study (MEASURE 2-J)

Mitsumasa Kishimoto¹, Atsuo Taniguchi², Brian Porter³, Sibylle Haemmerle⁴, Shigeto Kobayashi⁵

¹St. Luke's International University and St Luke's International Hospital, ²Tokyo Women's Medical University, ³Novartis Pharmaceuticals Corporation, ⁴Novartis Pharma AG, ⁵Juntendo Koshigaya Hospital

Conflict of interest: Yes

[Object] To assess the clinical efficacy, safety and tolerability of secukinumab (SEC) subcutaneous injections up to 52 weeks in Japanese patients with active AS [Methods] Thirty Japanese patients with active AS fulfilling modified NY criteria, with a score ≥4 on BASDAI and ≥4 cm spinal pain score on a VAS despite current or previous treatment with NSAIDs and/or anti-TNFα (TNFi) agents, were included. Patients received open-label SEC150mg at W0, 1, 2, 3, and 4, followed by treatment every 4 weeks. The primary outcome was ASAS20 response rate at W16. Overall safety and tolerability were also assessed [Results] Twenty-five subjects completed treatment up to W52. Response for the primary endpoint ASAS20 (70.0%) improved relative to baseline at W16. SEC was efficacious in both TNFi naïve patients and patients who failed prior TNFi therapy. These improvements were maintained throughout W52. ASAS20 response rate of HLA-B27 positive patients was 64.3% versus negative 75.0% at W16. AE rate was 86.7%, and 3 SAEs were reported. The most frequent AE was nasopharyngitis (50%) [Conclusions] SEC treatment improved the signs and symptoms of active AS in Japanese patients, with a similar safety profile as seen in past global SEC studies, demonstrating that SEC is a beneficial treatment option in AS

W44-2

Efficacy and safety of ixekizumab (IXE) in patients (pts) with active ankylosing spondylitis (AS)/radiographic axial spondyloarthritis (16-week results): COAST-V, a phase-3 randomized, active and placebo (PBO)-controlled study

Tetsuya Tomita¹, Ayako Konomi², Ko Nakajo², Fangyi Zhao³, Hilde Carlier³

¹Department of Orthopedic Biomaterial Science, Osaka University Graduate School of Medicine, Osaka, Japan, ²Eli Lilly Japan K.K., Kobe, Japan, ³Eli Lilly and Company, Indianapolis, IN, USA

Conflict of interest: Yes

[Object] To report efficacy and safety at Wk16 from the first 52 Wk phase-3 study to treat active AS pts with IXE. [Methods] Biologic DMARD-naïve pts with established diagnosis of AS with sacroiliitis defined radiographically via modified New York criteria were included. Pts were randomized to PBO, 80mg IXE Q2W or Q4W, or 40mg Q2W adalimumab (ADA). Primary endpoint was ASAS40 response at Wk16 and major secondary endpoint (msEP) included ASAS20, BASDAI50, etc. [Results] Of 341 randomized pts, 97% completed Wk16. Baseline demographics and disease characteristics were comparable among study arms (age:41.7yr, disease duration:16.0yr, BASDAI:6.7 [mean]). Significantly more pts achieved ASAS40 at Wk16 with IXEQ2W (52%) and IXEQ4W (48%) than with PBO (18%, p<.001). ASAS40 at Wk16 in ADA (36%) was also higher than PBO. Both IXE arms showed significantly greater improvements for all msEPs at Wk16 vs PBO. Among 7 pts enrolled in Jp, 1 pt enrolled in IXEQ4W arm achieved ASAS40, ASAS20 and BASDAI50 at Wk16, whereas 3 pts in PBO arm failed to respond. TEAE/SAE frequency was comparable among all arms. Majority of TEAE reported were mild or moderate. [Conclusion] Via 16 Wk IXE treatment, significant improvements in the signs and symptoms of AS were observed with no unexpected safety signals.

W44-3

Analysis of factors involved in radiographic changes in patients with ankylosing spondylitis

Kurusu Tada¹, Shigeto Kobayashi³, Eri Hayashi¹, Hisashi Inoue², Ken Yamaji¹, Naoto Tamura¹

¹Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, ²Department of Orthopaedic Surgery, Juntendo University School of Medicine, ³Department of Internal Medicine, Juntendo Koshigaya Hospita

Conflict of interest: None

[Object] The objective is to evaluate the radiographic change of ankylosing spondylitis patient with mSASSS (modified Stoke Ankylosing Spondylitis Spine Score) and to analyze factors involved in the radiographic progression. [Methods] We examined 46 patients who fulfilled the modified New York criteria and taking X-ray of the spine at intervals of 2 years or more. We evaluated radiographic changes with mSASSS, and classify patients with mSASSS increased by 2 or more in 2 years as progression group, less than 2 as non-progressive group. We analyzed the characteristics of each groups and factors involved in radiographic change. [Results] Of the 46 patients, 40 were male, the overall age was 41.7years old, and 38 patients (82.6%) were HLA-B27 positive. The observation interval of X-ray was 4.7years, the overall mSASSS change/2years was 2.36. In the mSASSS progression group, the change of score was 4.22, in the non-progressive group, the change was 0.93. Syndesmophyte at baseline was found in 17 patients (85%) in the progressive group and 12 (46.2%) in the non-progressive group, showing a significant difference. [Conclusions] The baseline syndesmophyte was associated as factor involved in the progression of radiographic changes in patients with ankylosing spondylitis.

W44-4

Risk factors for arthropathy in ulcerative colitis patients after post-total colectomy; a retrospective, a single center study

Kentaro Noda, Yuki Mizutani, Naohiro Sugitani, Yasuo Suzuki, Ayako Nakajima

Center for Rheumatic Diseases, Mie University Hospital

Conflict of interest: None

[Object] Ulcerative colitis (UC) is generally thought to become remission when patients undergo total colectomy. However, in clinical practice, patients often suffered from arthropathy which is thought as extra-colorectal findings even after total colectomy. In this study, we aimed to clarify the frequency and the risk for the occurrence of arthropathy after colectomy. [Methods] We analyzed the risk factors for arthropathy using patient background, activity of intestinal lesion, clinical and endoscopic severity classification by multivariate analysis retrospectively, among UC patients who underwent total colectomy in our hospital from January 2007 to November 2011. [Results] Among 123 patients after operation, 26 patients (22.2 %) patents have arthropathy, peripheral type in 15 (57.7 %), axial type in 2 (7.7 %), mixed type in 9 (34.6 %). Median [IQR] onset age of arthropathy was 39.0 (28.3-52.4) years, duration from operation to onset of arthropathy was 0.5 (0.2-1.1) years. The risk factors for arthropathy were grade of endoscopic severity (OR 5.0, p<0.05) and history of biologic therapy (OR 5.0, p<0.05). [Conclusions] High disease activity of endoscopic classification was risk factor of arthropathy. Thus, Disease activity of UC should be controlled to avoid developing arthropathy.

W44-5

Clinical features of Spondyloarthritis associated with inflammatory bowel disease in our institution

Masatoshi Kadoya, Takuya Yanagida, Satoshi Omura, Atsushi Omoto, Wataru Fukuda

Center for Rheumatic Disease, Japanese Red Cross Society Kyoto Dai-ichi Hospital, Kyoto, Japan

Conflict of interest: None

[Object] Spondyloarthritis (SpA) is a common extraintestinal complication in patients with inflammatory bowel disease (IBD). We examined the clinical features of IBD-related arthritis. [Methods] 11 patients with IBD-related arthritis visiting our institution were enrolled in the study. We investigated their clinical characters, clinical courses and treatments. [Results] The average age of patients was 49.8±16 years, and 3 were male. Among 11 cases, 9 cases were ulcerative colitis. 10 patients were peripheral SpA. Only one case was positive for ACPA (Anti-Citrullinated Protein Antibodies). 6 cases out of 11 were positive for ANA (anti nucleolar antibody). Their ANA patterns were homogenous and/or speckled. As for clinical courses, those who were positive for ANA, arthritis tend to occur later than those who were not. Concerning about treatments for IBD-related arthritis, 2 patients were observed without any medications. MTX was used in two cases, and Tacrolimus was administered in one case. Biologics were used in 6 cases. [Conclusions] Patients with IBD-related arthritis, their clinical courses may differ according to their ANA positivity.

W44-6

The prevalence or severity of clinical and radiographic axial spondyloarthritis in patients with inflammatory bowel disease

Tadashi Okano¹, Kentaro Inui¹, Koji Mandai¹, Yutaro Yamada¹, Yuko Sugioka², Tatsuya Koike^{2,3}, Hiroaki Nakamura¹

¹Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan, ²Center for Senile Degenerative Disorders (CSDD), Osaka City University Graduate School of Medicine, Osaka, Japan, ³Shirahama Foundation for Health and Welfare, Wakayama, Japan

Conflict of interest: None

[Object] The prevalence or severity of clinical and radiographic axial spondyloarthritis in patients with inflammatory bowel disease (IBD) such as ulcerative colitis (UC) and Crohn's disease (CD), was reserched by X-ray and MRI. [Methods] A total of 56 subjects, including 39 UC patients (19 males, 20 females) and 17 patients of CD (10 males, 7 females) were included. Imaging evaluation was performed blindly by two readers in X-ray and MRI. [Results] In X-ray, the average mSASSS score was 8.9 in patients with inflammatory back pain (IBP), and 6.5 (p = 0.257) in patients without IBP. There were 11 patients on bilaterally Grade 2 or uni-

lateral Grade 3 on mNY, 3 (27.3%) in patients with sacroiliac pain and 8 (17.8%) ($p = 0.477$) in the patients without sacroiliac pain. In spine MRI, there were 9 (42.9%) patients with SPARCC score more than 2 in patients with IBP and 9 (25.7%) ($p = 0.184$) in patients without IBP. In sacroiliac MRI, there were 1 (9.1%) patients with SPARCC score more than 2 in patients with sacroiliac pain and 12 (26.7%) ($p = 0.216$) in patients without sacroiliac pain. [Conclusions] Even without clinical symptoms, significant inflammatory findings were detected by MRI. Imaging might be important regardless of the presence or absence of clinical symptoms in patients with IBD.

W45-1

A subgroup analysis in the basis of the presence or absence of airway and ear involvement may be important for classification and treatment of relapsing polychondritis

Jun Shimizu¹, Yoshihisa Yamano², Kimito Kawahata³, Noboru Suzuki¹

¹Department of Immunology and Medicine, St. Marianna University School of Medicine, ²Institute of Medical Science, St. Marianna University School of Medicine, ³Division of Rheumatology and Allergology, St. Marianna University School of Medicine

Conflict of interest: None

[Object] We conducted an epidemiological survey of 239 patients with RP and obtained clinical information in 2014. Based on these data, we addressed how organ involvement in RP patients related to one another. [Methods] We assigned the numbers 1 and 0 to describe the presence and absence, respectively, of organ involvement and obtained a correlation matrix. [Results] From the correlation matrix, we found a significant inverse relationship between airway involvement and ear involvement. We then applied a subgroup analysis in the basis of airway involvement (A subgroup) and ear involvement (E subgroup). A and E subgroups included 19.7% and 49.4% patients, respectively. The remaining 29.3% patients formed third subgroup (O subgroup) with both A and E involvement. In the clinical data, progressive disease course were frequently observed in A and O subgroup compared with E subgroup. Two major poor prognostic factors, cardiovascular and CNS involvement, were frequently observed in E plus O subgroups compared with A subgroup. A subgroup patients did not develop cardiovascular involvement. [Conclusions] Subgroup analyses of patients with RP may provide new insights into the classification and treatment of RP.

W45-2

Clinical features of elderly onset Still's disease

Sayaka Takenaka, Takehisa Ogura, Chihiro Imaizumi, Yuto Takakura, Yuki Inoue, Hideki Ito, Norihide Hayashi, Ayako Hirata, Hideto Kameda Ohashi Hospital

Conflict of interest: None

[Object] It is said that the age of onset of adult onset Still's disease (AOSD) is often distributed between 16 and 35 years old. However, there are cases of onset in the elderly, therefore its clinical features are examined. [Methods] From May 2011 to October 2018, we extracted 20 cases of AOSD. In 6 cases of aged onset over 65 years old (age of onset is Age 65 to 84 years old, median 70.5 years old, 5 women) and 14 cases of under 65 years of age (age of onset is 26 to 53 years old, median 38 years old, 12 women). [Results] Typical eruption was 50% (80% under 65 years old) and lymph node swelling 50% (79% same) tended to be less in elderly onset cases. Therefore, comparing the number of applicable items of Yamaguchi et al's classification criteria, the median value of 5 items (7 items) was significantly lower in older onset ($p = 0.0056$). With regard to treatment, steroids were administered in all cases except for one case initiated at other hospitals, and pulse therapy was 20% (42.9% of the patients) with an aging episode, and the initial dose of steroids was 50 mg median prednisolone / day, And tocilizumab use was 20% (35% same). [Conclusions] The elderly onset AOSD tended to be less prone to typical rash or lymph node swelling.

W45-3

Steroid-sparing Effect of Tocilizumab on the Treatment of Adult Onset Still's Disease

Hiroshi Kataoka, Tomoko Tomita, Makoto Kondo, Masaya Mukai
Rheumatology and Clinical Immunology, Sapporo City General Hospital

Conflict of interest: None

[Object] To assess the efficacy and safety of Tocilizumab (TCZ) on the treatment of adult onset Still's disease. [Methods] Fifty-two patients who were registered as adult-onset Still's disease (AOSD) in the electric record in our hospital were listed for this study and in 24 patients of them, who had received treatment for over 3 months with complete data to evaluate treatment efficacy, we retrospectively analyzed CRP, ferritin in each of corticosteroid (CS) monotherapy group, CS+methotrexate (MTX) group and TCZ group. This study was certified by the ethical committee in our hospital. [Results] Seven patients of CS monotherapy (4 females; mean age 47, 3 males; mean age 33), 8 patients of CS+ MTX (all females; 57 y.o.) and 9 patients of TCZ (5 females; average age 48, 4 males; 37 y.o.) were analyzed in this study. There were no difference in initial CRP, ferritin and CS dose among three groups. In any of treatment group, CRP and ferritin were decreased by 3-month therapy. TCZ showed an advantage in lowering effect of CRP and tapering CS dose compared with MTX without serious health issue ($p=0.0092$ for CRP, $p=0.064$ for CS reduction). [Conclusion] In real world experience, TCZ was found to have promising CS sparing effect.

W45-4

Recovery period for prolonged thrombocytopenia in TAFRO syndrome: five encountered cases and literature review

Yuta Yamaguchi, Yuichi Maeda, Yumiko Mizuno, Mayu Yagita, Yusuke Manabe, Takayoshi Morita, Masayuki Nishide, Hyota Takamatsu, Toru Hirano, Masashi Narazaki, Atsushi Kumanogoh
Department of Respiratory Medicine and Clinical Immunology, Osaka University Medical Hospital, Osaka, Japan

Conflict of interest: None

[Objective] TAFRO syndrome is a newly proposed disease that is different from Castleman's disease. Generally, high-dose corticosteroids are used for treatment; however, other immunosuppressive therapies are administered in refractory cases. We aimed to determine the period required to recover from prolonged thrombocytopenia in TAFRO syndrome. [Methods] We included five encountered cases in this study; furthermore, we also evaluated 60 peer-reviewed reports that were obtained from PubMed. Recovery from thrombocytopenia was defined as a platelet count of more than 50,000/ μ L. Mortality and the cause of death were also monitored. [Results] Thrombocytopenia tended to last longer than other symptoms. In our four cases, the median period for the recovery was 43 days. In 41 cases of literature review, recovery from thrombocytopenia required 40 days. In our two cases, it suggested that D-dimer titers and platelet counts might be inversely correlated. Seven out of 60 cases were fetal, and 4 cases were due to infection. [Conclusions] It takes approximately 40 days to recover from thrombocytopenia associated with TAFRO syndrome. Therefore, when other symptoms are improving, physicians should not easily administer another immunosuppressant only for treatment of persistent thrombocytopenia.

W45-5

A case of autoimmune pancreatitis and autoimmune salivary glanditis by administration of nibormarb

Yuki Shimada¹, Yuji Akiyama²

¹Department of Supportive Oncology and Palliative Medicine, Saitama Medical University International Medical Center, Hidaka, Japan, ²Division of Rheumatology, Department of Internal Medicine, Ogawa Red Cross Hospital, Ogawa Town, Japan

Conflict of interest: None

[Case] A 75-year-old man. Nephrectomy was performed on renal cell carcinoma and treated with chemotherapy, but it was ineffective and changed to nibormab. He was aware of dry mouth and epigastralgia. In

blood test, Amylase 656U/l. Anti nuclear antibody and anti SS-A antibody, anti SS-B antibody were negative. IgG4 was 13.9 mg/dl. MRI revealed pancreatic head enlargement and a stenotic image in the main pancreatic duct. IgG4 was normal but diagnosed as AIP. Salivary gland scintigraphy showed a decrease in accumulation in salivary glands. Lip biopsy could not be done. Dry eye was diagnosed. He was diagnosed with autoimmune salivary glanditis. Administration of prednisolone (PSL) 1mg/kg/day to AIP was started. Symptoms improved, pancreatic enzymes decreased on the 2nd day of administration. Imaging findings also improved. Dry mouth improved, and salivary gland function improved. Pancreatic symptoms and dry mouth improved with PSL, but dry eye did not change. [Clinical significance] Adverse events of nibormab are versatile, adverse events due to immune reactions are often negative for autoantibodies. In this case an autoimmune mechanism may be considered. Since it may improve with PSL, we should be careful of dry mouth. after administration of nibormab.

W45-6

The ratio of serum MMP-3 to CRP is useful for distinguishing PMR-mimicking EORA from true PMR at the onset

Takeshi Suzuki¹, Yu Ser¹, Akitake Suzuki²

¹Division of Allergy and Rheumatology, Japanese Red Cross Medical Center, ²Department of Rheumatology, Mitsui Memorial Hospital

Conflict of interest: None

[Object] To determine the usefulness of serum MMP-3/CRP ratio, which may represent the proportion of synovial inflammation to whole (synovial and extra-synovial) inflammation, in distinguishing PMR-mimicking EORA from true PMR. [Methods] The medical records of patients who visited our hospitals for examination of PMR-like symptoms were retrospectively reviewed to identify patients who fulfilled the requirements: (i) 2012 PMR classification criteria were met; (ii) 2010 RA classification criteria were not met (Score <6); (iii) serum MMP-3 and CRP were measured on the same day before starting treatment with corticosteroids or DMARDs; (iv) the final diagnosis was confirmed as PMR or RA by the agreement between two certified rheumatologists who reviewed the clinical data during the one-year follow-up. [Results] Eight PMR-mimicking EORA patients and 29 PMR patients were found and analyzed. MMP-3/CRP ratio was significantly higher in PMR-mimicking EORA than in PMR (126×10^{-4} [127×10^{-4}] vs 29.2×10^{-4} [33.7×10^{-4}], median [IQR], $p=0.0021$). ROC analysis for MMP3/CRP ratio demonstrated AUC of 0.845 (95% CI: 0.641-1). [Conclusions] MMP-3/CRP ratio may be useful for distinguishing PMR-mimicking EORA from true PMR even when the classification criteria are not met.

W46-1

Clinical characteristics of late-onset patients having adult-onset Still's disease

Dai Kishida, Takanori Ichikawa, Satoru Ushiyama, Noriko Sakaguchi, Kenichi Ueno, Yasuhiro Shimojima, Yoshiki Sekijima
Department of Neurology and Rheumatology, Shinshu University School of Medicine, Matsumoto, Japan

Conflict of interest: None

[Object] Adult-onset Still's disease (AOSD) usually occurs in young adult. But we sometimes encounter patients of advanced age. Our aim was to evaluate the clinical characteristics about late-onset AOSD patients. [Methods] We retrospectively analyzed clinical features about 32 patients with AOSD between April 2008 and September 2018. Patients were divided into two groups based on the age of disease onset (65 years and older or not). [Results] Eleven patients (34.4%) experienced their first symptom at age ≥ 65 years. High fever (100%), arthritis (90.9%), and rash (90.9%) were common symptoms among them. The percentage of serositis (36.4%), hemophagocytic syndrome (36.4%), high ratio of neutrophils (72.7%), and elevated serum ferritin level (more than 3,000 ng/ml) (72.7%) were higher than early-onset patients. However, they indicated higher frequency in more than 3 cycles of methylprednisolone pulse therapy than early-onset patients despite lower that in administering immunosuppressant (54.3%) such as tocilizumab (18.2%). Infections required hospital treatment (54.5%) was more frequent in the late-onset

group. [Conclusions] Late-onset patients with AOSD tend to be more severe condition. They were treated mainly with glucocorticoids and we need to manage to decrease infections.

W46-2

Clinical significance of serum interleukin-18 level in the differential diagnosis of adult Still's disease and hemophagocytic syndrome

Toshihiko Shiga, Kazuya Kishimoto, Yuji Nozaki, Koji Kinoshita, Masanori Funauchi, Itaru Matsumura
Kindai University Hospital, Faculty of Medicine, Osaka, Japan

Conflict of interest: None

[Object] Adult Still's disease (ASD) is a systematic inflammatory disease that is associated with activation of macrophage. It has been suggested that IL-18 is associated with the pathogenesis of ASD. ASD shares several clinical and laboratory variables with hemophagocytic syndrome (HPS). So, It is difficult to differentiate these diseases. We evaluate the clinical significance of serum IL-18 level to differentiate ASD and HPS. [Methods] Thirty-six patients with ASD and Twenty-one patients with HPS, who were admitted to our hospital between January 2012 and October 2019, were enrolled. ASD patients were diagnosed according to Yamaguchi criteria. Serum concentration of CRP, LDH, GOT, GPT, ferritin, sIL-2R, IL-6 and IL-18 was determined in both ASD and HPS. [Results] The serum IL-18 level in ASD patients was significantly higher than that in HPS patients ($p<0.0001$), and that of sIL-2R was lower ($p<0.0001$). Between ASD and HPS, serum concentrations of CRP, LDH, GOT, GPT, ferritin, and IL-6 were not significantly different. IL-18 serum levels in AOSD patients positively correlated with serum ferritin levels ($r=0.6$, $p<0.0001$). [Conclusions] We argue that IL-18 can be a biomarker for differential diagnosis between AOSD and LAHS and be associated with activation of macrophage.

W46-3

The utility of serum IL-18 as a disease activity marker in adult onset Still's disease -IL-18 reflects remaining fever and rash in inactive patients-

Nanami Mino¹, Hiroaki Hatano², Hiroyuki Yamashita¹, Shinji Izuka¹, Toshiaki Kobayashi¹, Sotaro Nakajima¹, Kyoko Motomura¹, Shunta Kaneko¹, Yuko Takahashi¹, Hiroshi Kaneko¹

¹Department of Rheumatology, National Center for Global Health and Medicine, Tokyo, Japan, ²Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Conflict of interest: None

[Object] Monitoring of disease activity is crucial for preventing flares of adult-onset Still's disease (AOSD). This study aimed to reveal the utility of serum interleukin (IL)-18. [Methods] Twenty-seven patients treated at our hospital from 2014-2018 were enrolled. Serum markers [ferritin, C-reactive protein (CRP), and IL-18] and disease activity were analyzed. Patients were classified by Pouchot's score: ≥ 3 , active; <3 , inactive. Inactive patients with fever or evanescent rash were defined as "smoldering", and those without as "remission". [Results] The mean age was 38.2 years and there were seven males. IL-18 showed a moderate correlation with ferritin and CRP ($r_s=0.497$, 0.379 , respectively; both $p<0.001$) by Spearman's correlation test. IL-18 and ferritin showed a significant difference between active and inactive patients ($p<0.001$) by Mann-Whitney U-test. However, a significant difference between "smoldering" and "remission" patients was observed only in IL-18 ($p=0.004$), with a sensitivity of 70.4% and a specificity of 82.3% (IL-18 cutoff: 10807 pg/mL). [Conclusions] IL-18 was correlated with ferritin and CRP and was useful for evaluating AOSD activity. Moreover, IL-18 remained high in inactive cases with fever and rash; thus, IL-18 might be involved in their pathogenesis.

W46-4

Clinical features of 5 cases of immune checkpoint inhibitor-induced inflammatory arthritis

Takashi Hosokawa¹, Takeshi Kaneko¹, Tomomi Tada¹, Kenji Funakoshi¹, Shinichiro Nameki¹, Jun Fukui¹, Koji Nomura^{1,2}, Hiroshi Fujiwara¹

¹Division of Rheumatology, Osaka General Medical Center, Osaka, Japan, ²Division of Orthopedic Surgery, Osaka General Medical Center, Osaka, Japan

Conflict of interest: Yes

[Objectives] We aimed to determine the clinical features of immune checkpoint inhibitor-induced inflammatory arthritis. [Method] We analyzed the records of patients who were administered anti-PD-1 (programmed cell death-1) antibodies (nivolumab, pembrolizumab) and admitted to our hospital between September 2014 and October 2018. We examined patients showing an exacerbation of RA/polymyalgia rheumatica (PMR), as well as patients with new-onset arthritis resembling RA and PMR. [Results] We identified 4 patients with lung cancer and 1 with esophagogastric junction cancer. Two patients presented with exacerbation of pre-existing RA/PMR, 2 with new-onset arthritis similar to RA, and 1 with new-onset arthritis similar to PMR. Patients with new-onset arthritis demonstrated rapid improvement following the administration of 10-20 mg of prednisolone (PSL). However, patients presenting with exacerbation of pre-existing RA/PMR did not show noticeable improvement despite the administration of increased PSL doses. [Conclusion] New-onset arthritis and exacerbation of pre-existing arthritis after the administration of anti-PD-1 antibodies respond differently to low-dose PSL therapy. Further examination of patients is necessary in this regard.

W46-5

Usefulness of DMARDs for refractory polymyalgia rheumatica

Sho Tomozawa, Shohei Watanabe

Department of Orthopaedic Surgery, Japan Community Health Care Organization Uwajima Hospital

Conflict of interest: None

[Objective] This study is aimed to evaluate the usefulness of DMARDs for refractory polymyalgia rheumatica (PMR). [Methods] 60 patients (28 males, 32 females) of PMR were evaluated. The average age was 73.1 years old. Doses of 10-15mg oral prednisolone (PSL) were administered and decreased gradually. Remission and relapse was defined as, PSL free at the final examination and cases of exacerbation during treatment and PSL increased and/or DMARDs were added, respectively. Clinical laboratory tests, medication and clinical conditions were checked at both start and end of examinations. [Results] Before treatment, the average titers of CRP, ESR, RF and anti-CCP antibodies were 7.3 mg/dl, 72.1 mm/h, 11.4 U/ml and 15.6 U/ml, respectively. At the final examination, the average titers of CRP and ESR were 0.2 mg/dl and 20.6 mm/h, respectively. Cases of remission and relapse were 30 and 37, respectively. In relapsed cases, 22 were administered with DMARDs (IGU 15, TAC 7), and in 19 cases (IGU 12, TAC 7) doses of PSL were reduced to 5mg/day or less, 5 cases (IGU 2, TAC 3) were having remissions. [Conclusions] About half of PMR cases were having remissions. Using IGU and TAC for refractory PMR, doses of PSL were reduced or withdrawn. Both IGU and TAC were considered to be useful for PMR.

W46-6

Clinical characteristics of recent-onset polymyalgia rheumatica (PMR) -especially focused on peripheral joint involvement, ultrasonography (US) findings, and glucocorticoid-resistant cases-

Takayuki Wakabayashi, Noriko Sasaki, Yasuo Suzuki
Division of Rheumatology, Tokai University Hachioji Hospital, Tokyo, Japan

Conflict of interest: None

[Object] PMR is an inflammatory disease that affects the shoulder and pelvic girdles in aged persons and is accompanied by peripheral joint involvement with pitting edema mimicking RS3-PE syndrome. To clarify the clinical feature, US findings, and response to glucocorticoid (GC), we reviewed 45 patients (M/F=17/28) with PMR recently referred to our hospital between 2014 and 2018. [Methods] Clinical symptoms including shoulder and pelvic pain, peripheral arthritis, and swelling of hands, bursitis (BS) / tenosynovitis (TS) of shoulders by US, and response to GC were investigated. [Results] The mean age was 72.1 years. Clinical fea-

tures include shoulder pain 100%, pelvic pain 68.3%, peripheral arthritis 71.1%, and swelling of hands 35.6%. Either BS or TS was demonstrated by US in 61.5%. Mean dose of prednisolone was 12.7mg/day at the start of therapy and was tapered to 3.1mg/day at the second year. Patients who occurred the relapse during GC tapering were complicated with peripheral joint involvement at high frequency and in such cases, salazosulfapyridine (SASP) was effective for GC tapering. [Conclusions] Peripheral arthritis and swelling of hands mimicking RS3-PE syndrome was common in PMR patients. SASP might have steroid sparing effects in GC-resistant PMR patients

W47-1

Comparison of clinical characteristics between RS3PE syndrome and elderly-onset rheumatoid arthritis

Tomoki Origuchi¹, Masataka Umeda¹, Tomohiro Koga¹, Shin-ya Kawashiri¹, Naoki Iwamoto¹, Kunihiro Ichinose¹, Kazuhiko Arima¹, Mami Tamai¹, Hideki Nakamura¹, Toshiaki Tsukada², Taiichiro Miyashita³, Toshiyuki Aramaki⁴, Yukitaka Ueki⁴, Munetoshi Nakashima⁵, Masako Furuyama⁶, Akinari Mizokami⁷, Nozomi Iwanaga⁸, Fumiko Shomura⁹, Atsushi Kawakami¹

¹Nagasaki University, Nagasaki, Japan, ²Aino Memorial Hospital, Unzen, Japan, ³Miyashita Rheumatology Clinic, Omura, Japan, ⁴Sasebo Central Hospital, Sasebo, Japan, ⁵Kurume University Medical Center, Kurume, Japan, ⁶Nagasaki Kita Hospital, Nagasaki, Japan, ⁷Isahaya General Hospital, Isahaya, Japan, ⁸Nagasaki Medical Center, Omura, Japan, ⁹Ureshino Medical Center, Ureshino, Japan

Conflict of interest: None

[Object] We compared the clinical characteristics between remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome and elderly-onset RA (EORA). [Methods] We performed a retrospective chart review of 47 RS3PE syndrome patients and 50 EORA patients between January 2003 and December 2017. Clinical characteristics of disease and associated complications were assessed. [Results] Patients with RS3PE syndrome were more likely to be male compared to the EORA group (60% vs 24%; $p = 0.0004$). Serum C-reactive protein (CRP) concentration of RS3PE syndrome was higher than that of EORA (7.6mg/dl vs 2.3mg/dl, $p < 0.0001$). Fever was more common in the RS3PE syndrome group (51% vs 6%; $p < 0.0001$). Inflamed joints were similar, but hip joints were affected in only one patient with RS3PE syndrome. The RS3PE syndrome group was more complicated with cancer (32% vs 12%, $p = 0.0255$). On the other hand, the rate of interstitial pneumonia in the RS3PE syndrome was less than that in the EORA group (0% vs 20%, $p = 0.0012$). [Conclusions] These results suggested that fever was more commonly observed, hip joints were less affected, and interstitial pneumonia was not a frequent complication in patients with RS3PE syndrome compared to EORA.

W47-2

A randomised, double-blind, placebo-controlled phase III trial of tocilizumab in patients with adult-onset Still's disease refractory to glucocorticoid treatment

Yuko Kaneko¹, Hideto Kameda², Kei Ikeda³, Tomonori Ishii⁴, Kosaku Murakami⁵, Hyota Takamatsu⁶, Yoshiya Tanaka⁷, Tsutomu Takeuchi¹

¹Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, ²Division of Rheumatology, Department of Internal Medicine, Toho University Ohashi Medical Center, ³Department of Allergy and Clinical Immunology, Chiba University Hospital, ⁴Clinical Research, Innovation and Education Center, Tohoku University Hospital, ⁵Department of Rheumatology and Clinical Immunology, Kyoto University, ⁶Department of Respiratory Medicine and Clinical Immunology, Osaka University, ⁷The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health

Conflict of interest: Yes

[Object] To evaluate the efficacy and safety of tocilizumab in patients with adult-onset Still's disease (AOSD). [Methods] Patients with AOSD refractory to glucocorticoids were randomised to intravenous tocilizumab at a dose of 8 mg/kg or placebo every 2 weeks during the 12-week, double-blind phase. Patients received open-label tocilizumab for 40 weeks

subsequently. Primary outcome was ACR50 response at week 4. Secondary outcomes included ACR20/50/70, systemic feature score, glucocorticoid dose, and adverse events at each point. [Results] Twenty six patients in each group were included in the efficacy analysis. ACR50 at week 4 was achieved in 61.5% in the tocilizumab group and 30.8% in the placebo group ($p=0.24$). The mean changes in systemic feature score at week 12 were -4.1 in the tocilizumab group and -2.3 in the placebo group ($p=0.003$). The dose of glucocorticoids at week 12 decreased by 46.2% in the tocilizumab group and 21.0% in the placebo group ($p=0.017$). At week 52, the rates of ACR20, ACR50 and ACR70 were 84.6%, 84.6%, and 61.5%, respectively, in both groups. Serious adverse events were infections, aseptic necrosis in the hips, exacerbation of AOSD, drug eruption, and anaphylactic shock. [Conclusions] The study suggests that tocilizumab is effective in AOSD.

W47-3

Clinical features of 22 patients with Parvovirus B19-associated arthritis

Kenji Funakoshi¹, Takashi Hosokawa¹, Takeshi Kaneko¹, Tomomi Tada¹, Shinichiro Nameki¹, Jun Fukui¹, Koji Nomura^{1,2}, Hiroshi Fujiwara¹

¹Division of Rheumatology, Osaka General Medical Center, ²Department of Orthopedic Surgery, Osaka General Medical Center

Conflict of interest: None

Objectives: We analyzed the clinical features of Parvovirus B19 (PVB19)-associated arthritis (PVB19 arthritis) in 22 patients. **Methods:** We retrospectively reviewed patients aged ≥ 16 years who visited our hospital between April 2008 and March 2018 with arthralgia and showed a positive PVB19 immunoglobulin M antibody test. **Results:** The study included 28 patients and 22 were diagnosed with PVB19 arthritis. Most patients (91%) presented with associated symptoms including fever (59.1%), edematous extremities (50%), rash (45.5%), posterior cervical pain (18.2%), cervical lymphadenitis (13.6%), and pharyngalgia (9.1%). Of these patients, approximately 31.8% reported a history of contact with an infected individual. The anti-cyclic citrullinated peptide (CCP) antibody (14 patients) was negative. The rheumatoid factor test was positive only in 13.6% of patients. Other laboratory tests showed no leukopenia, anemia in 27.3%, hypocomplementemia in 68.8% (11/16), and a positive antinuclear antibody test in 71.4% (15/21) patients. **Conclusions:** History taking and physical examination play a key role in diagnosing PVB19 arthritis. A negative anti-CCP antibody test or hypocomplementemia may help to distinguish PVB19 arthritis from other similar conditions.

W47-4

Calcineurin Inhibitors for Adult-onset Still's Disease: A Multi-center Epidemiological (CHANCE) Study

Yuichiro Fujieda¹, Hiroyuki Nakamura², Masato Tarumi³, Shin Furukawa³, Ryo Hisada⁴, Yuka Shimizu⁴, Ikuma Nakagawa⁵, Akito Tsutsumi⁵, Takashi Kurita⁶, Hiroshi Kataoka⁷, Masaya Mukai⁷, Hideki Kasahara⁸, Atsushi Noguchi⁹, Yoshiharu Amasaki⁹, Tatsuya Atsumi¹

¹Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine Hokkaido University, ²Internal Medicine, Tomakomai City Hospital, ³Internal Medicine, Kushiro Red Cross Hospital, ⁴3rd Department of Internal Medicine, Obihiro Kosei Hospital, ⁵Internal Medicine, Takikawa City Hospital, ⁶Internal Medicine, Kitami Red Cross Hospital, ⁷Division of Rheumatology and Clinical Immunology, Sapporo City General Hospital, ⁸NTT Sapporo Medical Center, Department of Rheumatology, ⁹Department of Rheumatology, Tonan Hospital

Conflict of interest: None

[Object] To elucidate the efficacy and safety of calcineurin Inhibitors for patients with adult-onset Still's disease (AOSD). [Methods] This is a multi-center historical cohort study comprised of the consecutive patients with AOSD from 2000 diagnosed according to Yamaguchi classification criteria. The endpoints were set as the time from the initiation of treatment to recurrence and safety. These endpoints were evaluated for each recurrent event. [Results] 151 patients with 212 events were enrolled in the study. Median age was 42 years old, female ratio was 70%, and median follow-up period was about 3 years. Calcineurin inhibitors were used

in 67 events (tacrolimus: 54, cyclosporine: 13) with recurrent history, serious leukocytosis, high ferritin level and/or disseminated intravascular coagulation. Calcineurin inhibitors led to significantly longer recurrent-free survival (78% versus 65% at 3rd year. log-rank test, $p = 0.01$). Adverse events occurred in 21% of patients treated with calcineurin inhibitors and 10% without ones (chi-square test, $p = 0.04$). [Conclusions] Calcineurin inhibitors would be an additional option for AOSD, but might increase adverse events.

W47-5

HLA phenotype of 30 patients with SAPHO syndrome

Masao Tamura, Takahiro Yoshikawa, Teppei Hashimoto, Mai Morimoto, Naoto Azuma, Masayasu Kitano, Kiyoshi Matsui
Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, Hyogo, Japan

Conflict of interest: None

[Objectives] To assess the clinical and laboratory features, HLA phenotype in Japanese patients with SAPHO syndrome. [Methods] Thirty patients (female/male:20/10, mean age at diagnosis: 51.8years) were diagnosed with SAPHO syndrome from September 2014 to October 2018 at our hospital. We examined the HLA phenotype and assessed the clinical and laboratory features. [Results] Among the 30 patients, 23 had cutaneous involvement, 22 had palmoplantar pustulosis, 1 had acne, and 7 had no cutaneous involvement. Bone symptoms involved mainly the anterior chest wall ($n=27,90\%$), spine ($n=9,30\%$), and sacroiliac joints ($n=3,10\%$). 11 had peripheral arthritis. 4 patients had comorbid disease (Crohn's disease, ulcerative colitis, relapsing polychondritis, Behcet's disease). We treated 5 patients with biologics (2 with Adalimumab, 1 with Secukinumab, 2 with Guselkumab) for intractable cases. HLA-A26 was present in 13 patients (43%), B61 in 10 (33%), B62 in 7 (23%). [Discussion] HLA-A26, B61, B62 were frequently detected, these may be disease-sensitive genes. Also, refractory cases were associated with HLA-B51, B61, B62. We conduct much accumulation and want to examine a tendency of HLA in the SAPHO syndrome of this country in future.

W47-6

Clinical features and treatment results of the patients with SAPHO syndrome in Ehime university hospital

Takuya Matsumoto¹, Jun Ishizaki¹, Koichiro Suemori¹, Eiji Sada², Katsuto Takenaka¹, Hitoshi Hasegawa¹

¹Department of Hematology, Clinical Immunology, and Infectious Diseases, Ehime University Graduate School of Medicine, Toon, Ehime, Japan, ²Department of Medical Technology, Ehime Prefectural University of Health Sciences

Conflict of interest: None

[Object] [Methods] Synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome was proposed by Chamot et al. in 1987. This disease is characterized by pustular skin lesions and osteoarticular lesions. We analyzed 19 patients with SAPHO syndrome in our hospital. [Results] Nineteen patients (12 females, 7 males) were between 21- and 76-year-old (mean 54). Osteoarthritis symptoms occurred in the anterior chest in 14 patients (73%), spine in 8 (42%), and extremities in 8 (42%). The frequency of these symptoms was almost same with the other reports. All patients had received multiple NSAIDs and the following DMARDs: 4 patients with corticosteroids; 9 with methotrexate; and 8 with sulfasalazine. Some patients were effective with these treatments, but others had continued the pain of osteoarthritis. In the refractory cases, six patients were treated with TNF inhibitors (3 with infliximab, 2 with adalimumab, and 1 with etanercept). TNF inhibitors were effective for all patients. [Conclusions] Since patients having SAPHO syndrome may be accompanied with strong pain and bone fracture, early diagnosis and therapy are important to prevent the pain, joint deformities, and other complications. We report clinical features and treatment results in our hospital with a review of the literature.

W48-1

Naifold videocapillaroscopy in our institution

Yuji Yoshioka, Yuji Uzawa, Daisuke Kanai, Akiko Suda, Shohei Nagaoka
Yokohama Minami Kyosai Hospital

Conflict of interest: None

[Object] Various naifold capillary abnormalities are pointed out in connective tissue diseases. We investigated Naifold videocapillaroscopy (NVC) in our institution. [Methods] 79 cases examined NVC from April 2015 to September 2018 were included. We examined for naifold capillaries of both sides 2-5 fingers, enlarged ($>20\mu\text{m}$), giant capillary ($>50\mu\text{m}$), hemorrhages, capillary loss (<9), ramified capillaries. [Results] The average age was 62.9 years old (± 15.7), women were 65 cases (82.9%). 27 systemic sclerosis, 15 systemic lupus erythematosus, 12 Sjogren's syndrome, 8 rheumatoid arthritis, 6 polymyositis/dermatomyositis, 6 microscopic polyangitis were included, 17 cases were not diagnosed any connective tissue diseases. Enlarged capillary was observed in 43 cases (54.4%), giant capillary in 21 cases (26.6%), hemorrhages in 36 (45.6%), capillary loss in 20 cases (25.3%), ramified capillaries in 39 cases (49.4%). 11 cases (13.9%) had no capillary abnormality. In systemic sclerosis giant capillary and capillary loss had significant odds ratio; 6.94 (95%CI:2.31-20.8, $p=0.001$), 3.29 (95%CI:1.15-9.43, $p=0.027$) respectively. Ramified capillaries were related significant odds ratio 3.53 (95%CI:1.02-12.3, $p=0.047$) in systemic lupus erythematosus. [Conclusions] We reported NVC in our institution.

W48-2

Symmetrical MCP joints tenosynovitis determined by MRI is a predictor of RA development in patients with undifferentiated arthritis

Mami Tamai¹, Vincent Grundeken², Kazuhiko Arima¹, Robin Ten Brinck², Annette H.m. Van Der Helm-van Mil², Nozomi Oki¹, Masataka Uetani¹, Atsushi Kawakami¹

¹Nagasaki University, Nagasaki, Japan, ²Leiden University, Leiden, The Netherlands

Conflict of interest: None

Objectives. We investigated whether MRI-detected tenosynovitis at the level of MCP or wrist joints predicts progression to RA in UA patients. **Methods.** Clinical, serological and bilateral gadolinium-enhanced 1.5T-MRI data were obtained at baseline from 91 UA-patients (not fulfilling the 2010 EULAR/ACR RA classification criteria) whom included in the Nagasaki Early Arthritis Cohort. Tenosynovitis in MCP and wrist joints were scored according to the RA MRI scoring system. The collected data was analyzed for progression to RA during 1-year follow-up. **Results.** Twenty-nine patients (31.9%) progressed to RA. Univariate analysis showed higher MCP tenosynovitis-scores ($p=0.011$) and MCP flexor tenosynovitis-scores ($p=0.019$) in patients that developed RA. Also, symmetrical MCP tenosynovitis was more frequent in the progression group ($p=0.016$). In multivariate analysis, symmetric tenosynovitis at MCPs was independently associated with RA-development (OR 3.9). Sensitivity of symmetrical MCP tenosynovitis was low (35%), however, specificity was high (87%) and negative predictive value was 74%, positive predictive value was 56%. **Conclusions.** MRI-detected tenosynovitis in MCP joints, especially symmetrical MCP tenosynovitis, in UA is predictive for RA-development.

W48-3

AI-guided diagnosis of joint X-ray radiographs

Toru Hirano, Masayuki Nishide, Atsushi Kumanogoh

Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University

Conflict of interest: None

[Purpose] To judge joint destructions on radiographs by machine learning [Method] One hundred and fourteen digital X-ray radiographs of hand fingers of 62 patients with rheumatoid arthritis were used. Area around DIP, PIP, MCP, carpal bones and wrist were clipped, and these pictures were amplified by horizontal flipping Thus 3632 pictures were prepared. These pictures were processed by machine learning to judge

joint space narrowing (JSN) and erosions by reference to Sharp/van der Heijde method. The method of machine learning was processing of images with Open-Cv and convolution neural network with 50 repeated times, by open source neural network module, Chainer. [Result] Joint areas of DIP, PIP and MCP was correctly identified with a probability of $>90\%$ (DIP 90%, PIP 98%, MCP 96%), whereas joint areas of carpal bones was difficult to identify. Accuracy of JSN score and erosion score by AI was 70-90%, and the errors were evident in images with severe joint destructions. Decrease of the errors stopped in 30th stage of machine learning, suggesting over-fitting. [Discussion] AI-guided assessment of hand radiographs was available, however much more samples with balanced measurements and setting of parameters of machine learning were needed to deal with accuracy and errors.

W48-4

Development of peripheral joint imaging technique using HR-pQCT and 3D workstation

Hiroaki Mizuno¹, Shigenori Tamaki¹, Takashi Kato², Motokazu Kai³, Kunikazu Ogawa³, Hisaji Oshima⁴, Ikuko Tanaka¹

¹Nagoya Rheumatology Clinic, ²Department of Radiology, National Center for Geriatrics and Gerontology, Obu, Japan, ³Mie Rheumatology Clinic, Suzuka, Japan, ⁴Department of Connective Tissue Disease, Tokyo, Japan, Tokyo Medical Center

Conflict of interest: None

[Objective] We used HR-pQCT (Xtreme CT II, Scanco Medical) to image all joints from the wrist joint to the DIP joint. Those images were reconstructed using a 3D workstation. We present 3 arthritis cases and report the usefulness of this imaging technique. [Case 1] 41-year-old female, finger pain appeared 3 months ago, ACPA 11.9 U / mL, RF 10 IU / mL. Three bone erosion were recognized by horizontal section and coronal section in wrist, but it could not be found by simple X - ray. [Case 2] 50-year-old female, about 10 years ago, the deformation of the DIP joint has occurred and pain has appeared recently in the PIP joint. Osteophyte formation and bone erosion of the DIP · PIP joint were confirmed by coronary section. Pencil in Cup deformity was observed in the sagittal section, and it was diagnosed as peripheral spondyloarthritis. [Case 3] 52-year-old female, visited by fever and wrist arithritis. Calcification was found in the triangular fibrous ligament and around the carpal bones in HR - pQCT, which was diagnosed as pseudogout. [CONCLUSIONS] This imaging technology was thought to be useful for the diagnosis of arthritis and the understanding of the pathology by examining all the joints from the wrist joint to the DIP joint in detail.

W48-5

The relation analysis of bone micro-architecture by HR-pQCT and synovitis, bone destruction, bone mineral density in rheumatoid arthritis

Naoki Iwamoto¹, Mizuna Otsuka¹, Momoko Okamoto¹, Yushiro Endo¹, Sosuke Tsuji¹, Ayuko Takatani¹, Toshimasa Shimizu¹, Remi Sumiyoshi¹, Tomohiro Koga¹, Shin-ya Kawashiri¹, Takashi Igawa¹, Kunihiro Ichinose¹, Mami Tamai¹, Hideki Nakamura¹, Nozomi Oki², Kounosuke Watanabe³, Ko Chiba³, Tomoki Origuchi⁴, Makoto Osaki³, Atsushi Kawakami¹

¹Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ²Department of Radiological Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ³Department of Orthopedic Surgery, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ⁴Department of Physical Therapy, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: None

[Object] To investigate bone micro-architecture detected by High Resolution peripheral Quantitative CT (HR-pQCT) in RA. [Methods] This study included 21 RA patients. HR-pQCT imaging analyses quantified bone micro-architecture in 2,3 Metacarpal Head. We measured the BMD of lumber spine and femoral neck using DXA. Synovitis and bone destruction were assessed by ultrasonography (US) and X-ray, respec-

tively. [Results] BMD of femoral neck was correlated with trabecular volumetric densities (Tb.vBMD) ($r=0.84$, $p<0.01$). The patients with US-proven active synovitis ($PD\geq 2$) showed less Tb.vBMD, trabecular number (Tb.N) and trabecular thickness (Tb.Th) as compared with the patients with $US-PD<2$ synovitis (Tb.vBMD: 121.5 mg/cm^3 vs 145.3 mg/cm^3). These tendencies were also shown in bone destruction measured by x-ray. The longitudinal analysis of 10 patients revealed that Tb.vBMD and Tb.N were improved along with improvement of disease activity, but Tb.Th was not improved. [Conclusions] This study revealed that bone destruction and synovitis were associated with bone micro-architecture, and the difference of treatment response by parameter of bone micro-architecture. However, this study was mainly transverse analysis and small samples, we need longitudinal analysis using larger samples.

W48-6

Quantitative analysis of juxta-articular osteoporosis by HR-pQCT in patients with rheumatoid arthritis

Kounosuke Watanabe¹, Ko Chiba¹, Naoki Iwamoto², Nozomi Oki³, Masataka Uetani³, Atsushi Kawakami², Makoto Osaki¹

¹Department of Orthopedic Surgery, Nagasaki University Graduate School of Biomedical Sciences, Japan, ²Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Japan, ³Department of Radiological Sciences, Nagasaki University Graduate School of Biomedical Sciences, Japan

Conflict of interest: None

[Object] HR-pQCT is a high-resolution CT dedicated to human extremities. It has been used for the study of osteoporosis and RA as well, enabling quantitative analysis of bone microstructure. The purpose of this study is to analyze the juxta-articular osteoporosis in patients with RA by HR-pQCT. [Methods] 21 patients with RA (68.7 years, 21 female) and 17 controls (65.9 years, 17 female) participated in this study. The second and third MCP joints were scanned by HR-pQCT (XtremeCT II, Scanco Medical, Switzerland) at the voxel size of $61\ \mu\text{m}$. We analyzed microstructure of metacarpal head: volumetric bone mineral density (vBMD), bone volume fraction (BV/TV), trabecular thickness (Tb.Th), trabecular number (Tb.N), structure model index (SMI), connectivity density (Conn.D), and compared measured values between RA patients and healthy controls. [Results] Mean values of vBMD in RA patients and healthy subjects were 118.0 , 161.1 mg/cm^3 , BV/TV 0.86 , $0.97/\text{mm}$, Tb.Th 204.6 , $210.4\ \mu\text{m}$, Tb.N 0.86 , $0.97/\text{mm}$, and SMI 1.73 , 1.31 , respectively. [Conclusions] Patients with RA had lower density, number, connectivity of trabecular bones, and rod-like structure. Quantitative evaluation of bone microstructure by HR-pQCT would be useful for the pathophysiological research and drug development of RA.

W49-1

Clinical results and radiographic changes after malleolar osteotomy/fracture at total ankle arthroplasty in rheumatoid arthritis cases

Makoto Hirao¹, Jun Hashimoto², Kosuke Ebina¹, Hideki Tsuboi³, Koichiro Takahi⁴, Hiroyuki Nakaya⁴, Takaaki Noguchi², Yasuo Kunugiza⁵, Shigeyoshi Tsuji², Hideki Yoshikawa¹

¹Department of Orthopedics, Osaka University Graduate School of Medicine, ²Orthopaedics, Rheumatology, National Hospital Organization, Osaka Minami Medical Center, ³Orthopaedics, Rheumatology, Osaka Rosai Hospital, ⁴Orthopaedics, Rheumatology, National Hospital Organization, Toneyama Hospital, ⁵Department of Orthopaedics, JCHO Hoshigaoka Medical Center

Conflict of interest: None

[Object] This study aimed to investigate the clinical results and changes of the radiographic shape of the ankle joint after osteotomy/fracture at the medial/lateral malleolus at TAA. [Methods] 70 ankles with rheumatoid arthritis followed for 6.9 years (1-15 years) after TAA was investigated. JSSF RA foot and ankle and SAFE-Q score were determined along with radiographic parameters of the ankle/hindfoot. [Results] 31 (26 osteotomy, 5 fracture) showed discontinuity in the medial malleolus, while 13 (5 osteotomy, 8 fracture) in the lateral malleolus. Tibial medial malleolus (TMM) angle was significantly decreased [30.3° to 19.1°] after valgus correction [TC angle: -1.7° to 0.8°] by medial mal-

leolar osteotomy. Medial malleolar fracture was completely healed, except for one ankle that could also not achieve bony union at the site of lateral malleolar osteotomy. [Conclusions] Medial malleolar osteotomy contributes to not only controlling the soft tissue balance, but also providing the stabilized shape of the ankle joint. Lateral malleolar osteotomy was also effective for varus correction, but internal fixation is needed to prevent progression of valgus deformity and non-union if a medial malleolar fracture and a bony gap at the site of osteotomy occur simultaneously.

W49-2

Correction loss of toe arthroplasty for rheumatoid arthritis forefoot deformity

Kota Shimomura^{1,3}, Mitsuyasu Iwasawa¹, Takeomi Nakamura¹, Satoru Ohashi¹, Tetsuro Yasui²

¹Department of Orthopedic Surgery, Sagami National Hospital, Sagami, Kanagawa, Japan, ²Department of Orthopaedic Surgery, Teikyo University Hospital, Mizonokuchi, Japan, ³Department of Orthopaedic Surgery, Sapporo Medical University, Sapporo, Japan

Conflict of interest: None

[Object] To examine the loss of correction following toe arthroplasty for rheumatoid forefoot deformities. [Methods] 56 patients (72 toes) underwent surgery between 2014-2017. They were examined pre-operation, post-operation, and at 1, 3, 6, and 12 months. The loss of correction, and the correlation in all groups were measured. [Results] The loss of correction in the 1/3/6/12 month period was: RA group: 8/10/10/11, Non-RA group: 7/10/11/12, Conservative group: 8/10/10/11, Resection group: 16/19/20/21 degrees. A significant loss of correction was seen in the 1-month period following surgery in all groups. It was also significant in the Resection group throughout. A correlation was present between loss of correction and both the preoperative HVA value and the postoperative length of the gap between the 1st-2nd metatarsus. Results showed no significant difference between the RA and the Non-RA toes, plus a tendency for resection to cause loss of correction. The differences in the patients' backgrounds may affect the results. [Conclusions] Equivalent results can be expected when using conservative toe arthroplasty on both RA and Non-RA patients. Care should be taken during surgery planning and aftercare in cases where loss of correction may easily occur.

W49-3

Risk factors contributing to the deterioration of the hallux valgus angle after the metatarsal osteotomy with temporary fixation for hallux valgus

Takuya Tomizawa¹, Hiromu Ito^{1,2}, Koichi Murata^{1,2}, Masayuki Azukizawa¹, Shuichi Matsuda¹

¹Department of Orthopaedic Surgery, Kyoto University Graduate School of Medicine, Kyoto, Japan, ²The Department of Advanced Medicine for Rheumatic Diseases, Kyoto University Graduate School of Medicine, Kyoto, Japan

Conflict of interest: None

[Object] Collagen diseases such as rheumatoid arthritis (RA) often causes a hallux valgus (HV). After metatarsal osteotomy with temporary fixation (MOWTF), some patients relapse hallux valgus. But there are few reports on the risk factor of recurrence. [Methods] From January 2011 to August 2018, 54 feet performed MOWTF at Kyoto University Hospital were examined. We recorded the age, gender, collagen disease including RA, methotrexate (MTX) dose, steroid-use, and biologic-use. On X-rays, we evaluated the hallux valgus angle. Then, we collected the correction angle (CA), correction-loss angle (CLA), length of distal metatarsal bone after osteotomy (LDMB), permanent placement of implants (PI). On univariate analysis and multivariate analysis, CLA was applied as a target variable. On multivariate analysis, we adjusted for age, gender and collagen disease. [Results] On univariate analysis, LDMB, CA, and PI were significant factors. On multivariate analysis, LDMB, and CA were extracted as significant risk factors. [Conclusion] Regardless of collagen disease or fixed implants, after MOWTF for HV, we should be careful with the patients performed osteotomy at more proximal sites and the person corrected larger hallux valgus angle. Because

they might be easy to relapse HV.

W49-4

The gap between theoretical and actual shortening of the first metatarsal in rotational closing-wedge osteotomy

Haruki Tobimatsu, Katsunori Ikari, Koichiro Yano, Ken Okazaki
Department of Orthopedic Surgery, Tokyo Women's Medical University

Conflict of interest: None

[Object] Since 2010 we have had favorable results at our hospital with rotational closing-wedge osteotomy of the first metatarsal accompanied by distal oblique osteotomies of the second to fifth metatarsals. In this study, we examined the discrepancy between theoretical and actual degrees of shortening that resulted from rotational closing-wedge osteotomy of the first metatarsal. [Methods] We studied 37 foot of 37 patients that underwent rotational closing-wedge osteotomy of the first metatarsal. If θ is IMA and a is the width of the distal cut, the shortening b should theoretically be $b = (a/2) \sin \theta$. We measured actual shortening and assessed that against the theoretical shortening, using a paired t-test. [Results] Mean theoretical shortening was 1.82 ± 0.47 mm, mean actual shortening was 3.19 ± 0.93 mm, and the mean difference was a significant increase of 1.37 ± 1.1 mm ($P < 0.01$). [Conclusions] Rotational closing-wedge osteotomy of the first metatarsal is an excellent procedure, providing a way to correct varus deformity of the first metatarsal in a pre-planned way. Shortening of the metatarsal is unavoidable and shortening of the second metatarsal is not to be included, realizing the potential error of the theoretically calculated degree of shortening.

W49-5

The effect of forefoot arthroplasty for the balance and gait function in patients with rheumatoid arthritis

Motohiro Suzuki¹, Tetsuya Ichikawa², Tetsuyuki Nagafusa², Eiji Torikai⁴, Shigeyuki Miyamoto⁵, Ryou Okabayashi¹, Yukihiko Matsuyama¹

¹Department of Orthopaedics, Hamamatsu University School of Medicine, ²Department of Rehabilitation, Hamamatsu University School of Medicine, ³Department of Orthopaedics, Narita Memorial Hospital, ⁴Department of Rheumatology, Iwata City General Hospital, ⁵Department of Orthopaedics, Kikugawa City General Hospital

Conflict of interest: None

[Object] We assessed the effect of forefoot arthroplasty for the balance and gait function in patients with rheumatoid arthritis (RA) by gravicorder and foot print gait analyser. [Methods] We measured 16 RA patients (20 feet) performed forefoot arthroplasty by gravicorder (gravicorder GP6600; ANIMA) and foot print gait analyser (ZenoWalkwayZ-212; ProtoKinetics). We measured following indices in the pre-and post-operative course. We assessed differences of the balance and barycentric orbit in standing position by gravicorder and walking cycle, walking speed, and rate of both single and bilateral leg support by gait analyser. [Results] The primary load of pre-operative course were 5 feet (25%) on the diseased side, 10 feet (50%) on the unaffected side, and 5 feet (25%) on the bilateral side equally. The improvement of primary load was observed in 18 feet (90%) after forefoot arthroplasty. The movement of balance was improved after operation. On the other hand, walking cycle, walking speed, and rate of both single and bilateral leg support showed no differences statistically between pre-and post-operative course. [Conclusions] The forefoot arthroplasty in RA affected the improvement of balance movement in standing position. On the other hand, it did not affect the gait function.

W49-6

Setting target of JSSF RA foot ankle score for foot surgery in patients with rheumatoid arthritis based on patient-reported physical function

Toshihisa Kojima¹, Hajime Ishikawa², Sakae Tanaka³, Nobuhiko Haga⁴, Keiichiro Nishida⁵, Masao Yukioka⁶, Jun Hashimoto⁷, Hisaaki Miyahara⁸, Yasuo Niki⁹, Tomoatsu Kimura¹⁰, Hiromi Oda¹¹, Koji Funahashi¹², Shuji Asai¹, Masayo Kojima¹³, Naoki Ishiguro¹

¹Department of Orthopaedic Surgery and Rheumatology, Nagoya Univer-

isty, Graduate School of Medicine, ²Orthopedic Surgery, Niigata Rheumatic Center, ³Orthopaedic Surgery and Spinal Surgery, The University of Tokyo Hospital, ⁴Rehabilitation Medicine, The University of Tokyo Hospital, ⁵Orthopedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ⁶Orthopedic Surgery, Yukioka Hospital, ⁷Department of Rheumatology, National Hospital Organization Osaka Minami Medical Centre, ⁸Orthopedic Surgery, National Hospital Organization Kyushu Medical Centre, ⁹Orthopedic Surgery, Keio University, School of Medicine, ¹⁰Orthopedic Surgery, University of Toyama, Faculty of Medicine, ¹¹Orthopaedic Surgery, Saitama Medical University, ¹²Orthopedic Surgery, Kariya Yoyota General Hospital, ¹³Medical Education, Nagoya City University Graduate School of Medical Sciences

Conflict of interest: None

[Object] The aim of this study is to set the target value of JSSF RA foot ankle score (JSSF-RA) based on patient subjective physical function. [Methods] This research is a multicenter prospective, observational study conducted as a research by the Japanese Ministry of Health, Labor and Welfare. As a preoperative evaluation of foot surgery for RA patients, JSSF-RA, Timed Up & Go test (TUG), pain, global patient evaluation, physical function (HAQ), QOL (EQ-5D), and depression (BDI-II) were collected. Correlation of each parameter was examined. The relationship between HAQ remission ($HAQ \leq 0.5$) and JSSF-RA was examined with UNIANOVA adjusted for age and gender. [Results] Analysis was conducted on 417 RA patients. Mean values of age, disease duration, and DAS 28 were 64.1 years, 16.9 years and 3.01, respectively. JSSF-RA showed significant correlation with age, disease duration, HAQ, EQ-5D, and TUG. In patients with HAQ remission, mean JSSF-RA adjusted age and gender, was 77.6 (95% CI: 74.3-80.9). EQ-5D (0.68 vs 0.59) and TUG (9.0 s vs 13.1 s) were significantly better in patients with JSSF-RA ≥ 74 (95% CI lower limit). [Conclusions] The value of JSSF-RA for HAQ remission was considered to be at least 74. It could be an important value as the target of the RA foot surgery.

W50-1

Distance from femoral nerve to acetabular margin -cadaveric anatomical study-

Kensuke Yoshino, Junichi Nakamura, Shigeo Hagiwara, Yuya Kawarai, Masahiko Sugano, Kento Nawata, Masahiko Suzuki, Seiji Ohtori
Department of Orthopaedic Surgery, Graduate School of Medicine, Chiba University

Conflict of interest: None

[Object] To demonstrate safer areas in the anterior acetabulum by measuring the distance between the femoral nerve and the acetabular margin. [Methods] Eighty-four cadaveric hips from 44 formalin embalmed human specimens were dissected. The iliopsoas muscle and the femoral nerve were exposed. The tensor fascia latae and rectus femoris muscles were detached, the anterolateral joint capsule was resected to see the bony acetabular rim and the femoral head. The measurement points were determined along the acetabular rim every 30 degrees drawing a reference line from the anterior superior iliac spine through the center of the acetabulum, describing the intersection as 0 degrees. The minimum distance to the femoral nerve margin was measured by a divider at each measurement point. [Results] The mean minimum distances were 33.2 ± 5.1 mm (0 degrees), 24.4 ± 5.0 mm (30 degrees), 18.4 ± 4.2 mm (60 degrees), 16.6 ± 3.6 mm (90 degrees), 17.9 ± 4.0 mm (120 degrees) and 23.2 ± 5.0 mm (150 degrees). It was significantly shorter at 90 degrees point than at the others (Linear mixed effects model, Tukey's test, $p < 0.05$). [Conclusions] Considering the anatomical distance, it is relatively safe for the femoral nerve to avoid the anterior acetabulum from 90 degrees area in insertion and placement of retractors.

W50-2

Change of lumbar and femoral bone mineral density after total hip arthroplasty in patients with rheumatoid arthritis and osteoarthritis

Hyonmin Choe, Ken Kumagai, Shunsuke Yamada, Akira Morita, Arata Usui, Akiko Nagaoka, Yutaka Inaba

Department of Orthopaedic Surgery, Yokohama City University

Conflict of interest: None

[Object] We evaluated the change of lumbar and femoral bone mineral density (BMD) after total hip arthroplasty (THA) in patients with rheumatoid arthritis (RA) and osteoarthritis (OA). [Methods] 80 hips (26 with RA and 54 with OA) were enrolled in this study. Lumbar and femoral BMD was measured before and 1 year after THA. From the treatment for osteoporosis, patients were divided into no treatment, vitamin, and bisphosphonate group. Changes of lumbar and femoral BMD after THA were compared between RA patients and OA patients in each group. [Results] Femoral BMD were significantly decreased after THA in no treatment group or vitamin group, whereas femoral BMD in bisphosphonate group were not decreased after THA. The reduction of BMD in no treatment group was significantly higher in OA patients than that in RA, although BMD in bisphosphonate group had no difference between RA and OA patients. [Conclusions] Without treatment for osteoporosis, femoral BMD in RA and OA patients were significantly decreased after THA. Medication for osteoporosis is necessary in both RA and OA patients after THA so that they can prevent the bone fragility fractures that may severely disable daily activity of patients.

W50-3

The rotational alignment of femoral component of total knee arthroplasty decided with 3D-MRI

Yoshikazu Tsuneizumi
Chiba Rehabilitation Center

Conflict of interest: None

[Object] Objects were 101 primary TKAs. Diagnoses were 90 knees of OA and 11 knees of RA. [Methods] The angles between posterior condylar axis (PCA) and SEA, CEA were measured with preoperative 3D-MRI. The external angle of the femoral component was set to be between SEA and CEA. The preoperative plan for TKA was made with 3D-CT software ZedKnee, and the alignment of component was examined with ZedKnee postoperative mode. The rotation angle with respect to the preoperative SEA was examined. The difference between the theoretical angle of femoral component rotation from SEA in preoperative MRI and the postoperative rotational angle by CT was examined. [Results] The mean rotation alignment of the femoral component was 1.2° (SD 1.9°) external rotation from SEA. The error from the theoretical angle of the rotation was 0.3° (2.0) internal rotation and the absolute error value was 1.5° . Eighty-nine % of knees showed that the rotational alignment of femoral component was between CEA and 2° inner rotation from SEA. There was the significant weak correlation between the flexion alignment of the femoral component and the error of the rotation. [Conclusions] Accuracy of rotational alignment of femoral component decided with 3D-MRI was comparable with conventional methods.

W50-4

Perioperative complications of joint replacement surgery for haemophilic arthropathy

Takuya Matsumoto, Nobunori Takahashi, Shuji Asai, Nobuyuki Asai, Yasumori Sobue, Tsuyoshi Nishiume, Mochihito Suzuki, Naoki Ishiguro, Toshihisa Kojima
Department of Orthopaedic Surgery and Rheumatology, Nagoya University Hospital

Conflict of interest: None

[Object] The aim of this study was to investigate the incidence of postoperative complications following large joint replacement for haemophilic arthropathy. [Methods] Thirty patients who underwent total knee replacement surgery (TKA) or total hip replacement surgery (THA) for haemophilic arthropathy from 1995 to 2017 and were enrolled and postoperative complications was investigated. [Results] The subjected joints were 32 TKA and 12 THA. Average age was 44.2 years, gender was all male, and average observation period was 11.4 years. All 31 cases were positive for HCV antibody and 7 cases (22.6%) were positive for HIV antibody. As postoperative complications, superficial infection were found in 8 joints (17.8%), deep infection in 3 joints (6.7%), intra-articular bleeding which requires interruption of rehabilitation or additional ad-

ministration of coagulation factors in 8 joints (18.2%), aseptic loosening in 7 joints (15.5%), removal of the implant in 2 joints, revision in 1 joint, and periprothetic fracture in 1 joint. No case developed venous thromboembolism. [Conclusions] The incident rate of complications such as postoperative infection and intra-articular bleeding is remarkably high in large joint replacement for haemophilic arthropathy. Careful postoperative observation is needed.

W50-5

Comparison of clinical outcomes of total knee arthroplasty between the patients of osteoarthritis and rheumatoid arthritis using new New Knee Society Score

Kohei Nishitani^{1,2}, Hiromu Ito², Shinichiro Nakamura², Koichi Murata^{1,2}, Motomu Hashimoto^{1,3}, Masao Tanaka^{1,3}, Tsuneyo Mimori³, Shuichi Matsuda²

¹Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, ²Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, ³Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University

Conflict of interest: None

[Object] The purpose was to evaluate clinical outcomes between total knee arthroplasty (TKA) for osteoarthritis (OA) and rheumatoid arthritis (RA) using New Knee Society Score (NKSS). [Methods] This study include 245 OA (age: 74 ± 7 , 199 females, BMI: 26.8) and 56 RA (age: 66 ± 11 , 49 females, BMI: 23.8) cases, who underwent primary TKA between 2012 to 2016, and whose pre-operative and 1-year post-operative NKSS were available. Among 245 OA cases, age, gender, and BMI matched 56 cases (age: 69 ± 7 , 49 females, BMI: 24.8) were extracted, and compared with RA cases. [Results] Preoperative NKSS showed no difference in symptom (OA 10.1 ± 5.9 , RA 9.1 ± 5.2 ($p=0.35$)), satisfaction (OA 15.0 ± 6.7 , RA 13.2 ± 6.47 ($p=0.18$)), but function was higher in OA (OA 48.1 ± 18.8) than RA (40.8 ± 17.5) ($p=0.04$). At 1-year, NKSS showed no difference in symptom (OA 20.8 ± 4.6 , RA 19.8 ± 5.2 ($p=0.53$)), satisfaction (OA 27.4 ± 8.5 , RA 26.3 ± 8.6 ($p=0.44$)) and in function (OA 71.2 ± 16.5 , RA 65.3 ± 19.3 ($p=0.10$)). One-year improvements of symptom (OA 10.7 ± 6.6 , RA 10.7 ± 7.3 ($p=0.99$)), satisfaction (OA 12.4 ± 8.0 , RA 13.1 ± 10.0 ($p=0.70$)), and function (OA 23.1 ± 17.6 , RA 24.5 ± 19.6 ($p=0.70$)) were comparable. [Conclusions] TKA for OA and RA was evaluated using NKSS. Comparable improvement in symptom, satisfaction and function is expected in RA.

W50-6

Examination of secondary sarcopenia preventive effect by branched chain amino acid (BCAA) nutritional intervention in the perioperative period of rheumatoid arthritis foot patients

Shigeyoshi Tsuji, Jun Hashimoto, Kentaro Isoda, Takaaki Noguchi, Shosuke Akita, Koji Yachi, Shiro Ohshima, Yukihiko Saeki
NHO Osaka Minami Medical Center

Conflict of interest: None

[Object] To investigate the preventive effect by supplementation with BCAA for muscle mass reduction and muscle weakness risk associated with inflammatory stress by foot surgery in RA. [Methods] The subject was 20 patients with rheumatoid arthritis undergoing foot surgery. This research is a randomized control study. It is divided into both BCAA administered group (10 cases) and BCAA nothing group (10 cases). In the BCAA administration method, BCAA 4000mg (20g/day) is taken orally for a total of 5 times before meal, bedtime and immediately after rehabilitation for a total of 16 days from the day before surgery to 2 weeks after surgery. Muscle mass measurement method DXA. Muscle mass measurement by body composition meter is performed before and 2 weeks after surgery. Muscular strength measurement methods are as follows: (1) average handed grip strength, (2) average knee extension strength (kg). [Results] For SMI, in the BCAA+ group, preop 5.02 / postop 4.92, $P=0.06$, in the BCAA -group, preop 5.09 / postop 4.73, $P=0.01$. [Conclusions] It was suggested that administration of BCAA for prevention of secondary sarcopenia in the RA foot surgery period may be useful.

W51-1

Erythrocyte methotrexate (MTX)-polyglutamates levels in patients with rheumatoid arthritis are related to polymorphisms in genes associated with MTX-metabolism

Miwa Nishida^{1,2}, Saori Hatachi^{1,2}, Soshi Takahashi¹, Yasuhiro Nohda¹, Katsuhiko Yoneda¹, Saki Mukohara¹, Norihiko Amano¹, Akira Onishi³, Shunichi Kumagai^{1,2}

¹Center for Rheumatic Diseases, Shinko Hospital, ²Shinko Institute for Medical Research, ³Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine

Conflict of interest: None

[Objects] To clarify the factors that effected the concentration of erythrocyte MTX-PGn and associated with MTX-hepatotoxicity. [Methods] Concentrations of erythrocyte MTX-PGn were detected by LC-MS/MS. MTX-PGn levels were measured in 189 RA patients with stable dosage of MTX which included 42 patients with elevated transaminases (>40 U/L), and the 9 SNPs including 5 SNPs in MTX-PG related genes were identified by RT-PCR. [Results] Total concentrations of MTX-PGn were 84.4±37.4 nmol/L (mean±SD) in 147 RA patients. In univariate analysis the concentration of MTX-PGn were correlated with dosage of MTX, BMI, RBC, Cr and SLC19A1c.80G>A (p=0.029). In multivariate analysis the concentration of MTX-PGn were correlated with dosage of MTX, BMI, RBC, Cr and GGH c.452C>T or FPGS c.*192T>C (p<0.05). In the hepatotoxicity group, the concentration of MTX-PG1 were higher than in the group of normal range transaminase and were correlated with dosage of MTX, Cr and GGH c.452C>T (p<0.035). [Conclusion] We revealed that erythrocyte MTX-PG concentration were also related to polymorphism of MTX-PG related genes, not just clinical characteristics such as dosage of MTX, BMI, RBC and Cr.

W51-2

Predictive factors for the adequate second-choice of bDMARD or JAK-inhibitor in the first bDMARD-IR patients with RA ~From First registry~

Kazuhisa Nakano¹, Shingo Nakayamada¹, Shigeru Iwata¹, Kentaro Hanami¹, Shunsuke Fukuyo¹, Satoshi Kubo¹, Ipppei Miyagawa¹, Akio Kawabe¹, Yusuke Miyazaki¹, Ayako Yamaguchi¹, Kazuyoshi Saito^{1,2}, Yoshiya Tanaka¹

¹The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, ²Internal Medicine, Tobata General Hospital

Conflict of interest: Yes

[Object] To find the predictors of the effectiveness of the second-line bDMARD or JAK-i in RA treatment. [Methods] The subjects were 513 RA pts (from 2011 to 2018) who switched to other bDMARDs or JAK-i because of failure or lack of efficacy and/or toxicity of the first bDMARD. The 1st EP is the retention rate and the REM or LDA achievement rate for each formulation at 6 months. As a 2nd EP, patient characteristics involved in achieving CDAI-REM or LDA at 6 months were analyzed. [Results] The overall age/disease duration was 62 (y)/116 (m), 80% of the first bDMARD was TNFi. Number of pts/age (y) / half-year retention rate (%) / CDAI-REM or LDA achievement rate (%) were ETN 52/68/81/79, ADA 80/57/85/81, GLM 47/64/77/74, CZP 51/56/80/69, ABT 125/67/85/72, TCZ 123/60/90/69, Tofa 27/59/89/70. Main factors that contribute to achieving CDAI-REM or LDA at 6 months are as follows: ETN: low pain (p)-VAS, low HAQ, ADA: low p-VAS, low HAQ, GLM: low p-VAS, CZP: low p-VAS, high ACPA, ABT: low p-VAS, high ACPA, TCZ: low p-VAS, low HAQ, high ESR, high ACPA. In Tofa, p-VAS was not a factor to determine effectiveness. [Conclusions] The effectiveness of all bDMARDs except for Tofa was influenced by the degree of pain. In CZP and ABT, TCZ, the high levels of ACPA was an indicator of good response.

W51-3

What affects joint destruction of the hip joints in rheumatoid arthritis - a 4-year longitudinal study from KURAMA cohort -

Kohei Doi¹, Hiromu Ito¹, Takuya Tomizawa¹, Masayuki Azukizawa¹, Koichi Murata^{1,2}, Kohei Nishitani^{1,2}, Motomu Hashimoto², Masao

Tanaka², Shinichiro Ishie¹, Tsuneyo Mimori³, Shuichi Matsuda¹

¹Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, ²Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, ³Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University

Conflict of interest: None

[Purpose] Rheumatoid arthritis (RA) is a chronic disease leading to joint destruction. Destruction of the hip joints leads to disability of daily life. The purpose of this study is to identify the factors influencing joint destruction of hip joints in patients with RA [Methods] We enrolled consecutive RA patients from the Kyoto University Rheumatoid Arthritis Management Alliance (KURAMA) cohort who participated both in 2012 and 2016. Clinical data in 2012 including age, BMI, SJC 28, SDAI and DAS28-ESR. The use/non-use of biological agent were also recorded. Radiographic progression was defined if Larsen Grade was progressed in four years or joints were received total joint arthroplasty. The effect of baseline characteristics on the incidence of radiographic progression was assessed. [Results] A total of 179 patients were enrolled in this study. Forty-three joints of 31 patients (17.3%) showed radiographic progression in hip joints. On multivariate regression models, the presence of radiographic progression in hip was significantly associated with older age, higher Larsen Grade, and lower BMI. [Conclusion] Patients with higher Larsen Grade, or lower BMI tend to suffer from hip joint destruction. We need more attention to these patients to prevent joint destruction of hip joints in RA.

W51-4

Genome-wide SNP analysis for prediction of responsiveness and second failures in tocilizumab-treated RA patients

Tomoyuki Kamenaga¹, Shinya Hayashi¹, Koji Fukuda¹, Yoshinori Takashima¹, Ryosuke Kuroda¹, Marowa Hashimoto³, Keiko Funahashi^{2,3}, Tsukasa Matsubara^{2,3}

¹Department of Orthopaedic Surgery, Kobe University Graduate School of Medicine, ²Matsubara Mayflower Hospital, ³Research Institute of Joint Disease

Conflict of interest: None

[Object] It is difficult to predict therapeutic effect of tocilizumab (TCZ) in RA patients before the treatment. This study aimed to identify single nucleotide polymorphisms (SNPs) predicting of long-term use of TCZ in RA patients. [Methods] Among RA patients treated with TCZ and followed-up for over 6 months, 71 patients in which SNP analysis was performed were included. Judged by CDAI at 6 months after initiation of TCZ, 41 patients with remission or low disease activity were classified into responder group. Among them, 7 patients whose agent was switched due to deterioration over 1 year after initiation of TCZ were classified into secondary non-responder group, and 19 patients who had continued to use TCZ for over 3 years were classified into long-term user group. Using genome-wide SNP analysis, SNPs strongly associated with the therapeutic effect of TCZ was detected. [Results] Associated with long-term use of TCZ, SNPs located on the genes of SEMA4A and MAGI2 were extracted. SEMA4A is involved in angiogenesis and activation of T cells. MAGI2 is involved in apoptosis via Fas/FasL signal pathway. [Conclusions] These results suggested that the detected SNPs were potential candidate for predicting the therapeutic effect of TCZ in RA patients before the treatment.

W51-5

Association between distribution of affected joints and disease activity score in rheumatoid arthritis patients-Answer cohort study-

Yuichi Maeda¹, Toru Hirano¹, Motomu Hashimoto², Wataru Yamamoto³, Kosuke Ebina⁴, Kosaku Murakami², Tohru Takeuchi⁵, Kenichiro Hata⁵, Yonsu Son⁶, Hideki Amuro⁷, Akira Onishi⁸, Sadao Jinno⁸, Masaki Katayama¹⁰, Yusuke Manabe¹, Yuta Yamaguchi¹, Yumiko Mizuno¹, Mayu Yagita¹, Ryota Hara⁹, Atsushi Kumanogoh¹

¹Department of Respiratory Medicine and Clinical Immunology, Osaka University, Graduate School of Medicine, ²Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto

Unuversity, ³Department of Health Information Management, Kurashiki Sweet Hospital, ⁴Department of Orthopaedic Surgery, Osaka University, Graduate School of Medicine, ⁵Department of Internal Medicine, Osaka Medical College, ⁶First Department of Internal Medicine, Kansai Medical University, ⁷First Department of Internal Medicine, Kansai Medical University, ⁸Department of Rheumatology and Clinical Immunology, Kobe University, Graduate School of Medicine, ⁹The Center for Rheumatic Diseases, Nara Medical University, ¹⁰Department of Rheumatology, Osaka Red Cross Hospital

Conflict of interest: None

[Object] It is unknown which part of the joints strongly contributes to increased levels of ESR and CRP in rheumatoid arthritis (RA) patients. [Methods] We analyzed retrospectively 56976 clinical data (5002 RA patients) who visited our hospitals in 2011 to 2018. We divided the joints into 6 sites (shoulders, knees, wrists, elbows, MCPs, PIPs) for further analysis. We investigated the correlation between swollen, tender joints and the disease activity-related score such as ESR, CRP, PtVAS (patient visual analogue scale) and DrVAS. We also analyzed relationship between affected joints and autoantibodies such as rheumatoid factor and anti-citrullinated peptide antibody. [Results] Interestingly, among the 6 sites, knees are the strongest factors which induce increased levels of ESR and CRP. By contrast, PIPs are the weakest factors which contribute to elevated levels of ESR and CRP. PtVAS and DrVAS strongly correlated with increased affected joints of hands and knees. Intriguingly, we also found that the levels of rheumatoid factor and anti-citrullinated antibody are correlated with the score of wrists. [Conclusions] Thus, these findings suggest that different joint distribution in RA patients leads to different results of disease activity score or autoantibody production.

W51-6

Systemic immune-inflammation index in rheumatoid arthritis patients: Relation to disease activity

Takahiro Yoshikawa, Maki Shibamoto, Kazuteru Noguchi, Rei Tadokoro, Kazuyuki Tsuboi, Mai Nakano, Chie Ogita, Mei Tani, Tetsuya Furukawa, Masao Tamura, Teppei Hashimoto, Mai Morimoto, Naoto Azuma, Masayasu Kitano, Kiyoshi Matsui
Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine

Conflict of interest: None

[Object] To assess systemic immune-inflammation index (SII) in rheumatoid arthritis (RA) patients and compare between active cases and those in remission. [Methods] In 734 RA patients registered in the database of our department from 2015 to 2016, a total of 437 eligible RA patients were included in this study, excluding 296 patients whose neither the RA disease activity or laboratory data were available. Correlations of SII with the disease activity of RA were evaluated. SII was calculated by the following calculation formula; $SII = \text{Neutrophils (\%)} / \text{Lymphocyte (\%)} * \text{Platelets (G/L)}$. [Results] The median age of patients was 65.0 (54.0-73.0) years and the median of disease duration was 9 (6-14) years. The DAS28-ESR was median 2.69 (1.94 - 3.49). SII was 618.3 (420.8 - 962.1). There was a significant correlation between SII and DAS28-ESR ($r=0.335$, $P<0.0001$), and SII was significantly elevated as disease activity increased (median 532.2 in remission, 579.9 LDA, 796.9 in MDA and 1261.1 in HDA, respectively; $P<0.00001$). The sensitivity and specificity of SII (cut-off, 688.6) for DAS28-ESR remission were 75.2% and 55.7%, respectively. [Conclusions] SII is an emerging inflammatory biomarker which could be used to evaluate disease activity in RA patients.

W52-1

Transcriptome analysis of peripheral blood mononuclear cells revealed connective tissue disease associated pulmonary arterial hypertension

Junko Maeda¹, Tomohisa Okamura^{1,2}, Yukiko Iwasaki¹, Yasuo Nagafuchi¹, Mineto Ota^{1,2}, Yusuke Takeshima^{1,2}, Haruyuki Yanaoka¹, Mai Okubo¹, Satomi Kobayashi¹, Harumi Shirai¹, Yusuke Sugimori¹, Hiroaki Hatano¹, Masahiro Nakano¹, Saeko Yamada¹, Ryochi Yoshida¹, Shuji Sumitomo¹, Hirofumi Shoda¹, Kazuhiko Yamamoto^{1,3}, Keishi Fujio¹
¹Department of Allergy and Rheumatology, Graduate School of Medi-

cine, The University of Tokyo, ²Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, ³Laboratory for Autoimmune Diseases, RIKEN Center for Integrative Medical Sciences

Conflict of interest: Yes

[Object] Pulmonary arterial hypertension (PAH) is characterized by arteriopathy in the small to medium sized distal pulmonary arteries. Anti U1-RNP antibodies are associated with several clinical characteristics like PAH. In this study, we aimed to assess the immunophenotypic characterization of connective tissue disease associated PAH (CTD-PAH) patients by flow cytometry (FCM) and transcriptome analysis. [Methods] Peripheral blood samples were obtained from 26 patients with anti U1-RNP antibodies (6 with PAH, 20 without PAH). Immunophenotypes were analyzed by FCM. Then RNA-seq of sorted cells was performed. [Results] Among 29 immune cell subsets, circulating regulatory T cells (Treg) tend to decrease in patients with anti-U1-RNP antibodies than HC, and the proportion of monocytes was significantly higher in those patients. Moreover, the expression profiles of profibrotic regulator genes was changed in monocytes from CTD-PAH patients with anti U1-RNP antibodies. [Conclusions] Treg dysfunction has been reported to induce activation of monocytes/macrophages in CTD-PAH. Our results suggest that the decreased number of regulatory T cells may be associated with the pathogenesis of CTD-PAH by activating monocytes and inducing the elevated expression profiles of profibrotic regulator genes.

W52-2

Pathogenic role of fractalkine in interstitial pneumonia

Soichi Yamada¹, Natsuko Kusunoki¹, Hiroshi Sato¹, Sei Muraoka¹, Toshio Imai², Shinichi Kawai³, Toshihiro Nanki¹

¹Division of Rheumatology, Department of Internal Medicine, School of Medicine, Faculty of Medicine, Toho University, Tokyo, Japan, ²KAN Research Institute, Inc, Kobe, Japan, ³Department of Inflammation & Pain Control Research, School of Medicine, Toho University, Tokyo, Japan

Conflict of interest: None

[Objective] Treatment for interstitial pneumonia (IP) associated with collagen diseases has not been established yet. It is expected to elucidate the pathogenesis of IP and development of novel therapy. We aimed to clarify the role of fractalkine (FKN) in IP. [Methods] Bleomycin (BLM) was intratracheally administered to C57BL/6 mice. Expression of FKN and the receptor CX3CR1 was analyzed immunohistochemistry. The mice were treated with anti-FKN mAb or control Ab intraperitoneally for 2 weeks. The lung was stained with hematoxylin-eosin, and collagen eluted from the lung was quantified. In vitro, mouse lung fibroblasts (MLFs) were stimulated with FKN. Production of collagen and the cell movement was examined. [Results] Expression of FKN and CX3CR1 was upregulated in BLM-induced IP. Treatment with anti-FKN mAb did not significantly alter inflammatory cell infiltration. However, collagen in the lung decreased. Stimulation with FKN did not alter the production of collagen from MLFs, but enhanced the cell movement significantly. [Conclusion] FKN might be involved in increasing collagen in the IP and cell movement of MLFs. It is suggested that FKN may contribute fibrosis of IP.

W52-3

Autoantibody-inducing CD4 T (*ai*CD4 T) cells which induce SLE contain follicular helper T cell in addition to IL-21-producing CXCR5^{hi}ICOS^{hi}PD-1^{hi} population

Ken Tsumiyama, Shunichi Shiozawa
Institute for Rheumatic Diseases

Conflict of interest: None

[Object] Autoantibody-inducing CD4 T (*ai*CD4 T) cell is indispensable for our 'self-organized criticality theory' that induces SLE. We previously showed that the *ai*CD4 T cell belongs to CD45RB^{lo}122^{lo} subpopulation. Here we further dissected the phenotype of *ai*CD4 T cell. [Methods] BALB/c mice were repeatedly immunized with OVA, and

SLE was induced. Cell surface marker and cytokine production of CD45RB^{lo} CD4 T cell were examined using flow cytometry and ELISA. These CD4 T cells were adoptively transferred into recipient mice, and anti-ds DNA antibody and urine albumin were detected. [Results] After repeated immunization with OVA, not only CXCR5⁺ICOS^{hi}PD-1^{hi} follicular helper T (Tfh) cell but also CXCR5⁺ICOS^{hi}PD-1^{hi} cell was increased in CD45RB^{lo} CD4 T cell. CXCR5⁺ICOS^{hi}PD-1^{hi} CD4 T cell highly produced IL-21 rather than Tfh cell. Both CD4 T cells were induced anti-ds-DNA antibody in the recipient mice. Further, CXCR5⁺ICOS^{hi}PD-1^{hi} CD4 T cell strongly induced kidney injury as compared to Tfh cell. [Conclusions] In addition to Tfh cell, IL-21-producing CXCR5⁺ICOS^{hi}PD-1^{hi} CD4 T cell was increased in line with induction of SLE. This novel CXCR5⁺ICOS^{hi}PD-1^{hi} CD4 T cell appears to be responsible for helping B cell to induce autoantibody and driving CD8 T cell to cause lupus tissue injury.

W52-4

The regulation of skin fibrosis in systemic sclerosis by extracellular ATP via P2Y2 purinergic receptor

Sei-ichiro Motegi, Osamu Ishikawa

Department of Dermatology, Gunma University Graduate School of Medicine

Conflict of interest: None

[Object] Objective was to elucidate the role of extracellular ATP, which can act as a damage-associated molecular pattern molecules (DAMPs), in skin fibrosis in systemic sclerosis (SSc). [Methods] Production of IL-6 and collagen in SSc or normal fibroblasts treated by ATP was analyzed. [Results] We identified that hypoxia enhanced ATP release, and extracellular ATP enhanced IL-6 production more significantly in SSc fibroblasts than in normal fibroblasts. Non-selective P2 receptor antagonist and selective-P2Y₂ receptor antagonists, kaempferol and AR-C, significantly inhibited ATP-induced IL-6 production and phosphorylation of p38 in SSc fibroblasts. Collagen type I production in SSc fibroblasts by ATP-induced IL-6/IL-6 receptor trans-signaling was inhibited by kaempferol and p38 inhibitor, SB203580. Amount of ATP in bleomycin-treated skin was increased, and administration of AR-C significantly inhibited bleomycin-induced dermal fibrosis in mice. [Conclusions] These results suggest that vasculopathy-induced hypoxia and oxidative stress might enhance ATP release in the dermis in SSc, and extracellular ATP-induced phosphorylation of p38 via P2Y₂ receptor might enhance IL-6 and collagen type I production in SSc fibroblasts.

W52-5

Elevated Serum Concentration of Amphiregulin in Patients with Idiopathic Inflammatory Myopathy and Systemic Sclerosis

Akito Kawamura, Norio Hanata, Yasuo Nagafuchi, Yusuke Sugimori, Satomi Kobayashi, Yukiko Iwasaki, Hirofumi Shoda, Keishi Fujio
Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Conflict of interest: None

[Object] Amphiregulin (AREG) belongs to the epidermal growth factor that seems to be involved in the pathophysiology of autoimmune diseases such as rheumatoid arthritis (RA), while there is a paucity of research to show the association of AREG in idiopathic inflammatory myopathy (IIM) and systemic sclerosis (SSc). In this study, we measured the serum concentration of AREG in patients with IIM and SSc. [Methods] Serum concentration of AREG in patients with 18 IIM, 6 SSc and 7 RA was measured by ELISA and compared to that of 6 healthy controls (HC). The relationship between the serum concentration of AREG and the clinical parameters such as autoantibody profiles, presence of interstitial lung disease (ILD), and serum creatine kinase (CK) value were analyzed. [Results] The serum concentration of AREG was significantly elevated in patients with IIM (33.2 ± 16.5 pg/ml, $p=0.0066$), SSc (25.4 ± 10.9 pg/ml, $p=0.025$) and RA (20.5 ± 7.95 pg/ml $p=0.044$) compared to that in HC (11.9 ± 3.47 pg/ml). In particular, there was a tendency that the serum concentration of AREG was elevated in IIM with ILD compared to that in IIM without ILD (37.3 ± 5.06 vs 24.9 ± 4.14 , $p=0.096$). [Conclusions] The serum concentration of AREG was significantly ele-

vated in patients with IIM and SSc compared to that in HC.

W52-6

Intravenous low-molecular-weight heparin PLGA micro-particles inhibit lung fibrosis of bleomycin-induced interstitial pneumonia

Takuya Kotani, Takayasu Suzuka, Shogo Matsuda, Takao Kiboshi, Koji Nagai, Kenichiro Hata, Tohru Takeuchi, Shigeki Arawaka
Department of Internal Medicine IV, Osaka Medical College

Conflict of interest: None

[Object] Interstitial pneumonia (IP) is a life-threatening pathological condition that causes respiratory failure when it progresses. The development of new treatments is thus required for IP from the viewpoint of the poor effect and adverse effects of the currently available treatments. Heparin promotes the production of hepatocyte growth factor (HGF) in various cells and is useful for not only promoting cell proliferation but also immune response modulating action and anti-fibrotic effect. We investigated the therapeutic effect of intravenous low-molecular-weight heparin PLGA micro-particles (LMWH/PLGA) in a mouse model of bleomycin-induced IP. [Results] Heparin increased HGF production in the culture supernatant of type 2 alveolar epithelial cells. LMWH/PLGA inhibited fibrosis in the lung. The levels of TNF- α , IL-6, IL-1 β , COL1 α 1, and TIMP mRNA expression at 28 days after BLM administration were significantly lower in LMWH/PLGA treated group compared with those in non-treated group. [Conclusions] Intravenous LMWH/PLGA showed anti-fibrotic effect on IP model mice.

W53-1

Intrapleural methylprednisolone injection in pleuritis associated with connective tissue diseases: report of three cases

Saki Minoda, Yoichi Nakayama, Hirofumi Miyake, Hiroyuki Akebo, Ryuichi Sada, Hiroyasu Ishimaru, Kazuhiro Hatta
General Internal Medicine, Tenri Hospital

Conflict of interest: None

[Case] (Case 1) A 79-year-old woman with rheumatoid arthritis (RA) presented with bilateral exudative pleural effusion. Although 0.8mg/kg of prednisolone (PSL) were not effective, bilateral intrapleural methylprednisolone injection (ip-mPSL-i, 125mg in each side) could reduce her pleural effusion. (Case 2) An 83-year-old woman with Sjogren's syndrome presented with right exudative pleural effusion. She did not have an indication of high dose PSL or pleurodesis because of her background. We performed 120mg of ip-mPSL-i, which reduced her pleural effusion and turned her exudative pleural effusion into transudate. (Case 3) A 70-year-old woman with SLE and stage 3 pharyngeal cancer presented with cytology-negative left exudative pleural effusion. Either 1mg/kg of PSL and 120mg of ip-mPSL-i were not effective, and, she died due to Klebsiella bacteremia and invasive aspergillosis after 4 weeks. [Discussion] Effectiveness of ip-mPSL-i for pleural effusion due to connective tissue diseases (CTDs) other than RA is still unclear. We performed the injection for 3 cases of CTDs-related pleurisy. 2 cases without advanced cancer achieved a therapeutic effect. [Clinical Significance] ip-mPSL-i is one of the useful options for pleural effusion caused by CTDs.

W53-2

Systemic AL Amyloidosis Mimicking Rheumatoid Arthritis

Mikiko Iguchi

National Hospital Organization Kyoto Medical Center

Conflict of interest: None

Systemic AL amyloidosis mimicking seronegative rheumatoid arthritis A-51-year-old woman suffered from symmetrical multiple joint swelling simulating rheumatoid arthritis. Treatment with prednisolone, methotrexate and tocilizumab was not sufficiently improved her arthritis. Further examination revealed Bence Jones Protein in urine without monoclonal protein on immunoelectrophoresis in serum. Bone marrow biopsy didn't show typical plasma cell infiltration and a synovial biopsy revealed amyloid deposition composed AL kappa-amyloid. From these

findings, She was finally diagnosed with amyloid arthropathy. Amyloid arthropathy was proved to be with a frequency of 3.5% in a cohort study in a large set of patients with multiple myeloma, but it is unknown that a frequency of amyloid arthropathy in primary systemic AL amyloidosis. Primary Systemic AL amyloidosis or myeloma associated AL amyloidosis may be important in the differential diagnosis of chronic polyarthritis.

W53-3

Six cases with Chlamydia-associated rheumatoid arthritis, who could stop disease-modifying antirheumatic drug

Naruhiko Takasawa^{1,2,3}, Junichi Kameoka³, Yukio Sekiguchi⁴, Takeshi Sasaki^{1,2}

¹Department of Internal Medicine, Tohoku Medical and Pharmaceutical University Wakabayashi Hospital, ²Department of Rheumatology, Tohoku Medical and Pharmaceutical University Wakabayashi Hospital, ³Division of Hematology and Rheumatology, Faculty of Medicine, Tohoku Medical and Pharmaceutical University, ⁴Department of Internal Medicine, Tohoku Medical and Pharmaceutical University Natorimori Hospital

Conflict of interest: None

Chlamydia infection often causes acute onset of polyarthritis. We have demonstrated that rheumatoid arthritis (RA) may occur in association with Chlamydia infection in some cases. We here report six cases with RA, who were all positive for anti-Chlamydia pneumoniae IgM antibodies at onset. The therapy using minocycline (MINO) and methotrexate (MTX) could bring them termed as Chlamydia-associated RA, into remission without any disease-modifying antirheumatic drug (DMARD) including MTX. Six cases were in their forties to seventies. They fell to the acute-onset RA, got swollen joints and met the diagnostic criteria for RA. Vascular signals of joint echo were recognized and matrix metalloproteinase 3 (MMP-3) was elevated in all six cases. Anti-cyclic citrullinated peptide (CCP) antibodies were negative in half of six cases. They were treated with MTX and MINO. The treatment was effective for all the cases and the administration with biological DMARD was unnecessary in any cases. Six to ten mg of MTX per week were administered to them and induced remission. The amount of MTX was reduced gradually and treatment with DMARD including MTX was ceased finally. These indicate that Chlamydia-associated RA may be a subtype of RA, which has good prognosis.

W53-4

Endotheliopathy Induces Renal Dysfunction Of TAFRO Syndrome: Clinicopathological Analysis Of 7 cases Of TAFRO syndrome

Hiroki Mizuno, Daisuke Ikuma, Shun Watanabe, Masahiko Oguro, Akinari Sekine, Masayuki Yamanouchi, Noriko Hayami, Eiko Hasegawa, Tatsuya Suwabe, Junichi Hoshino, Naoki Sawa, Kenmei Takaichi, Yoshifumi Ubara

Department of Rheumatology, Toranomon Hospital

Conflict of interest: None

[Object] TAFRO syndrome is subtype of multicentric Castelman disease, characterized by thrombocytopenia, anasarca, fever, reticulin fibrosis, organomegaly. Renal dysfunction is known as a manifestation of TAFRO syndrome, sometimes requiring hemodialysis, but pathophysiology has not been elucidated yet. [Methods] Design; case series. Subject; 7 cases of TAFRO syndrome treated in our hospital between April in 2014 and October in 2018. [Results] Median age was 53 y.o. (min 34, max 84), 3 cases were female. Body weight gain was 17.6 (8.3, 26.4) kg and platelet count was 4.1 (2.8, 11.5) × 10⁴/μL. Serum creatinine was 1.17 (0.77, 5.71) mg/dL and maximum level was 2.67 (1.43, 6.28) mg/dL. Hemodialysis was required in 5 cases. Severe endothelial injury with tuft occlusion was observed in all cases. All cases were treated by glucocorticoid and 6 cases by tocilizumab. Thrombocytopenia was treated by thrombopoietin receptor agonist in 5 cases. 1 case was died by aspiration pneumonia and hemodialysis was not required after the treatment in all cases. Critical hemorrhage was occurred in 4 cases and PRES was occurred in 1 case during the treatment. [Conclusions] Severe endothelial injury was commonly seen in all patients with TAFRO syndrome and renal dysfunction. This change is specific in TAFRO syndrome.

W53-5

Clinical significance of myositis-specific autoantibodies in idiopathic interstitial pneumonia

Yasuo Matsuzawa, Kotaro Kumano

Department of Internal Medicine, Toho University Sakura Medical Center, Sakura, Japan

Conflict of interest: None

[Object] To clarify clinical significance of myositis-specific autoantibodies in idiopathic interstitial pneumonia (IIP). [Methods] All IIP patients who visited our department between December, 2015 and July, 2018 were subjected to measurement of myositis-specific autoantibodies using EUROLINE test. [Results] 240 patients of IIP were subjected. The HRCT patterns (number of the patients) of the patients were UIP (65), possible UIP (48), inconsistent with UIP (80), OP (40), DAD (7). Myositis-specific autoantibodies: OJ, EJ, PL12, PL7, SRP, Jo-1, Mi2 were positive in 5, 3, 9, 14, 9, 1, 7 patients. 7 patients were positive for multiple autoantibodies. The HRCT patterns of the 40 patients were UIP (7), possible UIP (9), inconsistent with UIP (20), OP (3), DAD (1). Acute exacerbation was observed in 7 patients, and 9 patients have died. The risk factor for acute exacerbation were anti PL12 antibodies (OR 1.99, p=0.006) and anti PL7 antibodies (OR 1.5, p=0.04), and the risk factors for death was anti PL12 antibodies (OR 1.7, p=0.03) in multivariate analysis. [Conclusions] Myositis-specific autoantibodies was positive for 40 of 240 patients of IIP. Anti PL12 antibodies and anti PL7 antibodies were risk factors of acute exacerbation, and anti PL12 antibodies was poor prognostic factor.

W53-6

Sleep status in RA patients receiving steroid medication

Noriyuki Hayashi¹, Shinsuke Yamada¹, Norikazu Toi¹, Yutaka Furumitsu², Shinichi Yamauchi³, Masaaki Inaba¹

¹Department of Metabolism, Endocrinology and Molecular Medicine, Osaka City University Graduate School of Medicine, Osaka, Japan, ²Department of Internal Medicine, Ohno Memorial Hospital, Osaka, Japan, ³Department of Orthopedic Surgery, Ohno Memorial Hospital, Osaka, Japan

Conflict of interest: None

[Background] There are not so many reports that examine the association between prednisolone (PSL) use and sleep status in RA patients, though it is known that sleep disorder is one of the important side effects of PSL. [Object] We investigated the influence that steroid medication gave in sleep status in RA patients. [Methods] We examined 28 RA patients (PSL user/non-user number: 13/15, 64.9/61.3 years of age, DAS28 (CRP): 3.2/3.5). In all patients, subjective and objective sleep status were assessed by Pittsburgh Sleep Quality Index (PSQI) and single-channel EEG, respectively. [Results] PSQI levels was 6.6 ± 3.2 in 28 RA patients. Approximately 71% of them had a diagnosis of sleep disorder (PSQI ≥ 5.5). Although there was no significant difference in age and DAS28 between PSL user and non-user, nocturnal awakening tended to be longer in PSL user than in PSL non-user, and slow wave sleep (SWS) and δ-power as sleep quality parameter were higher significantly in PSL non-user than in PSL user. In multiple regression analysis including age, DAS28, and PSL use or not, only PSL use was associated significantly in a negative manner with δ power. [Conclusions] Steroid medication has a negative effect on sleep status in RA patients.

W54-1

Involvement of mast cells in the development of tissue fibrosis of Sjögren's syndrome via fibroblast immune function

Shinjiro Kaieda, Kyoko Fujimoto, Yumi Yoshida, Makiko Hayashi, Takuma Koga, Hiroaki Ida

Department of Medicine, Division of Respiratory, Neurology and Rheumatology, Kurume University School of Medicine

Conflict of interest: None

[Object] We examined whether mast cells (MCs) play a critical role in sialadenitis in patients with Sjögren's syndrome (SS). [Methods] Labial salivary glands (LSG) samples were collected from 22 individuals with

primary SS and 10 with sicca syndrome. The degree of fibrosis in LSG was graded on a quantitative scale as previously reported. Human mast cell line 1 (HMC-1) were stimulated with or without recombinant IL-33/SCF for 24 hours and HMC-1 conditioned medium was collected. Profibrotic factors and collagen synthesis in fibroblasts was evaluated. [Results] The number of MCs in LSGs of patients with SS was significantly increased. There was a significant negative correlation between the Saxton's test results and the MC density ($r=-0.6742$, $P=0.006$). Whereas there was no correlation between the focus score and the MC density ($r=0.01545$, $P=0.58$), a significant correlation between the MC density and the degree of fibrosis was observed ($r=0.5911$, $P=0.0038$). MCs were usually present in close proximity to EVG-stained fibrous tissue. Significant up-regulation of profibrotic factors and Col1a mRNA was observed in fibroblast cultured in HMC-1-conditioned medium. [Conclusions] MCs contribute to sialadenitis in patients with SS by induction of tissue fibrosis via fibroblast immune function.

W54-2

Studies on anti-carbamylated protein antibody and the joint destruction in Sjogren's syndrome patients

Kazuko Shiozawa¹, Yasushi Tanaka¹, Ryosuke Yoshihara¹, Miki Murata¹, Natsuko Nakagawa¹, Atsuo Uefuji¹, Toshiyuki Ota², Ken Tsumiyama³, Shunichi Shiozawa³

¹Rheumatology & Collagen Disease Center, Hyogo Prefectural Kakogawa Medical Center, ²Collagen & Rheumatic Disease Center, Iizuka Hospital, ³Institute for Rheumatic Diseases

Conflict of interest: None

INTRODUCTION Anti-carbamylated protein antibody (aCaPAb) reacts against homocitrulline an amino acid harbouring additional CH₂ residue on citrulline scaffold. aCaPAb has previously been detected in 20% of Japanese patients with primary Sjogren's syndrome (pSS). We here evaluated 20 aCaPAb-positive pSS patients in comparison with 78 aCaPAb-negative pSS patients to clarify the contribution of aCaPAb to the clinical features. **METHODS** The presence of IgG antibody reactive against carbamylated fibrinogen was measured by using ELISA. **RESULTS** Among aCaPAb-positive pSS, the positive ratios for rheumatoid factor, anti-SS-A Ab and ACPA were higher as compared with those negative for aCaPAb-negative pSS patients. The number of tender joints were; zero was 40% and 53.8%, 1~2 was 30% and 30.8%, >3 was 30% and 15.4% in the aCaPAb-positive and aCaPAb-negative patients, respectively. The modified Sharp score 0 was 50% and 72.4%, score 1 was 16.7% and 20.7%, and score more than 2 was 33.3% and 6.9%, respectively, among those with positive-aCaPAb (n=18) and those with negative-aCaPAb (N=58) ($p=0.03$). **CONCLUSION** The joint destruction appeared more progressive in aCaPAb-positive pSS patients as compared with those with negative for aCaPAb, which suggests that aCaPAb may reflect progressive joint destruction.

W54-3

Assessment of submandibular glands using shear wave elastography in patients with early-stage Sjögren's syndrome

Naoaki Hashimoto¹, Masayasu Kitano², Takashi Nakazawa³, Tsuyoshi Iwasaki⁴, Takenori Hashimoto¹

¹Hashimoto Rheumatology Clinic, ²Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, ³Department of Rheumatology, Osaka Saiseikai Nakatsu Hospital, ⁴Department of Pharmacy, Hyogo University of Health Sciences

Conflict of interest: None

Object: The submandibular gland (SG) ultrasonography is useful for the diagnosis of Sjögren's syndrome (SS) patients, but it is difficult to diagnose early-stage SS patients with normal saliva flow (JCR2016). We reported that the shear wave elastography (SWE) is useful for elucidating the SG lesion in SS patients (JCR2018, EULAR2018). The aim of this study was to elucidate the usefulness of SWE in early-stage SS patients. **Methods:** Seventeen non-SS and 80 SS patients classified according to saliva flow by gum test were studied (N/SS: <10mL/10min. (n=15), L/SS: 5-10mL/10min. (n=32), VL/SS: <5mL/10min. (n=33)). The SG was evaluated by US staging and PD grading score, and shear wave velocity

(Vs) and elasticity (E) by SWE. **Results:** There was no significant difference between non-SS and N/SS in early-stage SS by US staging and PD grading score. However, the Vs and E were significantly higher in N/SS than in non-SS (Vs: 1.73±0.18 vs 2.03±0.28 m/s, E: 9.38±1.17 vs 12.73±3.63 Kpa, $p<0.01$). The US staging score, PD grading score, Vs and E were correlated to saliva flow reduction in three SS groups. **Conclusions:** The present study demonstrated that the SWE may be a useful tool for the differential diagnosis between patients with non-SS and early-stage SS in contrast to conventional SGUS.

W54-4

Chronological changes in oral health-related quality of life in patients with Sjögren's syndrome

Naoto Azuma¹, Yoshinori Katada², Sachie Kitano¹, Aki Nishioka^{1,3}, Masahiro Sekiguchi^{1,4}, Masayasu Kitano¹, Hajime Sano^{1,5}, Kiyoshi Matsui¹

¹Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, ²Department of Rheumatology, Sakai City Medical Center, ³Department of Rheumatology, Nishinomiya Watanabe Hospital, ⁴Department of Rheumatology, Hyogo Prefectural Nishinomiya Hospital, ⁵Kyoto Okamoto Memorial Hospital

Conflict of interest: None

[Object] To assess oral health-related quality of life (OHRQoL) and evaluate changes in OHRQoL within three years in patients with Sjögren's syndrome (SS). **[Methods]** 35 SS patients and 23 controls (non-SS) were enrolled. OHRQoL were evaluated using a short version of the Oral Health Impact Profile (OHIP-14), which is a self-administered questionnaire. Higher scores indicate poorer OHRQoL. 22 patients and 14 controls were followed up for three years. **[Results]** In the SS group, the OHIP-14 score was significantly higher compared with the non-SS group (11.3 vs 7.1, $p=0.027$). Salivary flow rate in the severe group (score ≥ 14) was significantly higher than that in the mild group (≤ 13). Scores of "trouble pronouncing words", "uncomfortable to eat", "self-conscious", "diet unsatisfactory" in the SS group were significantly higher than those in the non-SS group. The OHIP-14 score significantly increased after three years in the SS group (10.2 vs 12.6, $p=0.040$). Such change was not observed in the non-SS group. Scores of "irritable with others", "difficulty doing jobs", "life unsatisfying", "unable to function" significantly increased in the SS group. **[Conclusions]** OHRQoL is impaired in SS patients. Sustained xerostomia can cause poorer OHRQoL associated with social disability and handicap.

W54-5

Effectiveness of abatacept for patients with secondary Sjögren's syndrome (SS) associated with rheumatoid arthritis (RA). An open label, multicenter, prospective study: ROSE (Rheumatoid Arthritis trial toward Sjögren's syndrome Endocrinopathy) trial

Fumika Honda¹, Hiroto Tsuboi¹, Kazuhisa Nakano², Yoshiya Tanaka², Hideki Nakamura³, Atsushi Kawakami³, Yuichiro Fujieda⁴, Tatsuya Atsumi⁴, Yasunori Suzuki⁵, Mitsuhiro Kawano⁵, Yuko Kaneko⁶, Tsutomu Takeuchi⁶, Hitomi Haraoka⁷, Masami Takei⁷, Naoto Tamura⁸, Yoshinari Takasaki⁸, Kazuhiro Yokota⁹, Toshihide Mimura⁹, Kosaku Murakami¹⁰, Tsuneyo Mimori¹⁰, Shiro Ohshima^{10,11}, Naoto Azuma¹², Hajime Sano¹², Susumu Nishiyama¹³, Isao Matsumoto¹, Takayuki Sumida¹

¹Department of Internal Medicine, Faculty of Medicine, University of Tsukuba, Ibaraki, Japan, ²The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, ³Unit of Translational Medicine, School of Medicine, Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ⁴Internal Medicine II, Hokkaido University, Sapporo, Hokkaido, Japan, ⁵Division of Rheumatology, Department of Internal Medicine, Kanazawa University Graduate School of Medicine, Kanazawa, Japan, ⁶Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, ⁷Division of Hematology and Rheumatology, Department of Medicine, Nihon University Itabashi Hospital, Tokyo, Japan, ⁸Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan, ⁹Department of Rheumatology and Applied Immunology, Saitama Medical University, Saitama, Japan, ¹⁰Department of Rheumatology and Clinical Immunology

gy, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ¹¹Division of Rheumatology, Osaka Minami Medical Center, National Hospital Organization, Osaka, Japan, ¹²Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, Hyogo, Japan, ¹³Division of Rheumatology, Kurashiki Medical Center, Okayama, Japan

Conflict of interest: Yes

[Objectives] To clarify the effectiveness of abatacept (ABT) for patients with secondary SS (sSS) associated with RA. [Methods] Patients with sSS with RA were enrolled in ROSE I/II trial designed as an open-labeled, multi center, prospective study. 1) The primary endpoint was the achievement of SDAI remission at 52 weeks (W) after treatment with ABT. 2) Secondary endpoint included Saxon's and Schirmer's test. 3) In ROSE II, ESSDAI and ESSPRI were also included in secondary endpoint. [Results] 61 patients (all female) were enrolled (36 in ROSE I and 25 in ROSE II). Among them, 43 patients (36 in ROSE I and 7 in ROSE II) who had completed the evaluation at 52W were analyzed in this study. 1) SDAI significantly decreased from 20.8±11.5 (0W) to 10.2±10.1 (52W), and patients who achieved SDAI remission significantly increased from 0 (0W) to 12 cases (27.9%) (52W) (N=43, p<0.05). 2) Saxon's and Schirmer's test significantly improved from 2034±1789 (0W) to 2405±1852 mg/2min (24W) (N=41, p<0.05) and 4.7±5.8 (0W) to 6.0±7.4 (24W) mm/5min (N=34, p<0.05), respectively. 3) ESSDAI significantly decreased from 9.6±5.4 (0W) to 3.6±2.3 (24W) (p<0.05), while ESSPRI did not significantly change (4.5±2.0 to 3.9±2.0) (N=7). [Conclusion] ABT was effective for both RA and SS manifestations of sSS with RA.

W54-6

Clinical characteristics of Sjögren's syndrome induced by immune checkpoint inhibitors

Mikito Suzuki, Takahisa Gono, Shinji Watanabe, Yuichiro Shirai, Seiji Kobayashi, Mitsuhiro Takeno, Masataka Kuwana
Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan

Conflict of interest: Yes

Objectives: We experienced two cases who developed Sjögren's syndrome (SS) after administration of ICI. The aim of this study is to identify clinical characteristics of ICI-induced SS by literature review. **Methods:** We investigated clinical information of our cases and published literature reporting ICI-induced SS. We conducted a Pubmed search on the following keywords: "Sjögren", "immune checkpoint inhibitor", "Ipilimumab", "Nivolumab", "Pembrolizumab", "Atezolizumab", "Avelumab", "Durvalumab". **Results:** A total of 16 cases including our 2 cases developed SS at 14 weeks of the median period after initiation of ICI. The mean age was 62 years and 50 % were female. The most common malignancy was melanoma in 8 cases. Five cases received combination therapy with CTLA-4 inhibitors and PD-1 inhibitors. CTLA-4 inhibitor or PD-1 inhibitor was received in 7 and 4, respectively. Regarding the treatment for SS, ICI was ceased in 2 cases. 10 cases received corticosteroid (CS). Pilocarpine and cevimeline were administered in 3 and 1 case, respectively. Sicca symptoms improved in 13 of 16 cases. **Conclusions:** Sicca symptoms developed more acutely and the response to the treatment with CS for SS was better in ICI-induced SS, different from clinical characteristics in classic primary SS.

W55-1

Comparison of effectiveness of biologic DMARDs stratified by disease activities using propensity score matching

Kazuyoshi Saito^{1,2}, Kazuhisa Nakano², Shingo Nakayamada², Shigeru Iwata², Satoshi Kubo³, Ippei Miyagawa⁴, Shunsuke Fukuyo², Yusuke Miyazaki², Kentaro Hanami^{1,3}, Ayako Yamaguchi², Akio Kawabe², Masao Nawata¹, Yuya Fujita¹, Yoshiya Tanaka²

¹Center for Rheumatic Disease, Tobata General Hospital Kitakyushu Japan, ²The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu Japan, ³Department of Rheumatology, Wakamatsu Hospital of the University of Occupational and Environmental Health, Kitakyushu Japan, ⁴Department of Emergency Medicine, University Hospital of Occupational and Environmental Health, Kitakyushu Japan

Conflict of interest: None

[Object] This study aimed to evaluate the effectiveness of biologics stratified by disease activities at induction in RA from our university cohort (FIRST registry). [Methods] We retrospectively examined patients treated with TNF inhibitors (TNFi; IFX 345, ETN 348, ADA 517, GLM 106, CZP 161), TCZ 490, ABT 49. After stratification with disease activities (H group; high disease activity DAS28ESR>5.1, ML group; 2.6-5.1) at induction, we compared the patients' background, CDAI at 2 and 52wks after treatment using PS matching. [Results] Patients were divided to two groups as TNFi (H;913, ML;564), TCZ (H;355, ML;135), ABT (H;309, ML;188). Shorter disease duration, higher ratio of bio-naïve and concomitant treatment with MTX in TNFi, higher titers of CRP, MMP in TCZ, higher age in ABT were observed in both H and ML group. After PS matching, however CDAI at both 2 and 52 wks were comparable in both H and ML group, effectiveness was TNF>TCZ, ABT at 2 wks and TNF, TCZ>ABT at 52 wks in H group. [Conclusions] Disease activity at initiation of biologics might be one of important factor for selection of biologics. Although, there was slight differences among biologics, we have to decide biologics after comprehensive consideration including adverse effects that we did not discussed in this study.

W55-2

Comparison of drug tolerability and discontinuation reasons between 7 biologics in elderly patients with rheumatoid arthritis -Data from Kansai consortium for well-being of rheumatic disease patients (AN-SWER cohort)-

Kosuke Ebina¹, Motomu Hashimoto^{1,3}, Wataru Yamamoto^{3,4}, Toru Hirano², Yuichi Maeda², Koichi Murata³, Ryota Hara⁵, Akira Onishi⁶, Sadao Jinno⁶, Yonsu Son⁷, Hideki Amuro⁷, Masaki Katayama⁹, Tohru Takeuchi⁸, Koji Nagai⁸, Makoto Hirao¹, Hideki Yoshikawa¹

¹Department of Orthopaedic Surgery, Osaka University, Graduate School of Medicine, Osaka, Japan, ²Department of Respiratory Medicine and Clinical Immunology, Osaka University, Graduate School of Medicine, Osaka, Japan, ³Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, ⁴Department of Health Information Management, Kurashiki Sweet Hospital, ⁵The Center for Rheumatic Diseases, Nara Medical University, ⁶Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, ⁷First Department of Internal Medicine, Kansai Medical University, ⁸Department of Internal Medicine IV, Osaka Medical College, ⁹Department of Rheumatology, Osaka Red Cross Hospital

Conflict of interest: Yes

[Object] To compare the tolerability and discontinuation reasons between 7 biologics in elderly (65 years of age or older) RA. [Methods] 1098 biologics treatment courses from 2009 to 2017 (female 80.8%, age 71.7y, RF positivity 81.1%, Bio naïve 60.2%, number of each agent; ABT 272, TCZ 234, ETN 184, GLM 159, IFX 101, ADA 97, and CZP 51) were included in this multi-center, retrospective study. Drug tolerability and discontinuation reasons were adjusted by potent confounding factors (age, sex, and switched biologics number) with a Cox proportional hazards model and evaluated at 36 months. [Results] Adjusted cumulative incidence rates of each discontinuous reason were as follows. Drug inefficacy (ABT 18.1%, TCZ 22.5%, GLM 23.4%, IFX 28.9%, ADA 33.0%, CZP 40.5%, ETN 42.6%; Cox P < 0.001), toxic adverse events (ABT 4.6%, CZP 6.5%, ETN 14.3%, TCZ 15.2%, GLM 15.5%, ADA 15.8%, IFX 21.5%; Cox P = 0.03), remission (IFX 8.4%, TCZ 7.0%, ETN 6.4%, ABT 5.7%, ADA 3.9%, GLM 3.2%, CZP 0.0%; Cox P = 0.46). Overall adjusted retention rates excluding non-toxic events and remission were ABT 78.1%, TCZ 65.8%, GLM 64.9%, ADA 56.3%, IFX 55.8%, CZP 55.0%, ETN 47.1% (Cox P < 0.001). [Conclusions] ABT showed lowest inefficacy and toxic events, and highest retention rate in adjusted model.

W55-3

The efficacy, safety and adherence of biologic disease-modifying anti-rheumatic drugs, infliximab, tocilizumab and abatacept, in elderly patients with rheumatoid arthritis

Takuma Wada¹, Yu Funakubo¹, Mayumi Matsuda¹, Hiroaki Yazawa¹, Yoshinobu Nakao², Noritsune Kozu³, Keita Okamoto¹, Takashi

Maruyama¹, Yoshihiro Yoshida¹, Kazuhiro Yokota¹, Yasuto Araki¹, Hiroshi Kajiyama¹, Kojiro Sato¹, Yuji Akiyama⁴, Toshihide Mimura¹
¹Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University, Saitama, Japan, ²Department of Rheumatology, Saga University Hospital, Saga, Japan, ³Kouzu Orthopedic Clinic, Chiba, Japan, ⁴Department of Rheumatology, Ogawa Red Cross Hospital

Conflict of interest: None

[Objective] It is known if biologic disease-modifying anti-rheumatic drugs (bDMARDs) can be used to the elderly rheumatoid arthritis (RA) patients safely and effectively in the world. The purpose of this study is to examine the efficacy, safety and adherence of bDMARDs in elderly RA patients. [Methods] RA patients (n=253) who received bDMARDs were divided into 2 groups, the younger group and the elderly one. We analyzed retrospectively the efficacy, safety and adherence of those bDMARDs in the 2 groups. [Results] In elderly group, the rate of MTX use was lower and the rate of PSL use was higher than younger group significantly (p<0.001) before bDMARDs. CDAI and HAQ-DI significantly decreased in both groups during 1 year after bDMARDs exposure (P<0.001). There was no significant difference in the prevalence of patients who achieved CDAI remission and the continuation rate of bDMARDs between the 2 groups. The average doses of PSL at baseline were significantly decreased after 1 year in both groups (p<0.001). The total number of withdrawals of bDMARDs within 1 year, the number of inefficacy or adverse events were not significantly different between the 2 groups. [Conclusion] The efficacy, safety and adherence of bDMARDs in elderly patients were not inferior to those in younger patients.

W55-4

Reduced renal function in patients with rheumatoid arthritis treated with biologic agents

Eigo Kikuchi, Naoko Aoki, Taro Yoshioka, Takahiro Okai
Center for Rheumatology and Joint Surgery, Kawakita General Hospital, Tokyo, Japan

Conflict of interest: None

[Object] We aimed to examine the reduction of renal function and its risk factors in patients with rheumatoid arthritis (RA) treated by biologic agents. [Methods] We used biologic agents to treat patients with RA who had visited our hospital between 2011 and 2016. All patients had exhibited eGFR values of ≥ 70 (mL/min/1.73 m²) prior to use of biologic agents. The end point was decline in eGFR by $\geq 20\%$ for ≥ 3 months; moreover, the patients were analyzed according to their age (≥ 65 years old vs <65 years old) and the presence or absence of NSAID use. [Results] Overall, 180 patients (153 females, 85.0%, average age 57.6 \pm 16.1 years, ABT 23 cases, ADA 19 cases, CZP 19 cases, ETN 54 cases, GLM 16 cases, IFX 18 cases, TCZ 31 cases) were enrolled in this study. The longest cumulative incidence of reduced renal function in the 60-month period was 45.4%. The cumulative incidence was 68.1%, among patients aged ≥ 65 years (n = 66) and 33.4% in those <65 (n = 114) [p < 0.001 (log-rank test)]. The cumulative incidence in NSAIDs users (n = 70) was 61.6%, whereas in non-NSAIDs users (n = 110), it was 36.9% (p = 0.016). [Conclusions] It is recommended that renal function should be closely monitored in elderly patients who are undergoing treatment for RA with biologic agents and are taking NSAIDs.

W55-5

Current situation and secular change of biosimilars in NinJa

Toshihiro Matsui¹, Atsushi Hashimoto¹, Atsushi Kaneko², Shigeto Tohma³
¹Department of Rheumatology, National Hospital Organization Sagami-hara National Hospital, ²Department of Orthopedic Surgery, National Hospital Organization Nagoya Medical Center, ³National Hospital Organization Tokyo National Hospital

Conflict of interest: Yes

[Object] To investigate the current situation and secular change of biosimilars in patients with rheumatoid arthritis (RA) in Japan. [Methods] Using the data of NinJa (National Database of Rheumatic Disease in Ja-

pan) from 2014 to 2017, we compared the actual use and users' background of between infliximab (IFX) and infliximab BS (IFX-BS). [Results] The number of patients registered in each fiscal year of NinJa was 15023 (2014) \rightarrow 15100 (2015) \rightarrow 15341 (2016) \rightarrow 15185 (2017), respectively. Total number and percentage of IFX or IFX-BS users gradually decreased from 490 [3.3%] \rightarrow 449 [3.0%] \rightarrow 406 [2.6%] \rightarrow 324 [2.1%]. IFX users decreased from 490 \rightarrow 437 \rightarrow 362 \rightarrow 278, but IFX-BS users showed an increasing trend from 0 \rightarrow 12 \rightarrow 44 \rightarrow 46, and the rate of bio-similar users (IFX-BS/IFX + IFX-BS) also increased from 0 \rightarrow 2.7% \rightarrow 10.8% \rightarrow 14.2%. Comparison of IFX users and IFX-BS users in NinJa 2017 revealed that there were no significant differences in age, disease duration, disease activity (DAS28-ESR), patient global assessment, body weight, dose per body weight, and the number of vials used. Meanwhile, for IFX-BS users, the usage rate of steroid was lower (10.9% vs 25.9%, p < 0.05) and physical function (mean mHAQ) was better (0.172 vs 0.339, p < 0.05). [Conclusions] The use of biosimilars showed an increasing trend gradually.

W55-6

Drug tolerability of secondary biologics in patients with rheumatoid arthritis who were primarily treated by non-TNF inhibitors biologics -Data from Kansai consortium for well-being of rheumatic disease patients (ANSWER cohort)-

Kosuke Ebina¹, Motomu Hashimoto², Wataru Yamamoto^{2,7}, Toru Hirano^{3,5}, Yuichi Maeda³, Koichi Murata³, Ryota Hara⁴, Akira Onishi⁵, Sadao Jinno⁵, Yonsu Son⁶, Hideki Amuro⁶, Masaki Katayama⁹, Tohru Takeuchi⁸, Koji Nagai⁸, Makoto Hirao¹, Hideki Yoshikawa¹

¹Department of Orthopaedic Surgery, Osaka University, Graduate School of Medicine, Osaka, Japan, ²Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, ³Department of Respiratory Medicine and Clinical Immunology, Osaka University, Graduate School of Medicine, ⁴The Center for Rheumatic Diseases, Nara Medical University, ⁵Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, ⁶First Department of Internal Medicine, Kansai Medical University, ⁷Department of Health Information Management, Kurashiki Sweet Hospital, ⁸Department of Internal Medicine IV, Osaka Medical College, ⁹Department of Rheumatology, Osaka Red Cross Hospital

Conflict of interest: Yes

[Object] To compare the tolerability of secondary biologics in patients with rheumatoid arthritis (RA) who were primarily treated by non-TNF inhibitors. [Methods] 146 biologics treatment courses who were primarily treated by non-TNF inhibitors (TNFi) (ABT 57 cases, TCZ 89 cases) from 2009 to 2017 (female 82.6%, age 59.5y, RF positivity 73.9%, MTX 29.5%, PSL 21.9%) were included in this multi-center, retrospective study. Biologics were classified as TNFi, ABT, or TCZ, and tolerability was estimated using a Kaplan-Meier method at 36 months. [Results] ABT was switched to TNFi (33 cases) or TCZ (24 cases), and TCZ was switched to TNFi (61 cases) or ABT (28 cases). Main cause of discontinuation was inefficacy (89.0%) for 1st biologics, whereas inefficacy (49.5%), non-toxic reasons (25.8%), and toxic reasons (20.6%) for 2nd biologics. Overall retention rates excluding non-toxic reasons at 36 months were ABT to TNFi (57.1%) vs. ABT to TCZ (70.9%) (Log-rank P = 0.40), and TCZ to TNFi (35.8%) vs. TCZ to ABT (63.0%) (Log-rank P = 0.17). [Conclusions] Although ABT \rightarrow TCZ and TCZ \rightarrow ABT tended to show higher persistency compared to switching to TNFi, no significant differences were observed in drug tolerability of secondary biologics who were primarily treated by non-TNF inhibitors in RA.

W56-1

Effect of biologic agents on synovial tissues from patients with rheumatoid arthritis

Ayako Kubota¹, Toru Suguro¹, Arata Nakajima², Masato Sonobe², Hiroshi Takahashi¹

¹Toho University Omori Medicine Center, Tokyo, Japan, ²Departments of Orthopaedics and Rheumatology, Toho University Sakura Medical Center, Chiba, Japan

Conflict of interest: None

[Object] We examined the inflammation of synovium before and after biologic agents in the patients with rheumatoid arthritis (RA) and to investigate the association between synovial histopathology and disease activity. [Methods] Synovial tissues were collected from 34 RA joints before and after biologics. The average age and disease duration of the study subjects were 64 and 22.5 respectively. Histopathological changes in the synovial tissues were compared based on Rooney's score. We examined correlation between pathological findings in RA synovium and disease activity under biologics. [Results] Rooney score between before and after biologic agents improved from 28.4 to 12.0 showing significant difference. Significant improvement in Rooney score was observed in all items. After the use of biologic agents, MDA group had significantly higher in scores of focal aggregates of lymphocytes, diffuse infiltrates of lymphocytes, and Rooney total scores than Remission and Low disease activity groups. [Conclusions] The study results demonstrated that biologics agents significantly decreased inflammatory changes in the synovial lining layers and sublining layers. In addition, the results suggested that histopathological findings in the subsynovial tissue reflected disease activity.

W56-2

Serum levels of ROM, an oxidative stress marker at 12 weeks during treatment with tocilizumab is a useful biomarker to predict the clinical remission at 52 weeks

Arata Nakajima, Masato Sonobe, Hiroshi Takahashi, Shinji Taniguchi, Manabu Yamada, Shiho Nakano, Koichi Nakagawa

Department of Orthopaedic Surgery, Toho University Sakura Medical Center

Conflict of interest: None

[Object] Tocilizumab (TCZ) strongly suppresses inflammatory reaction; however, clinicians sometimes see discrepancy between the improved laboratory data and actual symptoms of patients. Therefore, it is necessary to develop a novel biomarker other than CRP to predict the future clinical remission during early treatment. [Methods] A total of 46 RA patients (mean age: 60.1 y.o., disease duration: 8.1 y) during treatment with TCZ including 32 naïve and 14 switched from other biologics were enrolled in this study. Associations between serum levels of ROM, CRP, and MMP-3 at 4 and 12 weeks and the remission by DAS28-ESR, CDAI, SDAI and Boolean at 52 weeks were investigated. [Results] There were no significant differences in CRP, MMP-3, and ROM between remission and non-remission groups at 4 weeks. ROM levels at 12 weeks in the DAS-, SDAI-, and Boolean-remission groups were significantly lower than those in their non-remission groups. ROC curves demonstrated the AUC of ROM was 0.735 ($p = 0.024$) and its cut-off value was 305.5 (sensitivity: 70%, specificity: 72.2%). Neither CRP nor MMP-3 was able to predict clinical remission at 52 weeks. [Conclusions] ROM at 12 weeks during treatment with TCZ was a useful biomarker to predict the DAS-remission at 52 weeks.

W56-3

Increase of serum bone alkaline phosphatase level after tocilizumab treatment; from comparison study of serum biomarkers between infliximab and tocilizumab

Naoshi Nishina, Keiko Yoshimoto, Tsutomu Takeuchi

Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] To elucidate the differences of the mechanism of action between infliximab (IFX) and tocilizumab (TCZ) by comparing time course of serum biomarkers. [Methods] Patients with rheumatoid arthritis who started IFX or TCZ as the first biological agent from 2010 to 2013 at our institution were included. Serum samples were collected at week 0, 6, 22, and 54 for IFX and at week 0, 4, 24, and 52 for TCZ, respectively. Serum biomarkers (interleukin [IL]-6, tumor necrosis factor α , soluble IL-6 receptor, vascular endothelial growth factor [VEGF], Bone alkaline phosphatase [BAP], and osteocalcin) were measured by electrochemiluminescence assay. [Results] The rate of methotrexate use was significantly higher in IFX group ($n=57$) than in TCZ group ($n=70$) (96% vs 76%).

Median IL-6 level decreased in IFX group (8.9 pg/ml at week 0 to 1.2 pg/ml at week 54), but increased in TCZ group (from 5.2 to 15.3 pg/ml). VEGF level decreased in both group. Median BAP level remained at the same level in IFX group (from 17.9 to 15.6 ng/ml) although significant increase was observed in TCZ group (from 7.9 to 86.6 ng/ml) ($p<0.01$). [Conclusions] Serum BAP level increased after TCZ treatment in contrast to IFX treatment. These two agents may have different effect on bone in spite of same clinical benefit.

W56-4

Improvement of matrix metalloproteinase-3 at 12 weeks is an independent predictive factor for achievement of low disease activity at 52 weeks after starting abatacept treatment in rheumatoid arthritis

Nobunori Takahashi

Nagoya University Graduate School of Medicine

Conflict of interest: Yes

[Object] Japanese PMS reported that effectiveness of abatacept in bio-switch RA patients was significantly lower than that in bio-naïve patients. We investigated predictive factors for good clinical effectiveness of abatacept in the bio-switch RA patients. [Methods] Participants were consecutive 423 RA patients treated with abatacept and observed for longer than 52 weeks, in the TBC Registry system. Multivariate logistic regression analysis was used to study predictive factors for achievement of low disease activity at 52 weeks, separately in bio-naïve and bio-switch group. [Results] ROC analysis revealed that MMP-3 improvement rate at 12 weeks had highest AUC and cut-off value of 20.0%. In bio-naïve group, DAS28-CRP score at baseline was the only predictive factor, while 20% improvement of MMP-3 at 12 weeks was an independent predictive factor (adjusted OR: 3.550, $p=0.005$) in addition to DAS28-CRP in the bio-switch group. [Conclusions] In bio-switch patients, we sometimes have difficulty to obtain good clinical response of abatacept and it would be even more important to judge whether to continue abatacept as early as possible. Our results suggested that the improvement of MMP-3 at 12 weeks would be a key to predict good clinical effectiveness of abatacept at 1 year.

W56-5

The efficacy and safety of abatacept in patients with rheumatoid arthritis and interstitial lung disease

Sho Sasaki, Yasushi Kondo, Takayoshi Kurabayashi, Yasushi Koyama, Chiho Yamada, Shinji Sato

Division of Rheumatology, Department of Internal Medicine, Tokai University School of Medicine

Conflict of interest: None

[Object] To assess the efficacy and safety of abatacept in patients with rheumatoid arthritis (RA) and interstitial lung disease (ILD) associated to RA. [Methods] We enrolled 24 patients with RA who were treated with abatacept between 2011 and 2017 at Tokai University Hospital. We compared the efficacy and safety between RA patients with ILD and without ILD. We retrospectively evaluated the disease activity using the change in DAS28-CRP and PSL dose at ABT initiation 0 month and after 12 months (12M). The safety was assessed using continuing rate of ABT. [Results] There were no statistically significant differences in gender, age, duration of disease, DAS28-CRP score, MTX and PSL dose between the two groups. At the 12 months after ABT initiation, there was a significant improvement in DAS28-CRP score (5.0 ± 1.0 vs. 3.5 ± 1.4 , $P=0.006$). There was a significant reduction in the mean dose of PSL ($8.5\text{mg}\pm 2.0$ vs. $5.4\text{mg}\pm 1.8$, $P=0.007$). There was no significant difference in reduction rate of Δ DAS28-ESR between RA patients with and without ILD groups (-1.6 ± 1.4 vs. -1.3 ± 0.5 , $P=0.3$). No significant difference in continuing rate between both groups at the 12 months was observed (11 [69%] vs. 4 [50%]). [Conclusions] ABT showed the equivalent efficacy and safety for RA with ILD as well as RA without ILD.

W56-6

Abatacept in rheumatoid arthritis patients with collagen disease

Kazunori Yamada^{1,2}, Kiyooki Ito², Yasunori Suzuki³, Fae Suzuki⁴, Satoshi

Hara², Ichiro Mizushima², Hiroshi Fujii², Takashi Kawane⁵, Kazuaki Mizutomi³, Mitsuhiro Kawano²

¹Department of Advanced Research in Community Medicine, Kanazawa University Graduate School of Medical Sciences, ²Department of Rheumatology, Kanazawa University Hospital, ³Kaga Medical Center, ⁴Kim Clinic, ⁵Toyama Red Cross Hospital

Conflict of interest: None

[Object] To retrospectively evaluate the efficacy of abatacept (ABT) in rheumatoid arthritis (RA) patients (pts) with other collagen diseases (CDs). [Methods] Forty-five RA pts who were treated with ABT were enrolled in this study; of these, 23 had other CDs (CD group, methotrexate [MTX] 43.5%) and 22 did not (non-CD group, MTX 50.0%). We evaluated disease activity at 0, 24, 52, and 104 weeks (wks) after ABT therapy and the persistence rate. [Results] The mean ages were 55.9 and 63.3 years in the CD and non-CD groups, respectively. The mean DAS 28-CRP (DAS) before ABT therapy was 4.0 ± 0.7 and 4.2 ± 1.5 in CD and non-CD groups, respectively, with no significant difference. The mean DAS at 24, 52, and 104 wks were 2.88, 2.52, and 2.04, respectively, in the CD group and 2.97, 3.29, and 2.41, respectively, in the non-CD group, indicating significant reduction from the baseline values. The changes in DAS at 24 and 52 wks in the CD group showed no significant differences from those in the non-CD group. Changes in DAS were also not significantly different between the pts who received and those who did not receive MTX. Persistence rates at 104 wks were 100% and 77.3% in the CD and non-CD groups, respectively. [Conclusions] ABT was effective in RA pts with other CDs regardless of MTX use.

W57-1

Actual dosage and adverse effect of methotrexate in patients with juvenile idiopathic arthritis: single center experience

Ai Ohnishi, Seira Hattori, Kenichi Nishimura, Ryoki Hara, Shuichi Ito
Department of Pediatrics, Yokohama City University

Conflict of interest: None

[Object] We examined actual status of Methotrexate (MTX) treatment among juvenile idiopathic arthritis (JIA) patients in our institute and analyzed the background why patients decreased or discontinued MTX. [Methods] We retrospectively reviewed the electric medical chart of 53 JIA patients who started MTX from April 2011 to March 2018 and collected the data. The target dose of MTX defined as 10 mg/m²/week, max 16mg/week. [Results] 53 JIA patients (male 20, female 33) were classified into; systemic (n=9), polyarticular (n=21), oligoarticular (n=15) and psoriatic/ enthesitis-related (n=8). Median age starting MTX was 8.5 years old (range 1.5~18.8). Median dose of maximum MTX was 8.9mg/m²/week. Adverse effects were observed in 36 (68%). 15 patients (28%) were forced to reduce or discontinue MTX due to adverse effect and 16 patients (30%) consequently needed biologics. Half of patients who started folic acid when MTX started, had nausea/vomiting. At the last observation, targeted dose was achieved only in 9 (9%), but 29 (55%) maintained remission using MTX below the target dose. [Conclusions] Many patients failed to achieve the target dose, resulted in adding biologics. Optimal dose varies widely by patient's background, disease activity and concomitant therapy.

W57-2

Adverse event reports of oral Methotrexate (MTX) using the database of the Pharmaceuticals and Medical Devices Agency (PMDA)

Naonori Tsuda¹, Shigeko Inokuma^{1,2}, Kenichi Hiraga¹, Yoshinori Masui¹, Toshikazu Kano¹

¹Department of Rheumatology, Kohnodai Hospital, National Center for Global Health and Medicine, ²Department of Allergic Disease and Rheumatology, Chiba Central Medical Center

Conflict of interest: None

[Object] The Japanese Adverse Event Report database (JADER) in the Pharmaceuticals and Medical Devices Agency (PMDA) collects information on drug adverse events throughout Japan. We analyzed the various adverse events of oral Methotrexate (MTX), which is the important

drug in rheumatoid arthritis treatment, according to its clinical contents. [Methods] From the list of adverse event reports of oral MTX published at JADER on PMDA, the number and the clinical contents of adverse events were analyzed within 2004 to 2008 (5 years), 2009 to 2013 (5 years), and 2014 to 2017 (4 years). We reorganized the categories partly to suit the clinically appropriate classification. [Results] The median of adverse events of oral MTX was 436 within 2004 to 2008, 668 in 2009 to 2013 and 1471 in 2014 to 2017. The details were in the order of blood / lymphatic system disorder 25% (blood cytopenia 24%), infection 25%, and respiratory disorder 24% (interstitial lung disease 20%) in 2004 to 2008, whereas neoplastic diseases were 40% (lymphoproliferative disorder (LPD) 34%), infectious diseases 17% and blood / lymphatic system disorders 13% (cytopenia 12%) in 2013 to 2017. [Conclusions] Reported adverse events of oral MTX were changing over time. LPD is increasing recently and caution is required.

W57-3

Diagnosis for chronic hepatic disorder induced by methotrexate (MTX)

Masayuki Miyata
Fukushima Red-Cross Hospital

Conflict of interest: None

[Object] Hepatic disorder is most frequent side effect in MTX Tx. Acute hepatic disorder can be noticed and dissolved by addition of folic acid, on the other hand, chronic hepatic disorder is hard to be noticed. Histopathology of this closely resembles that of non-alcoholic steatohepatitis (NASH). Fibrosis marker, Fibrosis-4 index (FIB-4) could be applied for diagnosis of chronic hepatic disorder. [Methods] FIB-4 was screened in non-alcoholic RA patients and the average was calculated. Fourteen patients, who have high FIB-4 and agreed to take liver biopsy, were enrolled. All patients quit taking MTX after liver biopsy. Three of them underwent 2nd biopsy in 2 years. [Results] Thirteen of 14 patients showed NASH-like hepatic disorder. The one showed simple steatosis. Almost of all patients decreased FIB-4 values after discontinuation of MTX. Second biopsies showed improvement of NASH, suggesting that FIB-4 seems valuable marker. Multivariate linear regression analysis identified the following factors as being significantly associated with FIB-4: Age, Class and CRE. [Conclusions] In order to monitor the degree of fibrosis of MTX-induced chronic hepatic disorder, FIB-4 was valuable. Combination with other fibrotic markers and diagnostic imaging may improve the safety in the MTX treatment.

W57-4

2-year real-world observation of disease control with optimizing dose of methotrexate (MTX) while reducing or discontinuing prednisolone (PSL) in patients with rheumatoid arthritis (RA)

Shintaro Hirata¹, Kei Araki¹, Hiroki Kohno¹, Kazutoshi Yukawa¹, Tadahiro Tokunaga¹, Tatsuomi Kuranobu¹, Katsuhiko Ohi¹, Yusuke Yoshida¹, Tomohiro Sugimoto¹, Sho Mokuda¹, Keisuke Oda^{1,2}, Takaki Nojima^{1,3}, Eiji Sugiyama¹

¹Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan, ²Department of Internal Medicine, Hiroshima Clinic, Hiroshima, Japan, ³Nojima Internal Medicine Clinic, Hiroshima, Japan

Conflict of interest: Yes

[Object] At JCR2018 we reported that PSL could be reduced without deterioration of RA with optimized MTX at 1-yr. Herein we investigated 2-yrs results of disease control and medication. [Methods] RA patients who had regularly visited our clinic for ≥ 1 yr were consecutively registered during Sep-Oct 2016. Clinical demographics as well as disease status and medication at baseline (BL), yr-1- and -2 were collected. Basic therapeutic strategy was to increase MTX while reducing PSL based on patient's consent. bDMARDs/JAKi were allowed if required. [Results] 70 patients were enrolled. Age (median [IQR]) 62 [51, 68] yrs; female 69%; disease duration 6.8 [3.4, 13.7] yrs. MTX users at BL, 1 and 2 yrs were 57, 67 and 59%, whereas doses (mean \pm SD) were 9.8 \pm 3.2, 11.6 \pm 3.7 and 10.5 \pm 3.8 mg/w, respectively. PSL users were 56, 26 and 10%, whereas doses were 3.6 \pm 3.4, 2.9 \pm 2.6 and 3.6 \pm 2.8mg/d. bDMARDs/JAKi users

were 16, 18 and 26, newly initiated in 2 and 8 during BL-1-2yrs. CDAI / SDAI / DAS28-REM at BL, 1- and 2- yrs were; 24, 39, 49% / 27, 41, 52% / 35, 41, 48%, respectively. MTX was withdrawn due to renal dysfunction or neoplasms. [Conclusions] Optimizing MTX with bDMARDs/JAKi if required resulted in discontinuation of PSL in 90% of the patients, whereas PSL might delay clinical decision-making.

W57-5

Iguratimod (IGU) add-on therapy for RA patients inadequately controlled with bDMARDs

Ken Hasegawa

Department of Orthopaedic Surgery, Meinan Hospital, Nagoya, Japan

Conflict of interest: None

[Object] If the treatment target is not achieved with the bDMARD therapy, another bDMARD should be considered by the treatment guideline for RA. A csDMARD add-on is also a treatment option in daily clinical practice. Efficacy and sustainability of IGU add-on therapy were evaluated in RA patients treated by bDMARDs. [Methods] IGU was added on bDMARD in 6 patients (3 male, 3 female, 54.7±15.8 years old, disease duration 13.1±7.1 years, bDMARD therapy duration 21.0±20.4 months). Disease activity score (SDAI), RF value and MMP-3 value were compared between before and after the IGU therapy. Drug persistency rate were estimated by Kaplan-Meier method (Start point was defined as the introduction of IGU, end-point was defined as the discontinuation of IGU or bDMARD). [Results] At the start of IGU/at 6 month later, SDAI were 14.0±10.4/7.0±5.1 (P=0.35), RF were 389.7±562.1U/mL/160.3±231.0U/mL (P=0.27), MMP-3 were 238.1±172.5ng/ml/103.4±79.2ng/ml (P=0.09). SDAI 50/70/85 achievement rate were 67/33/0% at 6 months (LOCF method). Persistency rate were 67%/67% at 6/12 months. IGU combination with bDMARD was effective and sustainable in most cases. [Conclusions] IGU add-on therapy could be one of valuable treatment options in daily clinical practice when the previous bDMARD therapy was failed.

W57-6

Experiences of Iguratimod (IGU) therapy in elderly patients aged 75 and over with rheumatoid arthritis

Toshihiko Hidaka, Yayoi Hashiba, Kazuyoshi Kubo, Hiroshi Kuroda
Insutitution of Rheumatology, Zenjinkai Shimin-no-Mori Hospital, Miyazaki, Japan

Conflict of interest: Yes

[Objectives] We assessed the efficacy of Iguratimod (IGU) in patients with elderly rheumatoid arthritis (ERA) aged 75 or over. [Methods] One hundred and nine RA patients who had been treated with IGU were evaluated. These patients were divided into two groups; group U (G-U, n=76): patients aged under 75, group O (G-O, n=33): aged 75 and over. We compared the SDAI, ACR response, EULAR response and adverse effects (AEs) of G-O with G-U until 1-year treatment. [Results] G-O was significantly longer in disease duration, higher in Class, DAS28-ESR and combination rate of steroid, and lower combination rate of MTX than G-U. G-O was significantly lower in SDAI remission rate than G-U (G-U: 50%, G-O: 21%, P<0.05). There were no significant difference in SDAI low disease activity rate, ΔSDAI, EULAR good and moderate response rate and ACR 20/50/70 response rate between G-O and G-U. There was no significant difference in AEs rate between G-O and G-U (G-O: 29%, G-U: 22%, ns). There was no significant difference in AEs rate between G-O and G-U (G-O: 29%, G-U: 22%, ns). There was no significant difference in retention rate at 1-year treatment between G-O and G-U (G-O: 73%, G-U: 80%, NS). [Conclusion] IGU therapy is safe and clinically effective for even older RA patients aged 75 and over.

W58-1

A multicenter, prospective study of clinical features of Japanese systemic sclerosis with progressive disease activity in the early clinical stage

Akira Utsunomiya¹, Minoru Hasegawa¹, Yoshihide Asano², Osamu Ishikawa³, Hirahito Endo⁴, Yasushi Kawaguchi⁵, Masataka Kuwana⁶,

Daisuke Goto⁷, Shinichi Sato², Hiroki Takahashi⁸, Kazuhiko Takehara⁹, Sumiaki Tanaka¹⁰, Manabu Fujimoto¹¹, Hironobu Ihn¹²

¹Department of Dermatology, School of Medicine, Faculty of Medical Sciences, University of Fukui, Fukui, Japan, ²Department of Dermatology, University of Tokyo Graduate School of Medicine, Tokyo, Japan, ³Department of Dermatology, Gunma University Graduate School of Medicine, Gunma, Japan, ⁴Department of Rheumatology, Jusendo General Hospital, Fukushima, Japan, ⁵Department of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, ⁶Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, ⁷Department of Internal Medicine, Faculty of Medicine, University of Tsukuba, Ibaraki, Japan, ⁸Department of Rheumatology, Sapporo Medical University School of Medicine, Hokkaido, Japan, ⁹Department of Molecular Pathology of Skin, Faculty of Medicine, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, Kanazawa, Japan, ¹⁰Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine, Kanagawa, Japan, ¹¹Department of Dermatology, Faculty of Medicine, University of Tsukuba, Ibaraki, Japan, ¹²Department of Dermatology and Plastic Surgery, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan

Conflict of interest: None

Object: Racial differences may perturb the overall clinical course and physical disability of systemic sclerosis, particularly in cases with early progressive disease. Methods: We enrolled 248 patients with aggressive clinical states in the early disease stage, and monitored their symptoms and laboratory states each year for 7 years in 10 facilities. Results: 193 (78%) were female with the mean age at the study registration of 49.3 years. Anti-topoisomerase I antibody and anticentromere antibody were detectable in 145 (58%) and 22 (9%), respectively. 171 (69%) had interstitial lung disease. Comparing between registration and final assessment points, subjects receiving monotherapy with corticosteroid were 57% and those having a combined therapy with corticosteroid and immunosuppressants were 11%, although the latter increased to 29%. MRSS decreased from 18.5 to 12.8 by 1-year, and became constant at around 10. Serum KL-6 level was stable, whereas %VC, digital ulcer, and HAQ-DI were gradually exacerbated. Conclusion: Japanese systemic sclerosis with early progressive disease activity tended to resolve their skin sclerosis during 7-year follow up. However, the physical disability was aggravated by respiratory dysfunction and digital ulceration.

W58-2

Characteristics of CRP positive systemic sclerosis

Kae Takagi¹, Yasushi Kawaguchi², Manabu Kawamoto², Yuki Ichimura², Akiko Tochimoto², Chikako Fukasawa², Hisashi Yamanaka²

¹Internal Medicine, Tokyo Women's Medical University Medical Center East, ²Rheumatology and Clinical Immunology, Tokyo Women's Medical University Hospital

Conflict of interest: None

[Object] Some of the patients with systemic SSc exhibit elevated levels of CRP. However, roles of CRP in the clinical features of SSc remains controversial. The purpose of this study is to clarify the characteristics of CRP-positive SSc patients. [Methods] Four hundred and twenty-five SSc patients were involved in this study. The cases accompanied by infection were excluded. Clinical features were compared between CRP-positive 100 cases and CRP-negative 318 cases. [Results] The frequency of arthritis (p 0.00658, OR 2.109), interstitial pneumonia (IP) (p 0.00163, OR 2.166), pulmonary hypertension (PH) (p 0.01289, OR 2.525) and lower gastrointestinal tract failure (p 0.02999, OR 2.837) was significantly higher in the CRP-positive group. The patients with rheumatoid arthritis (p=0.00389, OR 3.114), systemic lupus erythematosus (p 0.00771, OR 4.153) and anti-DNA antibody positivity (p 0.04365, OR 2.536) was also significantly higher in the CRP-positive group. The frequency of *TBX21* rs11650354 CC genotype was not significantly different between these groups. [Conclusions] SSc patients with an elevated level of CRP positive was associated with IP or PH that determine poor prognosis. This therefore suggests CRP is a useful marker to predict for the prognosis or disease activity of SSc.

W58-3

Evaluation of renal dysfunction in patients with anti-centromere antibody positive limited cutaneous systemic sclerosis

Taro Horino, Satoshi Inotani, Tatsuki Matsumoto, Yoshiko Shimamura, Kosuke Inoue, Yoshio Terada
Department of Endocrinology, Metabolism and Nephrology, Kochi Medical School, Kochi University

Conflict of interest: None

[Object] Anti-centromere antibody positive limited cutaneous systemic sclerosis (lcSSc) tends to be neglected because of the mild range and degree of skin symptoms compared to diffuse cutaneous type. Clinical features of renal dysfunction in patients with centromere antibody positive lcSSc (ACA-lcSSc) are examined. [Methods] 80 patients who had hospitalized in our outpatient clinic from 2012 to 2018 were enrolled. All patients met the American College of Rheumatology classification criteria for lcSSc. We assess their clinical characteristics and data. [Results] Female were 74 (92.5%). Mean age was 67.6 years old. Clinical characteristics; Incidence of Raynaud phenomenon and sclerodactylia were 76 and 89.3%. Organ damages; interstitial pneumonia, pulmonary hypertension, PBC, Sjogren syndrome, Hashimoto's disease, CKD were 30.0%, 33.3%, 46.2%, 55.5%, 36.2% and 46.2%, respectively. Incidence of overt proteinuria was 31.2%. Renal biopsy was performed in 7 cases, in which 6 cases had lupus nephritis and one had non-IgA mesangial proliferative glomerulonephritis. [Conclusions] To our knowledge, there is no report that studies case series of ACA-lcSSc with LN. Our data suggested that in ACA-lcSSc, SLE was thought to merge at a relatively high rate.

W58-4

Prognosis and causes of deaths of Systemic sclerosis patients with interstitial pneumonia

Shigeki Makino¹, Hidehiko Makino², Takeshi Shoda³, Takaaki Ishida², Takuya Kotani², Tohru Takeuchi², Shigeki Arawaka²
¹Division of Internal Medicine, Osaka Medical College Mishima-Minami Hospital, Takatsuki, Osaka, Japan, ²Department of Internal Medicine IV, Osaka Medical College, Takatsuki, Osaka, Japan, ³Division of Rheumatology, Yodogawa Christian Hospital, Osaka, Japan

Conflict of interest: Yes

[Background] We aim to know the influence of interstitial pneumonia (IP) involvement on prognosis of Systemic sclerosis (SSc). [Methods] We reviewed clinical data concerning about prognosis and causes of deaths of SSc-IP patients of our institute from August 2008 to July 2018. [Results] Total SSc-IP patients are 212 (34 males, average 69.7 years). Comparing SSc patients without IP (479 cases, 41 males, average 63.6 years), SSc-IP patients were older and male dominant. Total dead cases were 25 (7 males). 5-year survival rate of SSc-IP patients was 91.4%, 10-year survival rate was 80.2%. Concerning about the causes of deaths of SSc-IP patients, chronic progression of IP were 6 cases, acute exacerbation of IP were 1, pulmonary hypertension were 1, lung cancer were 2, other malignancy were 3, infection were 1, cardiac disease were 2. [Conclusions] SSc-IP patients of our institute were older and male dominant compared to SSc patients without IP. 5-year survival rate of SSc-IP patients was 91.4%, 10-year survival rate was 80.2%. Leading cause of deaths of SSc-IP patients were chronic progression of IP 6 cases. Total death due to pulmonary lesion were 10 (40%). So pulmonary involvement of SSc influence on prognosis of SSc-IP patients.

W58-5

Efficacy and Safety of Tocilizumab for the Treatment of Systemic Sclerosis (SSc) in Japanese Patients: Results from a Phase 3 Randomized Controlled Trial

Masataka Kuwana¹, Yoshihito Shima², Yoshiya Tanaka³, Kazuhiko Takehara⁴, Norihiro Okada⁵, Hiroko Igarashi⁶
¹Department of Allergy and Rheumatology, Nippon Medical School, ²Thermo-therapeutics for Vascular Dysfunction, Osaka University Graduate School of Medicine, ³The First Department of Internal Medicine, University of Occupational and Environmental Health, ⁴Department of Dermatology, Kanazawa University, ⁵Clinical Information & Intelligence

Department, Chugai Pharmaceutical Co., Ltd, ⁶Clinical Science & Strategy Department, Chugai Pharmaceutical Co., Ltd

Conflict of interest: Yes

[Object] To investigate the efficacy and safety of tocilizumab (TCZ) for Japanese patients (JP) with diffuse cutaneous SSc (dcSSc). [Methods] Patients with disease duration of ≤ 5 years were randomly assigned 1:1 to receive weekly double-blind injections of subcutaneous TCZ 162 mg or placebo (PBO) for 48 wks. [Results] 210 patients (ITT) were treated with TCZ ($n=104$, JP: $n=12$) and PBO ($n=106$, JP: $n=8$). Mean baseline values were: disease duration, 22.64 months; modified Rodnan skin score (mRSS), 20.35; and percent predicted forced vital capacity (ppFVC), 82.12%. Mean change in mRSS from baseline to wk 48 (primary endpoint) was -6.14 with TCZ (JP: -7.89) and -4.41 with PBO (JP: -4.63); the difference in mean change between TCZ and PBO was -1.73, $p = 0.098$ (JP: -3.26). Mean change in ppFVC from baseline to wk 48 (secondary endpoint) was -0.38% with TCZ (JP: 3.76%) and -4.58% with PBO (JP: -0.83%); the difference in mean change for the ITT population was 4.2% (95%CI: 2.0, 6.4). No new safety signal with TCZ treatment was observed. [Conclusions] The primary endpoint was not met, but the results favor TCZ over PBO for improvement in mRSS, and clinically meaningful differences in FVC were shown with no safety concern. Results of the JP were consistent with the ITT population.

W58-6

Efficacy and safety of combination therapy with prednisolone and oral tacrolimus or azathioprine for progressive interstitial pneumonia with systemic sclerosis

Takao Kiboshi¹, Takuya Kotani¹, Junichi Konma³, Reiko Wakura¹, Takeshi Shoda³, Tomohiko Kuboyama¹, Hidehiko Makino¹, Shogo Matsuda¹, Takayasu Suzuka¹, Takaaki Ishida¹, Youhei Fujiki¹, Koji Nagai¹, Kenichiro Hata¹, Shigeki Makino², Tohru Takeuchi¹, Shigeki Arawaka¹
¹Department of Internal Medicine IV, Osaka Medical College, Takatsuki, Osaka, Japan, ²Department of Internal Medicine, Osaka Medical College Mishima-Minami Hospital, ³Department of Rheumatology, Yodogawa Christian Hospital

Conflict of interest: None

Objectives: We retrospectively investigated efficacy and safety of combination therapy with prednisolone (PSL) and tacrolimus (TAC) or azathioprine (AZA) for progressive interstitial pneumonitis with systemic sclerosis (SSc-PIP). Methods: Eighteen patients were TAC and 19 were AZA treated groups. Results: In TAC treated group, 17 patients were women with the median age being 65 (range 38-81) years. Ten patients had diffuse type of SSc. The median period from the appearance of respiratory symptoms to the start of treatments (disease duration) was 31 (range 8-373) weeks. In response to treatment 1 year after, IP improved in 6 patients, stable in 12 patients. Presently, 12 patients who could be followed up. IP improved in 6, stable in 5 patients, and deteriorated in 1 patient. In AZA treated group, 13 patients were women with the median age being 69 (range 56-77) years. Eleven patients had diffuse type of SSc. The median disease duration was 28 (range 1-141) weeks. In response to treatment 1 year after, IP improved in 5 patients, stable in 11 patients. Presently, 16 patients who could be followed up. IP improved in 5, stable in 11 patients. Conclusions: Combination therapy with PSL and TAC or AZA appeared to be well tolerated and effective in suppressing the disease activity of SSc-PIP.

W59-1

Follow up study of 30 patients with eosinophilic granulomatosis with polyangiitis

Hiroki Mukoyama, Keisuke Nishimura, Kaoru Mizukawa, Keiichiro Kadoba, Tomohiro Yoshida, Daisuke Waki, Toshihiko Yokota
Department of Endocrinology and Rheumatology, Kurashiki Central Hospital, Kurashiki, Okayama, Japan

Conflict of interest: None

[Objectives] We analyzed the long-term prognosis of eosinophilic

granulomatosis with polyangiitis (EGPA). [Methods] To analyze the clinical features of 30 patients with EGPA treated in our hospital from 2000 to 2018 retrospectively. [Results] Average age was 65.6 ± 13.2 years old. Male/female were 6/24. Time after starting treatment was 65 ± 56 months. ACR criteria was used for diagnosis. Twenty-seven patients had asthma, 27 had peripheral nerve involvement, 24 had motor neuropathy, nine had lung involvement, four had cardiac involvement and four had gastrointestinal involvement. Fifteen patients had a positive test for MPO-ANCA. On Baseline, five factor scores 2009 (FFS) were 0 (n=7), one (n=11), two (n=11), and three (n=1). BVAS version 3 was 18.0 ± 5.4 . Glucocorticoids were administered in all the patients, and intravenous methylpredonisolone in 13 patients. Immunosuppressants for remission induction therapy were administered in 16 and intravenous immunoglobulin was administered in nine. Relapses occurred in 13 patients. Remission induction treatment with immunosuppressants was associated with significantly less frequent relapses ($p=0.03$). [Conclusions] Remission induction treatment with immunosuppressants was associated with significantly less frequent relapses in EGPA patients.

W59-2

Prognosis of organ involvement due to eosinophilic granulomatosis with polyangiitis (EGPA)

Hironobu Nobata, Asako Kachi, Masako Koshino, Naoya Matsuoka, Hirokazu Sugiyama, Mayumi Ito, Makoto Yamaguchi, Shiho Iwagaitsu, Takayuki Katsuno, Shogo Banno, Yasuhiko Ito
Nephrology and Rheumatology, Aichi Medical University

Conflict of interest: None

[Object] EGPA is a disease characterized by multiple organs involvement, which lung, sinus, heart, kidney and GI involvement, also polyneuritis. We decided therapeutic target for mainly polyneuritis, but sensory disorder highly remain. [Methods] For the patients with EGPA treated at our hospital, we investigated retrospectively about clinical symptoms, examinations, organ damage, treatment and prognosis. [Results] Twenty cases (M/F 8/12). Data are expressed as median. Age 61yro. Preceding asthma 19 cases and 7 of them were exacerbated one year before onset. Lung involvement were 16, sinus 15, heart 4, kidney 2, GI 2, sensory peripheral nerve disorder 17 (with motor nerve 12) cases. Laboratory data: eosinophil count $8588/\mu\text{L}$, CRP 5.92mg/dl , IgE 1230mg/dl , ANCA positive 11 cases, RF positive all cases. Treatment: steroid pulse 17 cases, IVCY 3, AZA 7, IVIg 13 cases (days to first time are day 9), mepolizumab only one case. Results: Lung, cardiac, kidney, GI involvement improved in all cases, exacerbation of asthma was none within 1 year, but 6 cases exacerbated after that. IVIg could improve subjective symptoms in all cases, but 13 cases remained numbness. All cases could recover to walk. [Conclusions] Prognosis of organ involvement except sensory disorder is satisfied in most cases.

W59-3

The analysis of 3 cases which improved the neurologic symptoms by mepolizumab to eosinophilic granulomatosis with polyangitis which recurred by conventional therapy

Noboru Kitamura, Takamasa Nozaki, Natsumi Ikumi, Atsuma Nishiwaki, Kaita Sugiyama, Yosuke Nagasawa, Shoen Yoshizawa, Hiroshi Tsuzuki, Marina Hamaguchi, Masashi Oshima, Yutaka Tanikawa, Shinya Asatani, Kumiko Akiya, Mitsuhiro Iwata, Hitomi Haraoka, Masami Takei
Division of Hematology and Rheumatology, Department of Medicine, Nihon University

Conflict of interest: Yes

[Object] Mepolizumab acquired approval of additional adaptation to eosinophilic granulomatosis with polyangitis (EGPA) in 2018. But clinical evidence of each complication of EGPA was unknown. We considered improvement of clinical manifestation, laboratory findings and complication treated with mepolizumab by which 3 case of EGPA recurred during tapering prednisolone. [Methods] We analyzed CRP, c eosinophil count, serum IgE, Exhaled NO, FEV1.0% and improvement of complication of EGPA between pre and post 24 weeks treatment of mepolizumab. [Results] Although CRP, count of eosinophil, serum IgE, Exhaled NO were improved, FEV1.0% was not improvement. Skin eruption was improve-

ment by 2 of 3 cases. Subjective symptom of the neurologic symptoms estimated in global scale was improved. [Conclusion] Although it was existed to the evidence of restraint recurrence and maintenance of remission, evidence of each laboratory findings and complication of EGPA was unknown. Especially, it's important to estimate improvement of neurological disorder which is the most important complication of EGPA. In this report, we are checking it only by a subjective symptom used global scale. In future, I'd like to estimate using peripheral nerve communication speed and skin perfusion pressure measurement.

W59-4

Low-dose mepolizumab as maintenance therapy with eosinophilic granulomatosis with polyangiitis

Yutaka Goto, Yukiko Takakuwa, Takeshi Suzuki, Kanako Suzuki, Takayasu Ando, Harunobu Iida, Marina Uchida, Yusa Asari, Hisae Fujimoto, Kana Ishimori, Keiichi Sakurai, Hiromi Matsushita, Tomofumi Kiyokawa, Kumiko Tonooka, Mitsuru Imamura, Yoshioki Yamasaki, Seido Ooka, Hiroko Nagafuchi, Kimito Kawahata
Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine

Conflict of interest: None

[Objectives] Mepolizumab is an anti-IL-5 monoclonal antibody targeting eosinophilic inflammation, which was shown to be an effective maintenance therapy of EGPA in the phase 3 clinical trial. However, the dose of mepolizumab used in this trial was 3-fold higher than 100mg dose approved for severe asthma. Here, we investigated the efficacy and safety issue of low-dose mepolizumab for patients with EGPA. [Methods] We retrospectively examined EGPA patients who met the 2012 Chapel Hill classification and treated with mepolizumab 100mg/4 weeks for severe asthma from 2017 to 2018. We evaluated efficacy and safety for 6 months. [Results] Nine patients (3 female, 59 ± 13 years old) with EGPA (33% ANCA-positive) requiring maintenance PSL or immunosuppressive drug were included in this analysis. All patients had neurological involvement. The dose of PSL at initiation of mepolizumab was 9 ± 1 mg, which by 6 months had fallen to 6 ± 2 mg. Two patients were able to discontinue an immunosuppressive drug. Blood eosinophil counts reduced from $1089 \pm 949/\mu\text{L}$ at initiation of mepolizumab to $45 \pm 39/\mu\text{L}$ at 6 months. No episodes of vasculitis or disease exacerbations and severe adverse events occurred for 6 months. [Conclusions] Low-dose mepolizumab might be effective in maintenance therapy for EGPA.

W59-5

Efficacy and safety of Cyclophosphamide and Rituximab in the initial remission induction therapy for ANCA-associated vasculitis (AAV)

Yuri Sadanaga¹, Nobuyuki Ono¹, Yukiko Takeyama^{1,11}, Yasushi Inoue², Tomoya Miyamura³, Kensuke Oryoji⁴, Naoyasu Ueda⁵, Shuji Nagano⁶, Hisako Inoue⁷, Mariko Sakai¹, Yoshinobu Nakao¹, Akihito Maruyama¹, Syuichi Koarada¹, Yutaka Chifu¹¹, Takuya Sawabe¹⁰, Shun-ichiro Ohta⁸, Seiji Yoshizawa⁹, Kyoko Otsuka¹², Yasutaka Kimoto¹³, Katsuhisa Miyake¹⁴, Takahiko Horiuchi¹³, Hitoshi Nakashima¹⁴, Hiroaki Niiro¹², Yoshifumi Tada¹

¹Department of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan, ²Division of Connective Tissue Disease, Fukuoka Red Cross Hospital, Fukuoka, Japan, ³Department of Internal Medicine and Rheumatology, National Hospital Organization Kyusyu Medical Center, Fukuoka, Japan, ⁴Division of Rheumatology, Matsuyama Red Cross Hospital, Matsuyama, Japan, ⁵Department of Internal Medicine, Miyazaki Prefectural Miyazaki Hospital, Miyazaki, Japan, ⁶Center for Rheumatology, Iizuka Hospital, Iizuka, Japan, ⁷Department of Rheumatology, Saiseikai Fukuoka General Hospital, Fukuoka, Japan, ⁸Department of Rheumatology, Shimonoseki City Hospital, Shimonoseki, Japan, ⁹Department of Rheumatology, Hamanomati Hospital, Fukuoka, Japan, ¹⁰Division of Rheumatology, Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital, Hiroshima, Japan, ¹¹Department of Internal Medicine, Saiseikai Karatsu General Hospital, Saga, Japan, ¹²Department of Medicine and Biosystemic Sciences, Kyusyu University Graduate School of Medical Sciences, Fukuoka, Japan, ¹³Department of Internal Medicine and Immunology, Kyusyu University Beppu Hospital, Beppu, Japan, ¹⁴Division of Nephrology and Rheumatology, Faculty of Medicine, Fukuoka University, Fukuoka, Japan

Conflict of interest: None

[Object] To evaluate the efficacy and safety of Cyclophosphamide (CY) and Rituximab (RTX) in the initial remission induction therapy for ANCA associated vasculitis (AAV). [Methods] Using a multicenter cohort database of AAV (KVAS cohort) mainly conducted in our hospital, we retrospectively extracted patients who used CY or RTX as initial induction therapy from May 2010 to May 2018, classified into CY or RTX groups, and evaluated clinical features, remission rates, adverse events. [Results] CY was used in 47 patients and RTX in 20 patients. The average age was 67.6 (26-86) years old in CY group, and 71.5 (54-88) years old in RTX group, male was 49% in CY group and 50% in RTX group. CY group had 36 (63%) MPA, 15 (26%) GPA and 6 (11%) UCAAV. RTX group had 11 (55%) MPA and 9 (45%) GPA. The average of BVAS was 17.1 (4-49) in CY group and 17.7 (8-32) in RTX group. Remission rate at 6 months was 66.7% in CY group and 80% in RTX group, and the average PSL dose at 6 months was 11.6 (4-50) mg/day in CY group and 8.8 (4-18) mg/day in RTX group. The adverse events were 36 in 23 patients in CY group and 14 in 7 patients in RTX group. [Conclusions] RTX treatment had comparable remission rates and adverse events compared with CY.

W60-1

Analysis of clinical features in ANCA-associated vasculitis treated with rituximab: single center experience

Soko Kawashima, Kazuhito Fukuoka, Yoshinori Komagata, Shinya Kaname
First Department of Internal Medicine, Kyorin University School of Medicine

Conflict of interest: None

[Object] Rituximab therapy (RTX) in ANCA-associated vasculitis (AAV) has increased, and the scenes to consider how to use it are increasing. Thus, we analyzed our patients treated by RTX. [Methods] We retrospectively analyzed the clinical database of the 28 patients with AAV who were treated by RTX to our hospital after 2014 were followed up. At the onset, all patients fulfilled the Chapel Hill Consensus Conference (CHCC) classification criteria for MPA and GPA. And also, compared the clinical features between RTX group and non-RTX group. [Results] RTX induction age was 70 years old. RTX was used in 10.8% for the initial AAV. The average of total RTX dose for initial induction was 2g. For maintenance therapy, regular dosing every 6 months or irregular dosing at intervals of 6 months or more were done. some relapses at irregular administration were seen. Though main reasons for RTX discontinuing was infection, many cases had remission and decreasing steroid dosage. In comparison between RTX usage example and RTX unused example, death: 10.7% vs 14.0%, dialysis withdrawal: 60% vs 0%, relapse: 10.7% vs 16.3%. [Conclusions] These results showed that AAV treated by RTX is good tend. But, we should evaluate the efficacy and safety of treatment and consider the better ways to use RTX.

W60-2

A Single Center, Retrospective Analysis of RTX Treatment for Japanese Patients with ANCA-associated vasculitis

Kei Hirose¹, Manami Hirata¹, Kazuyuki Fujita², Noriya Momoki¹, Akiko Ueno¹, Masahiro Yamamura¹

¹Department of Internal Medicine, Okayama Saiseikai General Hospital, ²Fujita Clinic

Conflict of interest: None

[Object] To determine the real world practice of RTX treatment for Japanese patients with AAV. [Methods] This study included 30 MPA and 4 GPA patients (17 males and 17 females; 33 MPO-ANCA positive), with the median age of 77 years. [Results] For the initial RTX cycle, only one infusion in 8, 2 in 17, 3 in 2, and 4 in 7. At 6 months, 71.4% (15/21) reached remission, and PSL was 4.5mg/day. At RTX start, 3, 6, 12, 18, and 24 months, PSL levels were 40.0mg/day, 6.0mg/day, 1.75mg/day, 2.5mg/day, and 0mg/day. 3 relapsed (1 within 6 months, 2 within 18months). 14 patients discontinued RTX by 6 months, due to 9 AEs, 1 death by MPA, 2 for other hospitals, 1 remission and 1 unknown, 4 with

in 6-12 months (3 AEs, 1 unknown) and 3 over 12 months (1 AE, 2 for other hospitals). Severe AEs included 1 CMV colitis, 3 sepsis (1 died), 3 herpes zoster, 2 bacterial pneumonia, 1 pneumocystis pneumonia, 1 IP, 1 skin eruption and 1 pulmonary tuberculosis. [Conclusions] Low dose of RTX had been used as initial therapy and relapse for Japanese patients with MPA and GPA, but were effective and could reduce PSL doses. However, monitoring of opportunistic infections needs for safe treatment.

W60-3

The efficacy and safety of rituximab as remission induction therapy in patients with ANCA associated vasculitis

Takahiko Kurasawa, Yusuke Okada, Akiko Shibata, Kentaro Chino, Hirofumi Takei, Tsuneo Kondo, Koichi Amano
Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan

Conflict of interest: None

[Object] Aim is to reveal the efficacy and safety of rituximab (RTX) as a remission induction therapy in patients with ANCA associated vasculitis (AAV). [Methods] The medical records of 23 AAV patients (13 MPA and 10 GPA) who were treated with RTX as a remission induction therapy were analyzed. Observation periods were 6 months from the start of RTX. [Results] At the time of RTX induction therapy, the mean age was 66.1 years old, the mean PSL dose was 32.7 mg/day, and BVAS score was 14.1. Twenty one cases were in remission (BVAS=0). Four cases had a relapse. At month 6, the mean PSL dose was 5.7 mg/day. The adverse events were as follows: CMV 7, herpes zoster 1, HBV reactivation 1, PCP 1, Mycobacterium avium complex 1 and malignancy 1. As glucocorticoid-related complications, 10 hypertension, 6 diabetes and 8 hyperlipidemia were newly diagnosed or worsened. The risk factors of the severe infection at baseline were number of lymphocytes (P=0.0016), RPGN (P=0.0029), mPSL pulse therapy (P=0.0401) and age (P=0.0045). [Conclusions] RTX was effective for AAV, and infection rate was higher as compared to the result of Remit-JAV cohort. But severe infection rate was similar to previous reports.

W60-4

The efficacy and safety of rituximab as maintenance therapy in patient with ANCA associated vasculitis

Takahiko Kurasawa, Yusuke Okada, Akiko Shibata, Kentaro Chino, Hirofumi Takei, Tsuneo Kondo, Koichi Amano
Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan

Conflict of interest: None

[Object] To assess the efficacy and safety of rituximab (RTX) as maintenance therapy in patients with ANCA associated vasculitis (AAV). [Methods] We investigated the medical records of 15 AAV patients (6 MPA and 9 GPA) who had visited our hospital from June 2005 until September 2018, and treated with RTX as maintenance therapy. [Results] Observation period was 397 person-months. At the start of maintenance therapy, mean age was 63.4 years old and mean PSL dose was 7.3 mg/day. Two cases experienced relapse of AAV. The adverse events were as follows, PCP 1 (dead), HBV reactivation 1, bacterial pneumonia 1, and common cold/bronchitis 5, malignant tumor 1, and cerebral infarction 1. Serum CRP level (P=0.0434) at the start of maintenance therapy was extracted as a risk factor for relapse of AAV. The risk factors of infectious events were PR3-ANCA titer (P=0.0009), MPA (P=0.0107), serum KL-6 level (P=0.0232), serum creatinine level (P=0.0341), number of lymphocytes (P=0.0459). [Conclusions] The flare rate of AAV patients treated with RTX as maintenance therapy was lower as compared to the results of Co-Remit-JAV cohort. The frequency of infectious diseases was high, but it was 13.3% only for serious infections which was equal to previous reports.

W60-5

Study of RTX maintenance therapy for patients with ANCA-associated vasculitis

Yukiko Takeyama^{1,2}, Nobuyuki Ono¹, Yuri Sadanaga¹, Yasushi Inoue³,

Tomoya Miyamura⁴, Kensuke Oryoji⁵, Naoyasu Ueda⁶, Shuji Nagano⁷, Hisako Inoue⁸, Mariko Sakai¹, Yoshinobu Nakao¹, Akihito Maruyama¹, Syuichi Koarada¹, Shun-ichiro Ohta⁹, Seiji Yoshizawa¹⁰, Takuya Sawabe¹¹, Kyoko Otsuka¹², Yasutaka Kimoto¹³, Katsuhisa Miyake¹⁴, Takahiko Horiuchi¹³, Hitoshi Nakashima¹⁴, Hiroaki Niiro¹², Yoshifumi Tada¹

¹Department of Rheumatology, Faculty of Medicine, Saga University, Saga, Japan, ²Department of Internal Medicine, Saiseikai Karatsu Hospital, Karatsu, Japan, ³Division of Connective Tissue Disease, Fukuoka Red Cross Hospital, Fukuoka, Japan, ⁴Department of Internal Medicine and Rheumatology, National Hospital Organization Kyushu Medical Center, Fukuoka, Japan, ⁵Division of Rheumatology, Matsuyama Red Cross Hospital, Matsuyama, Japan, ⁶Department of Internal Medicine, Miyazaki Prefectural Miyazaki Hospital, Miyazaki, Japan, ⁷Center for Rheumatology, Iizuka Hospital, Iizuka, Japan, ⁸Department of Rheumatology, Saiseikai Fukuoka General Hospital, Fukuoka, Japan, ⁹Department of Rheumatology, Shimonoseki City Hospital, Shimonoseki, Japan, ¹⁰Department of Rheumatology, Hamanomachi Hospital, Fukuoka, Japan, ¹¹Division of Rheumatology, Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital, Hiroshima, Japan, ¹²Department of Medicine and Biosystemic Sciences, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan, ¹³Department of Internal Medicine and Clinical Immunology, Kyushu University Beppu Hospital, Beppu, Japan, ¹⁴Division of Nephrology and Rheumatology, Department of Internal Medicine, Faculty of Medicine, Fukuoka University, Fukuoka, Japan

Conflict of interest: None

[Object] We investigated the efficacy and safety of RTX maintenance therapy for ANCA-associated vasculitis (AAV). [Methods] We used a multicenter cohort database of AAV (KVAS cohort) and retrospectively extracted patients who used RTX as maintenance therapy. The doses of PSL, relapses, and adverse events (AE) were examined. [Results] Among 141 patients who achieved remission, RTX was used in 16 cases (12 GPA, 3 MPA, 1 unclassified AAV) as maintenance therapy. Average age was 71.2 (62-83) years old (female 69%). 11 were positive for MPO-ANCA, and 5 for PR3-ANCA. 14 had been treated with RTX remission induction therapy. The average PSL dose before maintenance therapy was 7.1 (2.5-12.5) mg/day, MTX in 5 cases and TAC in 1 case were used. The average PSL dose after 6 months was 2.9 (0-8) mg/day, 5 cases withdrew corticosteroids and there were no recurrence within 6 months. At the final observation, the average PSL dose was 3.3 (0-7.5) mg/day. Six cases withdrew corticosteroids, but 3 relapses appeared among them. The occurrence of severe AE was 4 incidents in 4 cases in 6 months and 7 incidents in 6 cases in total. [Conclusions] We proved that RTX maintenance therapy was useful and safe in Japanese AAV patients. But it is considered that corticosteroid withdrawal will be a subject for further study.

W60-6

Study on administration status of rituximab in ANCA-associated vasculitis

Kazuki Fujioka, Tomoya Sagawa, Akiko Kasahara, Shunya Kaneshita, Takuya Inoue, Takashi Kida, Hidetake Nagahara, Makoto Wada, Masataka Kohno, Yutaka Kawahito
Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

Conflict of interest: None

[Object] Rituximab (RTX) can be used as a therapeutic option for ANCA-associated vasculitis (AAV), and the cases treated with it are increasing in recent years. However, the optimal administration protocol for Japanese is not clear. [Methods] We investigated the clinical profiles of AAV patients who were treated with RTX in our hospital. [Results] The traceable AAV cases treated with RTX were 6 cases (MPA 2, GPA 3, OMAAV 1; Average Age is 72.3). 3 cases had RTX as initial induction therapy; the others were used as re-induction because of relapse. In all cases, improvement of disease activity (mean BVAS 18.5 point to 7.7 point) was observed in 1 month after the initial treatment of RTX. As maintenance therapy, 3 cases had only PSL, and in the other cases RTX was administered again. Immunosuppressive agents were not added in all cases. In 4 out of 6 cases, the timing and frequency of RTX therapy was adjusted from CD19 (+) cells percentage and clinical course. Adverse

events were 3 infection cases and 1 leukopenia. Throughout the study period, there were no case of relapse or who require PSL increase. [Conclusions] RTX therapy for AAV is useful for both induction and maintenance therapy. Adjustment of administration pattern based on clinical course and laboratory data can be possible.

W61-1

Analysis of sequential development of pulmonary lesions in patients with rheumatoid arthritis

Ayae Tanaka, Yuta Takamura, Tomoyuki Miyao, Ryutarō Yamazaki, Satoko Arai, Takayoshi Owada, Reika Maezawa, Masafumi Arima, Kazuhiro Kurasawa
Department of Rheumatology, Dokkyo Medical University

Conflict of interest: None

[Object] To clarify the sequential developmental pathway of pulmonary abnormalities in RA. [Methods] Subjects were consecutive 208 RA patients treated with biological DMARDs (Bio) and received HRCT scan before and during the therapy. Pulmonary abnormalities were classified into 20 lesions. Cluster analyses were conducted according to pre-existing and newly developing of pulmonary lesions. A checkerboard analysis was conducted to examine the relationship between pre-existing and newly developing lesions. [Results] Subjects were 64 male and females with age of 59.2 y and disease duration of 7.9 y (mean). Pulmonary lesions were found in 70.2% of RA patients before starting Bio. AD was commonly accompanied with the other lung abnormalities. Newly developing pulmonary abnormalities were observed in 11.1/100 person years. The new lesions were developed in several patterns, not at random. Bronchiolitis and curved linear opacity were developed in patients without pre-existing pulmonary lesions. In patients with pre-existing diseases, various lesions were developed, which had relation to the pre-existing ones. [Conclusions] Pre-existing pulmonary lesions induced new pulmonary lesions. Airway diseases, particularly bronchiolitis, might be an important initial lesion that induces ILD.

W61-2

The Impact of Immunosuppressants and Biologics on the Prognosis of Interstitial Lung Disease Associated with Rheumatoid Arthritis

Keiichiro Kadoba, Keisuke Nishimura, Kaoru Mizukawa, Hiroki Mukoyama, Tomohiro Yoshida, Daisuke Waki, Toshihiko Yokota
Department of Endocrinology and Rheumatology, Kurashiki Central Hospital

Conflict of interest: None

[Object] To assess the prognosis of interstitial lung disease (ILD) associated with rheumatoid arthritis (RA). [Methods] We reviewed the medical records of RA patients who visited our department from January 2008 to July 2018. Among the patients diagnosed as RA for the first time at our department, 41 patients had ILD at the initial presentation. We retrospectively reviewed the clinical features of 40 ILD patients with non-specific interstitial pneumonia (NSIP) or organizing pneumonia (OP) pattern on chest CT scan. [Results] Fifteen patients had ILD requiring hospitalization. Among them, 14 patients received increased doses of glucocorticoid, 12 patients received calcineurin inhibitors (CNIs), and four patients received other immunosuppressants. Two patients suffered severe relapse requiring hospitalization during follow-up (they had received CNI and cyclophosphamide, respectively). Thirteen patients required biologics to control their arthritis (TNF inhibitors 7, abatacept 7, tocilizumab 5). Among them, only two patients under treatment with TNF inhibitors suffered relapse requiring hospitalization. [Conclusions] Most patients with RA-ILD received CNIs, with fair prognosis and few relapses. The use of TNF inhibitors for RA patients with ILD is a potential risk for relapse.

W61-3

The assessment of the influence of biologics to the pre-existing interstitial pneumonia in rheumatoid arthritis

Kentaro Kuzuya, Eri Oguro, Yasutaka Okita, Hidetoshi Matsuoka, Satoru Teshigawara, Maiko Yoshimura, Yuji Yoshida, Kentaro Isoda, Yoshinori

Harada, Shiro Ohshima, Jun Hashimoto, Yukihiko Saeki
Rheumatology and Allergology, National Hospital Organization Osaka
Minami Medical Center

Conflict of interest: None

Objective: To assess the influence of biologics (Bio) to the pre-existing interstitial pneumonia (IP) in rheumatoid arthritis (RA). **Methods:** RA patients with pre-existing IP treated by Bio in our hospital from 2008 to 2018 were divided into three groups (TNF inhibitor, IL-6 inhibitor and T cell inhibitor). Retrospective cohort study was conducted and the primary endpoint was the exacerbation of IP. The 58 patients were recruited; TNF inhibitor (TNFi), n=17, IL-6 inhibitor (IL-6i), n=16, and T cell inhibitor (Tci), n=25. Log-rank test to compare the Kaplan-Meier curves whose horizontal were the event-free time were conducted. **Results:** In the baseline data, the median of the age, sex, disease duration, CT score, KL-6, dose of corticosteroids were not significantly different. The results of Log-rank test were the followings: whole exacerbations were not significantly different among the three groups (p=0.201), but the acute exacerbations were significantly common when compared the TNFi and the non-TNFi group (p=0.0204), and all the acute exacerbations (n=2) were happened in TNFi group. **Conclusion:** Acute exacerbations were significantly common in TNF inhibitor group, which may indicate that non-TNFi is safer than TNFi in RA patients with pre-existing IP.

W61-4

Prognosis and causes of deaths of rheumatoid arthritis patients with interstitial pneumonia

Shigeki Makino¹, Koji Nagai², Takeshi Shoda³, Hidehiko Makino², Takayasu Suzuka², Kenichiro Hata², Takuya Kotani², Tohru Takeuchi², Shigeki Arawaka²

¹Division of Internal Medicine, Osaka Medical College Mishima-Minami Hospital, Takatsuki, Osaka, Japan, ²Department of Internal Medicine IV, Osaka Medical College, Takatsuki, Osaka, Japan, ³Division of Rheumatology, Yodogawa Christian Hospital, Osaka, Japan

Conflict of interest: Yes

[Background] We aim to know the influence of interstitial pneumonia (IP) involvement on prognosis of rheumatoid arthritis (RA). **[Methods]** We reviewed clinical data concerning about prognosis and causes of deaths of RA-IP patients of our institute from August 2008 to July 2018. **[Results]** Total RA-IP patients are 255 (114 males, average 73.5 years). Comparing RA patients without IP (1433cases, 285 males, average 61.0 years), RA-IP patients were older and male dominant. Total dead cases were 40 (22males). 5-year survival rate of RA-IP patients was 83.6%, 10-year survival rate was 59.8%. Concerning about the causes of deaths of RA-IP patients, chronic progression of IP were 7 cases, acute exacerbation of IP were 7, lung cancer were 7, other malignancy were 4, pneumonia were 4, other infection were 3, cardiac disease were 3. **[Conclusions]** RA-IP patients of our institute were older and male dominant compared to RA patients without IP. 5-year survival rate of RA-IP patients was 83.6%, 10-year survival rate was 59.8%. 3 major causes of deaths of RA-IP patients were 7 chronic progression of IP, 7 acute exacerbation of IP and 7 lung cancer. Total death due to pulmonary lesion were 25 (62.5%). So pulmonary involvement of RA profoundly influence on prognosis of RA-IP patients.

W61-5

Incidence of microalbuminuria and disease activity in patients with RA

Ryo Inoue¹, Yuhei Fujisawa¹, Yasushi Kakuchi¹, Hiroshi Fujii², Kazunori Yamada², Mitsuhiro Kawano²

¹Division of Internal Medicine, Ishikawa-ken Saiseikai Kanazawa Hospital, ²Department of Internal Medicine, Kanazawa University Graduate School

Conflict of interest: None

[Object] The chronic inflammation causes endothelial dysfunction, and may result in albuminuria. This study aims to examine the relationship between the disease activity and the incidence of microalbuminuria

in rheumatoid arthritis (RA). **[Methods]** We retrospectively examined the relationship between the disease activity score (DAS) and incidence of microalbuminuria in 304 RA patients. Patients were divided into two groups: group 1, including patients that their average disease activity score 28-erythrocyte sedimentation (DAS28-ESR) was <3.2 and group 2, the patients that their average DAS28-ESR was >3.2. The outcome of interest was incidence of microalbuminuria. We evaluated incidence of CKD using Kaplan-Meier curves, and calculated hazard ration using Cox proportional hazards models. **[Results]** The incidence of microalbuminuria in group 1 was higher than that in group 2 (p=0.041) High average DAS28-ESR was an independent predictor of the incidence of CKD (hazard ratio, 2.96; 95% confidence interval 1.24-8.59, p=0.035). **[Conclusions]** High disease activity was a significant risk factor for incidence of microalbuminuria.

W61-6

The incidence of malignant tumors that can be indicated for immune checkpoint inhibitors in patients with rheumatoid arthritis

Yukitomo Urata

Tsugaru General Hospital

Conflict of interest: None

[Object] To clarify the incidence of malignant tumors that can be indicated for immune checkpoint inhibitors (IC) in rheumatoid arthritis (RA) patients **[Methods]** In RA patients, the development of malignant tumors that can be indicated for IC was investigated at every year from September 2014, (September 2014 - August 2015: 2014 group; September 2015 - August 2016: Group 2015; September 2016 - August 2017: 2016 Group; September 2017 - August 2018: 2017 group). Patients with a history of malignant tumor treatment within 10 years were excluded at registration. IC adaptation was judged by the presence or absence of IC adaptation approval at diagnosis of malignant tumor. **[Results]** The number of RA patients, age (year), malignant tumor incidence (%), IC adaptive malignant tumor incidence (%) of each group are shown; [n=479, 68 (61-77), 9 (1.9%), 0 (0%)], [n=504, 68 (61-77), 12 (2.4%),0 (0%)], [n=514, 68 (61-77), 7 (1.4%), 1 (0.2%)], [n=526, 67 (60-76), 37 (7.0%), 9 (1.7%)]. **[Conclusions]** The incidence of IC-adapted malignancy has increased in RA due to an increase in malignant tumor incidence, development of a new IC (methods), combined use of IC and other cancer treatment methods, and expansion of IC indication diseases.

W62-1

Incidence of malignancy in patients with systemic sclerosis: A single-center study

Shota Kurushima¹, Katsumi Eguchi¹, Kanako Kojima¹, Yoshika Tsuji¹, Toshiyuki Aramaki¹, Kaoru Terada¹, Atsushi Kawakami², Yukitaka Ueki¹
¹Rheumatic Collagen Disease Center, Sasebo Chuo Hospital, ²Department of Immunology and Rheumatology, Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: None

[Object] To evaluate the profile and frequency of malignancy among patients with systemic sclerosis (SSc), and the association between disease-specific autoantibodies and malignancies. **[Methods]** We conducted a single-center retrospective study of SSc patients who visited our institution between 2008 and 2017. **[Results]** The total observation period was 1,344 person-years. Among 166 patients with SSc, 58% were positive for anticentromere antibodies, 16% were positive for anti-Scl-70 antibodies and 5% were positive for anti-RNA polymerase III antibodies. Of the 166 patients, 25 malignancies (15.1%) were observed. Breast cancer (n=9) was the most frequent, followed by lung cancer (n=5) or gastric cancer (n=4). As for the prevalence of malignancy, there were no statistical differences among the types of autoantibodies. Cancer developed after the diagnosis of SSc in 60% of patients and 40% had occurred before the diagnosis of SSc. About intervals between the diagnosis of SSc and malignancy, 56% of cancer developed within 50 months of SSc diagnosis. **[Conclusions]** SSc is associated with the increased incidence of cancer, particularly of the breast and lung. Investigations for underlying malignancy should be considered in medical care for SSc.

W62-2

Association of Anti-RNA Polymerase III Antibody and Malignancy in Patients with Systemic Sclerosis

Yoshihito Tanaka, Masanari Koderu

Department of Dermatology, JCHO Chukyo Hospital

Conflict of interest: None

[Object] Systemic Sclerosis (SSc) patients with anti-RNA polymerase III (RNAP) antibody have been reported to have an increased risk of malignancy. The aim of this study was to investigate the relationship between disease-specific autoantibodies and malignancy, and to examine the expression of RNAP in tumor tissues in SSc patients. [Methods] Among 156 Japanese SSc patients in our hospital, 13 were positive for RNAP antibody, 35 were positive for anti-topoisomerase I (Topo I) antibody and 108 were positive for anticentromere antibody (ACA). We examined the incidence of malignancy in these patients. Malignant tumor tissues were stained using an anti-POLR3A antibody (Atlas antibodies, Sweden). [Results] The prevalence of malignancy was significantly higher in patients with RNAP antibody (6/13, 46.2%) than in those with Topo I antibody (2/35, 5.7%) and in those with ACA (7/108, 6.5%). Importantly, three patients with RNAP antibody and malignancy developed malignancy from 2 years before to 1 years after SSc onset. Expression of POLR3A protein was observed in the tumor tissue. [Conclusions] SSc patients with RNAP have an increased risk of malignancy. POLR3A protein was expressed frequently in tumor tissues. We thought that RNAP antibody could be a tumor maker in SSc patients.

W62-3

Exploring the prominent genes for pathogenesis of pulmonary arterial hypertension in systemic sclerosis. ~ Shedding on the “exercise induced pulmonary hypertension”

Yoshinobu Koyama, Toshie Higuchi

Rheumatology, Center for Autoimmune Diseases, Japan Red Cross Okayama Hospital

Conflict of interest: None

[Object] To detect candidate genes involved in the pathogenesis of exercise-induced pulmonary hypertension (exPAH) at the early stage of SSc. [Methods] Total of 88 patients who had not met PAH criteria with Raynaud phenomenon, skin sclerosis or SSc-related autoantibody was enrolled. Exercise Doppler echocardiography was carried out to segregate exPAH from normal response group (exN) with using the reported definition. Differentially expressed genes (DEGs) between exPAH and exN group were applied to several gene analysis methods. [Results] After applying 1204 DEGs to hierarchical clustering analysis, 93% of exPAH samples were segregated into one cluster. WGCNA analysis revealed 6 co-expression modules. By pathway analysis, the modules were significantly enriched with genes of several pathways, such as Wnt, endothelin, TLR, EGF and VEGF-A. Volcano plots indicated that expressions of TMEM176A and TMEM176B were prominent in exPAH patients, and these genes were highly correlated with each other. [Conclusions] TMEM176A and TMEM176B were found initially to be a regulator for DC maturation in mice, but functions of human ortholog remain still unclear. It is interesting that accumulation of plasmacytoid DC was reported around blood vessels in the lungs from SSc-PAH patients.

W62-4

Impaired vasculogenesis of endothelial cells derived from iPSc in a patient with systemic sclerosis associated pulmonary artery hypertension

Yuki Kudo, Masaru Kato, Yuhei Shibata, Masatoshi Kanda, Wen Shi Lee, Michihiro Kono, Eri Sugawara, Michihito Kono, Yuichiro Fujieda, Toshiyuki Bohgaki, Olga Amengual, Kenji Oku, Shinsuke Yasuda, Tatsuya Atsumi

Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Conflict of interest: Yes

[Object] Systemic sclerosis associated pulmonary arterial hypertension (SSc-PAH) is associated with less favorable outcome, compared to other PAH, and with comorbidities including venous, cardiac and lung involvement. We aimed to clarify the pathogenesis of SSc-PAH using disease-specific induced pluripotent stem cells (iPSc). [Methods] Peripheral blood mononuclear cells obtained from a 76 y.o. female SSc-PAH patient with venous, cardiac and lung comorbidities and a healthy donor were transfected with sendai virus vector containing Oct3/4, Sox2, Klf4 and L-Myc to establish iPSc. Endothelial cells (EC) were differentiated with the culture system of BMP-4, Activin, bFGF, CHIR99021, Y-27632, VEGF and SB431542. The vasculogenesis of EC was evaluated by tube formation assay in vitro. The tube length was measured by image processing software. [Results] EC differentiated from the SSc-PAH patient and those from the healthy donor were morphologically similar. However, the vasculogenesis was significantly impaired in the SSc-PAH patient compared to the healthy donor with 33.5% reduced tube length (31.2±2.0 (mm) vs 47.0±1.3 (mm), $p < 0.01$, $n = 3$). [Conclusions] We detected the impaired vasculogenesis of EC in SSc-PAH using disease-specific iPSc, which might be involved in the pathogenesis of SSc-PAH.

W62-5

A new concept of M1 and M2 monocytes in systemic sclerosis

Naoki Iwamoto¹, Mizuna Otsuka¹, Momoko Okamoto¹, Yushiro Endo¹, Sosuke Tsuji¹, Ayuko Takatani¹, Toshimasa Shimizu¹, Remi Sumiyoshi¹, Tomohiro Koga¹, Shin-ya Kawashiri¹, Takashi Igawa¹, Kunihiro Ichinose¹, Mami Tamai¹, Hideki Nakamura¹, Tomoki Origuchi², Atsushi Kawakami¹

¹Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ²Department of Physical Therapy, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: None

[Object] Recently, the relation with M2 macrophage and fibrosis have been reported in several diseases. Similar with macrophages, monocytes can be classified into M1 and M2 subset. We attempted to investigate relationship among M1 or M2 in systemic sclerosis (SSc). [Methods] This study included 23 RA patients and 20 healthy donors. Using fluorescence-activated cell sorting, we defined CD14, CD68 and CCR2 positive cells as M1 monocytes and CD14, CX3CR1 and CD163 positive cells as M2 monocytes. We also examined the ability of cytokines, chemokines and TGF- β secretion of CD14 positive cells from SSc and M2 monocytes from healthy donors by multiplex bead array assay. [Results] SSc patients had higher M2/M1 ratio as compared with healthy control (7.00 vs 1.63, $P < 0.05$). And, there was tendency that M2/M1 ratio was higher in SSc patients complicated with interstitial pneumonia. Furthermore, the ability of TGF- β secretion of M2 monocytes was higher than that of M1-dominant monocytes. [Conclusions] Our present study suggested that the imbalance of M1/M2 monocytes might contribute to pathogenesis of SSc.

W62-6

Cyclin-dependent kinase 4/6 inhibitor ameliorates dermal fibrosis in murine models of systemic sclerosis

Akio Yamamoto, Fumitaka Mizoguchi, Kimito Kawahata, Tetsuya Saito, Hitoshi Kohsaka

Department of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University (TMDU)

Conflict of interest: None

[Object] In the skin lesions of early systemic sclerosis (SSc), increased proliferation of fibroblasts is observed. The objective of this study was to examine the effects of cyclin-dependent kinase 4/6 inhibitor (CDKI) on SSc dermal fibroblasts and the therapeutic effect in murine models of SSc. [Methods] Effects of palbociclib, a CDKI, on fibroblasts were examined in the presence or absence of TGF β in vitro. Hypochlorous acid-induced (HOCl) model and bleomycin-induced model were used to study the effect of palbociclib as monotherapy or in combination with galniserib, a TGF β receptor inhibitor, on skin fibrosis in vivo. [Re-

sults] Palbociclib suppressed the proliferation of fibroblasts. TGFβ-induced increase of *ACTA2* expression was suppressed in the presence of palbociclib, while phosphorylation of Smad2/3 was not. Palbociclib decreased dermal thickness and collagen contents, and suppressed fibroblast proliferation in murine models of SSc. The combination therapy with galunisertib was more effective than either monotherapy in HOCl model. [Conclusions] CDKI suppressed the proliferation of fibroblasts and the differentiation to myofibroblasts in vitro. CDKI ameliorated the skin fibrosis in vivo. These results should encourage the use of CDKI to treat human SSc.

W63-1

Quantitative evaluation of mRNA expression of MEFV gene product pyrin in human tissues

Naoko Nakano^{1,2}, Kazunaga Agematsu³, Akihiro Yachie⁴, Kiyoshi Migita⁵, Takeshi Urano⁶, Tomohiro Koga⁷, Atsushi Kawakami⁷, Junya Masumoto²

¹Department of Pediatrics, Ehime University Graduate School of Medicine Shitsukawa Toon Ehime Japan, ²Department of Pathology, Ehime University Graduate School of Medicine Toon- Ehime Japan, ³Department of Infectious Immunology, Shinshu University- Graduate School of Medicine Matsumoto- Nagano Japan, ⁴Department of Pediatrics, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University School of Medicine, Kanazawa, Ishikawa, Japan, ⁵Department of Rheumatology, Fukushima Medical University School of Medicine, Fukushima, Japan, ⁶Department of Biochemistry, Shimane University School of Medicine Izumo- Shimane Japan, ⁷Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University, Nagasaki, Japan

Conflict of interest: None

[Object] Familial Mediterranean fever (FMF) is a hereditary disease characterized by periodic episodes of fever accompanied by acute inflammatory attacks of serosa and synovium. Although a candidate gene *MEFV* product pyrin was identified, pyrin expression has not been still fully elucidated. To understand the pathogenesis of FMF, we studied on expression of pyrin in normal human tissues. [Methods] We isolated total RNA from formalin-fixed and paraffin-embedded normal human tissues, and performed real-time PCR. Transcripts of *MEFV* was evaluated using specific TagMan Gene Expression analysis. In addition, interleukin (IL)-1β and IL-18, both were expected as down-stream cytokines of pyrin, were also evaluated. [Results] Pyrin was highly expressed in appendix of acute appendicitis where a lot of neutrophil infiltrated. Lower expression was detected in subserosa of gastrointestinal tracts. Trace amount of expression was detected in all tissues we studied. A significant correlation between quantitative mRNA expression of pyrin and IL-18 but not IL-1β was observed. [Conclusions] mRNA of *MEFV* gene product pyrin was more or less ubiquitously expressed, and its expression level correlated with IL-18 production in each tissue, which may reflect FMF pathogenesis.

W63-2

Specific cytokine secretion patterns for detecting pathogenic MEFV variants

Takayuki Tanaka¹, Takeshi Shiba¹, Ryuta Nishikomori¹, Hiroaki Ida², Hirofumi Shibata¹, Kazushi Izawa¹, Takahiro Yasumi¹

¹Department of Pediatrics, Kyoto University Graduate School of Medicine, ²Department of Respiratory, Neurology, and Rheumatology, Kurume University Faculty of Medicine

Conflict of interest: None

[Background] FMF is an autoinflammatory disorder caused by MEFV mutation. As many as 340 sequence variants have been reported regarding MEFV, but only a few mutations, such as M694I, are relevant to FMF, and the significance of most variants are unclear. [Object] To clarify the characteristics of FMF-patients derived hematopoietic cells, and then recapitulate the phenotype with MEFV-mutant iPS cell-derived macrophages (iPS-MPs) [Methods] We obtained monocytes and monocyte-derived macrophages from FMF patients. We also established iPS-MPs with MEFV mutations. [Results] The IL-1beta secretion was com-

parable between FMF and control monocytes, and colchicine failed to suppress the secretion from FMF monocytes. IL-1beta secretion from monocyte-derived macrophages were higher in FMF patients, and that was inhibited by colchicine. This phenotype was reproduced with patient-derived iPS-MPs. iPS-MPs with exogenous M694I MEFV expression also secreted more IL-1beta than iPS-MPs with transgene WT MEFV expression. [Conclusions] We revealed the characteristics of primary cells from FMF patients, and the phenotype of macrophages matches the clinical phenotypes. We recapitulated this cytokine response with iPS-MPs, and established a platform to evaluate various MEFV variants.

W63-3

The study of clinical feature and gene analysis in patients with Familial Mediterranean Fever (FMF)

Tatsuo Ishizuka¹, Kei Fujioka¹, Ichiro Mori¹, Tomofumi Takeda¹, Saori Inui¹, Koichiro Taguchi², Takahide Ikeda², Hiroyuki Morita², Tomoko Toma³, Akihiro Yachie³

¹Gifu Municipal Hospital, ²Department of General Internal Medicine, Gifu Graduate School of Medicine, ³Department of Pediatrics, Kanazawa Graduate School of Medicine

Conflict of interest: None

[Object] To clarify the association between various clinical symptoms and mutation of MEFV. [Methods] Genomic DNA were purified from white blood cells in FMF patients, and MEFV has been explored. [Results] We have analyzed *MEFV* in 6 patients with FMF. Case 1; female 17 yo, she had recurrent fever (RF) with chest pain at 11 yo. *MEFV* showed compound heterozygous mutations (L110P+E148Q/M694I) from each father/mother. Case 2; female 29 yo, she had chest pain, arthralgia, RF and positive rheumatoid factor. Because of severe diarrhea she needed canakinumab injection. *MEFV* indicated compound heterozygous mutations (E148Q/M694I) from father/mother. Case 3; male 16 yo, he had RF with headache. *MEFV* was heterozygous mutations (E148Q+P369S+R408Q) from only father. Case 4; female 36 yo, she had RF from 10 yo 2-3 times/year. *MEFV* showed E148Q+S503C from only father. Case 5; male 31 yo, he had RF per month one year before. *MEFV* could not show abnormality. Case 6; female 15 yo, she had RF with headache and chest pain every 3-6 months. *MEFV* showed homozygote of E148Q. [Conclusions] These results showed improvement of symptoms by the treatment of colchicine except for case 2. Two cases of FMF indicated positive rheumatoid factors with arthralgia, showing compound heterozygote of E148Q/M694I in *MEFV*.

W63-4

The interim analysis of post-marketing all-patient surveillance of canakinumab in Japanese patients with cryopyrin-associated periodic syndrome

Kazuko Matsumoto

Medical Division, Novartis Pharma K.K.

Conflict of interest: None

[Objectives] A post-marketing all-patient (pt) surveillance of canakinumab (CAN), a human Anti-interleukin-1β monoclonal antibody is ongoing to assess its safety and efficacy in Japanese pts with cryopyrin-associated periodic syndrome. This is an interim report of 6 years post-launch in daily medical practice. [Methods] A total of 90 pts (55 sites) were registered with 83 (50 sites) included in a database lock in June 2018. 80 pts were assessed as safety population and 77 were for efficacy assessment. [Results] Of 80 pts for safety, the mean age of pts at dosing initiation was 24.2 years. The number of pts with Familial cold autoinflammatory syndrome/Muckle-Wells syndrome/Neonatal onset multi-system inflammatory disease were 10/46/24, respectively. 3 were discontinued and 8 were cessation of CAN. Adverse drug reactions (ADRs) were seen in 22 pts (27.5%). Severe ADRs were 3.75% in 3 newly enrolled pts with pneumonia, RS virus Bronchiolitis, Rhabdomyosarcoma, Neutropenia and Fever. The death was seen in one NOMID 0-year boy with no causality, having circulatory collapse and sepsis. Of 77 pts for efficacy, at 24-104 weeks, 75-82% of new pts and 83-94% of pts from clinical study remained flare free after achieving remission. [Conclusions] The further assessment is required until the final report.

W63-5

The functional analysis of peripheral blood mononuclear cells in a patient with A20 haploinsufficiency (HA20) with a new mutation (Cys200Alafsx16)

Yuya Fujita¹, Kazunaga Agematsu², Junpei Temmoku¹, Makiko Furuya Yashiro¹, Naoki Matsuoka¹, Tomoyuki Asano¹, Shuzo Sato¹, Hiroko Kobayashi¹, Hiroshi Watanabe¹, Tomohiro Koga³, Atsushi Kawakami³, Kiyoshi Migita¹

¹Department of Rheumatology, Fukushima Medical University School of Medicine, Fukushima, Japan, ²Department of Infectious Immunology, Shinshu University Graduate School of Medicine, Matsumoto, Japan, ³Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: None

Objective: Heterozygous germline mutations in the TNFAIP3 gene cause HA20, which presents as early onset autoinflammatory disease resembling Behçet's disease. The aim of this study was to identify the mechanism of inflammation in HA20 using mononuclear cells (PBMCs) of a patient with a new mutation. **Case:** A 17-year-old Japanese boy had a 3-year history of recurrent painful oral ulcer and periodic fever. His mother and sister had exhibited similar symptom. He was diagnosed as HA20 with a new mutation (Cys200Alafsx16), which result in premature stop codon in the OUT domain of A20. **Method:** We isolated PBMCs from the patient and healthy subjects. PBMCs were stimulated with TNF- α (10 ng/ml) for 24 hr. Cellular supernatants were assayed for IL-1 β by ELISA and cellular lysates were subjected to immunoblot using anti-A20 or anti-I κ B- α antibodies. **Result:** A20 expression was reduced in PBMCs from the patient with HA20 compared to those from control PBMCs. TNF- α -induces degradation of I κ B- α was accelerated in PBMCs for HA20, which is associated with the increased IL-1 β production. **Conclusion:** TNFAIP3 mutation lead to impaired A20 expression, which could be responsible for the TNF- α -induced NF- κ B activation process due to the increased degradation of I κ B- α .

W63-6

Efficacy of the urinary N-telopeptide/urinary creatinine ratio in assessing disease activity in pediatric chronic recurrent multifocal osteomyelitis

Yoji Uejima, Satoshi Sato, Eisuke Suganuma, Yutaka Kawano
Division of Infectious Disease, Immunology, and Allergy, Saitama Children's Medical Center

Conflict of interest: None

[Objective] Chronic recurrent multifocal osteomyelitis (CRMO) is characterized by aseptic and non-tumor disease of the bone. Although CRMO has been established as an autoinflammatory disease, the markers of disease activity are unknown. We investigated the efficacy of the urinary N-telopeptide/urinary creatinine ratio (uNTX/uCr), a bone resorption marker for osteoporosis and bone metastasis, in assessing the disease activity of CRMO. [Method] We enrolled 6 patients (3F, 3M) diagnosed with CRMO between February 2014 and September 2018. [Results] The median age of disease onset and mean duration of symptoms before diagnosis were 10.2 years (3-13 years) and 9.8 months, respectively. The most common symptom was local pain (5/6). The mean value of uNTX/uCr at the time of diagnosis (494.5 nmol/mmol/Cr) decreased in 4 patients who showed remission. Among these, 2 showed improvement after additional therapy with alendronate and 2, after remission of the biologics. Among the remaining 2 patients, uNTX/uCr decreased in the patient whose symptoms improved, whereas it increased in the patient with no improvement. [Conclusion] uNTX/uCr increased during symptomatic exacerbation of CRMO and decreased at the time of remission. Thus, uNTX/uCr may be an indicator of the disease activity of CRMO.

W64-1

Magnetic resonance imaging of skeletal muscles in patients with dermatomyositis: characteristic findings and diagnostic performance

Taro Ukichi, Ken Yoshida, Kentaro Noda, Kazuhiro Furuya, Daitaro Kurosaka

Division of Rheumatology, Department of Internal Medicine, The Jikei University School of Medicine

Conflict of interest: None

[Object] To define characteristic findings on MRI of skeletal muscles in patients with dermatomyositis (DM) relative to those in patients with other idiopathic inflammatory myopathies (IIMs) and to assess their diagnostic performance in DM. [Methods] Differences in the frequency of various findings on MRI of proximal limb skeletal muscles between 36 DM, 17 amyopathic DM, 19 polymyositis (PM), and 16 non-IIM patients were analyzed. [Results] Characteristic MRI findings in DM patients were subcutaneous high signal intensity (HSI), fascial HSI, peripheral distribution of HSI in muscle, and heterogeneous pattern of HSI in muscle. Homogeneous HSI pattern in muscle was less frequently observed in DM patients compared with PM or non-IIM patients. Interobserver agreement in the interpretation of MRI findings ranged from substantial to almost perfect (κ 0.67 to 0.98). The likelihood of DM score \geq 3 (assessed by counting the number of characteristic MRI findings in DM patients) showed good diagnostic performance in DM (short-tau inversion recovery: sensitivity 72.2%, specificity 88.5%, AUC 84.9%; gadolinium-enhanced fat-suppressed T1-weighted imaging: sensitivity 81.2%, specificity 91.5%, AUC 89.9%). [Conclusions] Muscle MRI could be a useful tool for distinguishing DM from other IIMs.

W64-2

Clinical characteristics of patients who underwent conchotome biopsy in our hospital

Masami Tokura, Tomoko Niwano, Kenji Nagasaka
Department of Rheumatology, Ome Municipal General Hospital

Conflict of interest: None

[Background] We haven't frequently performed muscle biopsy, because of high invasiveness and difficult sample processing. Recently, minimally invasive and convenient procedure, conchotome biopsy, was introduced in Japan. [Object] To launch conchotome biopsy in our hospital. [Methods] Conchotome biopsy was started in January 2018. Patients performed conchotome biopsy until September 2018 were retrospectively analyzed. [Results] Nine cases were included. The average time for biopsy was 27 minutes, patients needed not be rest and no adverse event was occurred. Before muscle biopsy, we clinically suspected 7 cases as dermatomyositis (DM) or polymyositis (PM) (group A) and 2 cases as other than DM/PM (group B). Histopathologically, muscle fiber degeneration and inflammatory cell infiltration were observed in 5 cases in group A and 1 case in group B. T cell infiltration was observed in all cases in group A and 1 case in group B. Finally, we diagnosed all cases in group A as DM or PM (2 DM/ 5 PM). In group B, 1 case was diagnosed as immune-mediated necrotizing myopathy. The other case was no abnormal findings in histopathology and was diagnosed as scleroderma. [Conclusion] Conchotome biopsy can be performed safely and minimally invasive in a short time.

W64-3

The characteristics of RNA-seq transcriptomics related to myositis-specific autoantibodies (especially anti-MDA5 antibody) in each immune cell subset

Yusuke Sugimori¹, Yukiko Iwasaki¹, Yusuke Takeshima^{1,2}, Hiroaki Hatano¹, Junko Maeda¹, Mai Okubo¹, Satomi Kobayashi¹, Harumi Shirai¹, Mineto Ota^{1,2}, Yasuo Nagafuchi¹, Shuji Sumitomo¹, Hirofumi Shoda¹, Yuta Kochi³, Tomohisa Okamura^{1,2}, Kazuhiko Yamamoto³, Keishi Fujio¹

¹Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Japan, ²Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, Japan, ³Laboratory for Autoimmune Diseases, Center for Integrative Medical Sciences, RIKEN, Japan

Conflict of interest: Yes

[Background] Clinical phenotype of idiopathic inflammatory myopathy (IIM) markedly differ between myositis-specific autoantibodies. To

find common and different point of myositis-specific autoantibodies, we performed RNA-Seq of immune cell subsets in peripheral blood from IIM patients. [Methods] 45 IIM patients and 58 healthy controls (HCs) were picked up. 7 had anti-MDA5 antibody (MDA5-Ab) and 14/5/3 had anti-ARS/Mi-2/TIF1 antibodies. Among 7 MDA5-Ab positive patients, all had interstitial pneumonia and 4 were before treatment. RNA-Seq of each immune cell subset was performed with HiSeq2500. [Results] The percentage of plasmablast (PB) significantly increased in IIM, especially in MDA5-Ab positive patients. Weighted gene co-expression network analysis showed positive correlation between MDA5-Ab positivity and the module (groups of genes) comprised of type 1 IFN signature in almost all subsets. Machine learning showed type 1 IFN signature module of PB can distinguish MDA5-Ab from other autoantibodies most accurately among all modules from all subsets. [Conclusions] The characteristics of MDA5-Ab positive IIM was enhanced type 1 IFN signature in wide range of immune cell subsets. This approach would reveal the characteristics of other autoantibodies-positive IIM patients.

W64-4

Autoantibodies and cytokine profiles in dermatomyositis/polymyositis

Kazuhiro Kurasawa, Satoko Arai, Yuta Takamura, Tomoyuki Miyao, Ryutaro Yamazaki, Ayae Tanaka, Takayoshi Owada, Reika Maezawa, Masafumi Arima

Department of Rheumatology, Dokkyo Medical University

Conflict of interest: None

[Object] By autoantibodies, mastitis was classified into subgroups with characteristic clinical features. It is unknown whether subgroups have characteristic cytokine profiles. The purpose of this study was to answer the question and if so to determine the profile. [Methods] Cytokine levels in sera from myositis (anti-MDA5; 22, -ARS; 18, -TIF1-g; 5) and 8 controls were measured using multiplex-array. [Results] IP-10 levels were increased in myositis patients, but not in controls. In anti-MDA5 Ab + myositis, IL-6, IL-10, IL-15, TNF- α , IFN- α and MCP-1 level was increased. In anti-ARS Ab+ cases, IFN- β levels were elevated as well as TNF- α and MCP-1. Using the correlation coefficient between cytokines, cytokine groups was identified. In anti-MDA5 Ab+ cases, 2 cytokine groups were identified; one includes IFN- α , IL-15, TNF- α and IL-10, and the other involved IL-6, MCP-1. Both groups related to IP-10. In anti-ARS Ab+ cases, 2 groups were found; one included NF- α , MCP-1 and IP-10, and the other had IFN- β as sole component. [Conclusions] Cytokine profiles differ among subgroups in myositis. In anti-DDA5+ myositis, IL-15 and IFN- α with strong correlation and IL-6 were characteristic cytokines, while IFN- β was a unique one in anti-ARS+ one.

W64-5

Branched chain amino acids in the treatment of polymyositis and dermatomyositis: results from BTOUGH study

Naoki Kimura, Hitoshi Kohsaka

Department of Rheumatology, Tokyo Medical and Dental University, Tokyo, Japan

Conflict of interest: None

[Object] To assess the efficacy and safety of branched chain amino acids (TK-98) in the treatment of polymyositis and dermatomyositis (PM/DM). [Methods] Untreated adults with PM/DM were enrolled in a randomized, double-blind trial to receive either TK-98 or placebo in addition to the conventional therapy. After 12 weeks, patients whose average MMT score was under 9.5 were enrolled in an open label extension study for 12 weeks. The primary end point was the change of manual muscle test (MMT) score at 12 weeks. The secondary end point was the disease activity and the change of functional index (FI) that evaluates dynamic repetitive muscle function. [Results] Twenty-four patients and 23 patients were randomized to receive TK-98 and placebo, respectively. The change of MMT scores at 12 weeks were equivalent (0.70 ± 0.19 and 0.69 ± 0.18 , respectively). The MMT scores in both groups improved similarly throughout the extension study. The improvement of FI in shoulder flexion at 12 weeks was significantly better in the TK-98 group. The differential change of average FI per time was larger in the TK-98 group. No dif-

ference was found in the disease activity and the adverse events. [Conclusions] BCAA was effective on the improvement of dynamic repetitive muscle function in patients with PM/DM.

W64-6

The predictive factor of effectiveness of intravenous immunoglobulin therapy in dermatomyositis and polymyositis

Keiichi Sakurai, Seido Ooka, Yutaka Goto, Harunobu Iida, Takayasu Ando, Kanako Suzuki, Yusa Asari, Marina Uchida, Shoshi Shinagawa, Tomofumi Kiyokawa, Hiromi Matsushita, Kana Ishimori, Hisae Fujimoto, Yukiko Takakuwa, Kumiko Tonooka, Machiko Mizushima, Mitsuru Imamura, Takeshi Suzuki, Yoshioki Yamasaki, Hiroko Nagafuchi, Kimito Kawahata

St. Marianna University

Conflict of interest: None

[Object] For the treatment of dermatomyositis (DM) and polymyositis (PM), high-dose intravenous immunoglobulin therapy (IVIG) is often performed, and sometimes repeated. But immunoglobulin is the formulation made from human blood, so the social cost of IVIG is serious problem. [Methods] DM and PM patient who were diagnosed in our department and were performed IVIG therapy was analyzed. The clinical data of these patients, such as creatinine kinase (CK), aldolase, and myocardial departure enzymes, before and after IVIG. The primary invalid was defined as the case whose CK did not decrease after IVIG. The secondary invalid was defined as the case whose CK increased within 6months after IVIG. [Results] 23 case were analyzed. Average CK was 1014U/l before IVIG. The primary invalid cases were 3. Secondary invalid cases were 5. The average serum concentration of myosin light chain before IVIG in the primary invalid cases was 7.4ng/ml, that in the secondary invalid cases was 13.84ng/ml, and that in successful cases was 132.97ng/ml. The higher concentration of myosin light chain cause higher therapeutic effect. ($P= 0.0017$, Kruskal-Wallis test) [Conclusions] We found that the serum concentration of myosin light chain would be a predictive factor of the primary and secondary invalid of IVIG therapy.

W65-1

Usage of biological DMARDs by renal function for rheumatoid arthritis patients

Yasutaka Kimoto¹, Tetsushin Murakami¹, Daisuke Oryoji¹, Masahiro Ayano², Hiroki Mitoma², Mitsuteru Akahoshi², Yojiro Arinobu², Hiroaki Niino³, Koichi Akashi², Takahiko Horiuchi¹

¹Internal Medicine, Kyushu University Beppu Hospital, ²Department of Medicine and Biosystemic Science, Kyushu University Hospital, ³Department of Medical Education, Kyushu University Graduate School of Medical Sciences

Conflict of interest: None

[Background] It is known that renal function decreases with age. In Japan of super aged society, it is inferred that decline in renal function affects the treatment of rheumatoid arthritis (RA). [Objective] To examine the use of biological anti-rheumatic drugs (bDMARDs) by renal function of RA patients in our hospital. [METHODS] We examined the use of bDMARDs by age / eGFR for 203 cases of receiving bDMARDs as of September, 2018. [Results] Many of anti-TNF antibody preparations, which are considered to require MTX combination in terms of therapeutic effect, have been used for cases with poor renal function reduction. In addition, non - TNF preparations that are expected to be effective in monotherapy were also frequently used in cases with decreased renal function.

W65-2

Evaluation of factors of patient characteristics associated with renal dysfunction in patients with rheumatoid arthritis

Yosuke Hattori, Daihei Kida, Tomotaro Sato, Kenya Terabe, Koichi Mori, Shotaro Mori, Atsushi Kaneko

Orthopaedic Surgery and Rheumatology, National Hospital Organization Nagoya Medical Center

Conflict of interest: None

[Object] This study aimed to assess renal dysfunction in patients with rheumatoid arthritis (RA). [Methods] Our subject population comprised 1316 RA patients, for whom we assessed factors that could potentially affect the estimated glomerular filtration rate (eGFR), as follows: age, gender, disease duration, stage, class, RF, body mass index (BMI), MTX dosage, PSL dosage, Biologics use, HAQ, EQ-5D tender joint count, swollen joint count, patient global assessment, CRP, and DAS28-CRP. Stepwise multiple regression analysis was performed using eGFR as the dependent variable and all other variables as independent variables. [Results] We obtained the following values: age: 63.4±12.7 years, disease duration: 13.9±11.2 years, BMI: 21.5±3.4 kg/m², MTX dosage: 4.4±4.2mg/week, MTX use: 57.4%, PSL dosage: 1.2±2.4mg/day, PSL use: 32.4%, Biologics use: 43.5%, HAQ: 0.8±0.8, EQ-5D: 0.7±0.2, CRP: 0.7±1.6 mg/dl, DAS28-CRP: 2.8±1.1, and eGFR: 71.3±20.1ml/min/1.73 m². The adjusted coefficient of determination was 0.26. Standardized partial regression coefficients were as follows: age, -0.48; BMI, -0.11; MTX dosage, 0.10 (all significant at the 1% level). [Conclusions] Our findings suggest that factors of patient characteristics that impact renal dysfunction in patients with RA are age, BMI, and MTX dosage.

W65-3

The effectiveness of epoetin beta pegol (continuous erythropoietin receptor activator: CERA) in patients with rheumatic diseases complicated with chronic kidney disease (CKD)

Satoshi Ito¹, Yoichi Kurosawa^{1,2}, Eriko Hasegawa^{1,2}, Daisuke Kobayashi², Shinji Taniguchi¹, Asami Abe¹, Hiroshi Otani¹, Kiyoshi Nakazono¹, Akira Murasawa¹, Ichiei Narita², Hajime Ishikawa¹

¹Department of Rheumatology, Niigata Rheumatic Center, ²Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences

Conflict of interest: Yes

[Object] To analyze efficacy of CERA in patients with rheumatic diseases complicated with CKD. [Methods] Among 43 patients with rheumatic diseases (M3, F40) who received CERA, 11 patients died or transferred within 12M. Thirty two patients (M2, F 30) were followed up more than 12 M. There were 26 RA, 1 MPA with RA, 3 MPA, 1 OA, and 1 PMR patients. Their clinical data were analyzed. [Results] Patients were 78.0 ± 1.2 YO and disease duration was 17.9 ± 2.8 years. Mean BUN was 30.2 ± 2.5 mg/dl, Cr was 1.4 ± 0.1 mg/dl, and eGFR was 39.5 ± 3.6 ml/min. Serum iron and ferritin were not low (51.0 ± 6.7 µg/dl, 220.0 ± 52.8 ng/ml) and UIBC was not raised (173.6 ± 16.4 µg/dl). MCV was not decreased (90.4 ± 2.3) and serum erythropoietin (EPO) was not raised (20.2 ± 2.0 mIU/ml; n=19). There was no patient whose EPO was over 50 mIU/ml. By usage of CERA (41.9 ± 5.1 µg/M), Hb was raised from 8.7 ± 0.2 to 10.1 ± 0.2 (p<0.0001). Hb in patients without iron preparation (n=27) was also raised from 8.7 ± 0.2 to 10.0 ± 0.2 (p<0.0001). [Conclusions] CERA was effective in rheumatic patients complicated with CKD. Even with low Cr, we should suspect CKD and start CERA in the early stage. In RA patients, it might be possible to discontinue CERA with the intensification of the treatment of RA.

W65-4

Usefulness of assessment of the GERD symptom with the use of GerdQ interview sheet in rheumatic disease

Kazuya Kishimoto, Yuji Nozaki, Tetsu Itami, Kenji Sakai, Shinkai Ri, Asuka Inoue, Toshihiko Shiga, Koji Kinoshita, Masanori Funauchi, Itaru Matsumura

Department of Hematology and Rheumatology, Kindai University Faculty of Medicine, Sayama, Osaka, Japan

Conflict of interest: None

Objectives: We have a lot of opportunities to prescribe NSAIDs or DMARDs in rheumatic clinic, but it's difficult to ask a patient about his upper gastrointestinal symptom since a consultation hour is limited. There is a previous study that GERD scores of systemic sclerosis (SSc) and Behcet disease (BD) were increased in rheumatic diseases. Methods: We investigated the frequency of heartburn, regurgitation, epigastric pain, nausea, sleep disturbance, additional use of commercial drug by GredQ in 350 rheumatic patients. Patients were asked to recall symp-

toms during the last 7 days. The definition of treatment-resistant GERD is that total score is more than 8, and any of heartburn, regurgitation, sleep disturbance, use of commercial drug is more than 2 days. Results: 40 of 350 patients has a treatment-resistant GERD. Patients were diagnosed as RA (n=11), SSc (n=7), SLE (n=6), BD/MCTD/PMR/PM/DM (n=6), and other rheumatic disease (n=6). The Mean age was 59 years and the mean disease duration was 114 months. The administration rate of PPI was 65%. Conclusion: Even though an administration of PPI, a treatment-resistant GERD was recognized with GerdQ interview sheet in rheumatic diseases. Usefulness to evaluate symptoms and reconsider treatment content was suggested.

W65-5

Examination of 10 cases of interstitial emphysema secondary to autoimmune diseases

Kana Ishimori, Seido Ooka, Kanako Suzuki, Harunobu Iida, Takayasu Ando, Yutaka Goto, Marina Uchida, Yusa Asari, Hisae Fujimoto, Keiichi Sakurai, Hiromi Matsushita, Tomofumi Kiyokawa, Yukiko Takakuwa, Kumiko Tonooka, Mitsuru Imamura, Takeshi Suzuki, Yoshioki Yamasaki, Hiroko Nagafuchi, Kimito Kawahata

Rheumatology and Allergology, St. Marianna University School of Medicine

Conflict of interest: None

[Object] The intestinal emphysema is a state with the gas in intestinal wall and classified in idiopathy and a secondary. It is unknown what the outcome intestinal emphysema with collagen diseases is. We examined intestinal emphysema of this hospital. [Method] From January, 2010 to October, 2018, we investigated clinical data regarding the patients with intestinal emphysema diagnosed by CT at St. Marianna university school of medicine. [Results] Ten intestinal emphysema was detected, but there was no stomachache in 8 cases. Two cases with stomachache die with sepsis. Five scleroderma, four systemic lupus erythematosus, one dermatomyositis were included. The case that showed increase of the activity at an intestinal emphysematous diagnosis was one case, and most were found accidentally. And they are improved by rest. Four of five cases of scleroderma caused intestinal pseudo-obstruction. [Conclusions] As for the intestinal emphysema associated with collagen disease, most had a good prognosis. The possibility that stomachache, portal vein emphysema, sepsis had a poor prognosis was suggested.

W65-6

Relationship between serum oxytocin levels, disease activity, activity of daily life, quality of life and depression in patients with rheumatoid arthritis

Yusuke Miwa¹, Nobuyuki Yajima¹, Ryo Takahashi¹, Ryo Yanai¹, Sakiko Isojima¹, Masayu Umemura¹, Nao Oguro¹, Yoko Miura¹, Mayu Saito¹, Mika Hatano¹, Tomoki Hayashi¹, Kosuke Sakurai¹, Tsuyoshi Kasama¹, Michio Hosaka²

¹Division of Rheumatology, Department of Medicine, Showa University, School of Medicine, ²Psychosomatic Medicine, Katsuyama Clinic

Conflict of interest: Yes

[Object] Oxytocin (OXT) also referred to as a happy hormone. However, the relationship between depression and RA has not yet been clarified. The objective of this study was to investigate the relationship between serum OXT levels and disease activity, depression, ADL, and QOL in RA. [Methods] This study included 119 RA patients. We measured the following variables: baseline characteristics including age, sex, disease duration, smoking history, BMI, prednisolone dose, MTX dose, and serum levels of RF, MMP-3, CRP and ESR. The disease activity of RA was assessed using the SDAI; depression was assessed using the Hamilton Depression Rating Scale; ADL were assessed using the HAQ-DI; and QOL was assessed using the SF-36. Serum OXT levels were determined by ELISA. The subjects were divided into two groups according to the higher or lower of the serum OXT levels, and a retrospective study was performed. [Results] The serum OXT levels were correlated with the disease duration (r=0.443). Weak correlations of MTX dose (r=0.208), swollen joint count (r=-0.306), ESR (r=-0.245) and CRP (r=-0.283). The binominal logistic analyses findings were as follows: younger age (OR:

1.04) and longer disease duration (OR: 1.08). [Conclusions] The serum OXT levels were correlated with longer disease duration.

W66-1

The regulation of AMP-activated protein kinase by uric acid in mice
Yoshitaka Kimura, Daisuke Tsukui, Tamiko Yanagida, Hajime Kono
Department of Internal Medicine, Teikyo University

Conflict of interest: None

[Object] It's reported that AMPK activation protected against the development of atherosclerosis. Hyperuricemia is regarded as one of the risk factors of atherosclerosis. In this study, we clarified the association of uric acid with AMPK. [Methods] Secretable uricase (ssUOX) or intracellular uricase (intUOX) transgenic mice express extracellular or intracellular uricase that lead to reducing levels of the uric acid of outside or inside of the cells, respectively. The uricase transgenic mice and control mice were administered with 30% fructose solution for 5 days. In another experiment, Apoe^{-/-} mice were fed with high fat diet for 16 weeks with or without administration of 60 µg/ml allopurinol in the drinking water. In both experiments the activities of AMPK of the leukocytes were evaluated by western blot. [Results] In fructose experiment, activities of AMPK were significantly increased in both types of uricase transgenic mice. In high fat diet experiment, activities of AMPK were increased in mice with allopurinol. [Conclusions] Decreasing uric acid levels by expressing uricase or inhibition of xanthine oxidase inhibitor both activated AMPK of leukocytes in mice. It suggests that uric acid has a role in development of atherosclerosis via regulation of AMPK activity.

W66-2

A pilot survey about the method of synovial fluid crystal examination in Japan

Takayasu Kise¹, Naoto Yokogawa¹, Naoki Tanomogi¹, Masahiro Iida¹, Shuhei Sano¹, Yusuke Nakamichi¹, Tatsuo Mori¹, Nanase Honda¹, Michiru Kina¹, Eisuke Takamasu¹, Kae Onishi¹, Yuji Miyoshi², Satoshi Watanuki³, Masako Utsunomiya¹, Yoshiki Nagai¹, Kota Shimada¹, Ikuko Masuda⁴, Shoji Sugii¹

¹Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, ²Department of Rheumatic Diseases, Tokyo Metropolitan Health and Medical Treatment Corporation, Tama-Hokubu Medical Center, ³Division of Emergency and General Medicine, Tokyo Metropolitan Tama Medical Center, ⁴Center for Rheumatic Diseases, Jujo Takeda Rehabilitation Hospital

Conflict of interest: None

[Objective] We performed a pilot survey about the crystal examination method in Japan. [Method] We sent a questionnaire about the identification of crystals in synovial fluid to 173 institutions in Japan. The questionnaires are following; 1) Which department is seeing crystal-induced arthritis?, 2) Is microscopic examination used for the diagnosis of crystal induced arthritis?, 3) Who is examining the synovial fluid?, 4) Is a compensated polarized microscope available in own institutions?. [Results] We received the replies from 80/173 institutions (46.2%). The results were following; 1) orthopedic surgery 64, rheumatology (internal medicine 43, surgery 9), internal medicine or general internal medicine 10; 2) 6 did not use microscopic examination because of non-availability; 3) laboratory 49, outsourcing 27. physician 6; 4) laboratory 43, not available 26, own department 3, unknown 8. Contacting the laboratories, we found almost all institutions including outsourcing companies did not have compensated polarized microscopy and are using a light microscopy with polarized plates. Examination is often performed after centrifuging. [Conclusion] A standard crystal identification method is not used in Japan. The standardization of microscopic examination is urgent subject in Japan.

W66-3

Validation of the protocol for detecting monosodium crystal deposition in dual-energy computed tomography (DECT) and pitfalls in interpretation

Yohei Seto^{1,2}, Atsuo Taniguchi¹, Naomi Ichikawa¹, Hisashi Yamanaka¹

¹Institute of Rheumatology, Tokyo Women's Medical University, ²Tokyo Women's Medical University Yachiyo Medical Center

Conflict of interest: None

[Object] DECT has currently been recognized as a non-invasive imaging modality which enables detection of monosodium urate (MSU) crystal deposition. We report a validation study for a single-source DECT (Discovery CT 750HD, General Electric) using a sample extracted from a patient with tophaceous gout. [Methods] a 77 year-old man attended the clinic with subcutaneous mass in the right lateral malleolus, suspected of gouty tophus. Aspiration and microscopic examination revealed the presence of MSU crystal and confirmed the diagnosis. The supernatant and precipitation acquired by settled separation were scanned by DECT and compared with the reference standard derived from the chemical formula and mass attenuation coefficient of urate. [Results] The change in the Hounsfield Unit was similar between the reference standard and the precipitation, and the effective atomic number of the precipitation was more approximate to the reference than that of the tophus detected in vivo. Whereas, applying the sample including supernatant as a reference resulted in increased sensitivity and also detection of artefact. [Conclusions] Density of MSU crystal deposition in vivo should be considered for interpretation of DECT image despite our confirmation of the validation for the reference standard.

W66-4

Usefulness of musculoskeletal ultrasonography to evaluate chondrocalcinosis in acute calcium pyrophosphate crystal arthritis (pseudogout)

Yukiko Komano¹, Sayaka Ueno¹, Kaori Yanagawa¹, Aiko Kishida¹, Koichiro Ohmura², Toshihiro Mata¹, Ikuko Masuda¹

¹Center for Rheumatic Diseases, Jujo Takeda Rehabilitation Hospital, ²Department of Rheumatology and Clinical Immunology, Kyoto University

Conflict of interest: None

[Background] Demonstration of calcium pyrophosphate (CPP) crystals in synovial fluid and/or radiographic chondrocalcinosis (CC) has been the gold standard for the diagnosis of calcium pyrophosphate deposition (CPPD). Recently, potential utility of ultrasonography (US) in diagnosis of CPPD including pseudogout has been reported. [Object] To investigate the usefulness of US in diagnosis of pseudogout. [Methods] Retrospective study. 24 consecutive patients (July/2015~July/2018) diagnosed with pseudogout in our rheumatology clinic. Clinical records were reviewed. [Results] 18 patients (17 females) who underwent radiographic and US assessment were analyzed. Mean age was 86 y.o. The main sites where CPP deposition was detected by US are hands (11/21), knees (9/16), shoulders (3/4). Three patients fulfilled the above gold standard. In others, the diagnosis was based on symptoms and CC of affected joints (6 cases), CC of asymptomatic joints (2 cases), US identification of CPP deposition and CC of asymptomatic joints (4 cases), US identification of CPP deposition without CC (2 cases), solely in clinical symptoms (1 case). Detection rate of CPP deposition in affected joints by US is relatively high compared to that by radiography. [Conclusions] US is a useful diagnostic tool for pseudogout.

W66-5

Ultrasound-guided aspiration for diagnosis in Pseudogout of the hip; two case reports

Ryozo Harada¹, Keiichiro Nishida², Ryuichi Nakahara³, Yoshihisa Nasu², Koji Takasugi³, Misuzu Fujimori³, Kazuhiko Ezawa³, Shinichiro Fujita⁴, Kie Inoue⁴, Wataru Yamamoto⁵

¹Department of Rheumatic Disease Center, Orthopaedics, Kurashiki Sweet Hospital, ²Department of Orthopaedics, Okayama University Hospital, ³Department of Rheumatic Disease Center, Internal Medicine, Kurashiki Sweet Hospital, ⁴Department of Rehabilitation, Kurashiki Sweet Hospital, ⁵Department of Health Information Management, Kurashiki Sweet Hospital

Conflict of interest: None

[Introduction] Atraumatic acute inflammatory hip joint pain requires differential diagnosis of rheumatoid arthritis, crystal induced arthritis and infectious arthritis, and it may be difficult to diagnose. [Objective] We report two cases in which ultrasound-guided aspiration of the hip joint was useful for diagnosis and treatment. [Case 1] 92-year-old female couldn't move with right hip joint pain. X ray and CT showed no fracture, but fluid accompanied by calcification was observed in the anterior direction in hip joint. [Case 2] 81-year-old female with pelvic fractures in resting hospitalization, suddenly had right hip joint pain and couldn't move. we found a fluid accumulation around the hip joint. [Results] Ultrasound-guided aspiration of the hip joint was performed in both case 1 and 2. Calcium pyrophosphate was confirmed from the specimen, and no infectious findings. [Discussion and conclusion] There are many diagnostic information obtained by joint fluid examination. ultrasound-guided aspiration of the hip joint may be performed easily and safely, and useful for diagnosis and treatment of hip joint pseudogout.

W66-6

Giant Gouty Tophus of Bilateral Knee Requiring Surgical Treatment. Case Report

Yasuhiko Mizutani¹, Hiroshi Horiuchi², Tsuyoshi Toyota¹, Yoshiyuki Kotouda¹, Yoshiyuki Nakamura¹, Tsutomu Takizawa¹

¹Department of Orthopedic Surgery, Nagano Matsushiro General Hospital, Nagano, Japan, ²Department of Rehabilitation, Shinshu University Hospital

Conflict of interest: None

[Object] Giant Gouty Tophi have been rare in recent years by the contribution of improvement of gout treatment. We report a case of giant gouty tophus of bilateral knee requiring surgical treatment. [Case] 60-year-old man with a history of gout presented to our hospital with pain and mass of bilateral knee. Febuxostat, 20mg daily, was prescribed by a local clinic. He had no family history of hyperuricemia. The tumor existed on proximal and distal of bilateral patella, invading partially to the patellar tendon. In the surgery, the giant tumor of bilateral knee was removed. The tumor had a negative optical sign of birefringence under a polarized light microscope. Histologically, eosinophilic nodules were rimmed by giant cells. Gouty tophus was diagnosed. Postoperatively, bilateral knee pain disappeared. [Discussion] Tophi are chronic foreign body granuloma-like structures surrounded by inflammatory cells and connective tissue. Tophaceous deposition occurs typically in olecranon bursa, Achilles tendon, or metatarsophalangeal joint of hallux, relatively rarely in knee. The indication of surgery is based on pain, function disturbance, infection, or risk of fracture or tendon rupture. In this case, he had pain and risk of patellar tendon rupture. Thus, the surgical treatment was recommended.

W67-1

The study of liver fibrosis in rheumatoid arthritis (RA) patients with methotrexate (MTX) treatment using Combi-Elasto and liver fibrosis score

Motokazu Kai¹, Shigenori Tamaki², Kunikazu Ogawa¹, Takashi Kato⁴, Ikuko Tanaka^{2,3}

¹Initiative for Rheumatology and Osteoporosis, Mie Rheumatology Clinic, Suzuka, Mie, Japan, ²Initiative for Rheumatology and Osteoporosis Nagoya Rheumatology Clinic, ³IRO Integration Clinical Research Center, ⁴Department of Radiology National Center for Geriatrics and Gerontology

Conflict of interest: None

(Object) Liver injury due to MTX have exhibited NASH-like pathological feature, but the mechanism is incompletely understood. Biopsy is necessary for diagnosis, but it is invasive. Type 4 collagen 7S have been used as bio markers, but not suitable for dairy use. We investigated liver fibrosis in RA patients using Combi-Elasto that is a combination RTE and SWM and Fib-4 index which is liver fibrosis score. (Methods) The subjects were 60 RA outpatients with MTX treatment. Combi-Elasto was performed with ARIETTA 850 by Hitachi Ltd. LES, Vs value, LFI, Fib-4 index was measured. (Results) Female was 44 (73.3%), mean age was 55.5 years, mean cumulative MTX dose was 415.2mg. Mean AST/ALT

and platelet count was 38.4/32.2 IU/L and 19,000/ μ L. Mean Fib-4 index was 2.44, Vs value was 1.42, LFI was 1.90. Fib-4 index showed a positive correlation with age, AST/square root ALT, Vs value, LFI and mHAQ, a negative correlation with platelet count and eGFR. LFI showed a positive correlation with age and cumulative MTX dose. (Conclusions) Fib-4 index and elastography are effective for evaluating liver fibrosis in RA patients with MTX treatment. In addition, cumulative MTX dose, transaminitis, age, platelet count and renal disfunction is a risk factor, combination fib-4 index and Combi-Elasto is useful.

W67-2

Efficacy of Plasma Platelet-Derived Microparticles in the Diagnosis of Rheumatoid Arthritis

Hideyuki Horikoshi, Ko Takamatsu, Rika Suzuki, Yasuyoshi Kusanagi, Fumihiko Kimura, Kenji Itoh

Division of Hematology and Rheumatology, Department of Internal Medicine, National Defense Medical College

Conflict of interest: None

[Object] Platelet-derived microparticles (PDMP) are membrane vesicles that are released from the activated platelets and contain various inflammatory or angiogenetic factors. PDMP can be a possible new biomarker in the diagnosis of rheumatic disease. We analyzed the plasma PDMP levels obtained from 33 patients with rheumatoid arthritis (RA). [Methods] In total, plasma PDMP of 33 cases, including 11 RA, 8 polymyalgia rheumatica (PMR), 6 undifferentiated arthritis (UA), 8 others, and 5 healthy controls were analyzed using enzyme-linked immunosorbent assay. Additionally, we compared the PDMP levels with other biomarkers (CRP, ESR, and MMP3). [Results] The PDMP levels (mean \pm SD) for the disease and control groups were 57.16 \pm 13.06, 33.25 \pm 14.69, 5.27 \pm 1.69, 29.68 \pm 12.72, and 5.70 \pm 1.33 U/ml for RA, PMR, UA, other, and control, respectively. The PDMP levels for patients with RA were significantly higher than those for patients with UA. Further, the PDMP levels were negatively correlated with other biomarkers in patients with RA and PMR. Of interest, the PDMP levels were high in some patients with lower levels of other biomarkers. Thus, PDMP can be the candidate for an independent biomarker in the diagnosis of RA and PMR. [Conclusions] Plasma PDMP is useful in the diagnosis of RA.

W67-3

NUDT15 polymorphism related adverse events in patients with rheumatic diseases

Yukinori Unno¹, Mitsuhiro Takeno¹, Takashi Nawata^{1,2}, Yuichiro Shirai¹, Takahisa Gono¹, Masataka Kuwana¹

¹Department of Allergy and Rheumatology, Tokyo, Japan, Nippon Medical School, Graduate School of Medicine, ²Department of Medicine and Clinical Science, Ube, Japan, Yamaguchi University Graduate School of Medicine

Conflict of interest: None

[Backgrounds] We here report adverse events of azathioprine (AZA) which is related with the NUDT15 polymorphism in two patients with rheumatic diseases. [Case 1] A 78-year-old female with systemic lupus erythematosus started to receive 50 mg of AZA in addition to prednisolone because of persistent elevation of anti-DNA Ab titer. Four weeks later, she had pancytopenia and alopecia, which were subsided by supportive therapies after discontinuation of AZA. [Case 2] A 70-year-old male with periarthritis nodosa started to receive 25 mg of AZA in addition to prednisolone due to persistent positive CRP. Because of alopecia and leukopenia, AZA was discontinued, resulting in hematological recovery without serious infection. Genotyping of NUDT15 codon 139 revealed T/T (Cys/Cys) in both patients. [Discussion] NUDT15 p. Arg139Cys, particularly the Cys/Cys homozygous, which is found in about 1% of Japanese, is strongly associated with severe AZA adverse events such as severe acute leukopenia and alopecia. Because the NUDT15 polymorphism related adverse events emerge, irrespective of underlying diseases, the genetic screening is necessary before starting AZA in rheumatic diseases including SLE and vasculitis besides inflammatory bowel diseases.

W67-4

Examination of LPS binding protein and CD57 expressing NK cells in ACPA antibody negative RA patients

Masao Takemura¹, Masao Sato², Tomohiro Sasaki³, Tsuneo Watanabe⁴, Kuniaki Saito⁵

¹Advanced Diagnostic System Research Laboratory, Fujita Health University Graduate School of Health Sciences, Toyoake, Aichi, Japan, ²Ohashi-Tani Orthopedics, Gifu, Japan, ³Ota Orthopedics Clinico, Gifu, Japan, ⁴Gifu University School of Clinical Laboratory, Gifu, Japan, ⁵Department of Disease Control and Prevention, Fujita Health University Graduate School of Health Sciences, Toyoake, Aichi, Japan

Conflict of interest: None

[Object] There are reports that patients with rheumatoid arthritis (RA) have less onset of dementia. Accumulation of amyloid β (A β) is thought to be one of physiological phenomena accompanying aging and its relation to dementia has been studied. In this study, anti-A β autoantibody was measured and the relationship between NK cell and LPS binding protein (LBP) was examined. [Methods] The subjects were 127 patients with rheumatic outpatient clinical visits. Seventy two patients (age 55.6 \pm 16.9 years) diagnosed with RA, 55 cases of unknown arthritis (UA) (60.5 \pm 13.4 years). Routine clinical examination was conducted on the relationship with ACPA antibody, CRP, RF, IgG, IgA, IgM. [Results] The anti-A β -40 antibody concentration (Mean \pm SE) was 16.3 \pm 1.9 u in the RA group and was significantly higher compared with UA group; 12.8 \pm 1.9 u (p < 0.01). On the other hand, LBP was significantly (p < 0.05) high in the RA group 4.9 \pm 0.4 μ g / mL than in the UA group 3.6 \pm 0.2 μ g / mL. There was no significant difference between the RA group and the UA group for CD57 + / CD8 + cells (%). [Conclusions] These results imply that autoantibodies and cellular origin are involved in their pathogenesis complicatedly.

W67-5

The relationship between the onset of rheumatoid arthritis and the balance of blood monocyte subsets

Eriko Tanaka^{1,2}, Shiro Ohshima^{2,3}, Yukihiko Saeki^{2,3}

¹Department of Rheumatology, Ginnankai Clinic, ²Department of Clinical Research, NHO Osaka-Minami Medical Center, ³Department of Rheumatology and Allergology, NHO Osaka-Minami Medical Center

Conflict of interest: None

[Object] In humans, monocytes are composed of three distinct subsets based on their expression of CD14 and CD16; inflammatory (I), patrolling (P), phagocytic monocytes. To evaluate the correlation between blood monocyte subsets and the onset or the disease activity of RA in patients with new-onset arthritis. [Methods] The patients were diagnosed within one month from initial visit and divided into three groups which were RA (n=73), OA (n=47), and UA (n=47) groups. In fresh peripheral blood of all patients, the membrane molecules of monocytes were analyzed immediately using flow cytometry using the antibodies anti-CD14 and anti-CD16. [Results] The percentages of I monocytes in RA and UA group were significantly higher than that in OA group (p =0.001, p =0.036). While that of P monocytes in UA group was significantly higher than that in RA group (p =0.0004). The ratio of I/P in RA group was significantly higher than that in UA group (p =0.0003). Moreover the ratio of I/P was correlated with DAS28CRP (r =0.43, p <0.0001). [Conclusions] This study suggests that in human blood monocyte subsets the I-biased monocyte is possible to correlate with the onset of RA and disease activity of arthritis and P monocytes possibly prevent the development of RA from UA.

W67-6

Comparison between the usefulness of temporal artery biopsy and imaging tests for the detection of temporal artery lesion in giant cell arteritis

Ko Takamatsu, Hideyuki Horikoshi, Rika Suzuki, Yasuyoshi Kusanagi, Fumihiko Kimura, Kenji Itoh

Division of Hematology and Rheumatology, Department of Internal Medicine, National Defense Medical College

Conflict of interest: None

[Object] Temporal artery biopsy (TAB) and imaging tests are used for detecting temporal artery (TA) lesion in giant cell arteritis (GCA); however, the concordance rate remains unclear. We compared the efficacy of TAB and imaging tests in detecting TA lesion in GCA. [Methods] We retrospectively reviewed patient characteristics, clinical symptoms, imaging test results, and TAB for 6 patients diagnosed with GCA. [Results] Three men and 3 women, with a median age of 74.5 (25th-75th percentile, 70-79.8) were analyzed. Clinical symptoms included fever in 1 patient, malaise in 2, weight loss in 4, jaw claudication in 2, visual loss in 1, and complication with polymyalgia rheumatica in 5. Laboratory tests showed that the CRP level was 7.5 (3.50-12.23) mg/dL, ESR was 109.5 (92.75-117.25) mm/h, WBC was 7000 (6375-8525)/ μ L, Hb level was 10.7 (9.88-10.88) g/dL, and Plt level was 37.8 (30.83-39.50) \times 10⁴ / μ L. Imaging tests showed 1/5 (17%) of TA abnormality on MRI and 3/6 (50%) of TA wall thickening on ultrasonography (US); moreover, 5/6 (83%) patients demonstrated arteritis on TAB. Three patients without cranial symptoms were all TAB-positive, and 2/3 in lack of TA lesion on US were TAB-positive. [Conclusions] TAB is more useful than US for detecting TA lesion in GCA.

W68-1

The relationship between Anti-citrullinated peptide antibody and osteoporosis

Hiroyuki Nagata¹, Kentaro Inui², Tatsuya Koike^{2,3}, Yuko Sugioka², Tadashi Okano^{2,4}, Kenji Mamoto², Yutaro Yamada², Koji Mandai⁴, Masahiro Tada⁵, Hiroaki Nakamura²

¹Orthopedic Surgery, Osaka General Hospital of West Japan Railway Company, ²Orthopedic Surgery, Osaka City University Hospital, ³Orthopedic Surgery, Hamayuu Hospital, ⁴Orthopedic Surgery, Osaka City Society Hospital, ⁵Orthopedic Surgery, Osaka City General Hospital

Conflict of interest: None

[Object] The factor of osteoporosis of rheumatoid arthritis (RA) is various, but there are reports that a disease itself is risk of osteoporosis. This time, the relation between the bone density and Anti-citrullinated peptide antibody (ACPA) was investigated. [Methods] We use the data from TOMORROW (the positive cohort study which consists of 202 RA patients and 202 controls whose age and sex were matched: UMIN000003876). We divided into three groups by the titer of ACPA at base line (BL). We have performed a multiple regression analysis of the objective variable DXA value, as an explanatory variable clinical data of BL. We also have performed a multiple regression analysis as explanatory variables clinical data of BL and objective variable amount of change in seven years lower limb bone density (BMD). [Results] In the context of the BMD in the BL there is no correlation between 3 group (p =0.9,0.9). In the analysis of change in seven years, we also find the correlation between 3 group (p =0.3,0.5). [Conclusions] ACPA is not associated with osteoporosis, also involved in the bone loss of seven years was not observed.

W68-2

Clinical factors affecting the change of anti-CCP antibody in rheumatoid arthritis patients

Ichiro Nakamura^{1,4}, Katsumi Ito², Takuo Juji⁴, Naohiro Izawa⁴, Akihiro Uchio⁴, Takumi Matsumoto³, Jinju Nishino³, Sakae Tanaka³

¹Faculty of Medical Science, Teikyo-Hisei University, ²Department of Rheumatology, Heisei Yokohama Hospital, ³Department of Orthopedic Surgery, University of Tokyo, ⁴Department of Rheumatology, JCHO Yugawara Hospital

Conflict of interest: None

[Object] Anti-CCP antibody (ACPA) is widely used for diagnosis of rheumatoid arthritis (RA). There are few reports that ACPA values fluctuate due to RA treatment, whereas, in the clinical course, the values sometimes change dramatically. The purpose of this study is to clarify the clinical factors affecting the change of ACPA values in RA patients. [Methods] 234 patients (195 women, 39 men) with RA, in whom ACPA values were measured twice with an interval of more than five years,

were analyzed. The mean age of patients was 67.6 years old, and the mean duration of RA was 17.4 years. Five clinical factors including smoking history, periodontal disease, Brinkman index, family history of RA and usage of biologic agents were evaluated for the change of ACPA values. [Results] Among these factors, usage of biologic agents significantly reduced ACPA values. Smoking history and periodontal disease have a tendency to increase ACPA values. In 56 patients, ACPA increased more than twice, while, in 50 patients, it decreased to less than half. Between two groups, multiple logistic analysis was performed with above factors as explanatory variables, revealing that biologic agents significantly reduced ACPA to less than half. [Conclusions] Biologic agents have the potential to decrease ACPA values.

W68-3

Risk factors for CMV infection in autoimmune disorder

Sayuri Takamura¹, Daisuke Kobayashi¹, Shunsuke Sakai¹, Ayako Wakamatsu¹, Yukiko Nozawa¹, Hiroe Sato³, Takeshi Nakatsue¹, Yoko Wada¹, Takeshi Kuroda³, Masaaki Nakano², Ichiei Narita¹

¹Division of Clinical Nephrology and Rheumatology, Niigata University Medical and Dental Hospital, ²School of Health Sciences, Niigata University, ³Niigata University Health Administration Center

Conflict of interest: None

[Purpose] To identify the risk for CMV infection in patients with autoimmune disorders on steroid therapy. [Method] Forty-nine (Male: 19, Female: 30) patients with autoimmune disease who started taking prednisolone ($\geq 20\text{mg/day}$) in our hospital were enrolled. Weekly CMV pp65 antigen evaluation were performed. If summation of positive cells in 2 slides was ≥ 5 , they were diagnosed as positive in this study (CMV positive group). [Result] Patients with SLE; 11, ANCA-associated vasculitis (AAV); 8, MCTD; 6, interstitial pneumonia with anti-ARS-Ab; 5, rheumatoid arthritis; 4, IgG4 related disease; 3, clinically amyopathic dermatomyositis (CADM); 2, adult onset still's disease (AOSD); 2, and others; 8 were started taking prednisolone, and 8 patients (SLE;2, AAV;2, CADM;2, AOSD;1, and MCTD;1) became positive CMV antigenemia. Total lymphocyte count and serum albumin level were low ($710/\mu\text{l}$ vs $1210/\mu\text{l}$; $p=0.002$, 2.80 g/dl vs 3.55 g/dl ; $p=0.030$, respectively), and HbA1c was high (6.4% vs 5.8% ; $p=0.007$) in CMV positive group. All patients in CMV positive group received steroid pulse therapy ($p<0.001$). [Conclusion] Lymphocytopenia, hypoalbuminemia, high HbA1c, and receiving steroid pulse therapy were associated with the risk of CMV pp65 antigen positivity.

W68-4

Evaluation of human non-mercaptoalbumin in patients with rheumatoid arthritis and systemic lupus erythematosus

Hideto Takada, Suguru Honda, Masako Majima, Naoko Konda, Yasuhiro Katsumata, Michi Tsutsumino, Masayoshi Harigai, Hisashi Yamanaka
Department of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

Conflict of interest: None

[Background] Patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are at high risk of atherosclerosis and have high mortalities due to cardiovascular disease and stroke. Oxidative stress is involved in the progression of atherosclerosis and the percentage of human non-mercaptoalbumin (HNA%), the oxidized form of human serum albumin, has been drawing a strong attention as a biomarker of oxidative stress. Although previous studies have shown increased HNA% in the elderly and in patients with hemodialysis and liver diseases, HNA% in patients with rheumatic diseases has never been reported. [Object] To evaluate HNA% in patients with RA and SLE and identify associated factors. [Methods] We measured HNA% in healthy controls and patients with RA and SLE by using high-performance liquid chromatography. We used multivariate analysis to identify factors associated with HNA%. [Results] SLE patients had significantly higher HNA% than age-matched healthy controls, while RA patients did not. HNA% was significantly higher in SLE compared to RA. In SLE patients, HNA% was associated with dyslipidemia after adjusting for age and sex. [Conclusions] This study revealed the redox state of serum albumin in patients with RA and

SLE, and its association with dyslipidemia.

W68-5

Is alpha-defensin useful for differential diagnosis of arthritis exacerbation and suppurative arthritis in RA patients?

Tomohiro Ojima, Seigaku Hayashi

Department of Rheumatology, Fukui General Hospital

Conflict of interest: None

[Object] We investigated whether alpha-defensin, which is useful for the diagnosis of periprosthetic joint infection (PJI), can distinguish between arthritis exacerbation and suppurative arthritis in RA patients. [Methods] Thirty joints who developed acute and chronic arthritis in RA patients were included. Peripheral blood data, synovial fluid culture, presence/absence of crystals, white blood cell count, neutrophil fraction, alpha-defensin (lateral flow kit, Zimmer) of all cases were examined. Synovial biopsy and surgery were performed, and histopathological examination was added. The presence or absence of infection was performed according to the MSIS criteria (2013), and the diagnostic accuracy of alpha-defensin was evaluated. [Results] Despite multiple culture of synovial fluid, bacterial culture was negative except for one case of CNS positive. Alpha-defensin positivity was 67% (20/30) and infection was 40% (12/30) on MSIS criteria. The diagnostic accuracy of pyogenic arthritis of alpha-defensin was 60% sensitivity and 100% specificity. [Conclusions] The diagnosis of pyogenic arthritis occurring in patients with RA is problematic and there is no choice but to respond to case-by-case basis at present.

W68-6

Clinical significance of anti-DFS70 antibodies in connective tissue diseases and healthy individuals

Kenichi Uto¹, Nobuhide Hayashi², Yuji Nakamachi¹, Akio Morinobu³, Jun Saegusa^{1,3}

¹Department of Clinical Laboratory, Kobe University Hospital, ²Department of Medical Technology, Faculty of Health Sciences, Kobe Tokiwa University, ³Division of Rheumatology and Clinical Immunology, Department of Internal Medicine, Kobe University Graduate School of Medicine

Conflict of interest: None

[Object] The antinuclear antibody (ANA) test is clinically important for the diagnosis of connective tissue diseases (CTD). However, anti-DFS70 antibodies have been reported the higher prevalence in healthy individuals with high titers of indirect immunofluorescent test (FANA). In this study, we evaluated the clinical significance of anti-DFS70 antibodies in CTD patients and healthy individuals. [Methods] We studied 252 healthy individuals and 281 CTD patients. Anti-DFS70 antibodies and eight disease-specific antibodies were tested by ELISA. ANA screening and determination of dense fine speckled (DFS) pattern was tested by FANA. [Results] The positivity rate of anti-DFS70 antibodies was comparable in healthy individuals (16.7%) and CTD patients (16.7%). There was a significant correlation between anti-DFS70 ELISA titers and FANA titers only in healthy individuals. The prevalence of monospecific anti-DFS70 antibodies (anti-DFS70 ELISA positive/eight disease-specific antibodies negative) or DFS pattern was significantly higher in healthy individuals than CTD patients. [Conclusions] Anti-DFS70 antibodies are responsible for ANA positivity in healthy individuals. It is necessary to suspect the presence of anti-DFS70 antibodies in cases of DFS pattern in CTD screening by FANA.

W69-1

Predictors for complete clinical response of skin and muscle disease in patients with cancer-associated myositis (CAM)

Hiroko Kadota¹, Takahisa Gono^{1,2}, Yukie Yamaguchi³, Eri Watanabe², Yuka Okazaki¹, Yuichiro Shirai¹, Seiji Kobayashi¹, Mitsuhiro Takeno¹, Chihiro Terai², Masataka Kuwana¹

¹Department of Allergy and Rheumatology, Nippon Medical School, Tokyo, Japan, ²Department of Rheumatology, Saitama Medical Center, Jichi Medical University, ³Department of Environmental Immuno-Dermatolo-

gy, Yokohama City University Graduate School of Medicine, Yokohama, Japan

Conflict of interest: None

[Object] To identify significant predictors for complete clinical response (CCR) of skin and muscle diseases in CAM patients [Methods] 41 CAM patients whose malignancy was concomitant with myositis within the period of 3 months were enrolled retrospectively in this study. Demographic and clinical data were collected by using multicenter cohort database. [Results] The mean age at disease onset was 66 years old, female; 19 (46%), PM/DM/CADM; 4/29/8, and anti-TIF1- γ positive; 17 (47%). Twenty-five (61%) of 41 patients achieved CCR during the median follow up period of 17 months. Univariate analysis identified significant ($P < 0.10$) factors as follows: absence of dysphagia and skin rashes, lower levels of serum creatine kinase, combination of immunosuppressants (IAs), no administration of intravenous immunoglobulin (IVIG), malignancy at stage I/II, surgical resection and radiation therapy for malignancy. In multivariate analysis, combination of IAs ($p = 0.01$, OR 29.0, 95%CI 2.1-408.7), no administration of IVIG ($p = 0.03$, OR 26.6, 95%CI 1.3-526.1), and surgical resection ($p = 0.02$, OR 17.8, 95%CI 1.6-197.3) were identified. [Conclusions] IAs with the combination of corticosteroid as well as surgical resection of tumors is associated with CCR of skin and muscle diseases in CAM patients.

W69-2

Clinical characteristics of cancer-associated myositis in patients with synchronous multiple primary malignancies

Mita Sakuraba¹, Hiroko Kadota¹, Takahisa Gono^{1,2}, Yukie Yamaguchi³, Eri Watanabe², Yuka Okazaki¹, Shinji Watanabe¹, Yuichiro Shirai¹, Seiji Kobayashi¹, Mitsuhiro Takeno¹, Chihiro Terai², Masataka Kuwana¹

¹Department of Allergy and Rheumatology, Nippon Medical School, Tokyo, Japan, ²Department of Rheumatology, Saitama Medical Center, Jichi Medical University, Saitama, Japan, ³Department of Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine, Yokohama, Japan

Conflict of interest: None

[Object] To elucidate the clinical characteristics of cancer-associated myositis (CAM) in patients with synchronous multiple primary malignancies (MPM). [Methods] We retrospectively investigated the clinical data of 75 CAM patients. We compared clinical characteristics between CAM patients with synchronous MPM (individual malignancies are concomitant within 12 months) and without. [Results] Synchronous MPM were revealed in 5 (7%) of 75 patients with CAM. Out of these 5 patients, the mean age of diagnosis of myositis was 65 years old. Three patients were females. Two patients developed MPM within 6 months after diagnosis of myositis. Three patients presented with muscle weakness on extremities and dysphagia. All of the 5 patients had skin rash associated with dermatomyositis. Anti-TIF1- γ and anti-SRP antibodies were detected in 2 and 1, respectively. Although there were no statistically significant differences of clinical features between CAM patients with synchronous MPM and without, the mortality rate tended to be poorer in CAM patients with synchronous MPM than the other (40% versus 29%). [Conclusions] Clinicians should pay attention to development of synchronous MPM within 6 months after diagnosis of myositis, particularly DM, although this complication develops less frequently.

W69-3

Clinical features in patients with anti-TIF1-gamma antibody-positive dermatomyositis

Yumi Yoshida¹, Makiko Hayashi¹, Suzuna Sugi², Takuma Koga¹, Shinjiro Kaieda¹, Tomoaki Hoshino¹, Hiroaki Ida¹

¹Division of Respiratory, Neurology, and Rheumatology, Kurume University School of Medicine, Kurume, Japan, ²Division of Rheumatoid Arthritis and Rheumatology, Kurume University Medical Center, Kurume, Japan

Conflict of interest: None

[Purpose] Measurement of myositis-specific autoantibodies including

anti-ARS ab, anti-MDA-5 ab and anti-TIF1- γ antibody is useful to predict the prognosis and determine therapeutic strategy. We have analyzed the clinical features in anti-TIF1- γ antibody-positive dermatomyositis (DM) compared to anti-ARS or MDA-5 ab-positive DM. [Method] We analyzed nineteen patients with DM including six, four and nine in anti TIF1- γ ab, anti-ARS ab, and anti MDA-5 ab-positive patients, respectively. Clinical features including skin eruption and organ complication were analyzed. [Result] Truncal broad erythema and finger erythema were observed in five and four anti-TIF1- γ ab-positive DM, respectively. These skin eruptions were not observed in anti-ARS and anti-MDA-5 ab-positive DM. Complication of interstitial lung disease (ILD) was observed in all anti-ARS ab and anti-MDA-5 ab-positive DM patients, while no anti-TIF1- γ -positive DM developed ILD. [Conclusion] Anti TIF1- γ ab-positive DM patients developed specific skin manifestations compared to anti-ARS/MDA-5 ab positive DM. Recognizing the clinical features in anti-TIF1- γ ab-positive DM is useful to predict their paraneoplastic pathophysiology.

W69-4

Clinical characteristics of polymyositis and dermatomyositis associated with pneumomediastinum: a 26-year retrospective study

Kyoko Motomura, Hiroyuki Yamashita, Shinji Izuka, Toshiaki Kobayashi, Sotaro Nakajima, Nanami Mino, Shunta Kaneko, Yuko Takahashi, Hiroshi Kaneko

National Center for Global Health and Medicine

Conflict of interest: None

[Object] This study investigated predictors of pneumomediastinum and the prognosis in patients with polymyositis (PM) or dermatomyositis (DM). [Methods] A retrospective study of PM and DM patients admitted to our hospital between January 1992 and October 2018. [Results] Of 141 patients, 14 (six men, eight women) had pneumomediastinum. Of these, five had PM and nine had DM [four had clinically amyopathic DM (CADM)]. The median interval between the diagnosis of myositis and the occurrence of pneumomediastinum was 70.5 (25-3,009) days. During follow-up, eight patients had pneumoderma and three had pneumothorax. Nine patients improved with conservative treatment. On univariate analysis, interstitial lung disease ($p < 0.001$), CADM ($p = 0.006$), steroid pulse ($p = 0.002$), high C4 ($p = 0.04$), low CK ($p = 0.04$), low serum albumin ($p = 0.01$), and low peripheral blood lymphocytes (%) ($p = 0.02$) were associated with increased pneumomediastinum. Survival was significantly ($p = 0.01$) lower in patients with pneumomediastinum than in those without. [Conclusions] This study is the first to associate a high C4 level, low serum albumin, and low peripheral blood lymphocytes with pneumomediastinum.

W69-5

Clinical characteristics of patients with clinically amyopathic dermatomyositis (CADM) positive for anti-TIF-1r antibody

Miwa Kanaoka, Yukie Yamaguchi, Asami Akita, Yasushi Ootake, Nobuaki Ikeda, Michiko Aihara

Environmental Immuno-dermatology, Yokohama City University Graduate School of Medicine

Conflict of interest: None

[Object] To analyze the clinical features of patients with anti-TIF-1r antibody (Ab)-positive dermatomyositis (DM), especially in cases of CADM. [Methods] CADM cases were extracted from anti-TIF-1r Ab-positive DM and their clinical features were evaluated. [Results] Within 31 cases of DM patients positive for anti-TIF1 γ Ab in our department, there were 7 CADM cases (22.6%). In these cases, Gottron's papule, heliotrope rash, and periungual erythema tended to be highly observed compared to that in patients with non-CADM patients with this Ab. The prevalence of malignancy within 2 years before and after the onset of DM was 58.3% (14/24) in anti-TIF-1r Ab-positive non-CADM patients, while that was 14.3% (1/7) in anti-TIF-1r Ab-positive CADM patients, which was significantly lower ($P = 0.04$). Meanwhile, interstitial lung disease was observed in 4 out of 7 patients with CADM (57.1%), which was significantly higher than that in anti-TIF-1r Ab-positive non-CADM patients (3/24, 12.5%, $P = 0.01$). Finally, serum anti-TIF-1r antibody lev-

el was significantly lower in CADM patients than that in non-CADM cases (64.0 ± 47.0 , 104.1 ± 36.8 respectively, $P = 0.03$). [Conclusions] Anti-TIF-1r Ab-positive CADM cases may have different clinical features from the normally recognized antibody profile.

W69-6

Clinical characteristics of anti-Ro 52 antibody in dermatomyositis/polymyositis

Mariko Momohara, Yoshinao Muro

Department of Dermatology, Nagoya University Graduate School of Medicine

Conflict of interest: None

[Object] Anti-Ro 52 antibody is one of the most common antibodies in inflammatory myositis and known as associating with interstitial lung disease (ILD) and coexisting with anti-Jo1. We tried to clarify the clinical significance of anti-Ro52 in different inflammatory myositis specific autoantibodies (MSA)-positive groups. [Methods] Of all 229 dermatomyositis (DM) and polymyositis (PM) patients, 167 cases (DM 152, PM 10, juvenile DM 5) fulfilled the criterion of Bohan and Peter, and 62 clinical amyopathic DM patients fulfilled the criterion of Sontheimer. Anti-Ro52 was detected by ELISA. [Results] 46 patients were anti-Ro 52 positive (20 %). ILD was frequently complicated with anti-Ro 52 positive patients (35 of 46: 78 %) ($P < 0.0001$), and anti-Ro 52 was highly positive in anti-aminoacyl tRNA synthetase (ARS) antibodies positive group (19 of 32) ($P < 0.0001$). But ILD frequencies of anti-Ro 52 -positive and -negative groups were not statistically different in each coexisting MSA-positive patients. Anti-Ro 52 positive rates were similar in anti-Jo1 (61%) and other anti-ARSs (52%) ($P = 0.7$). [Conclusions] Although anti-Ro 52 was highly positive with anti-ARS antibodies, it was simultaneously present with other MSAs. Anti-Ro 52 did not contribute as the risk of ILD in each MSA-positive group.

W70-1

Analysis of chronological changes in J-HAQ and factors associated with achieving J-HAQ remission 5 years after disease onset in patients with rheumatoid arthritis using the IORRA cohort

Mai Abe¹, Eiichi Tanaka¹, Eisuke Inoue^{1,2}, Mika Kawano¹, Eri Sugano¹, Naohiro Sugitani^{1,3}, Kumiko Saka¹, Yoko Higuchi¹, Moeko Ochiai¹, Rei Yamaguchi¹, Naoki Sugimoto¹, Katsunori Ikari¹, Ayako Nakajima^{1,3}, Atsuo Taniguchi¹, Hisashi Yamanaka¹

¹Institute of Rheumatology, Tokyo Women's Medical University Hospital, Tokyo, Japan, ²Division of Medical Informatics, St. Marianna University School of Medicine, Kanagawa, Japan, ³Center for Rheumatic Disease, Mie University Hospital, Mie, Japan

Conflict of interest: None

[Object] To evaluate chronological changes in J-HAQ score and J-HAQ remission rates 5 years after rheumatoid arthritis (RA) onset using the IORRA cohort. [Methods] RA patients who first visited at our hospital in the year of RA onset were divided into two groups, 1) RA onset between 2000 and 2005 (former onset group: $n = 357$) and 2) RA onset between 2006 to 2010 (recent onset group: $n = 291$). J-HAQ and J-HAQ remission rate at baseline and 5 years after onset in each group were investigated, and factors associated with J-HAQ remission after 5 years were assessed. [Results] Average J-HAQ/J-HAQ remission rate at baseline and 5 years after onset were 0.659/54.6% and 0.430/71.4%, respectively, in the former onset group. J-HAQ/J-HAQ remission rate at baseline and 5 years were 0.705/52.2% and 0.316/78.4%, respectively, in the recent onset group. Significant factors associated with achieving J-HAQ remission after 5 years were patients in the recent onset group, male, younger, lower J-HAQ at baseline, and non-steroid user. [Conclusions] J-HAQ score improved with improvement of RA treatment strategy in recent years. In order to achieve J-HAQ remission after 5 years RA onset, treatment from early stage to prevent deterioration of J-HAQ and treatment without steroid seems to be important.

W70-2

Transitions of clinical characteristics, incidence and prognosis of 447 cases of AA amyloidosis complicating RA in Dohgo Spa Hospital

Yasuaki Okuda, Kenichiro Matoba, Kazuo Jouyama, Akihiro Yamada, Yosuke Murata, Naoya Sawada, Ayuko Sogabe, Atsushi Kondo, Makoto Onishi, Kiyoshi Takasugi
Internal Medicine, Center for Rheumatic Diseases, Dohgo Spa Hospital, Matsuyama, Ehime, Japan

Conflict of interest: None

[Objective] To investigate transitions of the clinical features, incidence and the prognosis of AA amyloidosis complicating RA (AA) in our hospital. [Methods] We divided the 447 AA patients into 4-decade interval group (1980,1990,2000,2010) by the year of the AA diagnosis and compared the clinical features, incidence and prognosis of each group. [Results] 1. RA onset age of AA was not different significantly in each decade group. 2. Interval from onset of RA to AA diagnosis was prolonged in recent onset groups. 3. Incidence of AA was significantly decreased in recent onset groups. 4. CRP values were decreased significantly by the lapse of time. 5. Prognosis (5-year survival rate) improved significantly in recent decade group. [Conclusions] Decreased incidence and improved prognosis of AA were demonstrated due to progress of treatment of RA in our epidemiologic study.

W70-3

Epidemiology of rheumatoid arthritis in Japan

Masayo Kojima

Department of Medical Education, Nagoya City University Graduate School of Medical Sciences

Conflict of interest: None

[Object] To identify the epidemiological characteristics of rheumatoid arthritis (RA) patients in Japan by using the data of the National Life Basic Survey. [Methods] Of the 224,208 households including 565,133 subjects, total of 272,558 men and 295,196 women excluding 672 age-missing people were selected. "RA patients" were defined as those who were attending hospitals or clinics for RA, based on the self-reported questionnaire. [Results] The number of RA patients over 16 year-old in Japan was estimated as 77.7 thousand (95% confidence interval 72.5-83.4). RA prevalence increased with age, the highest in 80-84 years, and decreased from the late 80s. Late elderly people over 75 year-old accounted for 36% of all patients with RA. The percentage of those who had any mental stress with daily life was higher in RA patients than in non-RA. [Conclusions] The present results were almost consistent with recent reports from Europe and the United States. The necessity to consider RA medical care in the framework of regional inclusive care system in the future.

W70-4

The risk of hospitalized infection in patients with systemic lupus erythematosus with hydroxychloroquine

Ryoko Sakai¹, Suguru Honda¹, Sho Suzuki^{1,2}, Masayoshi Harigai¹, Hisashi Yamanaka¹

¹Department of Rheumatology, Tokyo Women's Medical University, ²Tokyo Women's Medical University, Department of Public Health

Conflict of interest: Yes

[Object] To compare risk of hospitalized infection (HI) between users and non-users of hydroxychloroquine (HCQ) in systemic lupus erythematosus (SLE). [Methods] Using claims data provided by Medical Data Vision Co., Ltd (Tokyo, Japan), we defined individuals as SLE cases if they had at least one SLE diagnostic code and one prescription of predefined drugs for SLE and were 16 years old or over between September 2015 and July 2017 ($n = 17,483$). SLE cases who had at least one prescription of HCQ were defined as HCQ group ($n = 1,431$), and others were defined as non-HCQ group ($n = 16,052$). Among these SLE cases, propensity-score-matched cases were observed for 1 year in this study ($n = 1,331$ in each group). We compared the proportion of cases with HI between the two groups using chi square test, and calculated the odds ratio (OR) of the

HCQ group for HI after adjusting for patients' baseline data. [Results] The median age and percentage of female patients were 42 years old and 88% in the both groups. The proportions of cases with HI were similar (HCQ group, 4.8%; non-HCQ group, 5.4%; $p=0.481$). Adjusted OR of the HCQ group was 0.9 [0.6-1.3], which was not statistically significant. [Conclusions] This study revealed that use of HCQ did not significantly change the risk of HI in patients with SLE.

W70-5

Analysis for clinical characteristics and social productivity of patients with malignant rheumatoid arthritis, based on the clinical personal record database

Yoshiyuki Abe¹, Hiroaki Dobashi², Tamihiko Kawakami³, Taichi Hayashi⁴, Shinya Kaname⁵, Masayoshi Harigai⁶, Naoto Tamura¹

¹Department of Internal Medicine and Rheumatology, Juntendo University, Tokyo, Japan, ²Division of Hematology, Rheumatology, and Respiratory Medicine, Department of Internal Medicine, Kagawa University, Kagawa, Japan, ³Division of Dermatology, Tohoku Medical and Pharmaceutical University, Miyagi, Japan, ⁴Department of Internal Medicine, University of Tsukuba, Ibaraki, Japan, ⁵First Department of Internal Medicine, Kyorin University School of Medicine, Tokyo, Japan, ⁶Department of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

Conflict of interest: None

Object: To evaluate the clinical data and social activity of patients with malignant rheumatoid arthritis (MRA) in Japan, including the changes over time. **Methods:** Using the clinical personal record database stored in the Ministry of Health, Labor and Welfare from 2003 to 2014, we evaluated retrospectively and cross-sectionally about the patient background, treatment, and social activity. **Results:** The average age gradually increased from 62.0 years old in 2003 to 65.1 years old in 2014, and female rates were about 70 to 73%. The fulfilling rate of each component in MRA classification criteria almost did not change over time. As for the treatment, use of DMARDs and immunosuppressants were increased. In contrast, proportion of patients with surgery, doses of corticosteroid, use of NSAIDs, and use of plasma exchange were decreased. In social activities, "recuperation" and "hospitalization" were decreased, while "household worker" "worker" were increased. **Conclusion:** Evaluation of the time course of patients with MRA in Japan revealed that the increase in use of DMARDs and immunosuppressants. As for social activities, the results suggest that social productivity of MRA patients improved over time.

W70-6

The habits of smoking, drinking alcohol and caffeinated coffee consumption in rheumatoid arthritis (Comparison with healthy control.) - TOMORROW study -

Hitoshi Yoshimura¹, Kentaro Inui², Tatsuya Koike^{4,5}, Yuko Sugioka⁵, Tadashi Okano², Kenji Mamoto², Masahiro Tada³, Hiroaki Nakamura²

¹Department of Orthopaedic Surgery, Osaka Saiseikai Nakatsu Hospital, ²Department of Orthopaedic Surgery, Osaka City University Graduate School of Medicine, ³Department of Orthopaedic Surgery, Osaka City General Hospital, Osaka, Japan, ⁴Department of Orthopaedic Surgery, Search Institute for Bone and Arthritis Disease, Wakayama, Japan, ⁵Department of Orthopaedic Surgery, Center for Senile Degenerative Disorders, Osaka City University Medical School, Osaka, Japan

Conflict of interest: None

Purpose: The association between smoking and rheumatoid arthritis (RA) patients is well known, however there is few reports on lifestyle habits. In this study we analyze the consumption of smoking, coffee and alcohol in RA patients in relation to healthy control. **Methods:** We analyzed baseline data from the TOMORROW study (UMIN000003876), which is a 10-years prospective cohort for age and sex matched RA (n=208) and volunteers (Vo) (n=205). Data on smoking history and alcohol (Alc), caffeinated coffee, decaffeinated coffee and Japanese tea intake were self-reported on the questionnaires. Alc intake was categorized into 3 groups by calculating the amount per day using Alc unit (1 unit is pure Alc 20 mg). We categorized frequency of Alc intake per week into 3 groups, number of cups of coffee and Japanese tea intake per week into 4

groups each. We performed multivariate analysis. **Results:** We analyzed 191 Vo and 208 RA with complete data about luxury items. In multivariate analysis, smoking history (OR 5.03, $p=0.04$), 2-6 unit of Alc intake per day (OR 0.20, $p=0.04$) and 1-7 cup of caffeinated coffee intake per week (OR 0.26, $p=0.04$) were significantly different between RA and Vo. **Conclusions:** In RA patients smoking seems to be high and moderate intake of Alc and caffeine seems to be low.

W70-7

Longitudinal study of the effects of biological DMARDs on work productivity in rheumatoid arthritis patients in daily practice using the Institute of Rheumatology Rheumatoid Arthritis (IORRA) Cohort

Eiichi Tanaka¹, Eisuke Inoue^{1,2}, Mai Abe¹, Mika Kawano¹, Eri Sugano¹, Naohiro Sugitani^{1,3}, Kumiko Saka¹, Yoko Higuchi¹, Moeko Ochiai¹, Rei Yamaguchi¹, Naoki Sugimoto¹, Katsunori Ikari¹, Ayako Nakajima^{1,3}, Atsuo Taniguchi¹, Hisashi Yamanaka¹

¹Institute of Rheumatology, Tokyo Women's Medical University Hospital, Tokyo, Japan, ²Division of Medical Informatics, St. Marianna University School of Medicine, Kanagawa, Japan, ³Center for Rheumatic Diseases, Mie University Hospital, Mie, Japan

Conflict of interest: None

[Object] To conduct a longitudinal study of the effects of biologics on work productivity in Japanese RA patients in daily practice. [Methods] RA patients who participated in the IORRA and initiated biologics between 2012 and 2016 as well as who were paid workers were selected for the Bio group. For a control group, matching method by age, sex, and DAS28 score at baseline was used from RA patients who had never used biologics before. Changes from baseline at mean 15 months in the scores of absenteeism (AB), and presenteeism (PR) in both groups were calculated using the WPAI. The effects of biologics on these scores were analyzed. [Results] Among RA patients in the IORRA, 157 patients were selected each for the Bio and the control group. The changes in AB/PR scores were from 1.4%/20.1% at baseline to 2.0%/12.3% at mean 15 months in the Bio group and from 2.1%/20.1% at baseline to 2.7%/20.1% at mean 15 months in the control group. The introduction of biologics resulted in improvement in PR ($p=0.003$) score. [Conclusions] The introduction of biologics improved the work productivity, especially presenteeism, in RA patients based on data from an observational cohort representing daily practice in Japan.

W71-1

Incidence of malignant lymphoma and other malignancies in patients with rheumatoid arthritis

Atsushi Hashimoto¹, Toshihiro Matsui¹, Shigetoh Tohma²

¹Department of Rheumatology, National Hospital Organization Sagami-hara National Hospital, ²National Hospital Organization Tokyo National Hospital

Conflict of interest: Yes

[Object] Patients with rheumatoid arthritis (RA) have higher incidence of malignant lymphoma (ML) than the general population. We assessed the incidence of malignancies including ML in RA patients over time. [Methods] Using the data from a nationwide multicenter Japanese RA cohort database 'NinJa' from 2003 to 2017, we estimated standardized incidence ratio (SIR) of malignancies. Incidence of malignancies in the general population was obtained from Cancer Registry and Statistics (Cancer Information Service, National Cancer Center, Japan.). [Results] In 2017, 177 patients developed malignancies (including 27 ML) in a total of 15185 patients. Lung cancer (n=29, 16.4%) was most frequent followed by ML (15.3%), colon (n=26), breast (n=18) and gastric cancer (n=16, 9.0%). SIR of entire malignancies was 0.98 (95% confidence interval (CI) 0.84-1.13), which was approximately 1 as before. SIR of ML was 4.44 (95% CI 2.77-6.12), which was significantly higher than the general population as before. SIR of ML rose to 5 to 6 in 2014-15 and thereafter declined as in the past. SIR of colon cancer was 1.31 (95% CI 0.81-1.82). [Conclusions] RA patients have incidence of ML about 4 times as high as the general population constantly during the past 15 years.

W71-2

Association between activity of arthritis at onset of disease and titers of autoantibodies for elderly-onset rheumatoid arthritis

Kenji Yamazaki, Ryuhei Ishihara, Toshiaki Miyamoto
Seirei Hamamatsu General Hospital

Conflict of interest: None

[Object] We elucidate the association between activity of arthritis at onset of disease and titers of their autoantibodies in Elderly-onset rheumatoid arthritis (EORA) compared with young-onset rheumatoid arthritis (YORA). [Methods] We enrolled 315 patients who were affected arthritis first visited in our institution from September 2013 until August 2018. We set semi-quantitative results of musculoskeletal ultrasounds (Gray Scale: GS, Power Doppler: PD) as surrogate marker of activity of arthritis at onset of disease based on the evidence that results of ultrasounds is an independent predictor of structural damage in early RA. [Results] In YORA group, there is an association between RF titer and GS/PD score (GS; $\rho=0.17$, $p=0.029$ /PD; $\rho=0.22$, $p<0.01$). On the other hand, in EORA group, There is no association between RF titer and GS/PD score statistically (GS; $\rho=0.14$, $p=0.10$ /PD; $\rho=0.11$, $p=0.18$). When we analyzed sensitively by changing cut-off age from 60 years to 65 years and 70 years, the correlation coefficients tended to decline. With respect to ACPA, GS/PD score are associated with ACPA titer. [Conclusions] EORA has weaker association between activity of arthritis at onset of disease and RF titer than YORA. In EORA, RF titer may be useless for prognostic factor.

W71-3

Analysis of the oral microbiome in general population: focused on rheumatoid arthritis and anti-CCP Ab positivity

Mami Tamai, Shin-ya Kawashiri, Mako Nagayoshi, Atsushi Kawakami
Nagasaki University, Nagasaki, Japan

Conflict of interest: None

Objectives: To evaluate the oral microbiome in the subjects with rheumatoid arthritis and anti-CCP Ab (ACPA) positive from the general population. Methods: Salivary samples were obtained from 1219 subjects in general population, and 16S rRNA OTU analysis were carried out. There were 26 subjects with ACPA-positive, and 32 patients with RA (out of 10 ACPA-positive), then, age and gender adjusted subjects with ACPA-negative non-RA were selected ($n=52$). PERMANOVA analysis of the weighted UniFrac distance developed (p -value <0.05). microbial community composition Results: Median age 70y.o., %Female 63%, 11 current smokers, 27 subjects with dry mouth symptoms, 13 anti-HTLV-1 Ab positive subjects. Multivariate analysis showed the association of microbial community composition between RA and non-RA ($p=0.04$), especially ACPA positive RA. Cardiobacterium increased in RA group. Conclusions: Our analysis suggest that there was difference of the oral microbiome between patients with RA and non-RA subjects, especially remarkable for anti-CCP positive RA.

W71-4

Left Ventricular Diastolic Dysfunction in Japanese Rheumatoid Arthritis

Manami Hirata^{1,2}, Kei Hirose¹, Yuriko Yamamura¹, Noriya Momoki², Akiko Ueno¹, Masahiro Yamamura¹

¹Department of Rheumatology, Okayama Saiseikai General Hospital, ²Department of Nephrology, Okayama Saiseikai General Hospital

Conflict of interest: None

[Background] It has been reported from the other country that patients with rheumatoid arthritis (RA) are more likely to have left ventricular diastolic dysfunction (LVDD). We investigated LVDD in Japanese RA patients, without a history of HF. [Methods] We analyzed RA patients who underwent echocardiography examinations from April 2016 to March 2018, in a retrospective way. We evaluated LVDD by 2015 ASE/EACVI echocardiography guideline. [Ejection fraction (EF) exceeded 50%, a ratio of early diastolic transmitral velocity to early diastolic mitral annular velocity (E/e'ratio) >14 and $e'<7$.] [Result] The study included 39 RA subjects (29 female). Mean age was 76.8 ± 10.3 years old. RF

positive in 30, ACPA positive in 24. Mean disease duration was 6 years (Median 1-58years), tender $1.2 \pm 2.0/28$ joints, swelling $1.0 \pm 1.8/28$ joints. Hypertension 26, diabetes mellitus 10, hyperlipidemia 9, smoking history 11. No HF was included. Assessment of E/A ratio with pulse doppler, the former evaluation, LVDD 34 subjects (94%) included. Compared with ASE/EACVI 2015 evaluation, LVDD 14 subjects (36%) included. [Conclusion] LVDD is known as one of the predictor of heart failure with preserved EF. We reported that the prevalence of LVDD in Japanese RA is approximately the same frequency with previous reports.

W71-5

The causes of death in deceased patients with RA by NinJa 2017 cohort

Atsushi Kaneko¹, Toshihiro Matsui², Shotaro Mori¹, Yosuke Hattori¹, Tomotaro Sato¹, Masao Katayama³, Shigeto Tohma⁴

¹Department of Orthopaedic Surgery and Rheumatism, Nagoya Medical Center, ²Department of Rheumatology, Sagami National Hospital, ³Department of Collagen Disease and Rheumatology, Nagoya Medical Center, ⁴Department of Rheumatology, Tokyo Medical Center

Conflict of interest: None

[Objectives] The purpose of the present study is to evaluate the age at death and the cause of death in patients with rheumatoid arthritis (RA) in NinJa2017 [Methods] 135 Japanese deceased patients with RA, who were registered in the large cohort database (NinJa: National Database of Rheumatic Diseases by iR-net in Japan). We investigated the age at death, the causes of death of all patients. [Results] The mean age at death was 77.6 years old. The major cause of death in deceased patients was infection in 39 patients involving in pneumonia in 30 patients. Next was malignancy in 31 patients, respiratory dysfunction involving intestinal pneumonia in 15 patients, cardiovascular disease in 18 patients, unknown sudden death in 5 patients. [Conclusion] The life expectancy of Japanese patients with RA was getting better. But the average of RA onset is recently older, the duration from RA onset to death is shorter. The major causes of death were infection, especially pneumonia.

W71-6

Background of patients with rheumatoid arthritis undergoing joint arthroplasties -Analysis using the National Database of Rheumatic Diseases in Japan (NinJa)

Tetsuro Yasui¹, Atsuhisa Yamada¹, Shigeru Nakamura¹, Mitsuyasu Iwasawa², Sakae Tanaka³, Toshihiro Matsui⁴, Shigeto Tohma⁵

¹Department of Orthopaedic Surgery, Teikyo University Mizonokuchi Hospital, Kanagawa, Japan, ²Department of Orthopaedic Surgery, NHO Sagami National Hospital, Kanagawa, Japan, ³Department of Orthopaedic Surgery, Faculty of Medicine, The University of Tokyo, Tokyo, Japan, ⁴Department of Rheumatology, NHO Sagami National Hospital, Kanagawa, Japan, ⁵NHO Tokyo National Hospital, Tokyo, Japan

Conflict of interest: None

Object Number of arthroplasties for rheumatoid arthritis (RA) has been reducing. The purpose of this study was to clarify the difference in patient background and its secular change at each surgical site. Methods The background data of patients who underwent arthroplasty of knee (TKA), hip (THA), and elbow (TEA) from 2003 to 2017 were extracted from NinJa. Results 1,816 TKAs, 727 THAs, and 383 TEAs were performed. The average value of mHAQ was 0.86, 1.11, and 1.13 in TKA, THA, and TEA group, respectively. There was a significant declining trend in each group. The difference among groups tended to shrink recently. The average value of DAS28CRP was 3.4, 3.2, and 3.2 in TKA, THA, and TEA group, respectively. There was a significant declining trend in each group. The average value was relatively high in TEA group recently. The average duration of the disease was 16.2, 18.0, and 22.5 years in TKA, THA, and TEA group, respectively. The difference between THA group and TKA group had shrunk recently. Conclusions Patients in TKA group and THA group generally became mild as RA recently, and the numerical indexes in both groups tended to be closer. It is speculated that the elements of osteoarthritis (OA) may be growing in RA patients. TEA group had different trend probably because OA seldomly affects.

W71-7

Discontinuation of concomitant methotrexate in patients with rheumatoid arthritis treated with tocilizumab: a prospective interventional study (T-ReX study)

Shuji Asai¹, Toshihisa Kojima¹, Masatoshi Hayashi², Masahiro Hanabayashi³, Yasuhide Kanayama⁴, Toki Takemoto⁵, Yuichiro Yabe⁶, Tomone Shioura⁷, Hisato Ishikawa⁸, Yutaka Yoshioka⁹, Takefumi Kato¹⁰, Yuji Hirano¹¹, Takayoshi Fujibayashi¹², Yosuke Hattori¹³, Tomonori Kobayakawa¹⁴, Nobunori Takahashi¹, Takuya Matsumoto¹, Nobuyuki Asai¹, Yasumori Sobue¹, Tsuyoshi Nishiume¹, Mochihito Suzuki¹, Naoki Ishiguro¹

¹Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan, ²Department of Rheumatology, Nagano Red Cross Hospital, Nagano, Japan, ³Department of Rheumatology, Ichinomiya Municipal Hospital, Ichinomiya, Japan, ⁴Department of Rheumatology, Toyota Kosei Hospital, Toyota, Japan, ⁵Department of Orthopedic Surgery, Anjo Kosei Hospital, Anjo, Japan, ⁶Department of Rheumatology, Tokyo Shinjuku Medical Centre, Tokyo, Japan, ⁷Department of Rheumatology, Shizuoka Kosei Hospital, Shizuoka, Japan, ⁸Department of Rheumatology, Japanese Red Cross Nagoya Daiichi Hospital, Nagoya, Japan, ⁹Department of Rheumatology, Handa Municipal Hospital, Handa, Japan, ¹⁰Kato Orthopaedic Clinic, ¹¹Department of Rheumatology, Toyohashi Municipal Hospital, Toyohashi, Japan, ¹²Department of Orthopedic Surgery, Konan Kosei Hospital, Konan, Japan, ¹³Department of Orthopedic Surgery, Nagoya Medical Center, Nagoya, Japan, ¹⁴Department of Rheumatology, Chutoen General Medical Centre, Kakegawa, Japan

Conflict of interest: Yes

[Object] To evaluate the efficacy of discontinuation of concomitant methotrexate in patients with rheumatoid arthritis (RA) treated with tocilizumab. [Methods] T-ReX study, a multicenter, open label, uncontrolled, prospective study, included the RA patients who maintained low disease activity (CDAI \leq 10) for \geq 12 weeks with combination therapy with tocilizumab plus methotrexate. Methotrexate was stopped following biweekly dosing for 12 weeks. The primary endpoint was the proportion of patients maintaining low disease activity at week 36 (24 weeks after stopping methotrexate). Secondary endpoints included physical function outcomes, quality of life, and gastrointestinal symptoms. [Results] A total of 49 patients completed 36 weeks. The proportion of patients maintaining low disease activity at week 36 was 75.5% with a lower 95% confidence limit exceeding the assumed threshold response rate of 60%. There were no significant changes in HAQ-DI and EQ-5D score from week 0 to week 36. The prevalence of GERD defined as FSSG score \geq 8 was significantly decreased from week 0 to week 12 (27.1% to 18.4%; $P = 0.025$). [Conclusions] Discontinuation of concomitant methotrexate is feasible in the RA patients with stable low disease activity on tocilizumab.

W72-1

Investigation of immune cell subsets involved in Behcet's syndrome by comprehensive gene expression analysis

Mai Okubo¹, Shuji Sumitomo¹, Mineto Ota^{1,2}, Yusuke Takeshima^{1,2}, Haruyuki Yanaoka¹, Harumi Shirai¹, Satomi Kobayashi¹, Yusuke Sugimori¹, Junko Maeda¹, Hiroaki Hatano¹, Yasuo Nagafuchi¹, Yukiko Iwasaki¹, Hirofumi Shoda¹, Tomohisa Okamura^{1,2}, Kazuhiko Yamamoto³, Keishi Fujio¹

¹Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Japan, ²Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, Japan, ³RIKEN Center for Integrative Medical Sciences, Japan

Conflict of interest: Yes

[Object] The functions of immune cell subsets that participate in pathologic conditions of Behcet's syndrome (BS) are unknown in detail. We aimed to elucidate immune cell subsets involved in BS by flow cytometry (FCM) analysis and exhaustive gene expression analysis by RNA sequence (RNA-seq). [Methods] FCM analysis and cell sorting of 19 PBMC subsets were performed in BS patients ($n=23$, including 11 HLA-B51 positive patients) and healthy controls (HC; $n=28$). Neutrophils were obtained by magnetic cell separation. Comprehensive gene expression analysis with RNA-seq for a total of 20 subsets was performed. The rela-

tionship between gene expression and clinical parameter was analyzed. [Results] Th17 cells were significantly increased in BS compared to HC. From the network analysis based on the gene expression, gene modules that characterized BS were found in antigen presenting cell (APC) subsets such as dendritic cells, rather than Th17 cells. A module of genes correlated with HLA-B51 positivity was found in CD8 positive T cells. [Conclusions] The results of current analysis indicated the importance of Th17 cells and APCs in BS pathology. We aim to elucidate their functions, interactions and their relationship with genetic factors through further analysis.

W72-2

Mitochondrial DNA in membrane vesicles plays critical roles in pathogenesis for Behçet's disease

Hachirou Konaka^{1,2}, Jeong Hoon Park^{1,2}, Yasuhiro Kato^{1,3}, Hyota Takamatsu^{1,2}, Atsushi Kumanogoh^{1,2}

¹Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University Japan, ²World Premier International Research Center, Immunology Frontier Research Center, ³NTT West Osaka Hospital

Conflict of interest: None

Mitochondrial DNA (mtDNA) is known to induce inflammation via activating inflammasome and DNA sensors, leading to exacerbate various diseases. However, pathological significance of mtDNA in autoimmune diseases (ADs) has not been elucidated. In order to clarify the involvement of mtDNA in BD pathogenesis, we measured the amount of mtDNA in serum of ADs by quantitative PCR. We found that serum mtDNA level is high in BD compared to other ADs. We also found that mtDNA was detected in extracellular membrane vesicles (EMVs) purified by ultracentrifugation. Since EMVs are known to be important for the cell-cell communication, we stimulated THP1, monocytic cells, with BD-derived EMVs. We found that BD-derived EMVs could induce IL-1 β production, which was diminished in NLRP3-deficient THP1 cells. Then, we assessed the releasing mechanism of mtDNA in EMVs. The release of mtDNA from BD monocytes increased by ATP stimulation, which diminished by treatment with caspase1 inhibitor, suggesting that inflammasome activation causes the increased release of mtDNA in EMVs in BD. Collectively, we revealed a novel etiology of BD, namely, inflammasome activation increases the release of mtDNA in EMVs, which causes additional inflammation via activating NLRP3-inflammasome.

W72-3

Cluster analysis of Behçet's disease: 2218 cases from a Japanese clinical database of patients receiving financial aid

Mitsuhiro Takeno¹, Michiko Kurosawa², Yutaro Soejima³, Yohei Kirino³

¹Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, ²Department of Epidemiology and Environmental Health, Juntendo University, ³Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine

Conflict of interest: Yes

[Object] To determine subgroups of Behçet's disease (BD) by clinical manifestations. [Methods] We investigated the data of BD patients who were newly registered to the Japanese Ministry of Health, Labour and Welfare, from 2003 to 2014. Cluster analysis was performed for clinical manifestations, pathology test, and HLA-B51 by Hayashi's quantification third methods using HALBAU version 7. [Results] After screening 9045 cases, 2218 eligible cases (male 945, female 1231, mean age 39 y.o) including 65% of them with less than one year of disease duration. We identified 3 distinct clusters: group A (male, ocular inflammation, HLA-B51-positive, neurologic involvement), group B (female, genital ulcers, onset age: <30 years, ocular inflammation-negative, HLA-B51-negative, neurologic involvement-negative), and group C (onset age: 30-39 years, skin lesions, arthritis). [Conclusions] Because of short disease duration, clinical manifestations were little modified by therapies, while additional symptoms could appear later in this study population. Similar clustering patterns were observed in a Yokohama cohort. It is important to determine prognosis and genetic susceptibility for individual clusters,

leading to the establishment of precision medicine in future.

W72-4

Patients with intestinal involvement compose a distinct subset in Behçet's disease in Japan

Yutaro Soejima¹, Yohei Kirino¹, Mitsuhiro Takeno², Michiko Kurosawa³, Yuki Iizuka¹, Takeaki Uehara⁴, Ryusuke Yoshimi¹, Yukiko Asami⁵, Akiko Sekiguchi⁶, Atsushi Ihata⁷, Shigeru Ohno⁸, Toshihisa Igarashi⁹, Shohei Nagaoka¹⁰, Yoshiaki Ishigatsubo¹¹, Hideaki Nakajima¹

¹Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, ²Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, ³Department of Epidemiology and Environmental Health, Juntendo University Graduate School of Medicine, ⁴Department of Rheumatology, Chigasaki Municipal Hospital, ⁵Yokosuka Rheumatology Center, Yokosuka City Hospital, ⁶Department of Rheumatology, Fujisawa City Hospital, ⁷Department of Rheumatology, National Hospital Organization Yokohama Medical Center, ⁸Rheumatology Center, Yokohama City University Medical Center, ⁹Department of Rheumatology, Yamato Municipal Hospital, ¹⁰Department of Rheumatology, Yokohama Minami Kyosai Hospital, ¹¹Yokohama City University

Conflict of interest: None

[Object] Behçet's disease (BD) consists of subgroups with distinct sets of clinical manifestations, leading to different disease outcomes. This study aimed to determine the subgroups of BD patients in Japan. [Methods] We enrolled 691 BD patients (294 males, 397 females) who were under care at 7 hospitals, from 1991 to 2017 and mostly fulfilled the 1987 Japan revised diagnostic criteria. Patients were subgrouped according to clinical symptoms by a principal component analysis (PCA) [Results] PCA extracted three significant components: Group A "eye and/or neurological lesions", Group B "vascular or intestinal lesions", Group C "preferentially mucocutaneous symptoms without ocular and organ involvement". While gender difference was not evident in Groups A and B. Prevalence of HLA-B51 was significantly more in Groups A than other groups. Biologics were used in Group A and B, but not in C. Patients in Group A was gradually reduced, whereas those in Group B was increased. [Conclusions] We identified three distinct clinical subgroups in BD patients in Japan. There was the difference in patients' backgrounds and therapeutic intensity among the 3 groups. We will identify the pathogenesis and prognosis of each cluster.

W72-5

Clinical feature and treatment of vascular Behçet's disease

Hiroko Sato, Yousuke Hoshi, Tomoaki Machiyama, Yukiko Kamogawa, Yoko Fujita, Tsuyoshi Shirai, Hiroshi Fujii, Tomonori Ishii, Hideo Harigae
Department of Hematology and Rheumatology, Tohoku University Hospital

Conflict of interest: None

[Object] Vascular involvement is the causes of mortality and morbidity in Behçet's disease. The aim of this study is to investigate clinical characteristics and treatments of patients with vascular Behçet's disease. [Methods] 225 patients with Behçet's disease in Tohoku University hospital during January 2007 to December 2017 were enrolled to this study. Clinical characteristics, the subtypes of vascular involvement, treatments were retrospectively evaluated of vascular Behçet's disease. [Results] Among 225 patients, 24 patients had vascular involvements. 10 patients (41.7%) had venous disease and 17 patients (70.8%) had arterial disease. We looked the deep venous thrombosis (n=9), inferior vena cava thrombosis (n=1) and cerebral venous sinus thrombosis (n=1), aneurysm (n=10), arterian obstruction (n=6) and dissection (n=2), organ infraction (n=3). Duration between the first vascular event and onset of Behçet's disease was within less than a year in 13 cases. 23 cases used immunosuppressive agents. [Conclusions] In this study, arterial disease were more present than venous disease. Also, the first vasculature events occurred within less than a year from onset of Behçet's disease in more than half the cases.

W72-6

Efficacy of Apremilast for Oral Ulcers Associated With Active Behçet's Syndrome Over 28 Weeks in a Japanese Subgroup: Results From a Phase III Study

Hiroaki Dobashi¹, Yoshiya Tanaka², Hajime Kono³, Shoji Sugii⁴, Mitsumasa Kishimoto⁵, Sue Cheng⁶, Maria Paris⁶, Mitsuhiro Takeno⁷
¹Kagawa University, ²University of Occupational and Environmental Health, ³Teikyo University School of Medicine, ⁴Tokyo Metropolitan Tama Medical Center, ⁵Immuno-Rheumatology Center, St. Luke's International Hospital, ⁶Celgene Corporation, ⁷Nippon Medical School

Conflict of interest: None

[Object] Apremilast 30 mg BID (APR) was assessed over 28wks in a Japanese subgroup with Behçets syndrome and oral ulcers (OU). [Methods] Adults were stratified by region (Japan/other) and received APR or PBO for 12wks, followed by active treatment (tx). The primary endpoint was AUC_{Wk0-12}. Wk12 variables were prespecified without multiplicity adjustment. Nominal *P* values are given. Wk28 data are as observed. [Results] Included were 19 APR and 20 PBO patients (pts). Mean baseline OU count was 3.8 (APR) and 3.7 (PBO); mean pain VAS was 54.3 (APR) and 61.7 (PBO). AUC_{Wk0-12} was significantly lower for APR vs PBO (115.9 vs 253.3; *P*=0.0168). Significantly more APR pts had OU complete response at Wk12; between-group difference in OU pain was not significant. Efficacy was sustained with continued tx through 28wks. At Wk28, 65% (APR) and 53% (PBO) of pts had complete OU response; 64% and 30% had reduced OU pain. At 12wks, adverse event (AE) rates were similar (APR: 74%; PBO: 75%). Common AEs were diarrhea, upper respiratory tract infection, nausea, and headache. No new safety concerns were identified up to 28wks. [Conclusions] APR showed efficacy for OU in Japanese pts with Behçet's syndrome. Benefits were sustained up to 28wks with continued tx. Safety was consistent with APR's AE profile.

W73-1

The influence of malnutrition on serious infectious complications in patients with rheumatoid arthritis

Kentaro Isoda¹, Shiro Ohshima¹, Shigeyoshi Tsuji¹, Yuji Yoshida¹, Eri Oguro¹, Kentaro Kuzuya¹, Yasutaka Okita¹, Hidetoshi Matsuoka¹, Satoru Teshigawara¹, Maiko Yoshimura¹, Yoshinori Harada¹, Takaaki Noguchi¹, Shosuke Akita¹, Jun Hashimoto¹, Yukihiko Saeki²
¹Department of Rheumatology and Allergology, National Hospital Organization Osaka Minami Medical Center, ²Department of Clinical Research, National Hospital Organization Osaka Minami Medical Center

Conflict of interest: None

[Objective] To investigate the influence of nutritional status on serious infectious complications in patients with rheumatoid arthritis (RA). [Methods] This retrospective cohort study comprised 1315 patients (\geq 65 years old) with RA treated at our hospital at April 2016. Observation period is for 2 years. All patients were divided into infectious group complicated with severe infections requiring hospitalisation and non-infectious group without severe infectious events. Clinical findings and prognostic nutritional index (PNI) were compared in the 2 groups. Patients backgrounds were adjusted by propensity score (PS) matching. [Results] Infectious group included 66 patients, and non-infectious group 1466. Thirty-five patients of each group were chosen by PS matching. From the results of comparison in the adjusted groups, PNI of infectious group (median: 41.3, IQR: 38.9 - 45.2) was significantly decreased than that of non-infectious group (median: 46.3, IQR: 43.7 - 50.1) (*p* < 0.001). Infectious complication in patients with PNI < 45.0, cut-off value by ROC analysis, was higher than PNI \geq 45.0 (HR: 1.835, 95%CI: 1.136 - 2.972, *P* = 0.013). [Conclusion] Malnutrition is a risk factor for severe infectious complication in RA.

W73-2

Helicobacter cinaedi bacteremia associated with painful erythema in rheumatoid arthritis with malignant lymphoma

Shunichi Fujita¹, Hiroaki Hayashi², Shoko Tsuji¹, Mayuko Fukushima¹, Takahiko Akagi¹, Hiroshi Sawachika¹, Nami Kurosaki¹, Hiroyasu Hirano¹, Tomoyuki Mukai¹, Yoshitaka Morita¹

¹Department of Rheumatology, Kawasaki Medical School, Kurashiki, Japan, ²Department of Dermatology, Kawasaki Medical School, Kurashiki, Japan

Conflict of interest: None

A 69-year-old woman, in whom rheumatoid arthritis had been diagnosed 6 years previously and had received methotrexate, developed malignant lymphoma. She started to receive R-CHOP chemotherapy in September 2014. Two weeks after the first administration of this chemotherapy, she developed painful erythematous swelling of the thigh. The erythema improved spontaneously 2 weeks later, R-CHOP chemotherapy was repeated for 6 cycles. During these cycles, she developed recurrent fever and painful erythema in both thighs. She underwent a trial of prednisolone 20 mg/day, but developed new painful erythematous lesions on the skin of the abdomen in October 2015. Blood culture was positive for Gram-negative spiral bacillus. A diagnosis of *Helicobacter cinaedi* (*H. cinaedi*) bacteremia was made. The erythema improved following treatment with intravenous aminobenzyl penicillin, and she received this antibiotic for six weeks. Clinical significance: *H. cinaedi* bacteremia is often accompanied by skin manifestations, such as cellulitis and erythema nodosum-like eruptions. This case emphasizes the importance of recognizing this opportunistic infection in immunocompromised patients.

W73-3

Necrotizing fasciitis in three patients with rheumatoid arthritis treated with tocilizumab

Atsushi Omoto, Satoshi Omura, Takuya Yanagida, Masatoshi Kadoya, Wataru Fukuda

The Center for Rheumatic Disease, Japanese Red Cross Kyoto Daiichi Hospital

Conflict of interest: None

[Case 1] A 74-year-old woman with rheumatoid arthritis (RA) treated with tocilizumab (TCZ) was admitted as an emergency because of pain in the right leg with erythema. She was diagnosed with necrotizing cellulitis and started on intravenous antibiotics and debridement. skin swabs grew haemolytic group G streptococcus. [Case 2] A 68-year-old woman with RA treated with TCZ and end-stage renal damage was admitted as an emergency because of pain in abdomen with purpura. She was diagnosed with necrotizing cellulitis and started on intravenous antibiotics and debridement. skin swabs grew *Staphylococcus aureus*. [Case 3] A 71-year-old woman with RA and systemic sclerosis treated with TCZ was admitted as an emergency because of pain in the right leg with erythema and purpura. She was diagnosed with necrotizing cellulitis and started on intravenous antibiotics and debridement. skin swabs grew *Staphylococcus aureus*. (discussion) we report 3 cases of NF with RA treated with TCZ. 41 RA cases with NF were reported and 17 patients were used biologic DMARDs including TCZ. TCZ might lead to let NF get worse.

W73-4

The risk for urinary tract infection among rheumatic disease patients with asymptomatic bacteriuria

Tomohiro Yoshida, Keisuke Nishimura, Kaoru Mizukawa, Keiichiro Kadoba, Hiroki Mukoyama, Daisuke Waki, Toshihiko Yokota

Department of Endocrinology and Rheumatology, Kurashiki Central Hospital, Kurashiki, Okayama, Japan

Conflict of interest: None

[Object] Our aim is to clarify whether asymptomatic bacteriuria (AB) is the risk for urinary tract infection (UTI) among those who has rheumatic diseases (RD) and is receiving immunosuppressive therapy. [Methods] Inpatients with RD, who administered medium or high dose prednisolone ($\geq 0.5\text{mg/kg}$) from April 2015 to March 2018, were recruited. We divided them into 2 groups (AB in urinalysis before treatment or not) and examined retrospectively whether they developed UTI. [Results] Ninety-one RD patients were recruited (32 were AB positive, 59 were AB negative). ANCA-associated vasculitis (33.0%) and systemic lupus erythematosus (14.3%) were the most common. When started treatment, patients

with AB administered significantly more prednisolone. And their lymphocyte and serum albumin were significantly few. In both group some patients administered immunosuppressant (cyclophosphamide, methotrexate, etc). Patients with AB developed significantly more UTI than patients without AB (8/32 (25%) vs 5/59 (8.5%), $p=0.0165$). Within thirteen UTI patients, ten were female. Six had acute pyelonephritis, six had acute cystitis, and one had emphysematous cystitis. [Conclusions] Patients with AB may develop UTI significantly after immunosuppressive therapy, but there may be a possibility of overestimation.

W73-5

A prospective study of the standardized incidence ratio (SIR) of tuberculosis (TB) in patients with RA by NinJa cohort data for 15 years

Yasuhiko Yoshinaga¹, Tetsushi Aita¹, Susumu Nishiyama¹, Shoji Miyawaki¹, Akira Okamoto², Shigeto Tohma³

¹Rheumatic Disease Center, Kurashiki Medical Center, Kurashiki, Japan,

²Department of Rheumatology, Himeji Medical Center, National Hospital Organization, Himeji, Japan, ³Department of Rheumatology, Tokyo Medical Center, National Hospital Organization, Tokyo, Japan

Conflict of interest: None

[Object] To evaluate the characteristics of the newly developed tuberculosis (TB) in the registered patients in *NinJa* cohort study for rheumatoid arthritis (RA). [Methods] We calculated the standardized incidence ratio (SIR) of TB from the clinical data on National Database of Rheumatic Disease by iR-net in Japan (*NinJa*) prospectively from 48 facilities for 15 years. [Results] Among 141,047 patients registered from 2003 to 2017, 74 patients developed TB and the SIR of TB was 2.13 (95%CI:1.65-2.62). 8 patients (10.8%) were treated with biologic agents, and 26 patients (35.1%) were treated with MTX. The mean age of them was 71.4 years old and the mean duration of RA before the onset of TB was 10.3 years. Among 849 patients who have been administered JAK inhibitors (Tofacitinib 767, Baricitinib 82) since 2012, nobody has developed newly tuberculosis until 2017. [Conclusions] Similarly our last reports, the incidence of TB in RA patients was in the downward trend. By this study, in elderly, in patients with RA of long-term morbidity is the high risk of the newly developed TB.

W74-1

A therapeutic intervention of osteoporosis for patients with rheumatoid arthritis

Ayano Hayashi¹, Hidenori Tanigawa², So Nomoto²

¹Department of Nursing, Saiseikai Yokoamashi Tobu Hospital, ²Department of Orthopedic Surgery, Saiseikai Yokoamashi Tobu Hospital

Conflict of interest: None

[Object] Rheumatoid arthritis (RA) often occurs in combination with osteoporosis due to inflammatory cytokines increase and steroid usage. RA patients are easy to develop fractures compared to healthy people. We launched an OLSteam in 2016 for the prevention of fragile fractures. We encourage RA patients to undergo a bone density examination for an early diagnosis and early treatment of osteoporosis. [Objective] The aim is to report the current condition of osteoporosis combined with RA in our hospital and to report the result of therapeutic intervention for the RA patients. [Method] From 2014 to 2018, a bone density examination was performed on the RA patients with consent. We made a therapeutic intervention for the patients who needed a treatment of osteoporosis. [Results] We researched 211 patients that we were able to follow-up as of September 2018 (average age; 69.3 years, average disease duration; 12.3years, the number of medicated patients; 55, average dose of PSL; 4.1mg). We carried out a therapeutic intervention on the 123 patients that is 58% of all the RA patients. This study suggests the importance of early diagnosis and early treatment of osteoporosis in RA patients because fragility fractures decay patients' ADL.

W74-2

A status report on medical treatment for osteoporosis in rheumatic patients

Hiroshi Fujimaki¹, Akihiro Nakazawa¹, Motoharu Hirano², Yoshihiro Kusayama¹, Yutaka Inaba³

¹Department of Orthopaedic Surgery, Yokohama Municipal Citizen's Hospital, Yokohama, Japan, ²Department of Rheumatology, Yokohama Municipal Citizen's Hospital, Yokohama, Japan, ³Department of Orthopaedic Surgery, Yokohama City University, Yokohama, Japan

Conflict of interest: None

[Object] The aim of this study was to investigate the status of medical treatment for osteoporosis in rheumatoid arthritis (RA) patients. [Methods] A total of 119 RA patients over 40 years old (83 females and 36 males, average 69.3 years old) were enrolled. Fracture risk of each patient was evaluated using FRAX, and bone mineral density data of femoral neck was also available in 105 patients. The indication of treatment for osteoporosis was defined as follows; 1) patients with 15% or higher fracture risk estimated by FRAX, 2) patients who met diagnostic criteria for osteoporosis, regardless of the fracture risk level. We assumed that history of past fracture and corticosteroid (CS) use affect the osteoporosis treatment rate in RA patient cohort. [Results] We specified 71 patients who met the indication for osteoporosis treatment. However, 31 patients of those were without any anti-osteoporotic drug. The treatment rate for patients with a history of CS use (58.3%) was significantly higher than patients without CS ($p=0.02$). The presence of past fracture history did not affect the treatment rate. [Conclusions] The number of potential subjects for osteoporosis treatment was underestimated. We should consider osteoporotic treatment more seriously in RA patients with a high risk of fracture.

W74-3

The sufficiency level of vitamin D for collagen disease in our faculty

Daisuke Nozawa^{1,2}, Shigeru Hioki²

¹Department of Orthopedic Surgery, University of Tsukuba, Faculty of Medicine, ²Department of Orthopedic Surgery, Tsukuba Central Hospital

Conflict of interest: None

[Object] We report on the sufficiency level of vitamin D in patients with collagen disease among patients who could measure serum 25-hydroxyvitamin D (25 (OH) D) concentration at our facility. [Methods] We investigated 106 patients who measured 25 (OH) D between Female 89 cases, male 17 cases. There were 14 patients with collagen disease. The disease was 6 cases of rheumatoid arthritis, 1 case of Sjogren's syndrome, scleroderma, systemic sclerosis, dermatomyositis, IgA nephropathy, polymyalgia rheumatica, adult still disease, psoriasis respectively. Average 69.1 years old. Based on the judgment criteria for vitamin D deficiency / deficiency using serum 25 (OH) D concentration, 30 ng/ml or more is satisfied, less than 30 ng/ml is not satisfied, 20 ng/ml or more and 30 ng / ml was determined as vitamin D insufficiency, and less than 20 ng/ml was determined as vitamin D deficiency, and the proportion of each group was determined. [Results] The average concentration of 25 (OH) D was 15.8 ng/ml. Satisfied was only one person (7%), insufficiency 21% and deficiency 72%. In non-collagen disease group, there were 22% of insufficiency and 78% of deficiency. [Conclusions] It was thought that vitamin D sufficiency level was low in all patients, not only patients with collagen disease.

W74-4

Efficacy of denosumab in patients with rheumatic diseases for 36 months

Kotaro Shikano, Kaichi Kaneko, Mai Kawazoe, Keiko Koshiba, Shotaro Masuoka, Satoshi Mizutani, Soichi Yamada, Hiroshi Sato, Sei Muraoka, Toshihiro Nanki

Division of Rheumatology, Department of Internal Medicine, Toho University School of Medicine

Conflict of interest: None

[Object] We previously reported the efficacy of 12-month treatment

of denosumab, anti-RANKL mAb, for rheumatic diseases. We continued denosumab for 36 months, and analyzed the efficacy of the treatment. [Methods] One hundred patients with rheumatic diseases (52 RA, 14 SLE, 11 PMR, 5 PM/DM, 4 SS, 3 MCTD, 3 SSc, 2 vasculitis syndrome and 6 other diseases) extended denosumab therapy to 36 months. Serum levels of bone turnover markers and lumbar BMD in 33 patients were examined at 36 months. [Result] Serum levels of NTX, TRACP-5b, and BAP significantly decreased after 12 and 36 months. BMD significantly increased from baseline. Two patients developed compression fracture, and BMD was decreased in one patient. By multi regression analysis, the dosage of prednisolone was extracted as the inhibiting factor for increase of BMD. [Conclusions] Denosumab is effective for rheumatic diseases in 36 months. Higher dose of prednisolone may suppress increase of BMD by treatment with denosumab.

W74-5

The Report of the Treatment for Glucocorticoid-induced Osteoporosis in Our Hospital and the Interference in Insufficient Medication by the Pharmacist

Miho Manabe¹, Akiko Yoshida^{2,3}

¹Pharmaceutical Division, Medical Technology Department, Keishinkai Kyoto Kizugawa Hospital, ²Department of Rheumatology, Keishinkai Kyoto Kizugawa Hospital, ³Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University

Conflict of interest: None

[Object] Glucocorticoid (GC)-induced osteoporosis (GIO) is the important side effect of GC therapy. I investigated the treatment for GIO in our hospital. [Methods] Outpatients were registered who had visited the department of rheumatology in our hospital from June to August in 2018, and who had taken Predonine (PSL) for more than 3 months. This was retrospective study using medical records and the risk factor score of GIO was quoted from Guidelines for GIO of the Japanese Society (2014). [Results] 48 patients; RA (21), PMR (15), RS3PE syndrome (6), SLE, MCTD, PsA, Behcet's disease, IgG4-RD, and IgA vasculitis (each for 1 patient) were enrolled. The average age was 73.4 y.o. and man/woman ratio was 16/32. The average PSL dose was 4.3 ± 2.81 mg/day. 8 patients didn't take any drug for GIO, though they had more than 3 risk factors of GIO score. 20 patients took only bisphosphonates (BP), 5 patients took the combination of BP and vitamin D tablets (Vit.D) and 13 patients took Vit.D alone. 6 cases were measured their bone density. Medications were suitable for patients with renal failure. After hearing from the patients and the physician, treatments for GIO were adjusted properly. [Conclusions] The treatment for GIO in our hospital was insufficient, but pharmacists could try to change GIO treatment better.

W74-6

Anti-resorptive agents-related Osteonecrosis of the jaw (ARONJ) in RA patients

Megumi Itoi¹, Hideaki Oyabu², Tatsuya Hojo³, Kazuha Kizaki⁴, Noboru Funakoshi⁴, Fumiharu Yamashita⁵

¹Department of Orthopedic Surgery, Meiji University of Integrated Medicine, Kyoto, Japan, ²Department of Dentistry, Meiji University of Integrated Medicine, Kyoto, Japan, ³Department of Health and Sports Science, Doshisha University, ⁴Department of Orthopedic Surgery, Kyoto Shimogamo Hospital, ⁵Department of Rheumatology, Kyoto Shimogamo Hospital

Conflict of interest: None

[Object] Osteonecrosis of the jaw (ONJ) is caused by various factors including inflammation and osteomyelitis. In recent years, it has been suspected that therapeutic targets for bone resorption by osteoclasts, bisphosphonates (BP) and denosumab are associated with anti-resorptive agents-related osteonecrosis of the jaw (ARONJ). We analyzed the incidence of ONJ in our hospital and introduced two ONJ cases with RA. [Results] We identified 7 cases of ONJs out of 10670 patients (average 1255 patients per year) who visited the department of dentistry in our hospital from 2010 to 2018. The incidence rate was increased after 2016, 1 case in 2013, 3 cases in 2016, 1 case in 2017, 2 cases in 2018. The underlying disease was 4 cases of prostate cancer (denosumab), 2 cases of

RA (1 case denosumab, 1 case minodronate) and 1 breast cancer (zoledronate). Case1 RA 85 y.o. female ARONJ stage3 with fistula Case2 RA 69 y.o. female ARONJ stage2 [Clinical significance] In RA patients, steroids and immunosuppressive agents are frequently used for suppressing inflammation and it potentially increases the risk of ONJ. We believe that physicians and dentists should share patients' information provision, cooperating with each other. When ONJ occurs, it is necessary to examine withdrawal of anti-rheumatic drug.

W75-1

Investigation of the effects of Igaratimod in combination therapy for RA patients experiencing insufficient results with biologics

Daisuke Tomita¹, Tetsu Itami², Satoshi Tsutsumi¹, Kosuke Okuda¹, Yuji Nozaki², Masanori Funauchi², Itaru Matsumura², Tsukasa Matsubara¹

¹Matsubara Mayflower Hospital, Hyogo, Japan, ²Department of Hematology and Rheumatology, Kinki University Faculty of Medicine, Osaka, Japan

Conflict of interest: None

Purpose: We investigated of Igaratimod (IGU) combination treatment for RA patients already using biologics (Bio), who were unable to achieve low disease activity and we compared the effectiveness of each of the biologics. Methods: We added IGU to the treatment of RA patients already being treated with Bio more than 3 months, and retrospectively analyzed its effects on the 42 patients who were able to continue for 12 week. Baseline we use age, morbidity history, stage, class, MTX usage, MTX dosage, PSL usage, PSL dosage, DAS28-ESR, we evaluated using LDA rates and change in CDAI at 12 and 24 weeks after combined. Results: Background: Age 64.9, disease duration 16.7, MTX had used 56% and dosage was 7.5mg. PSL had used 42% and dosage was 3.4mg. Stage 2.63, Class 1.73. Bio type: 17 TNF inhibitors (IFX6, ETN 8, GLM 1, CZP 2), 15 ABT, 7 TCZ, 1 TOF are used. CDAI before IGU was 14.6±8.39, at 12 weeks 10.0±9.97, at 24 weeks 8.64±9.29. Before administration of IGU LDA was 30.77%, at 12 weeks 64.71%, and at 24 weeks 75.76%. It was suggested that TCZ is more effective in IGU combination therapy than ABT and TNF inhibitor. Conclusion: In cases in which biologics are not sufficiently effective, IGU can improve disease activity, and TCZ is suggested as being more effective than ABT and TNF inhibitor.

W75-2

Add-on iguratimod to patients with rheumatoid arthritis inadequately responding to biological DMARDs can expect equivalent effects regardless of the type of bDMARDs

Ayaka Yoshikawa¹, Koji Nagai¹, Kenichiro Hata¹, Takuya Kotani¹, Yoko Matsumura², Tohru Takeuchi¹, Motomu Hashimoto³, Wataru Yamamoto^{3,11}, Kosaku Murakami⁴, Toru Hirano⁵, Kosuke Ebina⁶, Yonsu Son⁷, Hideki Amuro⁷, Akira Onishi⁸, Kengo Akashi⁸, Ryota Hara⁹, Masaki Katayama¹⁰, Shigeki Arawaka¹

¹Department of Internal Medicine IV, Osaka Medical College, ²Department of Central, Osaka Medical College, ³Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, ⁴Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, ⁵Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University, ⁶Department of Orthopaedic Surgery, Graduate School of Medicine, Osaka University, ⁷First Department of Internal Medicine, Kansai Medical University, ⁸Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, ⁹The Center for Rheumatic Diseases, Nara Medical University, ¹⁰Department of Rheumatology, Osaka Red Cross Hospital, ¹¹Department of Health Information Management, Kurashiki Sweet Hospital

Conflict of interest: None

[Object] To examine whether the effectiveness of rheumatoid arthritis (RA) patients treated with iguratimod (IGU) during the use of biological DMARDs (bDMARDs) differ between bDMARDs. [Methods] 87 RA patients who used bDMARDs for more than 12 weeks and then added IGU for 24 weeks were included. We retrospectively analyzed the disease activity between bDMARDs from the ANSWER cohort. [Results] The

mean age was 64.3 ± 12.8 years, a female of 76.2%, mean disease duration was 9.6 ± 8.6 years, mean duration of bDMARD treatment was 1.4 ± 1.6 years. bDMARDs were (1) TNF- α inhibitor 43 cases, (2) TCZ 16 cases, (3) ABT 28 cases. The mean Δ DAS 28-ESR (0w-24w) was 1.12±0.8 ((1):1.02±0.7, (2):1.13±0.9, (3):1.26±0.89). The DAS 28-ESR remission rate was improved from 8.5% at baseline to 45.5% at 24 weeks' administration of IGU ((1):2.4→47.4, (2):25.0→53.9, (3):7.7→38.5), and the CDAI remission rate was significantly improved from 0.0% at baseline to 27.7% at 24 weeks' administration of IGU ((1):0→24.4, (2):0→28.6, (3):0→32.1), respectively (P <0.001). The patient background factor was not different except for the MTX amount, and the effectiveness was equivalent among the bDMARDs. [Conclusions] Add-on IGU to bDMARDs can be expected to can expect equivalent effects regardless of the type of bDMARDs.

W75-3

Biologic agent therapy of rheumatoid arthritis in the elderly with lung disease

Tatsuo Watanabe¹, Toshihisa Kojima², Nobunori Takahashi², Shuji Asai², Yasumori Sobue², Naoki Ishiguro²

¹Department of Orthopedic Surgery, Daido Hospital, ²Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine

Conflict of interest: None

[Object] Of the treatment of rheumatoid arthritis (RA), biologic agent therapies are chosen, if disease activity remains moderate or high despite csDMARDs therapy. Elderly and lung disease are the major risk factor for infection in biologic agent therapy. We investigate biologic agent therapy of rheumatoid arthritis in the elderly with lung disease. [Methods] Records of relevant patients with RA were collected from the Tsurumai Biologic Communication Registry, wherein the department of Nagoya University and 20 affiliated hospitals in Japan are enrolled. A total of 873 biologics-naïve and age 75 and older patients were recruited from January 2004 to December 2014. We studied the choice of the biologic agent year by, and baseline disease activity drug continuation rates. [Results] From 2005 to 2010, etanercept was used the most. After the advent of abatacept (ABT), ABT was used the most. Drug continuation rates in the group with lung disease were: 70.6% (2004-2007), 93.5% (2008-2010), 94.1% (2011-). [Conclusions] Increasing of drug continuation rates seemed for accumulation of experience.

W75-4

Ten-year retention rate and outcome of etanercept in patients with rheumatoid arthritis in clinical practice

Toki Takemoto¹, Takeshi Oguchi¹, Atsushi Kaneko², Yuji Hirano³, Yutaka Yokota⁴, Nobunori Takahashi⁴, Toshihisa Kojima⁴, Naoki Ishiguro⁴

¹Department of Orthopedic, Anjo Kosei Hospital, Anjo, Japan, ²Department of Orthopedic, National Hospital Organization Nagoya Medical Center, ³Department of Rheumatology, Toyohashi Municipal Hospital, ⁴Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine

Conflict of interest: None

[Object] Biologic agents (bDMARD) are regarded as a major advance in the treatment of rheumatoid arthritis (RA), but data on the long-term effects of bDMARD remain relatively scarce. So, the aim of this study is to evaluate the ten-year outcome of etanercept (ETN) in patients with RA. [Methods] RA patients who started ETN between 2005 and 2007 were investigated and 205 patients were enrolled. [Results] At baseline, average age 57.6 years old, DAS28-CRP was 5.4 and rate of concomitant MTX was 51%. Ten-year retention rate of ETN was 41% and 75 patients actually continue ETN at 10 year. There was higher retention rate in patient concomitant with MTX. After 10 years, there were 68% of RA patients who continue to visit our hospitals for treatment, and 10% patients who died. [Conclusions] In this study, the overall 10-year drug retention rate for RA patients treated by ETN results comparatively good and follow up rate at 10 year also results comparatively good.

W75-5

Short-term clinical effectiveness of biosimilar product of etanercept on rheumatoid arthritis patients

Akihiro Uchio¹, Takuo Juji¹, Katsumi Ito², Naohiro Izawa¹, Takumi Matsumoto³, Jinju Nishino³, Ichiro Nakamura⁴, Sakae Tanaka³

¹JCHO Yugawara Hospital, ²Heisei Yokohama Hospital, ³The University of Tokyo Hospital, ⁴Teikyo Heisei University

Conflict of interest: None

[introduction] In drug therapy of rheumatoid arthritis (RA), economical efficiency is an important factor as well as efficacy and safety. Biological agents are widely introduced in RA patients. However, due to its expensive medical expense, the usage of biologics is sometimes limited or even given up. In this study, we investigated the effectiveness and safety of its bio-similar (BS) product of etanercept. [Method] We targeted 39 patients who were using ETN at JCHO Yugawara Hospital, Heisei Yokohama Hospital, changed to BS and were able to follow the course of 3 months after change. We measured and compared CRP, RF, MMP-3, HAQ, DAS28CRP, SDAI, CDAI before BS and 3months after change. The reason for changing to BS, the presence or absence of side effects and the feeling after the change were also investigated. [Result] There was no difference in CRP, RF, HAQ and DAS28CRP, but there was significant difference in SDAI, CDAI and MMP-3. There were no cases in which arthritis exacerbated after BS change, which was consistent with international joint Phase III clinical trial. 30 people changed to BS for reasonable price. 11 patients had relieved injection pain and no new adverse events occurred. [Conclusion] BS was comparable with ETN.

W75-6

Differences of clinical performance between 50mg and 100mg of golimumab in patients with rheumatoid arthritis

Kengo Harigane¹, Yuichi Mochida¹, Kagayaki Sahara¹, Naoto Mitsugi², Ken Kumagai³, Hyonmin Choe³, Akiko Nagaoka³, Yutaka Inaba³

¹Center for Rheumatic Diseases, Yokohama City University Medical Center, ²Department of Orthopaedic Surgery, Yokohama City University Medical Center, ³Department of Orthopaedic Surgery, Yokohama City University

Conflict of interest: Yes

[Object] This study evaluated the differences of clinical performance between 50mg and 100mg of golimumab in patients with rheumatoid arthritis [Methods] The clinical background and the changes of disease activity score (DAS28-ESR) were analyzed for fifty-nine patients (50mg group; 37 cases, 100mg group; 32 cases) who were treated with golimumab at least three months. [Results] The rates of concomitant use of methotrexate (MTX) were 83.8% in 50mg group and 43.8% in 100mg group. The mean doses of MTX were 8.2 and 6.8 mg/week respectively. Also, the rates of concomitant use of prednisolone (PSL) were 56.8% in 50mg group and 53.1% in 100mg group. The mean doses of PSL were 4.4 and 4.0 mg/week respectively. The DAS28-ESR at baseline were 3.86 in 50mg group and 3.95 in 100mg group (n.s.). The rates of remission at 12 and 24 weeks were 42.4%, 45.8% in 50mg group and 50.0%, 54.1% in 100mg group. The averaged differences of DAS28-ESR from baseline at 12 and 24 weeks were -0.82, -1.18 in 50mg group and -1.30, -1.52 in 100mg group (n.s.). [Conclusions] Although there were no statistically significant results from our data, the administration 100mg of GLM tended to show better clinical efficacy in early period of treatment.

W76-1

Characteristics of the patients with Systemic lupus erythematosus (SLE) in our division and the efficacy of Belimumab

Hitoshi Kodera, Yoshifuji Matsumoto
Kuwana City Medical Center

Conflict of interest: None

[Object/Methods] To analysis the treatment of SLE patients who have consultations in our division for more than one year. Also to verify the effectiveness and safety of BEL. [Results] There were 32 subjects (female 29). Average age 47.6 years old, age at diagnosis 36.6 years old.

Lupus nephritis diagnosed by renal biopsy was 40.6% of them. In initial symptoms, skin rash tended to be more frequent in juvenile onset, and serositis tended to be higher in elderly ones. Hydroxychloroquine (HCQ) was used at 65.6 %, and its average age was 42 years old, which is younger than the non-use cases (58.5 years old). The steroid free was 40.6 % of the total, and there was a tendency of frequent use of combination of immunosuppressants. BEL was used for four cases (the average age was 29.8 years old), mainly because of the experience of side effects for immunosuppressive drugs or of planning of childbearing. One of the cases was the one with the difficulty of steroid tapering, but after 6 months, the case succeeded in decreasing prednisolone 5 mg/day. [Conclusions] There is a tendency to reduce the dose of steroid with the use of HCQ and immunosuppressant in our division. And it was confirmed that BEL is useful for some case with difficulty of steroid tapering.

W76-2

Clinical features and the efficacy in patients with systemic lupus erythematosus treated with belimumab

Taihei Nishiyama, Yuya Kondo, Shota Okamoto, Hirofumi Toko, Masaru Shimizu, Fumika Honda, Ayako Ohyama, Izumi Kurata, Mizuki Yagishita, Saori Abe, Masahiro Yokosawa, Atsumu Osada, Hiroto Tsuboi, Isao Matsumoto, Takayuki Sumida

Department of Internal Medicine, Faculty of Medicine, University of Tsukuba Hospital, Tsukuba, Ibaraki, Japan

Conflict of interest: None

<OBJECTIVE> To clarify the clinical features and the efficacy in systematic lupus erythematosus (SLE) patients treated with belimumab (BLM) <METHODS> This study included six cases with SLE treated with BLM in University of Tsukuba hospital. We retrospectively evaluated 1) baseline characteristics, 2) purpose of BLM therapy, 3) clinical course in two cases treated with BLM for 12 weeks, and 4) adverse events. <RESULTS> 1) The mean age was 34.2±12.8 years old. The mean of SLE disease activity index (SLEDAI) and of anti-DNA antibody titer were 4.83±3.58 and 43.8±50.9 IU/mL, respectively. The mean prednisolone (PSL) dose was 14.5±3.6mg/day. 2) BLM was used to treat arthritis flare-up in one case, nephritis in one case, thrombocytopenia in one case, and to reduce PSL dose in three cases. 3) In case 1 with arthritis flare-up, both SLEDAI and anti-DNA antibody titer were decreased. PSL could be reduced from 17.5 to 13 mg/day. In case 2 treated with BLM to reduce PSL dose, PSL could be reduced from 12.5 to 8 mg/day. 4) Three cases experienced cough, infusion reaction and lassitude, respectively. BLM was discontinued in case with lassitude. <CONCLUSION> Our observations suggested that BLM might be effective for the improvement of disease activity and the reduction of PSL dose in patients with SLE.

W76-3

Safety and Efficacy of Belimumab in Pediatric Patients with SLE: The BEL114055 Phase II, Randomized, Placebo-controlled and multinational Study of Belimumab in Pediatric Patients with SLE including the Japanese Children

Syuyi Takei¹, Masaaki Mori², Naomi Iwata³, Hiroaki Umebayashi⁴, Ken Clark⁵, Antonio Nino⁶, Anne Hammer⁶, Beulah Ji⁷, David Roth⁶

¹Pediatric Department of Kagoshima University Hospital, Japan, ²Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Japan, ³Department of Infection and Immunology Aichi Children's Health and Medical Center, Japan, ⁴Department of Rheumatology - Infectious Disease, Miyagi Children's Hospital, Japan, ⁵GSK Stevenage UK, ⁶GSK Upper Providence USA, ⁷GSK, Stockley Park UK

Conflict of interest: None

[Object] This study evaluated the efficacy and safety of belimumab (BEL) when added to standard of care therapy compared to placebo (PBO) over 52 weeks in pediatric SLE subj. incl. 6 Japanese (J) children (NCT0169765). [Methods] SLE subj. aged 5-17 years with a SLEDAI score of ≥ 6 , were to be dosed with BEL 10 mg/kg intravenously (IV) every 28 days through W48, with a final evaluation at W52. The primary endpoint was the SLE responder index (SRI) response rate at W52. Due to the rarity of the disease in children, the study was not

powered to detect statistical significance. [Results] 93 subj. were randomized to BEL [53 (J: 2)] and PBO [40 (J: 4)]. The SRI response rate at W52 was numerically higher for BEL [52.8%, 28/53] compared with PBO [43.6%, 17/40] (OR:1.49, 95%CI:0.64, 3.46). The outcome using PRINTO measures, a composite assessment specific to pediatric SLE, also showed positive effect in favour of BEL. The overall incidence of adverse events was similar between groups. The safety profile of subj. in BEL incl. the J children was generally favorable. [Conclusions] The efficacy and safety results in the study were consistent with those of in BEL IV adult studies. No new safety issues were identified in pediatric SLE subj. incl. J children. GSK funded this study.

W76-4

Study on the effect of mycophenolate mofetil (MMF) for neuropsychiatric SLE (NPSLE)

Tamao Nakashita, Akira Yoshida, Akira Jibatake, Shinji Motojima
Rheumatology and Allergy, Kameda Medical Center, Kamogawa, Japan

Conflict of interest: None

[Object] MMF is a standard regimen for the treatment of lupus nephritis. However, its effect on NPSLE has not been extensively studied. We studied the effect of MMF on NPSLE. [Methods] Patients with SLE were enrolled who used MMF for the treatment of LN for more than 6 months complicated with NPSLE. [Results] Subjects were 16 patients (male 2, female 14), with the mean age of 47.3 years. The purposes of MMF introduction were induction of CR in 2, maintenance of CR in 12, and treatment for relapse in 2. Episodes of NPSLE were classified as neurological symptoms in 8, diffuse neuropsychiatric symptoms in 12, and peripheral neuropathy in 1 according to the ACR criteria. The mean dose of PSL at the introduction of MMF was 16.8mg/day and 10 patients were on HCQ. The concentration of IL-6 in CSF was more than normal range in 6 with the mean of 162.3 pg/ml. Anti-ribosomal P antibody and anti-NR2 antibody were positive in 5/6 and 3/7, respectively. Abnormal EEG and MRI findings were seen in 9 and 4, respectively. The mean dose of MMF was 1421mg/day and the mean duration of administration was 691 days. The mean dose of PSL was significantly reduced to 6.84mg/day. SLEDAI score and patients' VAS were also improved significantly. [Conclusions] The usefulness of MMF on NPSLE was suggested.

W76-5

A comparative analysis between mycophenolate mofetil and intravenous cyclophosphamide in induction therapy for the patients with lupus nephritis

Mizuki Yagishita, Yuya Kondo, Taihei Nishiyama, Shota Okamoto, Hirofumi Toko, Masaru Shimizu, Fumika Honda, Ayako Ohyama, Saori Abe, Hiroyuki Takahashi, Masahiro Yokosawa, Atsumu Osada, Hiroto Tsuboi, Isao Matsumoto, Takayuki Sumida
Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: None

<Objectives> To compare efficacy and treatment continuation rate between mycophenolate mofetil (MMF) and intravenous cyclophosphamide (IVCY) in induction therapy for lupus nephritis. <Methods> We examined patients with lupus nephritis received induction therapy with MMF or IVCY between January 2010 and April 2018. We retrospectively investigated 1) patient characteristics, 2) treatment efficacy and 3) treatment continuation rate for 6 months. <Results> 1) Twenty six cases (MMF:13/IVCY:13) were included. Initial prednisolone dose was significantly lower in MMF group (39.1±16.9 vs 54.6±9.1 mg/day, p=0.02). In the other characteristics, there were no significant differences between two groups. 2) Complete remission defined as urinary protein ≤ 0.5g/day, albumin ≥ 3.5g/dL, eGFR ≥ 80mL/min/1.73m², and no cellular cast was achieved in 38.4% and 23.0% of respective groups (p=0.4). No significant differences in the change of SLEDAI, anti-DNA antibody, albumin, eGFR and urinary protein were observed between two groups. 3) Treatment continuation rate for 6 months was significantly higher in MMF group (100% vs 53%, p<0.01) <Conclusion> At 6 months after the treatment, there were no significant differences in efficacy between MMF and IVCY, and continuation rate was significantly higher in MMF.

W77-1

The utility of red cell distribution width in the patients with systemic sclerosis related interstitial lung disease

Tomoya Sagawa, Takashi Kida, Risa Sagawa, Akiko Kasahara, Shunya Kaneshita, Takuya Inoue, Kazuki Fujioka, Hidetake Nagahara, Makoto Wada, Masataka Kohno, Yutaka Kawahito
Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine

Conflict of interest: None

[Object] In the patients with systemic sclerosis (SSc) related interstitial lung disease (ILD), serum KL-6 may not reflect their severity in some cases. Recently, the utility of red cell distribution width (RDW) has been reported as the diagnostic marker of pulmonary hypertension in SSc patients. The aim of this study is to investigate the relationship between RDW and pulmonary function in the patients with SSc related ILD. [Methods] SSc patients with ILD who performed pulmonary function test at our hospital from April 2008 to September 2017 were enrolled. The medical records of 45 consecutive patients were reviewed retrospectively. Baseline demographic data, laboratory findings including RDW and %VC were obtained from medical records at the time of first pulmonary function test. [Results] With the exclusion of 28 patients for some reasons, 17 patients were reviewed. The median age was 54 (46-63) years and 15 patients were female. The median value of RDW, KL-6, and %VC was 13.3 (12.6-14.1), 460 (264-577) U/ml, and 84.5 (80.2-92) %, respectively. While there was no significant correlation between KL-6 and %VC, RDW and %VC had significant negative correlation (r = -0.54, p = 0.027). [Conclusions] RDW may correlate with the reduction of %VC in the patients with SSc related ILD.

W77-2

Change in breast muscle volume in patients with scleroderma associated with interstitial lung disease assessed using computed tomography

Takashi Nawata^{1,2}, Yuichiro Shirai¹, Masataka Kuwana¹

¹Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, ²Department of Medicine and Clinical Science, Yamaguchi University Graduate School of Medicine, Yamaguchi, Japan

Conflict of interest: None

[Object] We investigated the association between change in breast muscle volume and pulmonary function in systemic sclerosis (SSc) patients with interstitial lung disease (ILD). [Methods] Twenty five patients with SSc-ILD, who were underwent chest computed tomography (CT) and pulmonary function test, were assessed. Maximum diameter of diaphragm (MDD) and pectoralis major muscle area (PMMA) and skeletal muscle area (SMA) at the level of 12th thoracic vertebra were obtained using CT. [Results] In patients with SSc-ILD, MDD and PMMA and SMA decreased (p<0.01, p=0.016, p=0.031). The area of ILD also increased (p=0.016). The change of MDD and PMMA showed correlations with the change of both ILD area (p<0.01, p=0.045) and serum level of KL-6 (p=0.023, p=0.022). On the other hand, the change of SMA showed correlations with the initial ILD area (p<0.01) and the change of tidal volume (p<0.01). The patients whose initial ILD area were more than 10 % showed reduction of SMA (p=0.019). With regard to complications, gastrointestinal tract disorders decreased MDD (p=0.024). Myocardial disorders also decreased SMA (p=0.023). [Conclusions] Our study suggests the possibility that volume loss of breast muscle in SSc-ILD patients cause the decline in pulmonary function.

W77-3

Prognosis of Borderline Pulmonary Arterial Hypertension in Patients with Systemic Sclerosis

Sumiaki Tanaka, Yu Matsueda, Tatsuo Nagai, Kunihiro Yamaoka
Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine

Conflict of interest: Yes

[Object] To evolve the therapeutic strategy for borderline pulmonary arterial hypertension (PAH) associated with Systemic Sclerosis (SSc), we evaluated the long-term prognosis of borderline PAH (border-PAH) in SSc patients. [Methods] We selected 11 SSc patients who fulfilled the criteria for border-PAH by right heart catheterization in our hospital from 2011 to 2018. We performed survival analysis under retrospective cohort study design. [Results] Eligible patients were all females, and included 6 diffuse cutaneous and 5 limited cutaneous SSc patients. The age at diagnosis of border-PAH was 63±16 years old. All patients had no symptoms and had been treated with beraprost sodium. Mean pulmonary arterial pressure, pulmonary capillary wedge pressure, cardiac output and pulmonary vascular resistance levels were 22.4±4.2 mmHg, 7.5±4.2 mmHg, 5.0±1.1 L/min and 2.1 WU, respectively. In the observation period, no patient had been treated with PAH-specific drugs. Two patients had died of lung cancer and liver cancer. No patient had additional echocardiographic findings indicating PAH. [Conclusions] Our results show that no SSc patient developed of PAH from border-PAH, resulting in deliberate consideration for the indication for treatment of border-PAH in SSc patients.

W77-4

Identifying the factors to predict borderline pulmonary hypertension and evaluating clinical outcomes during a 5-years period in patients with systemic sclerosis

Katsuhiko Yoneda, Soshi Takahashi, Saki Mukohara, Norihiko Amano, Yasuhiro Nohda, Miwa Nishida, Saori Hatachi, Shunichi Kumagai
Department of Rheumatic Disease, Shinko Hospital, Hyogo, Japan

Conflict of interest: None

[Objective] To identify the factors for predicting pulmonary hypertension (PH) and borderline PH with mPAP more than 21mmHg (overt and borderline PH), and to evaluate clinical outcomes for 5 years in patients with SSc. [Method] Among 113 patients with SSc visiting our hospital between January 2011 and May 2014, we performed right heart catheterization (RHC) in 47 cases with consent. 3 patients with PCWP more than 15 mmHg were excluded. In 44 cases, relevant multivariate was carried out for identifying the factors for predicting overt and borderline PH. The clinical outcomes were tracked from medical records to investigate whether the predicting factors were effective. [Results] Among 44 patients, RHC demonstrated mPAP more than 21mmHg. Relevant multivariate revealed that %DLco, estimated systolic PAP (esPAP) and BNP were correlated with mPAP. Though one patient developed PH by left heart disease and one patient developed borderline PH in 17 patients with “less than 35mmHg of esPAP” and “more than 80% of %DLco”, there were no deaths in the original disease for 5 years. [Conclusion] Though it is important to detect the borderline PH with RHC, echocardiography and pulmonary function test may have predicting ability for the necessity of RHC and that for clinical outcomes.

W77-5

Clinical characteristics associated with esophageal function in systemic sclerosis (SSc)

Yuichiro Shirai, Masataka Kuwana
Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan

Conflict of interest: None

[Objective] To clarify clinical characteristics associated with esophageal function in SSc. [Methods] Among 227 SSc cases who visited our clinic between 2014 and 2018, we enrolled 39 consecutive cases in the study who underwent high resolution manometry. We analyzed associations between esophageal motility assessed by Chicago classification, upper and lower esophageal sphincter (UES and LES) pressure and clinical characteristics. [Results] Among 39 cases, 34 were women, 20 were diffuse cutaneous SSc (dcSSc), and 22 had interstitial lung disease (ILD). When we classified patients into normal (n = 12), ineffective esophageal dysmotility (n = 6), and absent contractility (n = 21), 3 groups were correlated with dcSSc, maximal esophageal diameter in CT scan, presence of ILD (P=0.026, 0.007, 0.029), and inversely with pulmonary function (%TLC, %FVC, %DLCO) (P=0.014, 0.028, 0.004). Reduced UES pres-

sure was correlated with age at onset and presence of ILD (P=0.043, 0.047) and inversely with proton pump inhibitors use (P=0.03). Reduced LES pressure was correlated with smoking (P=0.03). [Conclusions] In SSc, esophageal dysmotility was correlated with presence of ILD and reduced pulmonary function and it was prominent in dcSSc. Further studies are required to clarify causal relationship.

W77-6

Survey on Dysphagia Using Simple Questionnaire EAT-10 in Patient with Systemic Sclerosis

Tatsuaki Naganawa, Shunji Yoshida, Natsuko Watanabe, Masashi Suzuki, Ai Umeda, Konomi Ashihara, Megumi Kurumizawa, Daisuke Hirano, Takako Hashimoto, Jo Nishino, Shusaku Fukaya, Hidekata Yasuoka
Division of Rheumatology, Department of Internal Medicine., Fujita Health University School of Medicine

Conflict of interest: None

[Object] In Systemic Sclerosis (SSc), symptom of upper gastrointestinal tract is thought to be due to gastroesophageal reflex or motion dysfunction. However, swallowing function is not well evaluated. Our aim is to investigate the actual condition of dysphagia in patient with SSc. [Methods] 10 with SSc who randomly selected from patient visited during from November to December 2016. Polymyositis/Dermatomyositis (PM/DM) patients were selected as controls. The feature of dysphagia were evaluated by Self-assessment of feeling with difficulty at swallowing and the simple swallowing evaluation form, EAT-10. [Results] Based on self-assessment, 50% of patients with SSc felt difficulty of swallowing and 40% did not, whereas 28.6% of patients with PM/DM did and 50% did not in PM/DM. By EAT-10, there were 3 in SSc (30%) and 2 in PM/DM (14%) who were suspected to have dysphagia, which is a same trend with self-assessment. As for the contents of swallowing, there was no difference in difficulty with liquids or solids between SSc and PM/DM. However, swallowing difficulty of tablets was confirmed with 5 in SSc (50%), and 2 in PM/DM (14%). [Conclusion] Swallowing difficulty of patients with SSc comes from not only esophageal dysfunction but also oropharyngeal disorder, which may be different from PM/DM.

W78-1

Analysis of the optimal blood concentration of tacrolimus in systemic lupus erythematosus

Koichiro Taguchi, Hideki Tani, Takahide Ikeda, Hiroyuki Morita, Motochika Asano, Yoshihiko Kitada
Department of General Internal Medicine, Gifu University Hospital

Conflict of interest: None

[Object] We evaluated the optimal blood concentration of tacrolimus (TAC) in systemic lupus erythematosus (SLE). [Methods] SLE treated with TAC was 18 cases from April 2013 to May 2018. 6 cases discontinued TAC. 12 cases continued for 6 months, and divided into two groups, the TAC trough level < 5 ng/mL (A, 4 cases) and ≥ 5 ng/mL (B, 8 cases). [Results] 3 cases discontinued by the suspicion of the side effect. But those were not measured the trough level. The mean age of the groups was 36±12, all of the cases were women. Baseline characteristics were balanced between the groups. The mean dose of TAC at month 6 was 2.8 mg in the group A and 2.3mg in the group B. The amount of urine protein, SLEDAI and an average daily dose of prednisolone were significantly reduced in the group B at both month 3 and month 6. Otherwise, there was no significant difference between groups in the laboratory data and the rates of side effect. [Conclusions] These data suggested the trough level ≥ 5 ng/mL was the useful marker for the treatment of SLE. The side effect did not occur both groups. We assumed this was because the trough level was < 8 ng/mL except for 1 case. Two thirds of the cases treated with TAC 2 mg/day were the trough level ≥ 5 ng/mL. Therefore, we recommend TAC was started with 2 mg/day.

W78-2

Hydroxychloroquine modulates elevated expression of S100 proteins in systemic lupus erythematosus with lupus nephritis

Risa Wakiya, Tomohiro Kameda, Shusaku Nakashima, Kiyoko Ueda,

Hiroshi Shimada, Mikiya Kato, Taichi Miyagi, Hiroaki Dobashi
Department of Hematology, Rheumatology and Respiratory Medicine,
Department of Internal Medicine, Faculty of Medicine, Kagawa University

Conflict of interest: None

[Object] To clarify the effect of HCQ treatment on serum levels of S100A8 and S100A9 proteins in SLE patients with sustained remission of lupus nephritis (LN). [Methods] All patients enrolled in this study started HCQ treatment and had been receiving oral HCQ sulfate continuously for at least 3 months. There was no need for additional immunosuppressive treatments, including glucocorticoids, to any patient during the 3 months prior to starting HCQ because of sustained low disease activity in these patients. Immunological biomarkers, SELENA-SLEDAI and CLASI score were investigated in this study. Serum levels of S100A8 and S100A9 were measured at the time of HCQ administration as well as 3 or 6 months later using ELISA (CircuLex ELISA Kit, MBL). In addition, we investigate interferon- α . [Results] We enrolled 79 patients. 26 cases were sustained remission of LN patients. HCQ significantly lowered levels of S100A8 and S100A9. Elevated levels of S100A8 and S100A9 were seen in patients with LN and significantly lowered in LN patients regardless of sustained remission of LN. [Conclusions] HCQ lowered serum levels of S100 protein and might suppress disease activity in sustained remission of LN patients. We could define LN as complete remission by S100 proteins analysis.

W78-3

Research of each marker and free blys before and after administration of belimumab

Seiji Tanaka

Department of Pediatrics, Kurume University

Conflict of interest: None

[Object] We compare free blys and other marker in the acute period and revival and the maintenance period. [Methods] SLE patients from 16 years old to 21 years old. observation period 3 six months. We examine combination blys which soluble blys and sledai score and free fusibility blys which are not connected, the change in the stage of a disease and serum c3, c4, antids-dna antibody, b-cell number, the change of the memory b cells number. We perform sandwich elisa using blys and commercial antiblys antibody, and the measurement of free blys divides into free blys and combination type blys and compares it. [Results] As for the sledai score, two points accepted a point zero, ascent of c3 ($p=0.29$), ascent of c4 ($p=0.03$), an ascent of ds-dna ($p=0.53$) wbc ($p=0.71$) to two people in approximately blimmab use. We switch to balibmab solid-phase assay and enforce it again without being made solid-phase in the system of measurement using commercial blys. [Conclusions] We accepted improvement of c4 after balibmab use, but there was not the significant difference in c3. It is thought to be allowed to examine the dosage to the condition of a patient by the condition of a patient such as the drops of the complement at the time of the revival.

W78-4

The analysis of anti ds-DNA antibody evaluation between CLEIA and ELISA

Taichi Miyagi, Mikiya Kato, Risa Wakiya, Hiroshi Shimada, Syusaku Nakashima, Tomohiro Kameda, Hiroaki Dobashi
Kagawa University Hospital

Conflict of interest: None

[Object] ELISA system was used to evaluate serum anti-double stranded DNA antibody (ds-DNA ab) until 2017, and then it had changed into CLEIA system in our institution. After that changing, we experienced some cases which titer of ds-DNA ab had varied substantially. Therefore, we investigated the difference between CLEIA and ELISA. [Methods] We examined the SLE patients who had the same treatment within 6 months. We classified them into 3 groups according to the changes of ds-DNA ab titer between ELISA and CLEIA. Group A was increasing, B was decreasing, C was unchanged cases. We assessed dis-

ease activity of SLE by SELENA-SLEDAI (SLEDAI) and SLEDAI (-) which defined as exclude ds-DNA ab factor from SLEDAI. [Results] We could analyze 115 cases. Group A was 4, B was 27, and C was 84 cases. In group A, mean SLEDAI of 2 cases which had changed into positive was 20.50, and mean SLEDAI (-) was 18.50. In group B, mean SLEDAI of 18 cases which had changed into negative was 2.33, and mean SLEDAI (-) was 2.33. There exist 2 in latter 18 cases, who had high disease activity. They had the history of NPSLE. [Conclusions] The CLEIA was better than ELISA as for reflecting disease activity. However, it is necessary to pay much attention to the cases which ds-DNA ab dissociates from SLEDAI.

W78-5

Importance of serum phosphatidylserine-specific phospholipase A1 (PS-PLA1) as a novel biomarker of systemic lupus erythematosus (SLE)

Tetsuji Sawada¹, Harumi Shirai², Yukiko Iwasaki², Koichiro Tahara¹, Haeru Hayashi¹, Keishi Fujio²

¹Department of Rheumatology, Tokyo Medical University Hospital, ²Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo

Conflict of interest: None

[Object] To assess the utility of serum PS-PLA₁ in SLE diagnosis and disease activity monitoring. [Methods] We measured PS-PLA₁ using AIA-21 (Tosoh) in 146 patients (pts) with SLE (including 43 untreated pts), 80 disease control (35 active RA, 22 SSc, and 23 SS), and 237 healthy controls. [Results] PS-PLA₁ was significantly higher in SLE than in healthy controls and RA. Although PS-PLA₁ was significantly elevated in SSc and SS compared with healthy controls, PS-PLA₁ was significantly higher in untreated SLE than in healthy controls, treated SLE, and disease control. ROC analysis revealed that a cut-off value of 17.9 ng/mL distinguished untreated SLE from disease control (sensitivity 88% specificity 57%). SLEDAI was positively correlated with PS-PLA₁, anti-dsDNA Ab, and IgG, and inversely correlated with C3. PS-PLA₁ was significantly higher in SLE pts with high disease activity than in those with low disease activity. PS-PLA₁ decreased significantly in parallel with improvement of SLEDAI in 25 SLE pts whose paired serum samples were available pre- and post-treatment. [Conclusions] PS-PLA₁ is elevated in SLE in parallel with disease activity, suggesting that PS-PLA₁ may be a novel biological marker for SLE disease activity monitoring.

W78-6

Comparison of proposed ACR/EULAR new classification criteria for SLE with 1997 ACR and 2012 SLICC criteria

Hiroshi Doi¹, Takeshi Iwasaki¹, Yuya Tabuchi¹, Shuji Akizuki¹, Kosaku Murakami¹, Ran Nakashima¹, Motomu Hashimoto², Hajime Yoshifuji¹, Masao Tanaka², Wataru Yamamoto³, Koichiro Ohmura¹, Tsuneyo Mimori¹

¹Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ²Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ³Kurashiki Sweet Hospital

Conflict of interest: None

[Object] We aimed to examine the sensitivity of newly proposed ACR/EULAR criteria in Japanese patients and clarify the characteristics of patients who did not meet the new criteria. [Methods] We examined 319 SLE patients in Kyoto University Hospital whose clinical history and examination results were clearly described in charts. [Results] 313, 319, and 314 out of the 319 SLE patients met the 1997 ACR, 2012 SLICC, and new ACR/EULAR criteria, respectively, and their sensitivity was 98%, 100% and 98%, respectively. In the five patients who did not meet the new criteria, 3 were male, and ANA was <1:40 for 1 and 1:40 for 3 patients, whereas 1 patient showed ANA 1:160 but total score was only 9. The five patients' total score for 1997 ACR and 2012 SLICC criteria ranged from 4 to 8 (average 5) and from 6 to 8 (average 7.25), respectively. [Conclusions] Sensitivity of new classification criteria was reported to be 98% in Derivation cohort and 96% in Validation cohort, which was similar in our patients. 4 patients who did not meet new criteria due

to shortage of ANA titer satisfied both 1997 ACR and 2012 SLICC criteria and were clinically considered to be SLE. When new classification criteria were applied to diagnosis, careful consideration should be taken for patients with low ANA titer.

W79-1

Antiphospholipid antibody cross-reactive with DNA activates the TLR9 pathway leading to a thrombophilic state, which is suppressed by chloroquine

Tetsuo Kubota

Department of Immunopathology, Tokyo Medical and Dental University Graduate School of Medical and Dental Sciences, Tokyo, Japan

Conflict of interest: None

[Object] In the pathogenesis of antiphospholipid syndrome (APS), antiphospholipid antibodies (APAs) play a significant role by stimulating monocytes and vascular endothelial cells. This study aims to clarify how APAs activate the cells. [Methods] IgG monoclonal anti-CL- β 2-GPI antibody WB-6 was prepared from an (NZWxBXS)F1 mouse, and the specificity was tested by ELISA. PBMCs from healthy volunteers, monocytic leukemia cells THP-1, or vascular endothelial cells HUVECs were incubated with WB-6, and the effect of the antibody was estimated by fluorescence microscopy, flow cytometry, and measurement of cytokine expression. [Results] WB-6 was cross-reactive with DNA. Highly purified WB-6 without DNA contamination still bound to DNA. WB-6 entered monocytes, THP-1, and HUVECs, and the internalization was diminished by pretreatment of the cells with DNase I. WB-6 induced tissue factor expression in monocytes and THP-1, and this effect was suppressed by chloroquine. Culture supernatant of THP-1 incubated with WB-6 contained TNF- α , and this conditioned medium stimulated HUVECs to express ICAM-1 and VCAM-1. [Conclusions] APAs cross-reactive with DNA bind to cell surface DNA, enter living cells, and activate the TLR9 pathway, which may contribute to the thrombophilic state of APS.

W79-2

The Direct Effect of Anti-Sm Antibody on MMP-2 Up-regulation and claudin-5 degradation in Brain Endothelial Cells

Yoshiyuki Arinuma, Kunihiro Yamaoka

Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine

Conflict of interest: Yes

[Object] Breakdown of the blood-brain barrier (BBB) integrity is required for development of psychiatric manifestations in SLE. The aim of this study is to investigate the direct effect of anti-Sm antibody (Ab) on brain endothelium cells and the role in breakdown of BBB integrity. [Methods] A human brain hemangiosarcoma cell line was stimulated with monoclonal anti-Sm or anti-RNP Ab. Tight junction (TJ) composing protein, claudin-5 expression was measured by western blot. MMP-2 that is known to degrade TJ protein and claudin-5 mRNA were evaluated by q-PCR. [Results] Compared to control Ab, expression of claudin-5 protein was significantly reduced by anti-Sm Ab, and increased by anti-RNP Ab. Meanwhile, combinatory stimulation with anti-Sm Ab and anti-RNP Ab significantly reduced claudin-5 protein expression. Claudin-5 mRNA expression was increased by anti-RNP Ab, while anti-Sm Ab made no change. Interestingly, MMP-2 mRNA expression was significantly increased by anti-Sm Ab but not by anti-RNP Ab. [Conclusions] Depending on the notion of MMP2 on degradation of TJ protein and claudin-5 mRNA, anti-Sm Ab could directly affect brain endothelium cell through up-regulation of MMP-2 expression could cause degradation of claudin-5. On the other hand anti-RNP Ab could have a protective effect.

W79-3

Neuroinflammation as a potential target of neuropsychiatric systemic lupus erythematosus

Atsushi Nomura, Go Murayama, Asako Chiba, Sachiko Miyake

Department of Immunology, Juntendo University School of Medicine

Conflict of interest: None

Objective SLE causes disabling neuropsychiatric symptoms even in the quiescent phase. Innate immune-mediated inflammation has attracted attention as a pathogenic mechanism in neuropsychiatric diseases; therefore, we investigated the CNS of lupus-prone mice. Methods Fc γ RIIB^{-/-} *Yaa*, NZB/NZW, and MRL/lpr were used to analyze immunopathology in the CNS. The composition and activation status of immune cells in the CNS were analyzed by flow cytometry. Immunohistochemistry of brain sections and RNA-seq analysis of microglia were performed using Fc γ RIIB^{-/-} *Yaa* mice. Results Upregulation of MHC class I and PDCA1 were observed in microglia and CD11b⁺ myeloid cells, indicating they were activated in response to interferons (IFN). Microglial gene expression analysis revealed the upregulation of inflammation-related genes including *ApoE*, *Axl*, *Clec7a*, and *Itgax* as well as IFN responsive genes. Upregulated chemokine gene expressions including *Ccl5* and *Cxcl10* were concurrent with increased T cells and Ly6C^{lo} monocytes. Conclusion Microglia in lupus exhibit a unique phenotype characterized by up-regulated expressions of neurodegeneration-related genes and IFN responsive genes. Interaction with peripheral cells and brain resident cells was presumed to orchestrate neuroinflammation.

W79-4

Association of Soluble Programmed Death-ligand 1/2 and Interleukin 21 with Systemic Lupus Erythematosus

Shinya Hirahara, Yasuhiro Katsumata, Hidenaga Kawasumi, Akira Nishino, Masanori Hanaoka, Hirokazu Nishina, Yasushi Kawaguchi, Hisashi Yamanaka

Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] Programmed cell death protein 1 (PD-1) and PD-1 related molecules, which are expressed on T follicular helper cells, play a key role in pathology of systemic lupus erythematosus (SLE). We have reported that the serum levels of sPD-1 are higher in SLE patients and they are moderately correlated with the SLEDAI-2K scores and the anti-dsDNA antibody titers. We aimed to retrospectively evaluate the usefulness of soluble programmed death-ligand 1/2 (sPD-L1/L2) and IL-21 in SLE patients. [Methods] We measured the levels of sPD-L1/L2 and IL-21 by ELISA in sera of patients with SLE ($n = 73$) and systemic sclerosis (SSc), and healthy controls (HC), and compared them. We also analyzed the association of the levels of sPD-L1/L2, and IL-21 with clinical information and the serum sPD-1 levels in SLE patients. [Results] The levels of sPD-L2 in SLE patients with SLEDAI-2K ≥ 6 were significantly higher than those in SLE patients with SLEDAI-2K < 6 , SSc patients, and HC ($p < 0.05$). The levels of sPD-L2 were moderately correlated with the anti-dsDNA antibody titers, levels of C3 and C4, SLEDAI-2K, and serum sPD-1 levels. [Conclusions] The present study suggested an association of serum sPD-L2 with SLE and its disease activity and its usefulness as a diagnostic and activity biomarker for SLE.

W79-5

Expansion of Peripheral Helper T cells Associated with Disease Activity in Systemic Lupus Erythematosus

Ayako Makiyama^{1,2}, Asako Chiba¹, Go Murayama^{1,2}, Ken Yamaji², Naoto Tamura², Sachiko Miyake¹

¹Department of Immunology, Juntendo University School of Medicine,

²Department of Rheumatology, Juntendo University School of Medicine

Conflict of interest: None

[Object] To assess whether recently identified "peripheral helper" T (T_{PH}) cells are involved in the pathogenesis of systemic lupus erythematosus (SLE). [Methods] Peripheral blood mononuclear cells were obtained from patients with SLE and healthy subjects, and were analyzed by flow cytometry. We defined T_{PH} cells as memory CD4⁺T cells expressing PD-1^{hi} and lacking CXCR5. The frequency and activated status of T_{PH} cells were compared with B cell subsets and the disease activity. The cytokine production of T_{PH} cells was analyzed with intracellular staining. [Results] The frequency of T_{PH} cells was increased in SLE patients than

healthy controls. The T_{PH} cells had the capacity to produce IL-21. The proportion of activated T_{PH} cells was also elevated in SLE patients and was correlated with disease activity. The frequency of activated T_{PH} cells were correlated with that of plasmablasts and activated switched memory B cells. T_{PH1} (CXCR3⁺CCR6⁺T_{PH}) cells, that showed IFN- γ producing capacity, were increased in SLE patients and the frequency of activated T_{PH1} cells was positively correlated with that of plasmablasts. [Conclusions] As T_{PH} cells were associated with disease activity and B cell maturation in SLE, these cells may play an important role in lupus pathogenesis.

W79-6

DOCK8-Expressing CD4 T cell as Autoantibody-Inducing CD4 T (aiCD4 T) Cell That Causes Systemic Lupus Erythematosus (SLE): Proof of Concept of Self-Organized Criticality Theory as a Cause of SLE

Shunichi Shiozawa^{1,2}, Ken Tsumiyama¹, Keiichi Sakurai¹, Hidetoshi Kagawa³, Takashi Yamane⁴, Motohiro Oribe⁶, Koji Ishii⁷, Takahiko Horiuchi², Ryosuke Yoshihara⁵, Miki Murata⁵, Kazuko Shiozawa⁵
¹Institute for Rheumatic Diseases, ²Kyushu University Beppu Hospital, ³Himeji Red-Cross Hospital, ⁴Department of Rheumatology, Kakogawa City Central Hospital, ⁵Rheumatology & Collagen Disease Center, Hyogo Prefectural Kakogawa Medical Center, ⁶Oribe Rheumatology Clinic, ⁷Nephrology & Rheumatology, Oita University School of Medicine

Conflict of interest: None

[Object] To prove Self-Organized Criticality Theory where SLE develops as a natural consequence of routine but exaggerated immune response against antigen when stimulated maximally beyond immune system's self-organized criticality, we characterized the aiCD4 T cell. [Methods] DOCK8⁺ cell was identified by mass spectrometry of cell membrane and the *in vivo* transfer study. [Results] Transfer of DOCK8⁺ CD4 T cells into naïve mice induced autoantibodies including anti-dsDNA and anti-Sm antibodies and organ diseases such as WHO IV/V lupus nephritis, skin liquefaction degeneration, pericholangitis, pneumonitis, thyroiditis, perineuritis, panniculitis and splenic periarteriolar fibrosis with amyloid-like deposits, a classical Onion-skin lesion of SLE. Such manifestations subsided after anti-DOCK8 Ab therapy. The DOCK8⁺ CD4 T cell is a large lymphocyte with abundant ER and mitochondria, expressing ICOS, PD1, Ly6C and LFA1 but not CXCR5. The cell produced increased IFN γ , IL-4, IL-6, IL-17, IL-21 and IL-22, and its TCR repertoire was highly deviated. [Conclusions] The DOCK8-expressing CD4 T cell is the aiCD4 T cell that emerges as a natural consequence of exaggerated immune response against antigen when stimulated maximally beyond immune system's self-organized criticality, and causes SLE.

International Concurrent Workshop

ICW1-1

The genetic and clinical prediction models for efficacy and hepatotoxicity of methotrexate in patients with rheumatoid arthritis: a multi-center cohort study

Akira Onishi¹, Miwa Nishida², Keisuke Nishimura³, Kenta Misaki⁴, Yumiko Nobuhara⁵, Saori Hatachi², Takashi Nakazawa⁵, Goh Tsuji⁶, Akio Morinobu¹, Shunichi Kumagai^{2,7}

¹Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, ²Center for Rheumatic Diseases, Shinko Hospital, ³Department of Endocrinology and Rheumatology, Kurashiki Central Hospital, ⁴Department of Rheumatology, Kita-Harima Medical Center, ⁵Department of Rheumatology, Osaka Saiseikai Nakatsu Hospital, ⁶Tsuji Rheumatology Clinic, ⁷Shinko Institute for Medical Research

Conflict of interest: None

[Objectives] To develop combined genetic and clinical models to predict the efficacy and hepatotoxicity of MTX. [Methods] Patients with RA under the treatment of MTX according to Japanese guideline for the management of RA with MTX were enrolled. To predict the efficacy and hepatotoxicity, 1,971 polymorphisms of 246 enzymes/transporters potentially relevant to pharmacokinetics and pharmacodynamics of MTX were measured by the DMET microarray (Affymetrix Inc.) and direct-sequencing method and clinical variables at baseline were collected. The EU-LAR-CRP response criteria was used to classify patients with RA as responders (good response) and non-responders (moderate or no response). Hepatotoxicity was defined as either serum AST or ALT levels higher than 1.5 times the upper limit of the normal range. [Results] A total of 166 patients with RA was included from 4 institutes. The median age was 61.5 years with 81.3% of women. For efficacy, genetic prediction model using 7 SNPs showed area under the curve of ROC (AUC) was 0.822 with sensitivity of 74.3% and specificity of 76.8%, while combined clinical and genetic model indicated AUC was 0.844 with sensitivity of 81.5% and specificity of 76.9%. By incorporating clinical variables into the genetic model, overall category-free net reclassification improvement (NRI) was 0.700 ($P < 0.0001$) and overall integrated discrimination improvement (IDI) was 0.089 ($P = 0.0005$). For hepatotoxicity, genetic prediction model using 7 SNPs showed AUC was 0.783 with sensitivity of 70.0% and specificity of 80.0%, while combined clinical and genetic model indicated AUC was 0.906 with sensitivity of 85.1% and specificity of 87.8%. Overall category-free NRI was 1.122 ($P < 0.0001$) and overall IDI was 0.279 ($P < 0.0001$). [Conclusion] Genetic and clinical models showed higher predictive accuracy for both efficacy and hepatotoxicity of MTX. These models should be validated with a larger scale of prospective study.

ICW1-2

A comprehensive study of splicing quantitative trait loci (sQTL) effects in various immune cell subsets in peripheral blood mononuclear cells (PBMCs) of systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) patients

Hiroaki Hatano¹, Mineto Ota^{1,2}, Yusuke Takeshima^{1,2}, Yukiko Iwasaki¹, Yasuo Nagafuchi¹, Yuta Kochi^{1,3}, Hirofumi Shoda¹, Tomohisa Okamura^{1,2}, Keishi Fujio¹, Kazuhiko Yamamoto³

¹Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, ²Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, ³Laboratory for Autoimmune Diseases, Center for Integrative Medical Sciences, RIKEN, Kanagawa, Japan

Conflict of interest: None

[Object] Recently, genome-wide association studies (GWAS) have identified many loci associated with autoimmune diseases, such as SLE and RA. However, the effects of GWAS single nucleotide polymorphism (SNPs) on splicing isoforms in various subsets of immune cells in PBMCs have not been fully investigated. [Methods] We previously conducted sorting and RNA sequencing of 21 immune cell subsets in PBMC from 49 SLE and 30 RA patients and 36 healthy volunteers and also got their genotyping data from whole blood. Here, we analyzed cis-acting

sQTL effects of RA and SLE GWAS SNPs in this dataset. [Results] Many transcript-SNP-subset pairs were detected after FDR multiple testing adjustment. We confirmed some sQTL effects on the transcripts of the genes (e.g. NADSYN1, UBASH3A, SNRPC...) were shared in most cell subsets expressing the genes. On the other hand, several sQTL effects were observed only in parts of cell subsets. [Conclusions] Our results suggest some GWAS SNPs are associated with diseases through alternative splicing and such sQTL effects work in parts of immune cell subsets of PBMC.

ICW1-3

A phenome-wide association study of the MHC region in 166,190 Japanese using NGS-based classical and non-classical HLA imputation

Yukinori Okada^{1,2}, Saori Sakaue^{1,3}

¹Department of Statistical Genetics, Osaka University Graduate School of Medicine, ²Department of Statistical Immunology, IFReC, Osaka University, ³Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo

Conflict of interest: None

[Object] The major histocompatibility complex (MHC) region at chromosome 6 confers genetic risk on a variety of human complex traits, while detailed fine-mapping of the causal genetic variants and genes has yet to be elucidated. In this study, [Methods] We conducted NGS-based genotyping of the 33 human leukocyte antigen (HLA) genes of the Japanese population ($n = 1,120$), providing high resolution allele catalogue up to 6-digit HLA alleles of both classical and non-classical HLA genes. Together with population-specific deep whole-genome sequencing (WGS) data of Japanese ($n = 1,276$), we conducted NGS-based HLA, SNV, and Indel imputation of the large-scale genome-wide association (GWAS) genotype data of Japanese from BioBank Japan Project, a nation-wide hospital-based cohort of Japan ($n = 166,190$). Using imputed genotype data, we conducted a phenome-wide association study (PheWAS) assessing 106 clinical phenotypes including human complex diseases (e.g., rheumatoid arthritis, Graves' disease, type 1 diabetes, asthma, atopic dermatitis, and others), as well as anthropometric, biochemical, and hematological quantitative traits. [Results] The PheWAS identified significant genotype-phenotype associations across 52 phenotypes. Fine-mapping within the MHC region revealed multiple association patterns conferring independent risks from the classical HLA genes including those represented as non-classical HLA gene variants, non-HLA variants within MHC, and long-range haplotype spanning the entire MHC region. Novel MHC associations of the traits were also identified (pollinosis, hyperlipidemia, myocardial infarction, stable angina, type 2 diabetes, liver cancer, liver cirrhosis, and nephrotic syndrome). MHC region-wide heritability estimates and genetic correlation network analysis elucidated polygenic architecture shared across the phenotypes. [Conclusions] This study should contribute to our understanding of genetic and phenotypic landscape of MHC.

ICW1-4

Immune cell profiling of rheumatoid arthritis identified disease activity and treatment resistance related gene networks

Saeko Yamada¹, Yasuo Nagafuchi¹, Mineto Ota¹, Yusuke Takeshima¹, Hiroaki Hatano¹, Yukiko Iwasaki¹, Shuji Sumitomo¹, Tomohisa Okamura¹, Hirofumi Shoda¹, Kazuhiko Yamamoto², Keishi Fujio¹

¹Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, ²Laboratory for Autoimmune Diseases, Center for Integrative Medical Sciences, RIKEN

Conflict of interest: Yes

[Object] Rheumatoid arthritis (RA) is an autoimmune disease characterized by inflammatory synovitis and destruction of joint cartilage. In this study, we performed transcriptome analyses of cell subsets of peripheral blood taken from RA patients and tried to identify gene module networks closely associated with disease activity and treatment resistance. [Methods] Peripheral blood mononuclear cells were obtained from 37 healthy donors and 28 RA patients, who were just before the induction of bDMARDs or tsDMARDs. We isolated 16 cell subsets by fluorescence-

activated cell sorting (FACS), and RNA sequencing was performed. 16 out of 28 RA patients were reanalyzed 6 months after the induction of treatment. A network analysis WGCNA and differential expression analysis were performed for each subset. The expression of most highly connected "hub genes" was compared between before and after the treatment. [Results] WGCNA of the pre-treated patients revealed that a gene module including *STAT5B* and *CTBP1* in neutrophils correlated most to the DAS28-ESR disease activity (Spearman's rho (r) = 0.78, $p = 5e-04$). bDMARDs or tsDMARDs treatment decreased the expression of 32% (12/37) of the hub genes (FDR < 0.20). It is also revealed that the treatment resistance (low decrease of DAS28-ESR) was correlated most to a module containing NF κ B signaling genes in plasmacytoid dendritic cells (pDCs) and plasmablast subset ($r = -0.61$ and -0.54 , $p < 0.05$). Almost none of the hub genes in this module changed the expression after treatment (0% or 2% FDR < 0.20). [Conclusions] In this study, we identified candidate subset-gene networks that are independently related to disease activity or treatment resistance. Enhanced NF κ B signaling in pDCs and plasmablast could be a biomarker for treatment resistance and a novel therapeutic target for treatment-resistant RA.

ICW1-5

Upregulation of LINC00487 in Peripheral B cell Subsets Associated with Disease Activity among Patients with Primary Sjögren's Syndrome

Jun Inamo¹, Katsuya Suzuki¹, Masaru Takeshita¹, Yoshiaki Kassai², Maiko Takiguchi², Rina Kurisu², Yuumi Okuzono², Tsutomu Takeuchi¹

¹Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, ²Immunology Unit, Pharmaceutical Research Division, Takeda Pharmaceutical Company Limited

Conflict of interest: Yes

[Object] Although B cells are considered to play an important role in the pathogenesis of primary Sjögren's syndrome (pSS), the mechanism is still unclear. Here, we investigated the differential gene expression of peripheral B cell subsets in pSS patients. [Methods] We enrolled pSS patients ($n=6$) and healthy controls (HC) ($n=6$). Peripheral B cells were separated into 4 subsets: CD38⁻IgD⁻, CD38⁺IgD⁻, CD38^{high}IgD⁺ and CD38⁺IgD⁻. Total RNA was extracted and gene expression was measured using the Human Genome U133 Plus 2.0 Array (Affymetrix). [Results] After excluding HLA and interferon signature genes, LINC00487 was the most upregulated gene in all B cell subsets. Fold changes in CD38⁻IgD⁻, CD38⁺IgD⁻, CD38^{high}IgD⁺ and CD38⁺IgD⁻ were 8.4 ($p=0.038$), 11.3 ($p=0.014$), 8.5 ($p=0.089$) and 6.37 ($p=0.078$), respectively. In addition, the normalized intensity value of LINC00487 was significantly correlated with disease activity score in all pSS B cell subsets, namely CD38⁻IgD⁻ ($r=0.96$, $p=0.002$), CD38⁺IgD⁻ ($r=0.90$, $p=0.015$), CD38^{high}IgD⁺ ($r=0.81$, $p=0.049$) and CD38⁺IgD⁻ ($r=0.96$, $p=0.003$). [Conclusions] LINC00487 was upregulated in all pSS B cell subsets and correlated with disease activity. These results may suggest that long non-coding RNA contributes to B cell dysregulation in patients with pSS.

ICW1-6

SH3BP2 gain-of-function mutation ameliorates lupus in B6.MRL-Fas^{lpr} mice

Akiko Nagasu¹, Tomoyuki Mukai¹, Masanori Iseki², Hajime Nagasu³, Kyoko Kawahara¹, Shoko Tsuji¹, Shunichi Fujita¹, Naoki Kashiwara³, Katsuhiko Ishihara², Yoshitaka Morita¹

¹Department of Rheumatology, Kawasaki Medical School, Kurashiki, Japan, ²Department of Immunology and Molecular Genetics, Kawasaki Medical School, Kurashiki, Japan, ³Department of Nephrology and Hypertension, Kawasaki Medical School, Kurashiki, Japan

Conflict of interest: Yes

[Object] SH3BP2 (Src homology domain 3 binding protein 2) is an adaptor protein, which is dominantly expressed in immune cells, and regulates intracellular signaling pathways. We have previously reported that SH3BP2 regulates macrophage activation, TNF production, and autoantibody production in a murine arthritis model. To further investigate the role of SH3BP2 in other autoimmune diseases, we here tested a murine lupus model using SH3BP2 mutant mice. [Methods] SH3BP2 gain-of-

function mutant (P416R knockin; Sh3bp2^{KI/+}) mice and lupus-prone; B6.MRL-Fas^{lpr} mice were crossed to yield the double mutant (KI/+ Fas^{lpr}) mice. Serum anti-dsDNA antibody levels and a histopathological index of glomerulosclerosis were assessed at 48 weeks of age. B and T cell subsets in the lymph nodes were analyzed by flow cytometry. Splenic B cell proliferation was determined by CFSE assay. TNF mRNA expression in lymph nodes were analyzed by real-time PCR. [Results] SH3BP2 gain-of-function mutation alleviates lupus phenotypes, as shown by an increased survival rate, reduced proteinuria, and improved glomerulosclerosis. Serum anti-dsDNA antibody levels were significantly reduced in the KI/+ Fas^{lpr} mice (90.5% decrease compared to those in Fas^{lpr} mice). B220⁺CD4⁻CD8⁻ double-negative T (DNT) cell population, which is known as characteristic cells in the Fas^{lpr} mice, were decreased in the lymph nodes of the KI/+ Fas^{lpr} mice. Proliferation capacities of splenic B cells were comparable between Fas^{lpr} and KI/+ Fas^{lpr} cells. TNF mRNA expression in lymph nodes tended to increase in the KI/+ Fas^{lpr} mice compared to that in the Fas^{lpr} mice. [Conclusions] SH3BP2 gain-of-function mutation ameliorated clinical and immunological phenotypes of the lupus-prone mice. Elevated TNF production might compensate the impaired apoptosis of the DNT cells in the KI/+ Fas^{lpr} mice. Further analyses are required to reveal the immunoregulatory roles of SH3BP2.

ICW2-1

Impact of switching oral bisphosphonates to denosumab or daily teriparatide on the progression of radiographic joint destruction in patients with biologic-naïve rheumatoid arthritis

Kosuke Ebina, Makoto Hirao, Yuki Etani, Akira Miyama, Kenji Takami, Hideki Yoshikawa

Department of Orthopaedic Surgery, Osaka University, Graduate School of Medicine, Osaka, Japan

Conflict of interest: Yes

[Object] The aim of this study was to clarify the effects of switching oral bisphosphonates (BPs) to daily teriparatide (TPTD) or denosumab (DMAb) on the radiographic joint destruction in female, biologic-naïve, RA patients. [Methods] 155 patients were allocated depending on each physician's decision, to (1) BP-continue group (n=63), (2) switch-to-TPTD group (n=31), or (3) switch-to-DMAb group (n=61). Ninety patients (n=30 for each group; mean age 68.2 years, 96.7% postmenopausal, DAS28-CRP 2.4, methotrexate treatment 81.1%, prednisolone treatment 68.9%, lumbar T-score -2.0, prior BP treatment 44.8 months, TRACP-5b 286.4 (mU/dl), and modified total Sharp score (mTSS) 87.0) were retrospectively selected using propensity score to match the baseline clinical backgrounds. The primary endpoint was to clarify the change of the mTSS from baseline to 12 months (Δ 12M mTSS). [Results] After 12 months, the mean changes of the modified Sharp erosion score were significantly lower in the switch-to-DMAb group (0.2 ± 0.1 ; mean \pm standard error) than in the switch-to-TPTD group (1.3 ± 0.5 ; $P < 0.05$), and mTSS was significantly lower in the switch-to-DMAb group (0.3 ± 0.2) than in the BP-continue group (1.0 ± 0.3 ; $P < 0.05$) and the switch-to-TPTD group (1.7 ± 0.6 ; $P < 0.05$). Patients with Δ 12M mTSS ≥ 3 (Clinically relevant radiological progression) (%) were BP (10.0), TPTD (20.0), and DMAB (3.3), respectively (TPTD v.s. DMAB; $P < 0.05$). The percent change of TRACP-5b after 6 months (%) (Δ 6M TRACP-5b) were BP (-4.6), TPTD (64.9), and DMAB (-29.0), respectively. Among the factors which significantly correlated with Δ 12M mTSS (baseline DAS28-CRP, ACPA positivity, and Δ 6M TRACP-5b), logistic regression analysis revealed that Δ 6M TRACP-5b was a remaining significant factor associated with Δ 12M mTSS ($\beta=0.30$, 95% CI=0.002-0.016; $P < 0.01$). [Conclusions] The change of systemic bone turnover induced by osteoporosis agents may affect local joint destruction besides of inflammatory state.

ICW2-2

A prospective observational study on the incidence of beaking, a sign of atypical femoral fractures, in patients with rheumatoid arthritis

Chinatsu Takai¹, Hiroe Sato², Naoki Kondo³, Yoichi Kurosawa¹, Eriko Hasegawa¹, Shinji Taniguchi¹, Daisuke Kobayashi^{1,4}, Asami Abe¹, Satoshi Ito¹, Kiyoshi Nakazono¹, Akira Murasawa¹, Naoto Endo³, Ichiei Narita⁴, Hajime Ishikawa¹

¹Niigata Rheumatic Center, Shibata, Niigata, Japan, ²Niigata University Health Administration Center, Niigata, Japan, ³Division of Orthopedic

Surgery, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan, ⁴Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

Conflict of interest: None

[Object] The incidence of thickening of the lateral cortex of femora termed "beaking" is known to precede atypical femoral fracture (AFF). It is reported that beaking was detected in 8-10% of patients with autoimmune diseases taking bisphosphonates and glucocorticoid (GC), and bone absorption inhibitor and GC are generally considered as risk factors of AFF. However, the incidence of beaking in patients with rheumatoid arthritis (RA) is unknown. [Methods] A total of 209 patients with RA (female 78.9%, median age 67 years old, median disease duration 11 years, GC use 74.6% and bone resorption inhibitor use 67.5%) who were underwent anterior-posterior X-rays and dual-energy X-ray absorptiometry (DXA) at recruitment and at 1 year were enrolled. Focal lateral cortical thickening in femoral X-rays was defined as beaking. Statistical analyses were performed using Fisher's exact test and Mann-Whitney U test. [Results] Beaking was detected in 3 patients (1.4%) at recruitment and its incidence was increased to 6 patients (2.9%) at 1 year. Five of them were using bone absorption inhibitor (alendronate, 3; minodronate, 1; denosumab, 1) and 4 were taking GC. The significant higher incidence of beaking was found in patients taking more than 5 mg daily dose of prednisolone both at recruitment and at 1 year (4/47 patients vs. 2/162 patients, $p=0.024$, 4/50 patients vs. 2/159 patients, $p=0.031$), in patients who had received GC continuously more than 7 years (5/85 patients vs 1/124 patients, $p=0.042$), and in patients who received alendronate at recruitment (3/27 patients vs 3/182 patients, $p=0.030$). No significant difference was detected in the past history of bone resorption inhibitor use, duration of bone resorption inhibitor treatment or T-score of femoral neck measured by DXA. [Conclusions] This is the first report of prospective study about the incidence of beaking in patients with RA. Long-term or higher-dose use of GC could be risk factors in patients with RA.

ICW2-3

Five-year follow-up of beaking and osteoporosis in patients with autoimmune diseases treated with prednisolone and bisphosphonates

Hiroe Sato^{1,3}, Naoki Kondo², Naoto Endo², Shunsuke Sakai³, Sayuri Takamura³, Ayako Wakamatsu³, Daisuke Kobayashi³, Takeshi Nakatsue³, Yoko Wada³, Takeshi Kuroda¹, Masaaki Nakano⁴, Ichiei Narita³

¹Health Administration Center, Niigata University, ²Division of Orthopedic Surgery, Niigata University Graduate School of Medical and Dental Sciences, ³Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences, ⁴School of Health Sciences, Faculty of Medicine, Niigata University

Conflict of interest: None

[Object] Beaking is a localized femoral reaction that can lead to an atypical femoral fracture (AFF). Previously, we reported a high frequency of beaking in patients with autoimmune diseases treated with prednisolone (PSL) and bisphosphonates (BP). Here, we report 5-year follow-up data and retrospectively analyze the influence of the discontinuation of anti-resorption drugs on osteoporosis. [Methods] The study initially enrolled 125 patients with autoimmune diseases taking BP and PSL and 100 patients were re-examined 5 years later. The incidence of beaking was examined by femoral X-rays. Bone metabolic markers and bone mineral density (BMD) were compared between the groups in which anti-resorption drugs were discontinued and continued. Statistical analyses were performed using the *t*-test. [Results] Beaking was observed in 10 of 125 patients at recruitment and in 18 of 100 patients at 5 years. Complete AFF occurred in one patient. The BP was discontinued in 31 patients and the most frequent reason was beaking. Four were changed to denosumab and five were given teriparatide. At the 5-year follow-up, 27 patients were not taking anti-resorption drugs (discontinued group) and no clinically obvious osteoporotic fractures were seen after discontinuation. The annual change in BMD did not differ between the discontinued and continued groups. The serum NTx concentration was elevated at follow-up in both groups (discontinued vs. continued: from 9.6 ± 1.7 to 12.5 ± 2.9 , $p < 0.001$ vs. from 11.0 ± 4.3 to 13.6 ± 9.0 nmolBCE/L, $p=0.037$). Urine NTx was elevated only in the discontinued group (from 109.5 ± 87.8 to

165.6±121.3, $p=0.03$ vs. from 141.7±140.8 to 164.2±125.0 nmolBCE/nmol-Cr, $p=0.332$). The bone specific alkaline phosphatase concentration did not change significantly in either group. [Conclusions] The incidence of beaking was increased at 5 years in patients taking PSL and BP. Discontinuation of the anti-resorption drugs did not worsen the BMD and bone metabolic markers obviously.

ICW2-4

E3-Ubiquitin Ligase RNF146 links Bone to Energy Metabolism through regulation of the RUNX2 Transcriptional Activity controlled by the Wnt-FGF18-TAZ Axis

Yoshinori Matsumoto^{1,2}, Ken-ei Sada¹, Jun Wada¹

¹Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ²Princess Margaret Cancer Center, University of Toronto, Canada

Conflict of interest: None

[Object] Bone undergoes continuous remodeling equally regulated by osteoblast-mediated bone formation and osteoclast-mediated bone resorption. RUNX2, the osteoblastogenic master transcription factor, forms the critical complex with the transcriptional coactivator TAZ for osteoblast differentiation and skeletal formation. Here we uncover a genetic evidence showing that the E3-ubiquitin ligase RNF146 links bone to energy metabolism through regulation of the RUNX2-TAZ transcriptional activity. [Methods] We generated *Rnf146* conditional knockout mice (*Rnf146^{fl/fl} Osterix-Cre*) to examine the *in vivo* bone metabolism in the absence of RNF146 in osteoblasts. Micro-CT, histomorphometric analysis, ISH, IHC, Co-IP, ChIP, promoter assay, BrdU assay, ubiquitin/proliferation/differentiation assay, glucose tolerance test and ELISA were performed to investigate the molecular mechanisms in this study. [Results] We found that *Rnf146^{fl/fl} Osterix-Cre* shows phenotypic similarities to Cleidocranial Dysplasia, an autosomal dominant human disorder characterized by abnormal bone development due to defective osteoblastogenesis. Loss of RNF146 stabilized its substrate AXIN1, leading to impairment of WNT3a-induced β -catenin activation and reduced Fgf18 expression in osteoblasts. We show that FGF18 transcriptionally induces TAZ expression, leading to the complex formation with RUNX2 and another transcription factor TEAD for osteoblast differentiation and proliferation, respectively. Finally, these mice had increased fat stores and were glucose intolerant with severe osteopenia due to defective osteoblastogenesis and subsequent impaired osteocalcin production. [Conclusions] Our observation that RNF146 regulates bone and energy metabolism through regulation of the RUNX2-TAZ transcriptional activity could expand the concept that RNF146 links bone loss to abnormal glucose tolerance through reduced osteocalcin production by osteoblasts in patients with rheumatic diseases treated by glucocorticoids.

ICW2-5

Functional differences between osteoclasts and osteoclast-like cells from peripheral blood mononuclear cells in patients with rheumatoid arthritis

Kazuhiro Yokota¹, Shinya Tanaka², Kojiro Sato¹, Yoshimi Aizaki¹, Noritsune Kozu³, Hiromi Oda², Toshihide Mimura¹

¹Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University, ²Department of Orthopaedic Surgery, Saitama Medical University, ³Kozu Orthopaedic Clinic

Conflict of interest: None

[Object] Osteoclasts (OCs) are giant multinucleated cells formed from precursors of the monocyte/macrophage lineage, which play an important role of bone destruction in rheumatoid arthritis (RA). Previously, we reported that osteoclast-like cells (OLCs) are differentiated from mouse bone marrow macrophages stimulated with TNF α and IL-6, which have a bone resorption activity both *in vitro* and *in vivo*. The present study investigates functional differences between OCs and OLCs in peripheral blood mononuclear cells (PBMCs) from patients with RA and healthy controls (HCs). [Methods] PBMCs and CD14⁺ monocytes from 9 RA patients and/or HCs were stimulated with RANKL or TNF α and IL-6. The number of tartrate-resistant acid phosphatase-positive multinucle-

ated cells (OCs/OLCs) and bone resorption were assessed. The relationship between the number of OCs/OLCs and the modified total Sharp score or systemic bone mineral density (BMD) was also examined. [Results] The number of OCs and OLCs from PBMCs in RA patients was significantly increased compared with that in HCs (RA OCs 53.2±16.4 vs. HCs OCs 7.9±3.4, $p<0.01$; RA OLCs 19.6±4.2 vs. HCs OLCs 1.8±0.9, $p<0.01$). These cells showed bone resorption activity on dentin slices. Moreover, they showed significantly increased expression of *cathepsin K* mRNA compared with osteoclast precursors (OCPs) (OCs 9.4±3.5-fold, OLCs 2.3±0.5-fold vs. OCPs 1.0±0.0-fold, $p<0.01$, respectively). The number of OCs significantly negatively correlated with systemic BMD in RA patients ($r=-0.67$, $p<0.05$), while the number of OLCs significantly positively correlated with the modified total Sharp erosion score ($r=0.79$, $p<0.05$). [Conclusions] Our results demonstrated that PBMCs of patients with RA showed higher OC/OLC differentiation potential than that of HCs. Further, PBMCs-derived OLC bone resorption activity could likely play a potential role in the bone destruction in RA patients. OLCs could form a subpopulation of OCs, possibly different from conventional OCs.

ICW2-6

WW domain-containing protein 2 (Wwp2) maintains cartilage homeostasis in coordination with miR-140

Sho Mokuda^{1,2}, Merissa Olmer², Martin K Lotz², Eiji Sugiyama¹, Hiroshi Asahara^{2,3}

¹Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan, ²Department of Molecular Medicine, The Scripps Research Institute, La Jolla, CA, USA, ³Department of Systems BioMedicine, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan

Conflict of interest: None

[Object] The *Wwp2* gene encoding WW domain-containing protein 2 (Wwp2), which belongs to the HECT-type E3 ubiquitin ligase family, also encodes miR-140 generated from intron of its pre-mRNAs. Wwp2 is abundantly expressed in articular cartilage; however, its function remains unclear. We investigated the function of Wwp2 for cartilage homeostasis and the therapeutic potential of Wwp2 replacement against cartilage defects caused by arthritis. [Methods] We detected the expression of human WWP2 and mouse Wwp2 in damaged articular cartilage and investigated its contribution in cartilage homeostasis using Wwp2 knockout mouse and Wwp2-C838A enzyme dead mouse models generated with CRISPR/Cas9 system. We also examined the effect of *in vitro*-transcribed (IVT) Wwp2 mRNA in experimental osteoarthritis (OA) mouse model. The targets of Wwp2 and its cooperative function with miR-140 were elucidated using dual treatment with IVT Wwp2 mRNA/miR-140 mimic and integrated ChIP-seq/TargetScan database search. [Results] Human WWP2 and mouse Wwp2 protein expression levels were decreased in OA cartilages compared to healthy controls. Both Wwp2 knockout mouse and Wwp2-C838A enzyme-inactivated mouse exhibited aggravated cartilage damage. IVT Wwp2 mRNA injection into mouse joints reduced the severity of experimental OA. We also identified Runx2 as a Wwp2 substrate via Runx2 poly-ubiquitination and degradation. Dual treatment with IVT Wwp2 mRNA/miR-140 mimic and integrated ChIP-seq/TargetScan database analysis revealed that Wwp2 and miR-140 cooperatively regulate several genes such as *Adamts5*, *Gli3*, *Bmp2k*. [Conclusions] We propose that Wwp2 has a role in protecting cartilage from arthritis by suppressing Runx2-induced genes, especially *Adamts5*, via Runx2 poly-ubiquitination and degradation. The overlapping targets of the newly identified Wwp2-Runx2 pathway and miR-140 suggest that products from the *Wwp2* locus cooperatively regulate several cartilage-related genes at pre- and post-transcriptional stages.

ICW3-1

Risk assessment and long-term prognosis of patients with SLE-associated pulmonary arterial hypertension: A multi-center cohort study in China

Junyan Qian¹, Mengtao Li¹, Qian Wang¹, Jiuliang Zhao¹, Zhuang Tian², Wei Wei³, Xiao Zhang⁴, Xiaoxia Zuo⁵, Miaojia Zhang⁶, Ping Zhu⁷, Shuang Ye⁸, Wei Zhang⁸, Yi Zheng⁹, Wufang Qi¹⁰, Yang Li¹¹, Zhuoli Zhang¹², Feng Ding¹³, Jieruo Gu¹⁴, Yi Liu¹⁵, Xiaofeng Zeng¹

¹Department of Rheumatology, Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Science, Key Laboratory of Rheumatology and Clinical Immunology, Ministry of Education, Beijing, China, ²Department of Cardiology, Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Science, Beijing, China, ³Department of Rheumatology, the General Hospital of Tianjin Medical University, Tianjin, China, ⁴Department of Rheumatology, Guangdong Provincial People Hospital, Guangzhou, China, ⁵Department of Rheumatology, Xiangya Hospital, Central South University, Changsha, China, ⁶Department of Rheumatology, Jiangsu Provincial People Hospital, Nanjing, China, ⁷Department of Rheumatology, Xijing Hospital Affiliated to the Fourth Military Medical University, Xian, China, ⁸Department of Rheumatology, Ren Ji Hospital South Campus, Shanghai Jiao Tong University, Shanghai, China, ⁹Department of Rheumatology, Beijing Chao-Yang Hospital Affiliated to Capital Medical University, Beijing, China, ¹⁰Department of Rheumatology, Tianjin First Central Hospital, Tianjin, China, ¹¹Department of Rheumatology, the Second Affiliated Hospital of Harbin Medical University, Harbin, China, ¹²Department of Rheumatology, Peking University First Hospital, Beijing, China, ¹³Department of Rheumatology, Qilu Hospital of Shandong University, Jinan, China, ¹⁴Department of Rheumatology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China, ¹⁵Department of Rheumatology and Immunology, West China Hospital, Sichuan University, Chengdu, China

Conflict of interest: None

Objective: This study aimed to investigate the prognostic value of a multidimensional risk assessment in SLE-associated pulmonary arterial hypertension (PAH). **Methods:** This study involved fourteen high ranked rheumatology centers in China. All SLE patients were fulfilled the 1997 revised ACR criteria. PAH was diagnosed based on ESC/ERS guidelines by right heart catheterization. Baseline characteristics were collected. Patients underwent regular follow-up visits. The outcome was all-cause mortality. Two different methods of risk categorization, including low-risk criteria number of none to 4 and mean risk score of 1 (low-risk), 2 (intermediate-risk) or 3 (high-risk) based on the PAH risk categorization, were applied based on baseline data. According to first follow-up data, patients were further divided into increased risk, remained risk and decreased risk group. Kaplan-Meier survival curves and Cox analysis were conducted based on baseline risk categorizations and follow-up risk changes. **Results:** 282 patients were enrolled. The 5-year survival of patients categorized into none, 1, 2, 3 and 4 low risk criteria group were 42.7%, 64.8%, 86.1%, 90.2% and 91.7%, respectively (HR=0.59, 95% CI 0.44-0.78, $p<0.001$). When categorized according to the mean risk score at baseline, the 5-year survival of patients in low, intermediate and high-risk group were 92.3%, 60.4% and 50.0%, respectively (Log-rank, $p=0.001$). At first follow-up visit, 51 patients remained in the same risk group, 77 patients improved to lower risk group and 19 patients worsened into higher risk group. The 5-year survival of these three groups of patients were 65.4%, 88.1% and 23.8% respectively (log-rank, $p<0.001$). **Conclusion:** Our study, for the first time, validated the prognostic value of risk stratification strategy at baseline and follow-up visit in patients with SLE-associated PAH. Improving to low-risk group can be a future treatment target for SLE-associated PAH patients in clinical practice.

ICW3-2

The clinical feature of late-onset systemic lupus erythematosus: The LUNA registry study

Natsuki Sakurai¹, Ryusuke Yoshimi¹, Chiharu Hidekawa¹, Masaki Mitsuhashi¹, Yumiko Sugiyama², Yosuke Kunishita¹, Daiga Kishimoto¹, Yuki Iizuka¹, Takaaki Komiya¹, Hideto Nagai¹, Naoki Hamada¹, Naomi Tsuchida¹, Yutaro Soejima¹, Reikou Kamiyama¹, Kouji Kobayashi², Yukiko Asami¹, Yohei Kirino¹, Nobuyuki Yajima³, Ken-ei Sada⁴, Kunihiro Ichinose⁵, Shigeru Ohno², Hideaki Nakajima¹

¹Department of Hematology and Clinical Immunology, Yokohama City University School of Medicine, ²Center for Rheumatic Disease, Yokohama City University Medical Center, ³Division of Rheumatology, Department of Medicine, Showa University School of Medicine, ⁴Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ⁵Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: None

[Object] Late-onset systemic lupus erythematosus (SLE) has been considered to have the characteristics of atypical manifestations. In our previous single-center cross-sectional study, vasculitis occurred more frequently at onset, and immunosuppressants were less used as compared to early-onset SLE. Here we assessed the characteristic features of late-onset SLE using the multicenter database. [Methods] We collected demographic, clinical and laboratory data from LUNA registry, which is the integrated SLE registry by 6 facilities. The registered patients, who met the 1997 American College of Rheumatology criteria for SLE, were included in the study. We compared the data from patients with late-onset SLE (≥ 50 years old at onset; LO group) with those from patients with early-onset SLE (< 50 years old at onset; EO group). [Results] Among 559 patients who were enrolled, 98 and 461 belonged to LO and EO groups, respectively. There was no significant difference in male to female ratio and glucocorticoid usage between LO and EO groups (0.20 vs 0.13, $p = 0.17$, and prednisolone 6.6 ± 8.8 vs 7.0 ± 6.7 mg/day, $p = 0.59$, respectively). Immunosuppressants had been less used in LO group as compared to EO group (71.4% vs 80.6%, $p = 0.042$). Although the usage rates of cyclophosphamide and azathioprine showed no differences between the groups, mycophenolate mofetil (8.2% vs 18.7%, $p = 0.011$), tacrolimus (30.6% vs 43.6%, $p = 0.018$), rituximab (1.0% vs 6.1%, $p = 0.043$) were less used in LO group as compared to EO group. There was no significant difference in disease activity at onset between the groups (SLEDAI 13.8 ± 8.4 vs 12.6 ± 7.2 , $p = 0.52$). There were no significant differences in skin rash, serositis, vasculitis, anti-SS-A and anti-dsDNA antibody seropositivities. [Conclusions] Immunosuppressants were less used in late-onset SLE. There were no significant differences in clinical features which have been pointed out as being related to age of onset in the previous studies.

ICW3-3

A Retrospective Analysis of Treatment Efficacy in Different types of Cutaneous lupus

Navjeet Gill¹, Stephanie Keeling²

¹University of Alberta, Edmonton, Canada, ²Division of Rheumatology, Faculty of Medicine, University of Alberta, Edmonton, Canada

Conflict of interest: None

[Object] Cutaneous lupus (CLE) has various presentations and treatment options. The purpose of this study is to determine the ideal treatment for different types of CLE and specific cutaneous features. [Methods] A retrospective electronic medical record review (EMR) was performed on all patients with active CLE seen at the University of Alberta's rheumatology-dermatology clinic between 2012 to 2018. Data evaluated the achievement of one of three endpoints: improved cutaneous features, remission (or stability; no new disease features), or no effect at last consult. Variables collected included: patient demographics (age and gender), type of CLE, cutaneous features at presentation, histopathology, lupus serology results, previous agents tried, treatment regimen at endpoint, and number of flares after endpoint. [Results] A total of 41 patients (80% female; mean age 43 (SD 17)) were categorized as follows: 46% ($n=19$) chronic cutaneous lupus (CCLE), 22% ($n=9$) undefined CLE, 20% ($n=8$) subacute cutaneous lupus (SCLE), 10% ($n=4$) mixed discoid and SCLE, and 2% ($n=1$) acute cutaneous lupus. The most commonly used medications included hydroxychloroquine (HC; average end dose 329 mg for 327 days), topical steroids (class 3.3, 352), and prednisone (average start dose 33, 175) which achieved remission in 46%, 24%, and 22% respectively. Thirty-four percent ($n=14$) were on a single agent at endpoint, most commonly HC ($n=6$). Half of these patients achieved remission on a single agent. HC was the most successful agent in achieving remission in all three major categories of lupus represented in this study (CCLE, SCLE, undefined CLE) and specific manifestations including discoid lesions, alopecia, malar rash, and CLE with normal C-reactive protein (CRP). [Conclusions] The agents, dose, and duration of treatment is similar across different categories and features of CLE. HC is a mainstay in CLE treatment and has increased efficacy when combined with another agent - ideally prednisone.

ICW3-4

Crescent formation in active lupus nephritis is a poor prognostic factor of renal outcomes

Aya Nawata^{1,2}, Kazuhisa Nakano¹, Hiroko Yoshinari¹, Yoshino Inoue¹, Naoaki Ohkubo¹, Yurie Sato¹, Hiroaki Tanaka¹, Yasuyuki Todoroki¹, Hiroko Miyata¹, Masanobu Ueno¹, Atsushi Nagayasu¹, Takafumi Aritomi¹, Ryuichiro Kanda¹, Yuya Fujita^{1,5}, Masashi Funada¹, Ayako Yamaguchi¹, Taeko Azuma³, Keisuke Nakatsuka⁴, Masao Nawata⁵, Shingo Nakayamada¹, Yoshiya Tanaka¹

¹The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, ²Department of Pathology, University of Occupational and Environmental Health, Japan, ³Department of Internal Medicine, Kyushu Rosai Hospital, Moji Medical Center, ⁴Department of Internal Medicine, JCHO Fukuoka Yutaka Central Hospital, ⁵Department of Rheumatology, Tobata General Hospital

Conflict of interest: None

[Object] Lupus nephritis (LN) exhibits various histological findings including inflammatory lesions such as crescent formation and immune complex (IC) deposition lesions. In INS/RPS 2003 classification, both lesions are classified as class III, IV and V. In this study, we examine the association between the histological factors and renal remission at 52 weeks. [Methods] This is a retrospective study. 152 cases of LN class III, IV, and V out of 274 SLE performed renal biopsy in our department between 1995 to 2017 were registered. 52 weeks after biopsy, they were classified as renal remission (RR) and non-remission (NR) according to ACR and LUNAR remission criteria by eGRF or sCr and proteinuria. The primary endpoint was RR achieving rate, and the secondary endpoint was baseline histological and clinical factors related to NR. [Results] Baseline data: mean age 39, 135 females, histological class III:n=53, IV:n=58, pure V:n=12, III/IV+V:n=30. At 52 w, SLEDAI (16→2), BILAG (17→2) score was significantly decreased. PSL dose was reduced (48→9mg). At 52w, all cases were classified as RR (n=125,82%) and NR (n=27,18%). All of pure V reached remission. Histologically, III or IV (RR n=114;91% vs NR n=27;100%, p=0.01) and cellular/fibrocellular crescent (RR n=51;40% vs NR n=18;66% p=0.01) were more frequent in NR. Clinically, coexisting hypertension (RR n=7;6% vs NR n=9;33%, p<0.01) and higher urine protein level (RR 1.5g vs NR 2.2g, p<0.01) were detected in NR. IVCY improved remission rate (RR n=84;68% vs NR n=9;41%, p=0.03). After long-term, eGFR level were lower in NR (RR 81 vs NR 50, p<0.01, median:138 months). 3 cases developed ESRD showing crescent formation. [Conclusions] Histological factors contributing to NR were III or IV LN and crescent. This result suggested therapeutic response was better in cases with IC deposition than those with inflammatory lesions. The problems is it could not be pointed out crescent formation in current INS/RPS classification, further investigation is required.

ICW3-5

Predictors of neuropsychiatric flare in patients with systemic lupus erythematosus

Kuniyuki Aso, Michihito Kono, Michihiro Kono, Keita Ninagawa, Taiki Sato, Toshiyuki Watanabe, Yuka Shimizu, Yuichiro Fujieda, Masaru Kato, Kenji Oku, Toshiyuki Bohgaki, Olga Amengual, Shinsuke Yasuda, Tatsuya Atsumi

Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University

Conflict of interest: None

Objective: To explore the predictors of neuropsychiatric flare in Japanese patients with systemic lupus erythematosus (SLE). **Methods:** This retrospective study comprised 160 patients with adult-onset SLE who visited our hospital between 2006 and 2017. Overall event-free survival was estimated by Kaplan-Meier analysis. The event was defined as death or neuropsychiatric flare. The neuropsychiatric flare was defined using American College of Rheumatology case definitions and Aini criteria. Predictors of neuropsychiatric flare at diagnosis were analyzed by Cox regression model. **Results:** One hundred and forty-seven patients (91.9%) were female and mean age at diagnosis was 34.5 ± 12.3 years old. The median observation period was 8.4 years (lower and upper quartile: 5.0 and 12.1, respectively). Their mean SLEDAI at diagnosis was 13.0 ± 7.5.

Main clinical manifestations at diagnosis were lupus nephritis (25.6%), serositis (20.0%), neuropsychiatric SLE (NPSLE) (10.0%), anti-phospholipid antibody syndrome (9.3%). Simultaneously with diagnosis, 26 patients were treated with intravenous cyclophosphamide and glucocorticoid (GC) for induction, 11 patients with calcineurin inhibitors and GC, 6 patients with mycophenolate mofetil and GC, and 103 patients with GC monotherapy. Twenty-three patients (14.3%) experienced at least one neuropsychiatric flare during the observation period. The median period to neuropsychiatric flare was 2.0 years (lower and upper quartile: 0.9 and 4.9, respectively). The five- and ten-year event-free survival was 86.0% and 84.2%, respectively. Hypocomplementemia (p=0.02) and NPSLE (p=0.03) at diagnosis were independent poor predictors for event-free survival. **Conclusions:** The ten-year event-free survival was 84.2%. Hypocomplementemia and NPSLE at diagnosis were independent poor predictors for neuropsychiatric flare.

ICW3-6

Macrophage activation syndrome as the initial manifestation of juvenile systemic lupus erythematosus: from a single center study

Satoshi Sato, Yoji Uejima, Eisuke Suganuma, Yutaka Kawano
Division of Infectious Diseases and Immunology, Saitama Children's Medical Center

Conflict of interest: None

[Object] Macrophage activation syndrome (MAS) is a severe, potentially life-threatening complication of a juvenile systemic lupus erythematosus (jSLE). Little is known about the association between MAS and jSLE. The aim of this study was to determine the clinical features of MAS as the initial complication of jSLE. [Methods] During 2004 and 2016, we retrospectively reviewed the clinical and laboratory features of MAS that was diagnosed concomitantly with jSLE patients at the Saitama Children's Medical Center. These patients were compared with a control group composed of jSLE patients without MAS. [Results] 11 patients (24.9%) were diagnosed with MAS during the initial stage of jSLE. Fever, leukopenia, hyperferritinemia, increased aspartate aminotransferase (AST), and increased lactate dehydrogenase (LDH) were more frequently observed in patients having jSLE with MAS than in those having jSLE without MAS (P<0.01). No differences were observed in serum C3 and C4 levels, or erythrocyte sedimentation rate (ESR). Especially, six patients (54.6%) had neurologic symptoms that were significantly higher in those with MAS (P<0.01). All patients received corticosteroids when jSLE with MAS diagnosis was established, among whom six received pulse methylprednisolone therapy. Two patients were treated with IVIG. Eight patients with MAS were treated with immunosuppressants, including cyclophosphamide and mycophenolate mofetil, *azathioprine*. No patient involved in this study died. [Conclusions] MAS can be the initial manifestation of jSLE. MAS with jSLE should be suspected in patients with high fever, cytopenia, and a liver disorder. In addition, we found that in jSLE with MAS patients, they had more neurologic symptoms compared to jSLE without MAS. All patients with MAS were successfully treated with corticosteroids. Early diagnosis and intensive therapy is essential to improve the clinical outcome.

ICW4-1

Clinical Features and Risk Factors of Pulmonary Embolism in Patients with Systemic Lupus Erythematosus

Hanxiao You, Jiuliang Zhao, Qian Wang, Xiaofeng Zeng, Mengtao Li
Department of Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

Conflict of interest: None

[Object] To explore the clinical features and risk factors of pulmonary embolism (PE) in patients with systemic lupus erythematosus (SLE). [Methods] A case-control study was conducted in patients complicated with PE among SLE patients admitted to Peking Union Medical College Hospital from 2012 to 2017. Clinical and laboratory data of case group (SLE-PE) and age, sex, and entry-time-matched control group (SLE-non-PE) were analyzed by the single factor analysis and multivariate analysis to explore the risk factors of PE among SLE patients. A *p* value of 0.05

or less was considered to be statistically significant. [Results] 77 patients were eligible for enrollment into the case group and 231 contemporaneous SLE patients without PE as the control group. Among the SLE-PE group, the majority were female (63; 81.8%), with a mean SLE course of 29.04±6.61 months before PE events and a high mortality rate of 9.1% after PE. Multivariate analysis revealed that duration of SLE < 1.5 years (odds ratio (OR) 5.129, $p < 0.001$), lupus nephritis (OR 3.225, $p < 0.001$), thrombocytopenia (OR 3.121, $p < 0.005$), high hypersensitive c-reactive protein (hsCRP) (OR 6.937, $p < 0.001$), anti-SSA positive (OR 2.989, $p < 0.003$) and aPL positive (OR 9.15, $p < 0.001$) were independent significant risk factors of PE in SLE patients. [Conclusions] PE is a serious complication among SLE patients with a high mortality rate. The risk is higher during the first year immediately after the diagnosis of SLE. Shorter SLE course less than 1.5 years, positive antiphospholipid antibodies, lupus nephritis and elevated inflammatory markers are independent risk factors of PE among SLE patients.

ICW4-2

Effects of antiphospholipid antibodies and hematological abnormalities on short- and long-term mortality in blood-stream infections associated with commensal Streptococcal infection

Yu-min Kuo^{1,2}, Song-chou Hsieh², Jen-hao Chen³, Yen-chun Lin², Jean-san Chia⁵, Chiau-jing Jung⁴

¹Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, ²Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, ³Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, National Taiwan University Hospital Yunlin Branch, Yunlin, Taiwan, ⁴Department of Microbiology and Immunology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan, ⁵Graduate Institute of Immunology, College of Medicine, National Taiwan University, Taipei, Taiwan

Conflict of interest: Yes

[Object] Antiphospholipid (aPL) antibodies have been proposed to activate platelets and contribute to vegetation growth and embolization in infective endocarditis (IE). The presence of anticardiolipin (aCL) and anti- β 2-glycoprotein I (β 2GPI) antibodies have been reported to be associated with embolic events in IE. Besides, production of aPLs and anti-DNA were observed in the rats with bacteremia caused by *S. mutans* in our laboratory. Whether aPLs as well as anti-DNA were predictors of short- and long-term outcome of blood-stream infections with/without IE have not been evaluated. [Methods] We studied 51 patients with commensal streptococcal bacteremia with/without definite IE (Duke-Li criteria) from our prospective cohort (2002-2009). Serum aCL IgG and IgM and anti- β 2GPI IgG antibodies were detected by ELISA (Thermo Fisher). The relationship between antibodies as well as other clinical parameters and short- and long-term mortality were studied with Kaplan-Meier and Cox multivariate analyses. [Results] The mean follow-up periods were 296±314 weeks. At least one aPL antibody was found in 11 patients (21%). The 30- and 90-days mortality rates were 15.7% and 27.4% respectively. Risk factors predictive of 90-day mortality were leukopenia (Hazard ratio 3.0, 95% CI 0.8 to 15.2, $p = 0.09$), both presence of anti- β 2GPI IgG and leukopenia (Hazard ratio (HR) 4.6, 95% CI 0.9 to 23.1, $p = 0.06$), and presence of either leukopenia or thrombocytopenia but positive anti- β 2GPI IgG (HR 7.0, 95% CI 2.2 to 25.7, $p = 0.001$). Clinical parameters predictive of 10-year mortality were leukopenia (Hazard ratio 3.5, 95% CI 1.5 to 8.1, $p = 0.004$) and presence of thrombocytopenia (HR 2.4, 95% CI 0.9 to 6.2, $p = 0.07$), but not any presences of autoantibodies. [Conclusions] The presence of anti- β 2GPI IgG (not other aPLs and anti-DNA) and hematological abnormalities (either leukopenia or thrombocytopenia) could significantly predict 90-days mortality rate among patients with commensal Streptococcal infection.

ICW4-3

Factor Xa inhibitors for preventing recurrent thrombosis in patients with antiphospholipid syndrome: A longitudinal cohort study with propensity score-based analysis

Taiki Sato, Yuichiro Fujieda, Hiroyuki Nakamura, Naoki Ohnishi, Keita Ninagawa, Kuniyuki Aso, Nobuya Abe, Michihito Kono, Masaru Kato, Kenji Oku, Toshiyuki Bohgaki, Olga Amengual, Shinsuke Yasuda,

Tatsuya Atsumi

Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Conflict of interest: None

[Object] The clinical indications of factor Xa inhibitors for the patients with antiphospholipid syndrome (APS) are not fully established. The aim of this study was to clarify the efficacy and safety of factor Xa inhibitors for APS patients in real world. [Methods] This is a retrospective cohort study comprised of consecutive patients with APS between April 1990 and June 2018 in our Rheumatology department. Patients treated with factor Xa inhibitors were extracted from the cohort. As a control group, patients treated with warfarin were selected from the same cohort with matched age, gender, coexistence of SLE and having antiplatelet therapy. We used propensity score adjustment for each of the confounding factors for multivariate Cox proportional hazard model. Primary endpoint was set as thrombotic and haemorrhagic event-free survival for 5 years. [Results] Among 206 patients with APS, 10 had a history of anti-Xa therapy (4 rivaroxaban, 6 edoxaban). In all the 10 patients, factor Xa inhibitors were switched from warfarin. Event-free survival was significantly shorter on anti-Xa therapy than that on warfarin therapy in these 10 patients (Hazard ratio: 11.4, 95% CI: 1.6-233.2). Similarly, event-free survival in patients treated with factor Xa inhibitors was significantly shorter compared with controls (Hazard ratio: 6.8, 95% CI: 1.6-30.7). After adjustment, event-free survival in patients with anti-Xa therapy remained significantly shorter (Hazard ratio: 21.9, 95% CI: 2.2-264.7). [Conclusions] This study provided an unfavourable evidence on the efficacy and safety of factor Xa inhibitors for APS patients. From our findings, factor Xa inhibitors for APS may not be recommended and warfarin remains the mainstay treatment for APS.

ICW4-4

Prothrombin/MHC class II complexes expressed on procoagulant cells are one of the targets of pathogenic antiphospholipid antibodies

Naoki Ohnishi, Yuichiro Fujieda, Michihito Kono, Masaru Kato, Kenji Oku, Toshiyuki Bohgaki, Olga Amengual, Shinsuke Yasuda, Tatsuya Atsumi

Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Conflict of interest: None

[Objectives] Antiphospholipid syndrome (APS) is characterized by thrombosis or pregnancy morbidity and the presence of antiphospholipid antibodies (aPL). Phosphatidylserine-dependent antiprothrombin antibodies (aPS/PT) recognize the phosphatidylserine/prothrombin (PS/PT) complex, and are strongly correlated with APS. Recently, misfolded β 2-glycoprotein I (β 2-GPI) molecules transported to the cell surface with major histocompatibility complex class II (MHC II) were reported as targets of autoantibodies in patients with APS. APS patients with anti- β 2-GPI are highly likely to share the thrombophilic pathophysiology with those with aPS/PT, therefore we hypothesized that misfolded prothrombin (PT), likewise β 2-GPI, are transported to the cell surface by MHC II in procoagulant cells, consequently being targeted by aPS/PT. [Methods] 1) The interaction between PT and MHC II was analyzed by flow cytometry (FCM) and immunoprecipitation, using co-expression of PT and several alleles of MHC II in HEK293T cells. 2) Synthesis of PT in monocytes was investigated in phorbol-12-myristate-13-acetate (PMA) treated THP-1 cells by western blotting and FCM. 3) Cell surface transportation of synthesized PT was evaluated by FCM on THP-1 cells co-stimulated with PMA and interferon gamma. [Results] 1) Overexpressed PT/MHC II complexes were detected on THP-1 cell surface by a mouse monoclonal aPS/PT. The dependency of MHC II allele effects on aPS/PT binding was confirmed. 2) PMA-treated THP-1 cells synthesized PT with stronger binding to aPS/PT than to non-pathogenic monoclonal anti-PT antibody. 3) aPS/PT binding to PT/MHC II complexes were confirmed in co-stimulated THP-1 cells. No binding was observed between non-pathogenic monoclonal anti-PT antibody and PT/MHC II complexes. [Conclusion] PT proteins synthesized by monocytes were presented on the cell surface by MHC II. The expression of PT/MHC complexes on stimulated mono-

cytes might be considered as one of the targets for pathogenic aPS/PT.

ICW4-5

In vivo imaging of arterial thrombus formation in a murine arthritis model

Shoko Tsuji, Tomoyuki Mukai, Hiroyasu Hirano, Yoshitaka Morita
Department of Rheumatology, Kawasaki Medical School, Kurashiki, Japan

Conflict of interest: Yes

[Object] Although elevated incidence and mortality for cardiovascular diseases are reported in patients with rheumatoid arthritis, the mechanisms by which chronic inflammation induces thrombosis have not been fully elucidated. Recently, *in vivo* imaging technique was reported for the thrombus formation by using a *two*-photon excitation microscope. In the model, intravascular administration of hematoporphyrin and subsequent laser irradiation to the peripheral artery induce the local thrombus formation. To evaluate the effect of chronic inflammation on pro-thrombotic condition, we visualized and quantified the thrombus formation *in vivo* in TNF-transgenic arthritis mice. [Methods] Blood flow, platelets, and nucleated cells were visualized by rhodamine-labeled dextran, DyLight488-labeled anti-GPIIb/IIIa antibody, and Hoechst, respectively. After the hematoporphyrin injection, the testicular arteries were exteriorized and irradiated by the laser, and then the thrombus formation was quantified by the microscope. 16 week-old TNF-transgenic mice (n=4) and the wild-type mice (n=6) were used. One to four areas per each mouse were analyzed. [Results] Platelets adhesion to the vessel wall, thrombus formation, and subsequent obstruction of the vessels were observed within approx. 10 seconds. Initial platelet attachment times were 4.61 ± 3.53 sec in arthritis mice and 5.53 ± 3.74 sec in control mice ($P = 0.50$); vascular obstruction times were 37.60 ± 15.41 sec in arthritis mice and 28.23 ± 12.78 sec in controls ($P = 0.09$); speed of thrombus formation were 224.3 ± 113.6 $\mu\text{m}^2/\text{sec}$ in arthritis mice and 235.8 ± 169.1 $\mu\text{m}^2/\text{sec}$ in controls ($P = 0.15$). [Conclusions] The arterial thrombus formation in mice was visualized by the *in vivo* imaging technique. The presence of chronic arthritis did not significantly affect the severity of thrombus formation. This result might be caused by too strong induction of thrombosis, which could mask the pro-thrombotic status of arthritic condition.

ICW4-6

Cutaneous Collagenous Vasculopathy in Patients with Connective Tissue Disease: A diagnostic challenge

Noreen Walsh, Phillip Moss, Thai Yen Ly, Sylvia Pasternak, Peter J Green, Kerri Purdy, Christopher Gallant, Ariel Burns, Mary Lou Baxter, Colleen Kelly, Elana Murphy, John G Hanly
Dalhousie University, Halifax, Nova Scotia, Canada

Conflict of interest: None

Objectives: Cutaneous collagenous vasculopathy (CCV), a recently described, rare, superficial dermal microangiopathy of unknown etiology, shares clinical and histopathological features in common with cutaneous lupus erythematosus and dermatomyositis. Fewer than 50 cases have been reported in the literature. Concurrence of CCV and connective tissue diseases (CTD) may present a diagnostic quandary. Our objectives were to determine whether CCV cases at our center were associated with CTD and to identify distinguishing features between CCV and cutaneous manifestations of CTD. **Methods:** The laboratory information system at a single academic health care center (2000-2018) was searched to identify cases with a diagnosis of CCV. All pathological material and clinical charts were reviewed. The demographic, clinical and pathological data were documented. **Results:** We identified 6 cases of CCV (4 female, 2 male; median age 57 years). Clinically, a telangiectatic eruption was present in all patients, affecting the lower limbs and other sites (N= 5) and the abdomen and arms (N=1). All patients had been seen by a dermatologist and 3 by a rheumatologist. A concurrent CTD was present in 2 cases; Sjogren's syndrome (N=1) and undifferentiated connective tissue disease (N=1). In both, the clinical differential diagnosis included CCV and cutaneous involvement by the CTD. In all 6 cases, histopathological examination revealed a non-inflammatory vasculopathy, with PAS-positive, diastase resistant, hyaline thickening of ectatic superficial capillary

walls, and loss of pericytes. These hallmarks of CCV excluded skin disease attributable to CTD in the two relevant cases. **Conclusion:** Concurrence of CCV and CTD, though uncommon, presents a diagnostic challenge. The clinical distribution of the CCV eruption, favouring the lower limbs, and its non-inflammatory character histopathologically distinguish it from cutaneous involvement by a CTD.

ICW5-1

MMP-9 as a Potential Therapeutic Target in Giant Cell Arteritis

Ryu Watanabe¹, Toshihisa Maeda¹, Hui Zhang¹, Gerald Berry¹, Markus Zeisbrich¹, Robert Brockett², Andrew Greenstein², Lu Tian¹, Jorg Goronzy¹, Cornelia Weyand¹
¹Stanford University School of Medicine, ²Gilead Sciences Inc

Conflict of interest: Yes

[Object] Giant cell arteritis (GCA) is a granulomatous inflammation of medium and large arteries. Pathological consequences include fragmentation of elastic membranes and vessel wall destruction. Matrix metalloproteinases (MMPs) are implicated in pathogenesis by degrading extracellular matrices. MMP-9, a type IV collagenase, is produced in the GCA-affected arteries; however, it is unknown whether MMP-9 has a pathogenic role in vasculitis beyond matrix digestion. [Methods] Temporal arteries were collected from diagnostic biopsies, and blood samples were obtained from patients with GCA. An engineered basement membrane was built from collagen IV for cell invasion assay. A humanized chimera model was generated by grafting human medium-sized arteries into immunocompromised NSG mice. Vasculitis was induced by adoptive transfer of peripheral blood mononuclear cells from GCA patients. *In vivo* functions of MMP-9 were tested by blocking enzyme activity with a highly specific monoclonal antibody or by injecting recombinant MMP-9 (rMMP-9). [Results] GCA-affected temporal arteries contained high amounts of MMP-9 transcripts, and immunostaining localized MMP-9 to tissue-infiltrating macrophages. GCA monocytes showed an increased ability to penetrate through engineered basement membrane. GCA CD4+ T cells required MMP-9-producing monocytes to pass through the membrane. Blocking MMP-9 activity *in vivo* had profound antivasculitic effects, decreased the density of T cell infiltrates ($P < 0.001$), reduced microvascular neoangiogenesis ($P < 0.001$), and prevented intimal outgrowth ($P < 0.001$). In contrast, rMMP-9 promoted T cell infiltration ($P < 0.05$), enhanced microvessel formation ($P < 0.001$), and worsened intimal expansion ($P < 0.001$). [Conclusions] In GCA, invasion of vasculitogenic T cells, formation of new microvessel, and intimal hyperplasia all require MMP-9 activity, implicating this proteinase as a potential therapeutic target in GCA.

ICW5-2

A comprehensive LC-MS/MS lipid mediator analysis of lupus-prone mice revealed inhibitory effects of palmitoylethanolamide on Toll-like receptor 9-mediated inflammation

Takashi Ozaki^{1,2}, Keisuke Maeshima², Koji Ishii², Hirotaka Shibata², Takashi Kobayashi¹
¹Department of Infectious Disease Control, Faculty of Medicine, Oita University, Oita, Japan, ²Department of Endocrinology, Metabolism, Rheumatology and Nephrology, Faculty of Medicine, Oita University, Oita, Japan

Conflict of interest: None

[Object] In recent years, some lipid mediators are known to play critical roles in regulating inflammation, which could be new therapeutic approaches for inflammatory and autoimmune disorders. Our aim is to identify lipid mediators which might contribute to modulate inflammatory responses related to systemic lupus erythematosus (SLE). [Methods] We evaluated levels of lipid mediators in MRL/lpr mice (lupus-prone mice) and MRL/MpJ mice (wild type) by comprehensive liquid chromatography tandem-mass spectrometry (LC-MS/MS) analysis with method package software designed to analyze 158 compounds. Based on LC-MS/MS assay, we focused on significantly increase/decrease lipid mediators in MRL/lpr mice and assessed physiological effects of the mediators on Toll-like receptor 9 (TLR9) signaling which is known to be involved in the pathogenesis of SLE. [Results] Our LC-MS/MS analysis revealed

that the levels of palmitoylethanolamide (PEA), an endogenous *N*-acyl-ethanolamide, in both serum and spleen were reduced in MRL/*lpr* mice. PEA suppressed pro-inflammatory cytokine (IL-6, IL-12, and IL-23) production induced by TLR9 stimulation (CpG-ODN) in bone marrow derived dendritic cells (BMDC) in vitro. Moreover, upregulation of MHC class II, CD86 and CD40 induced by CpG-ODN in BMDC were significantly attenuated by PEA. In splenic B cells, in addition to inhibition of IL-6 production and surface marker upregulation, cell proliferation and IgM production were suppressed by PEA. To examine whether PEA reduces TLR9-mediated inflammation in vivo, we assessed serum IL-6 levels in mice injected with CpG-ODN and D-galactosamine, resulting in reduction of IL-6 levels by intraperitoneal administration of PEA. [Conclusions] In MRL/*lpr* mice, PEA levels are decreased in the serum and spleen compared to MRL/MpJ mice. PEA reduces TLR9-mediated pro-inflammatory cytokine production both in vitro and vivo, suggesting that PEA might be a novel therapeutic candidate to modulate inflammation related to SLE.

ICW5-3

Glutaminase 1 is a target for Th17-related autoimmune diseases

Michihito Kono^{1,2}, Nobuya Yoshida¹, Kayaho Maeda¹, Abel Suárez-fueyo¹, Vasileios C Kyttaris¹, George C Tsokos¹

¹Division of Rheumatology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Japan, ²Division of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine, Hokkaido University, Sapporo, Japan

Conflict of interest: None

[Object] Glutaminase 1 (Gls1) is the first enzyme in glutaminolysis. We previously showed that the selective Gls1 inhibitor Bis-2-(5-phenylacetamido-1,3,4-thiadiazol-2-yl)ethyl sulfide (BPTES) suppresses Th17 cell development and suppresses experimental autoimmune encephalomyelitis (EAE). However, the involved mechanisms and whether inhibition of glutaminolysis can be useful in the treatment of systemic lupus erythematosus (SLE) remain unknown. [Methods] MRL/*lpr* mice were treated by BPTES or vehicle control and disease activity was examined. Then naïve CD4⁺ T cells from patients with SLE were cultured under Th17 conditions with BPTES or the vehicle. Furthermore, using newly generated Gls1 conditional knockout mice in IL-17 producing cells, in vitro Th17 differentiation and EAE disease were investigated. The expression of hypoxia-inducible factor 1 α (HIF1 α) and the von Hippel-Lindau tumor suppressor protein (VHL) which degrades Hif1 α were examined. [Results] MRL/*lpr* mice with BPTES improved autoimmune pathology in a Th17-dependent fashion. T cells from patients with SLE treated with BPTES displayed decreased Th17 differentiation. Using the conditional knockout mice we demonstrated that both the in vitro Th17 differentiation and the development of EAE depend on Gls1. Gls1 inhibition reduced the expression of HIF1 α protein, while the expression levels of VHL were found to be increased suggesting excessive degradation of HIF1 α . [Conclusions] We have provided evidence that inhibition of glutaminolysis can be used to treat patients with SLE and Th17-related autoimmune diseases. Mechanistically we showed that glutaminolysis inhibition suppresses Hif1 α expression in Th17 cells by increasing VHL.

ICW5-4

Atypical complement receptor C5aR2 transports C5a to initiate neutrophil adhesion and inflammation

Yoshishige Miyabe

Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School

Conflict of interest: None

[Object] “Atypical” chemoattractant receptors (ACKRs) act as non-signaling chemokine sinks helping to maintain chemoattractant gradients. In addition, ACKR1 on endothelial cells (ECs) has been shown to transport chemokines produced in tissue across ECs and regulate neutrophil recruitment. Recently, we found that ACKR1 and “atypical” complement C5a receptor 2 (C5aR2) were highly expressed in the joint ECs of immune complex (IC)-induced arthritis. However, their roles in an inflammatory arthritis remain unclear. [Methods] We induced arthritis on wild-

type (WT), *C5ar2*- or *Ackr1*-deficient (KO) mice to study their roles in IC-induced arthritis. To determine their roles on hematopoietic vs. non-hematopoietic cells, we generated bone marrow chimeric mice and induced arthritis. How they collaborate to control neutrophil recruitment into the joint were defined using multi-photon intravital microscopy (MP-IVM). To directly study if C5aR2 transports C5a and ACKR1 transports CXCR2 ligands into the vessel lumen to initiate neutrophil recruitment, we used a superfusion assay and MP-IVM. Finally, we visualized the requirement for C5aR2 for the transport of C5a from the extravascular space into the lumen of vessels overlying the joint. [Results] Abrogation of C5aR2 and ACKR1 ameliorate IC-induced arthritis. C5aR2 and ACKR1 expressed on non-hematopoietic cells are required for IC-induced arthritis. C5aR2 is required for transporting tissue-derived C5a into the vessel lumen to induce C5aR1-mediated neutrophil arrest. In addition, ACKR1 transports CXCR2 ligands across the joint ECs to induce CXCR2-dependent neutrophil extravasation in the joints. C5a was visualized on the luminal surface of the joint ECs in the joints of WT and *Ackr1*-KO mice, but not in *C5ar2*-KO mice. [Conclusion] These findings provide new insights into how “atypical” chemoattractant receptors collaborate with “classical” signaling chemoattractant receptors to control the recruitment of neutrophils into inflamed joints.

ICW5-5

PI3K-Akt pathway plays a crucial role in production of collagen in Fli1 deficient condition and its inhibitor has the therapeutic potential in treating fibrosis

Yuko Ota, Warren Strober, Atsushi Kitani

Laboratory of Clinical Immunology and Microbiology, National Institutes of Health, Bethesda MD, USA

Conflict of interest: None

[Object] Systemic sclerosis (SSc) is a connective tissue disease characterized by fibrosis of the skin and internal organs. Previous studies have shown that dermal fibroblast in patients with SSc frequently shows decreased levels of Fli1 due to hypermethylation. We aimed to clarify the mechanisms underlying the regulation of Fli1 gene of fibrosis using Fli1 deficient cells and mice generated by the CRISPR/Cas9-mediated gene editing. [Methods] Fli1-deficient fibroblast cell line and mice were generated by CRISPR/Cas9 system using paired guide RNAs specific for Fli1 and a nickase Cas9. NIH3T3 cells were transfected with a LentiCRISPR v2 vector and then selected by puromycin. We evaluated collagen and profibrotic cytokine production in the absence of Fli1 by mRNA level. To reveal the mechanism for induction of collagen in Fli1 KO cells, we treated the cells with various antibodies and inhibitors and performed RNA-seq analysis. We evaluated the candidate drug using bleomycin-induced lung fibrosis model and collagen production in skin fibroblasts from patients with SSc. [Results] qPCR studies revealed that Col1A1, Col1A2, Fibronectin, TGF- β 1 and IL-6 mRNA levels were increased in Fli1 KO 3T3 fibroblasts. Antibody neutralization of TGF- β 1, IL-6/IL6R, each alone or in combination failed to suppress the increased collagen production. Surprisingly, Col1A2 mRNA was dramatically inhibited by a PI3K inhibitor but not MAPK inhibitors, suggesting a PI3K-Akt pathway was regulating collagen synthesis in KO cells. Furthermore, RNA-seq reveals several molecules to induce collagen via PI3K-Akt pathway. PI3K inhibitor attenuated bleomycin-induced lung fibrosis in Fli1 KO mice and also inhibited collagen production in skin fibroblasts from patients with SSc. [Conclusions] Lack of Fli1 expression activates the molecule that induces collagen accumulation through PI3K-Akt pathway. PI3K inhibitor showed the therapeutic potential in treating fibrosis.

ICW5-6

14-3-3 eta protein, a promising step forward in predicting response to Infliximab and its biosimilar? Results from two groups of patients diagnosed with rheumatoid arthritis in Romania

Bogdan I Gavrilă, Ciofu S Claudia, Liviu Macovei, Victor Stoica, Ioan Ancuta, Mihai Bojinca

Department of Internal Medicine and Rheumatology Cantacuzino Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Conflict of interest: None

[Object] testing predictive value of 14-3-3eta protein regarding response to Infliximab (IFX) and its biosimilar (Remsima) on 2 groups of patients diagnosed with rheumatoid arthritis (RA). [Methods] prospective and observational study, including 2 groups of patients with active RA, uncontrolled by csDMARDs, followed 12 months, 16 treated with IFX and 17 with Remsima. Clinical assessment was performed at 0,6,12 months according to ACR criteria and evaluation of treatment response according to EULAR criteria (good/moderate/nonresponder). [Results] 30 patients (90.91%) were women and 3 (9.09%) men. Following baseline 14-3-3eta titres and the response at 6 months, tests for identifying differences between groups showed that lower 14-3-3eta protein titres, in both groups of patients, had predictive value on achieving a good EULAR response at 6 months. For IFX, patients with good EULAR response had lower baseline titres (0.11±0.245 ng/ml) than patients with moderate response (0.70±0.705 ng/ml, p=0.049). For Remsima group, good responders had lower baseline titres (0.25±0.380 ng/ml) than nonresponders (1.67±0.615 ng/ml, p=0.004) or those with moderate response (0.25±0.401 ng/ml) Grouping patients in 2 categories (responders/nonresponders) only for IFX group, 14-3-3eta maintained value predicting a 6 months response (0.25±0.378 ng/ml), than nonresponders (1.67±0.615 ng/ml, p=0.0005). For 12 months, we didn't find significant differences between groups regarding baseline 14-3-3eta titres and the response obtained (IFX p=0.1483, Remsima p=0.2470) The status pretreatment (positive/negative) influenced the good response for IFX group at 6 months (p=0.005). Regarding the evolution of serum titres, we noticed a reduction, statistically close to significance for IFX (baseline 0.51±0.703 ng/ml, 12 months 0.13±0.439, p=0.064), but not for Remsima (p=0.153). [Conclusions] 14-3-3 eta, a new diagnostic biomarker, could be a major candidate to distinguish pretreatment patients who will or not respond to anti-TNF α therapy.

ICW6-1

Are there differences in efficacy and safety of biological disease-modifying antirheumatic drugs between elderly-onset and young-onset rheumatoid arthritis?

Sadao Jinno¹, Akira Onishi¹, Kengo Akashi¹, Motomu Hashimoto², Wataru Yamamoto^{2,9}, Koichi Murata², Tohru Takeuchi³, Takuya Kotani³, Yuichi Maeda⁴, Kosuke Ebina⁵, Yonsu Son⁶, Hideki Amuro⁶, Ryota Hara⁷, Masaki Katayama⁸, Jun Saegusa¹, Akio Morinobu¹

¹Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, ²Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ³Department of Internal Medicine IV, Osaka Medical College, Osaka, Japan, ⁴Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University, Osaka, Japan, ⁵Department of Orthopaedic Surgery, Osaka University Graduate School of Medicine, Osaka, Japan, ⁶First Department of Internal Medicine, Kansai Medical University, Osaka, Japan, ⁷The Center for Rheumatic Diseases, Nara Medical University, Nara, Japan, ⁸Department of Rheumatology, Osaka Red Cross Hospital, Osaka, Japan, ⁹Department of Health Information Management, Kurashiki Sweet Hospital, Kurashiki, Japan

Conflict of interest: None

[Object] To compare efficacy and safety of biological disease-modifying antirheumatic drugs (bDMARDs) between elderly-onset rheumatoid arthritis (EORA) and young-onset rheumatoid arthritis (YORA) patients. [Methods] Patients with rheumatoid arthritis (RA) aged ≥ 18 years enrolled in a Japanese multicenter observational registry between Sep 2009 and December 2017 who had ≥ 3.2 disease activity score in 28 joints-erythrocyte sedimentation rate (DAS28-ESR) when initiating bDMARDs were included. EORA was defined as RA with onset at 60 or over. A multivariate logistic regression model was performed to assess the relationship between age onset and clinical remission at 48 weeks. Clinical remission was calculated using DAS28-ESR, Simplified Disease Activity Index (SDAI), and Clinical Disease Activity Index (CDAI) scores. Biologic retention at 48 weeks was estimated using the Kaplan-Meier method. [Results] Of the 989 bDMARDs initiators, 364 patients (36.8%) were identified as EORA. Patients in the EORA group were older (73 vs 55, p<0.001) and more likely to have higher value of DAS28-ESR (5.1 vs 4.8, p<0.001), SDAI score (22.6 vs 20.9, p=0.03), modified Health Assessment Questionnaire (mHAQ) score (1.0 vs 0.8, p<0.001),

and lower rate of positive rheumatoid factor (74% vs 82%, p<0.001). CDAI score was similar (19.8 vs 18.9, p=0.19). Multivariate analysis demonstrated that EORA (OR 0.65, CI 0.45-0.97) was a negative predictor of the DAS28 remission, but not of the SDAI or CDAI remission. Drug maintenance rates (63% vs 61%) and adverse events discontinuation rates (2.7% vs 5.2%) were similar between the two age groups. [Conclusions] In RA patients initiating bDMARDs, there was no difference between EORA and YORA in achieving the SDAI or CDAI remission. The result that EORA was a negative predictor of the DAS28 remission could be attributed to the high weight of ESR in the DAS28. Drug maintenance and adverse events discontinuation rates were similar between the two age groups.

ICW6-2

Safety and Efficacy of Filgotinib in Japanese Patients Enrolled in a Global Phase 3 Trial of Patients with Active Rheumatoid Arthritis and Inadequate Response or Intolerance to Biologic DMARDs

Tsutomu Takeuchi¹, Tsukasa Matsubara², Tatsuya Atsumi³, Koichi Amano⁴, Naoki Ishiguro⁵, Eiji Sugiyama⁶, Kunihiro Yamaoka⁷, Mark C Genovese⁸, Kenneth Kalunian⁹, David Walker¹⁰, Jacques-eric Gottenberg¹¹, Kurt De Vlam¹², Neelufar Mozaffarian¹³, Beatrix Bartok¹³, Franziska Matzkies¹³, Jie Gao¹³, Ying Guo¹³, Chantal Tasset¹⁴, John S Sundry¹³, Yoshiya Tanaka¹⁵

¹Keio University School of Medicine, Tokyo, Japan, ²Matsubara Mayflower Hospital, Kato, Japan, ³Hokkaido University, Sapporo, Japan, ⁴Saitama Medical Center, Kawagoe, Japan, ⁵Nagoya University, Nagoya, Japan, ⁶Hiroshima University, Hiroshima, Japan, ⁷Kitasato University School of Medicine, Sagamihara, Japan, ⁸Stanford University, Stanford, CA, USA, ⁹University of California, San Diego, La Jolla, CA, USA, ¹⁰Northumbria Healthcare, UK, ¹¹Strasbourg University Hospital, Strasbourg, France, ¹²Universitair Ziekenhuis Leuven, Leuven, Belgium, ¹³Gilead Sciences, Inc., Foster City, CA, USA, ¹⁴Galapagos NV, Mechelen, Belgium, ¹⁵University of Occupational and Environmental Health, Kitakyushu, Japan

Conflict of interest: None

[Object] We report results of Japanese patients enrolled in the FINCH 2 study (ClinicalTrials.gov Identifier: NCT02873936) of filgotinib (FIL), an oral, selective, Janus Kinase 1 (JAK1) inhibitor in patients with RA and an inadequate response or intolerance to ≥ 1 biologic bDMARDs. [Methods] Patients (pts) with RA were randomized globally, including at sites in Japan, 1:1:1 to FIL 200 mg, FIL 100 mg, or placebo (PBO) once daily for 24 weeks; pts continued background conventional synthetic csDMARDs. The primary endpoint was the proportion of subjects who achieved an ACR20 response at Week (Wk) 12. [Results] Primary and all key secondary endpoints were met for both global (N=448) and Japanese patient populations (n=40; FIL200, n=12; FIL100, n=15; and PBO, n=13). ACR20 response rates (%; p-value vs PBO) in Japanese pts at Wk12 and 24 were: FIL200 83% (p=0.015), 92% (p<0.001); FIL100 53% (p=0.28), 60% (p=0.024); PBO 31%, 15%; respectively. At Wk 12, HAQ-DI LS mean changes from baseline were -0.55 (95% CI: -0.81, -0.29) and -0.30 (-0.53, -0.07) in the FIL200 and FIL100 groups, vs 0.09 (-0.16, 0.35) in PBO. At Wk 12, the percentage of Japanese pts with DAS28 (CRP) ≤ 3.2 was 67% FIL200 (p<0.001) and 47% FIL100 (p=0.007) vs PBO (0%). In Japanese patients, adverse event (AE) rates were similar for FIL200, FIL100 and PBO (75%, 60% and 77%, respectively) and there were no serious AEs; there was 1 case of uncomplicated herpes zoster (FIL200); and no venous thrombotic events, opportunistic infection/active TB, malignancy, GI perforation or death. [Conclusions] In this phase 3 study of pts with active RA and prior inadequate response/intolerance to bDMARDs, treatment with FIL over a 24-week period was associated with significant improvements in signs and symptoms of RA, with a safety and efficacy profile in Japanese pts consistent with that in the global population. Thus, FIL may provide a novel treatment option for pts who continue to have active RA despite prior biologic therapy.

ICW6-3

Filgotinib Week 132 Safety Data from a Phase 2b Open-Label Extension Study in Rheumatoid Arthritis

Yoshiya Tanaka¹, Arthur Kavanaugh², Mark C Genovese³, Kevin Winthrop⁴, Maria Greenwald⁵, Lucia Ponce⁶, Enriquez-sosa Favio⁷,

Mykola Stanislavchuk⁸, Minodora Mazur⁹, Alberto Spindler¹⁰, Regina Cseuz¹¹, Natalya Nikulenkova¹², Maria Glowacka-kulesz¹³, Istvan Szombati¹⁴, Anna Dudek¹⁵, Neely Mozaffarian¹⁶, Joy Greer¹⁶, Rebecca Kunder¹⁶, Di An¹⁶, Luc Meuleners¹⁷, Robin Besuyen¹⁷, Rieke Alten¹⁸, René Westhovens¹⁹

¹The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, ²University of California, San Diego, La Jolla, USA, ³Stanford University School of Medicine, Palo Alto, USA, ⁴Oregon Health and Science University, Portland, USA, ⁵Desert Medical Advances, Palm Springs, USA, ⁶Cons. Priv., Temuco, Chile, ⁷Clinstile SA de CV, Col.Roma, Mexico, ⁸National Pirogov Memorial Medical University, Vinnytsia, Ukraine, ⁹IMSP Inst. de Cardiologie, Chisinau, Moldova, ¹⁰Centro Méd. Priv. Reum., Tucumán, Argentina, ¹¹Revita Reumatológiai Kft, Budapest, Hungary, ¹²Vladimir Reg Clin Hosp, Shosse, Russian, Federation, ¹³Silesiana Centrum Medyczne, Wrocław, Poland, ¹⁴Qualiclinic Kft, Budapest, Hungary, ¹⁵AMED Medical Center, Warsaw, Poland, ¹⁶Gilead Sciences, Inc, Foster City, USA, ¹⁷Galapagos NV, Mechelen, Belgium, ¹⁸Schlosspark Klinik, Berlin, Germany, ¹⁹University Hospitals, Leuven, Belgium

Conflict of interest: None

[Object] Long-term safety and efficacy of the oral, selective Janus Kinase 1 (JAK1) inhibitor filgotinib (FIL) in patients (pts) with moderately to severely active RA is being evaluated in the DARWIN 3 (Phase 2b) open-label extension (OLE) study. [Methods] Eligible pts from the 24-week Phase 2b DARWIN 1 and 2 studies could enroll in DARWIN 3, where they received FIL 200 mg daily (100 mg for US males) as monotherapy or as add-on to methotrexate. We present cumulative safety data (from the patient's first dose of FIL in the DARWIN program through 20 Feb 2018) and efficacy data (from Day 1 to Week 132 of DARWIN 3). [Results] Of 877 pts from DARWIN 1 and 2,790 (90%) completed the study and 739 (84%) enrolled in DARWIN 3; 603 (82%) were female, mean age was 53 years. At analysis, 469 (64%) remained in the OLE. Cumulative patient-years of exposure (PYE) was 2081, median time on study drug was 1197 days. Overall treatment-emergent adverse event (TEAE) and serious TEAE rates/100PYE were 146 and 5.6, respectively. Specific rates/100PYE were: serious infections 1.0, malignancy 0.6, herpes zoster 1.5, deep vein thrombosis 0.05, pulmonary embolism 0.05, active tuberculosis 0.0, and death 0.2. The most common Grade 1 or 2 laboratory abnormalities were hemoglobin decrease (25%), alanine aminotransferase increase (24%), lymphocyte decrease (20%), and neutrophil decrease (12%). Grade 3 or 4 abnormalities of these parameters occurred in $\leq 1\%$ of pts, except for lymphocyte decrease (3%). There was no difference in the safety profile of FIL with or without concomitant methotrexate. No new trends or safety signals were identified. Efficacy data revealed that 89%, 70%, and 49% of pts had ACR20/50/70 responses, respectively, and 69% achieved DAS28 (CRP) ≤ 3.2 (observed case analysis). [Conclusions] Filgotinib continues to demonstrate a favorable safety and tolerability profile in pts with RA over a 2.5-year period, with maintenance of therapeutic response in the long term.

ICW6-4

Evaluation of response criteria in rheumatoid arthritis treated with biological disease-modifying antirheumatic drugs

Mariko Inoue^{1,2}, Hiroko Kanda^{1,2}, Shoko Tateishi^{1,2}, Keishi Fujii¹

¹Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, ²Department of Immunotherapy Management, Graduate School of Medicine, The University of Tokyo

Conflict of interest: Yes

[Object] There are several mechanisms of action in biologic disease-modifying anti-rheumatic drugs (bDMARDs) used for rheumatoid arthritis (RA) treatment. Interleukin-6 inhibitor (IL-6i) blocks the production of acute-phase reactant (APR) proteins, which are part of the composite measures of disease activity of RA. In this study, we examined agreement between the European League Against Rheumatism (EULAR) response based on ESR or CRP, the Simplified Disease Activity Index 50% (SDAI50), and the Clinical Disease Activity Index 50% (CDAI50) response measures in patients treated with IL-6i and other bDMARDs. [Methods] We enrolled 306 RA patients who started or switched bDMARDs. Treatment response at 6 months was analyzed. Kappa statistics

were used to evaluate the agreement between different response measures. The contribution of the APRs to improvement in disease activity scores was compared between different response measures. Change of Health Assessment Questionnaire (HAQ) score was analyzed in patients treated with IL-6i. [Results] There was good agreement between each response measure, with κ above 0.6 in patients treated with tumor necrosis factor inhibitors (TNFi) or cytotoxic T-lymphocyte-associated antigen 4 immunoglobulin fusion protein (CTLA4Ig). In patients treated with IL-6i, the agreement was low between the EULAR response (ESR) and the SDAI50 or the CDAI50 (κ , 0.43 and 0.37, respectively). Under IL-6i treatment, APR improvement accounted for 56.0% of total improvement of the DAS28-ESR. When discordance was found between the CDAI50 and EULAR response in IL-6i-treated patients, all patients were classified as EULAR-only responders. And there was no HAQ improvement in IL-6i-treated patients who only showed EULAR response and no CDAI50 response. [Conclusions] EULAR response criteria overestimate the response under IL-6i treatment because the APR improvement largely contributes to the DAS28 improvement.

ICW6-5

15-year changes in clinical outcome of bDMARDs in patients with rheumatoid arthritis ~from FIRST registry~

Shunsuke Fukuyo¹, Kazuhisa Nakano¹, Shingo Nakayamada¹, Shigeru Iwata¹, Kentaro Hanami¹, Satoshi Kubo¹, Ippei Miyagawa¹, Ayako Yamaguchi¹, Yusuke Miyazaki¹, Akio Kawabe¹, Kazuyoshi Saito², Yoshiya Tanaka¹

¹Department of First Internal Medicine, University of Occupational and Environmental Health, Japan, ²Institute of Rheumatology, Tobata General Hospital

Conflict of interest: Yes

Objective: The aim of this study was to explore changes in clinical outcome in RA patients treated with bDMARDs over a 15-year period. **Methods:** We used clinical data from FIRST registry which included all patients with RA who initiated bDMARDs therapy during 2003-2017 in our hospital. We divided 15 years into 5 terms every 3 years (2003-2005/2006-2008/2009-2011/2012-2014/2015-2017). The primary endpoint was the proportion of patients with CDAI remission at month 12 in each term. **Results:** In total 3067 patients were included. The mean age was increased over time (55.0→57.5→59.7→61.5→64.0 years). The mean CDAI score at baseline (BL) was approximately 30. 90 % of patients had moderate to high disease activity at baseline. The retention rates of bDMARDs at month 12 were almost 80 %. The proportion of patients with remission at month 12 increased over time (16.9→22.6→32.5→33.7→32.0%). In logistic regression analysis, the factors that associated with CDAI remission were low BL-CDAI, HAQ, oral GC use and high bio-naïve rate. CDAI, oral GC use and bio-naïve rate were decreased and HAQ was increased over time. The incident of adverse event (1000 person-years) was decreased over time (57.2→48.0→48.0→37.3→15.8). The incident of pneumonia (1000 person-years) was decreased over time (25.2→13.5→7.9→9.5→2.4). **Conclusions:** Elderly patients treated with bDMARDs have gradually increased for 15 years in the FIRST registry. The retention rate and effectiveness of bDMARDs sustained, whereas incidence of adverse events rather decreased. Increase in option of bDMARDs could lead to such 15-year improvement.

ICW6-6

Predictive factors for remission achievement by tocilizumab monotherapy in patients with rheumatoid arthritis after inadequate response to methotrexate: a post hoc analysis of the SURPRISE study

Masaru Kato¹, Yuko Kaneko², Yoshiya Tanaka³, Masayuki Inoo⁴, Hitomi Haraoka⁵, Koichi Amano⁶, Masayuki Miyata⁷, Yohko Murakawa⁸, Hidekata Yasuoka², Shintaro Hirata⁹, Hayato Nagasawa⁶, Eiichi Tanaka¹⁰, Nobuyuki Miyasaka¹¹, Hisashi Yamanaka¹⁰, Kazuhiko Yamamoto¹², Tatsuya Atsumi¹, Tsutomu Takeuchi²

¹Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan, ²Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, ³The First Department of Internal Medicine, University of Occupational and Envi-

ronmental Health, Kitakyushu, Japan, ⁴Internal Medicine, Utazu Hospital, Ehime, Japan, ⁵Division of Hematology and Rheumatology, Nihon University School of Medicine, Tokyo, Japan, ⁶Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan, ⁷Department of Internal Medicine, Fukushima Red Cross Hospital, Fukushima, Japan, ⁸Department of Rheumatology, Shimane University Faculty of Medicine, Izumo, Japan, ⁹Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan, ¹⁰Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, ¹¹Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, ¹²Department of Allergy and Rheumatology, Graduate School of Medicine, University of Tokyo, Tokyo, Japan

Conflict of interest: Yes

[Object] To identify predictive factors for clinical and structural remission by tocilizumab without methotrexate in patients with rheumatoid arthritis (RA). [Methods] This is a post hoc analysis of the SURPRISE study, a 2-year randomized, controlled study comparing the efficacy of tocilizumab with (ADD-ON) and without methotrexate (SWITCH) in active RA patients despite methotrexate therapy. The primary endpoint was the DAS28 remission (< 2.6) at week 24. The change in modified total Sharp score from baseline to week 52 (Δ mTSS/year) was also assessed as an endpoint. Patient characteristics and clinical parameters, including serum levels of CRP, IL-6, SAA, MMP-3, RF and IgG, were compared between patients who achieved DAS28 remission at week 24 and those who did not. [Results] In SWITCH (n = 96), SAA levels and DAS28 at baseline were significantly higher in patients who did not achieve DAS 28 remission at week 24 than those who did (85.0 mg/mL vs 15.3 mg/mL, p = 0.006; 5.7 vs 5.0, p = 0.01; respectively). Structural remission (Δ mTSS/year \leq 0.5) rate at week 52 was significantly higher in patients with SAA of < 85.0 mg/mL than those with SAA of \geq 85.0 mg/mL (71% vs 50%, p = 0.046). In contrast, in ADD-ON (n = 98), whereas DAS28 at baseline was also higher in patients who did not achieve DAS 28 remission (5.6 vs 4.9, p = 0.005), SAA levels were not relevant (25.6 mg/mL vs 24.7 mg/mL, p = 0.99). In patients with SAA < 85.0 mg/mL and DAS28 < 5.1 at baseline, both DAS28 remission (85% vs 81%, p = 0.77) and structural remission (77% vs 76%, p = 1.00) rate were comparable between ADD-ON and SWITCH. [Conclusions] SAA levels and disease activity at baseline can predict the necessity of concomitant methotrexate in tocilizumab initiation in patients with RA. Patients with both low levels of SAA and moderate disease activity at baseline may benefit similarly from tocilizumab therapy with and without methotrexate in terms of achieving clinical and structural remission.

ICW7-1

Long-term retention rates of biologic disease-modifying antirheumatic drugs in elderly and very elderly patients with rheumatoid arthritis from the FIRST registry

Akio Kawabe, Satoshi Kubo, Kazuhisa Nakano, Shingo Nakayamada, Shigeru Iwata, Kentaro Hanami, Shunsuke Fukuyo, Ipppei Miyagawa, Ayako Yamaguchi, Yusuke Miyazaki, Yoshiya Tanaka
The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan

Conflict of interest: None

[Object] Japan is facing a "super-aged" society, the wide use of bDMARDs for elderly RA patients is required. Here, we examined long-term retention rates (RRs) of bDMARDs to clarify the effectiveness and safety for elderly RA patients. [Methods] Data from patients (n=999) who were treated with abatacept (ABT), etanercept (ETN), and tocilizumab (TCZ) between February 2011 and October 2017 were retrospectively extracted from the FIRST registry. The elderly patients aged 65-74 and \geq 75 were 329 and 262, respectively. The primary endpoint was the RR, and the secondary endpoints were reasons for discontinuation and serial changes of CDAI. The Propensity Score Matching (PSM) and Inverse Probability of Treatment Weighting (IPTW) were used to accommodate selection bias. [Results] Patients characteristics (all ages/65-74/ \geq 75) were as follows: mean age 65/70/80 years, disease duration 9.6/10.8/10.3 years, SDAI 28.2/28.2/30.2, HAQ-DI 1.484/1.497/1.849, pre-existing lung disease 37/39/47%, and MTX use 64/59/60%. The

5-year RRs (all ages/65-74/ \geq 75) by Kaplan-Meier method were 50/52/43% (65-74 vs \geq 75, p=0.22). The 5-year RRs (ABT/ETN/TCZ) in the patients aged 65-74 and \geq 75 were 49/52/59% (no difference) and 52/34/20% (ABT vs ETN, p=0.03), respectively. In the patients aged \geq 75, the 5-year RRs (ABT/ETN) after the use of PSM and IPTW were 50/35% (p=0.02) and 52/37% (P=<0.001), respectively; the RR of ABT was significantly higher. The rates of the reasons of discontinuation (inadequate response/adverse events: AEs) were 17/4% in ABT, 16/21% in ETN, and 15/15% in TCZ; the rate of AEs in ABT tended to be lower. Serial changes of CDAI were similar between ABT, ETN, and TCZ. [Conclusions] ABT therapy showed the high RR in elderly patients aged \geq 75; fewer AEs might lead to the outcome. Therefore, bDMARDs should be selected differentially among ages, namely, careful consideration for 65-74 and \geq 75 years would be required to generate a better outcome.

ICW7-2

Discontinuation of oral glucocorticoid after initiation of biological DMARD due to a higher dose of methotrexate; a retrospective observational study based on data from a Japanese multicenter registry study

Mochihito Suzuki, Toshihisa Kojima, Nobunori Takahashi, Shuji Asai, Nobuyuki Asai, Takuya Matsumoto, Yasumori Sobue, Tsuyoshi Nishiume, Naoki Ishiguro
Department of Orthopedic Surgery, Nagoya University Hospital

Conflict of interest: Yes

[Object] In the treatment of rheumatoid arthritis (RA), glucocorticoid (GC) that provide anti-inflammatory effects in the early stage of treatment is an important drug. We recommend discontinuing of GC as much as possible within 6 months, but many patients have taken oral GC for the long term in daily clinical practice. The aim of this study is to examine association of methotrexate (MTX) dose with discontinuation of GC after one year since initiation of biological DMARD (bDMARD) as 1st bDMARD. [Methods] We established the large observational cohort, the Nagoya University orthopedic facility multicenter study (TBCR). 564 patients who used GC and MTX when bDMARD was initiated as 1st bDMARD were included. In the first study, we examined predictive factors of discontinuation of GC after one year since initiation of bDMARD by using multivariate analysis in the two groups, 400 patients continued to use GC and 164 patients discontinued to use GC. In the second study, we adjusted the background at the time of initiation of bDMARD by using propensity score matching (PS) in the two groups, MTX \leq 8mg (L group) and MTX >8mg (H group). [Results] In the multivariate analysis, age (Odds ratio (OR)0.98), MTX dose (OR1.09) and GC dose (OR0.88) were independently predictive factors of discontinuation of GC. When we adjusted age, disease duration, sex, disease activity, RF/ACPA, GC dose by using PS matching, 105 pairs were extracted. There were obvious significant differences between 24 patients (22.9%) in the L group and 43 cases (41.0%) in the H group (P = 0.007), where GC were discontinued at one year after the initiation of bDMARD. [Conclusions] In the clinical practice, MTX dose at the time of initiation of bDMARD was predictive factor of discontinuation of GC. A higher dose of MTX associated with discontinuation of GC in the patients treated with bDMARD.

ICW7-3

De-escalation of treatments after sustained remission in patients with RA - The FREE-J study, a real world prospective observational cohort study

Ayako Yamaguchi¹, Shintaro Hirata², Toshiaki Miyamoto³, Kazuhide Tanimura⁴, Hideyuki Iwai⁵, Yuko Kaneko⁶, Tsutomu Takeuchi⁶, Koichi Amano⁷, Naoki Iwamoto⁸, Atsushi Kawakami⁸, Miho Murakami⁹, Norihiro Nishimoto⁹, Tatsuya Atsumi¹⁰, Masahiro Yokosawa¹¹, Takayuki Sumida¹¹, Tsuneyo Mimori¹², Hisashi Yamanaka¹³, Keishi Fujio¹⁴, Kazuhisa Nakano¹, Yoshiya Tanaka¹

¹The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, ²Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Japan, ³Department of Internal Medicine and Rheumatology, Seirei Hamamatsu General Hospital, Japan, ⁴Department of Rheumatology, Hokkaido Medical Center for Rheumatic Diseases, Sap-

poro, Japan, ⁵Department of Medicine and Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, ⁶Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, ⁷Division of Rheumatology and Clinical Immunology, Department of Internal Medicine, Saitama Medical Center, Saitama Medical University, Saitama Japan, ⁸Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ⁹Department of Molecular Regulation for Intractable Diseases, Institute of Medical Science, Tokyo Medical University, Osaka, Japan, ¹⁰Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido, Japan, ¹¹Department of Internal Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan, ¹²Department of Rheumatology and Clinical Immunology, Kyoto University Graduate School of Medicine, Kyoto, Japan, ¹³Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, ¹⁴Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Japan

Conflict of interest: None

Objective: To investigate 1-year dose-reduction or discontinuation of DMARDs after sustained remission in RA patients in the FREE-J (drug-FREE remission in Japan) study. **Methods:** The FREE-J study is a real world prospective observational study focusing on tapering or withdrawal of MTX and/or bDMARDs after sustained remission in RA patients treated with both MTX (≥ 8 mg) and bDMARDs. After the sustained remission (DAS28-ESR <2.6) for at least 2 consecutive visits, different treatment strategies, including continuation, dose-reduction or withdrawal of MTX or bDMARDs, were selected according to shared decision making. The primary endpoint was the remission (DAS28-ESR <2.6) rates after 1 year of the study entry. **Results:** We recruited 436 patients with mean age 57.5 years, mean disease duration 105.3 months and mean DAS28-ESR score was 1.74 ± 0.57 . The number of patients for each strategy; 1) 80 continued all DMARDs, 2) 184 reduced dose of MTX, 3) 24 discontinued MTX, 4) 68 reduced bDMARDs, 5) 71 discontinued bDMARDs. The remission rate 1 year after the study entry was 1) 86%, 2) 82%, 3) 83%, 4) 75%, 5) 56%, respectively, in which only group 5), discontinuation of bDMARDs was significantly different from group 1), continuation of all DMARDs (OR:0.2, 95%CI:0.09-0.5, $p < 0.001$). By the multivariate analysis, the presence of bDMARDs, lower score of DAS28-ESR and lower value of anti-CCP at the study entry were significantly correlated with the maintained remission for 1 year after the de-escalation of DMARDs. There were no significant differences in the maintained remission among different bDMARDs. **Conclusions:** After sustained remission in RA patients treated with MTX and bDMARDs, the remission rate 1 year after dose-reduction of MTX or bDMARDs and withdrawal of MTX was statistically comparable to that of continuation of treatments and the use of bDMARDs significantly affected with the maintained remission for 1 year after the de-escalation of DMARDs.

ICW7-4

The effects of erythrocytes and platelets on disease activity in patients with rheumatoid arthritis - ANSWER longitudinal cohort study -

Akira Onishi¹, Kengo Akashi¹, Sadao Jinno¹, Yonsu Son², Hideki Amuro², Toru Hirano³, Yuichi Maeda³, Motomu Hashimoto⁴, Wataru Yamamoto^{4,5}, Kosaku Murakami⁶, Ryota Hara⁷, Masaki Katayama⁸, Tohru Takeuchi⁹, Takuya Kotani⁹, Yoshikazu Fujikawa¹, Takumi Nagamoto¹, Yuzuru Yamamoto¹, Hirotaka Yamada¹, Yoshihide Ichise¹, Ikuko Naka¹, Takaichi Okano¹, Yo Ueda¹, Sho Senda¹, Jun Saegusa¹, Akio Morinobu¹

¹Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, ²First Department of Internal Medicine, Kansai Medical University, ³Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University, ⁴Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, ⁵Department of Health Information Management, Kurashiki Sweet Hospital, ⁶Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, ⁷The Center for Rheumatic Diseases, Nara Medical University, ⁸Department of Rheumatology, Osaka Red Cross Hospital, ⁹Department of Internal Medicine IV, Osaka Medical College

Conflict of interest: None

[Objective] While experimental models suggest both erythrocytes and platelets can activate immune cells and enhance inflammation in inflammatory arthritis, no studies have demonstrated the number or form of erythrocytes and platelets predicts disease activity in patients with RA. Therefore, the objective of this multi-center cohort study is to identify the effects of erythrocytes and platelets on disease activity in RA patients. [Methods] Hemoglobin concentrations, platelet counts, red blood cell distribution (RBW), and mean platelet volume (MPV) were measured in RA patients. Disease activity was assessed using disease activity score 28-CRP (DAS28-CRP) for primary outcome. Linear mixed-effect models were used to examine whether the indices of erythrocytes and platelets on the previous visit predicted disease activity on the next visit when adjusted with the previous disease activity. The indices of erythrocytes and platelets, and disease activity were used as time-dependent variables while participant identification number and time from baseline were included as random factors. Age, sex, disease duration, RF, ACPA, and DMARDs were included as covariates. [Results] A total of 24288 samples (median sampling interval: 63.6 days) from 1927 patients was included. The median age at baseline was 66.0 years with 76.5 % of women. Regarding erythrocytes, lower hemoglobin concentrations predicted higher disease activity ($P = 0.001$) while RDW did not. As for platelets, the next disease activity was significantly higher in patients with higher platelet counts ($P < 0.001$) and lower MPV ($P = 0.002$) on the previous visit. [Conclusion] These results suggest the number or form of erythrocytes and platelets captures disease activity that remain unmeasured by established disease activity measures in RA. These may also support erythrocytes and platelets influence immune and inflammatory processes in patients with RA as well as the established opposite causal relationship.

ICW7-5

Difference in health care utilization in RA patients according to seropositivity

Hyounyoung Kim¹, Soo-kyung Cho¹, Seongmi Choi², Seul Gi Im³, Sunyoung Jung⁴, Eun Jin Jang³, Yoon-kyoung Sung¹

¹Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, ²Department of Statistics, Kyungpook National University, Daegu, Korea, ³Department of Information Statistics, Andong National University, Andong, Korea, ⁴College of Pharmacy, Chung-Ang University, Seoul, Korea

Conflict of interest: None

[Object] We aimed to compare health care utilization between patients with seropositive (SP) and seronegative (SN) rheumatoid arthritis (RA). [Methods] Using the Korean nationwide healthcare claims database between 2012 and 2016, we selected patients with SPRA and SNRA. We compared the three indices of healthcare utilization: current medications, clinic visits and hospitalization, and direct medical cost of the year. Changes of the indices from 2012 to 2016 in each SPRA and SNRA group were also analyzed. [Results] A number of 103,815 SPRA and 75,809 SNRA patients in 2016 were included. In current medications, methotrexate (MTX) and biologic agents were commonly used SPRA patients (73.2% and 7.9%, respectively) than SNRA patients (30.3% and 2.9%, respectively). However, the prevalence of glucocorticoids use was high in both groups; 81.9% of SPRA and 73.6% of SNRA patients. Patients with SPRA visited outpatient clinic more frequently than SNRA patients (6.0 ± 3.7 and 4.4 ± 4.0 times/year, respectively), while the number of hospitalization per person was similar in both groups (1.5 ± 1.1 /year of SPRA, 1.4 ± 1.2 of SNRA, respectively). Annual direct medical cost of 2016 for each SPRA patient was higher than that of SNRA patient (1,026.7 USD and 449.8 USD, respectively) and its increase between 2012 and 2016 was prominent in SPRA patients (820.6 to 1026.7 USD) than SNRA patients (327.5 to 449.8 USD). Another change in health care utilization between 2012 and 2016 was an increase in the number of patients with biologic agents use and it was prominent in SPRA patients (4,466 to 8,177 in SPRA and 1,291 to 2,209 of SNRA). [Conclusions] The seropositivity could lead to the differences in the healthcare utilization in RA patients. Patients with SPRA showed higher rates of MTX use, biologic agents use, and outpatient clinic visits than SNRA patients. Total direct medical cost for each patient was also higher

in SPRA patients than SNRA patients.

ICW7-6

Treatment Patterns in DMARD Naïve Rheumatoid Arthritis Patients: A Retrospective Analysis of US Claims Data

Robin K Dore¹, Jenya Antonova²

¹Division of Rheumatology, David Geffen School of Medicine, University of California, Los Angeles, California, USA, ²Health Economics and Outcomes Research Division, Gilead Sciences, Foster City, California, USA

Conflict of interest: None

[Object] To better understand recent advances in pharmacologic therapy for rheumatoid arthritis (RA), this study evaluated recent treatment patterns in RA patients (pts) who newly initiated a DMARD. [Methods] Adult pts with more than 2 claims for RA initiating their first DMARD between 1/2012-9/2016, with 12-months continuous enrollment pre- and post-ID and without DMARD claims 12 months pre-ID were extracted from a commercial database including medical and pharmacy health insurance claims covering about 40 million people annually. Use of conventional synthetic DMARDs (csDMARDs), TNF inhibitors (TNFi), anti-IL6 pathway antibodies, other biologic DMARDs (bDMARDs), and JAK inhibitors (JAKi), as monotherapy and in combination with csDMARDs, was described, with median therapy duration assessed via Kaplan-Meier curves. Drug discontinuation, switching, or addition of another DMARD marked end-of-treatment. [Results] Of 26,808 pts (74.2% female; mean age 51.9), most (97.7%) initiated monotherapy, with csDMARD (91.3%) and TNFi (6.6%) being the most frequently prescribed monotherapies. For combination therapy with csDMARDs, TNFi (88.0%) and other bDMARDs (7.3%) were most common. Median duration of index therapy did not significantly differ for monotherapy vs. combination therapy ($p = 0.110$). Therapy discontinuation was high; by day 90, only 71% (monotherapy) and 70% (combination) of patients remained on index therapy, and by day 360, fewer than 40% of patients remained on index therapy. Median treatment duration was 230 days (csDMARD monotherapy), 225 vs. 206 days (TNFi combination vs. monotherapy, respectively), 227 vs. 203 days (anti-IL6), 198 vs. 182 days (other bDMARDs), and 347 vs. 301 days (JAKi). [Conclusions] In a retrospective health claims study, RA pts initiating DMARDs had median duration of therapy of less than a year, suggesting a need for improved durability among treatments. However, compared to other therapies, JAKi demonstrated the longest median duration.

ICW8-1

Peripheral immunophenotyping in idiopathic inflammatory myopathies differs between myositis-specific antibodies

Yasuyuki Todoroki¹, Satoshi Kubo¹, Shingo Nakayamada¹, Yusuke Miyazaki¹, Ippei Miyagawa¹, Hiroko Yoshinari¹, Yoshino Inoue¹, Naoaki Ohkubo¹, Shigeru Iwata¹, Shunsuke Fukuyo¹, Kentaro Hanami¹, Akio Kawabe¹, Shin Tanaka⁴, Kazuhisa Nakano¹, Minoru Satoh^{1,2}, Kazuyoshi Saito^{1,3}, Yoshiya Tanaka¹

¹First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, ²Department of Clinical Nursing, School of Health Sciences, University of Occupational and Environmental Health, Japan, ³Department of Rheumatology, Tobata General Hospital, ⁴Department of Clinical Pathophysiology, School of Health Sciences, University of Occupational and Environmental Health, Japan

Conflict of interest: None

[Objective] Idiopathic inflammatory myopathies (IIMs) can be classified into subgroups according to myositis-specific antibodies (MSAs) and the pathological findings of muscles. The purpose of this study was to clarify the peripheral immune cell phenotype differences among these subgroups. [Methods] Peripheral blood mononuclear cells obtained from 82 patients with untreated IIMs were used for comprehensive flow cytometric analysis based on the Human Immunology Project Consortium. MSAs were detected by immunoprecipitation and ELISA. [Results] Overall, the proportion of activated CD4⁺ (especially, Th1, Th17 and Treg) and activated CD8⁺ T cells were higher in IIMs than in healthy

controls. Similarly, the proportion of IgD-CD27-B cells and plasmablast were increased. However, the immune cell phenotypes of subgroups classified by MSAs (Anti-ARS; n=30, Anti-MDA5; n=22, Anti-TIF1 γ ; n=12, Others; n=18) were different. The most remarkable immune dysregulation was observed in anti-TIF1 γ patients. In these patients, the proportions of activated T cells of CD4⁺/CD8⁺ T cells and plasmablast were significantly higher than other cases. Next, if we compared anti-ARS⁺ and anti-MDA5⁺ patients who had interstitial lung disease, the proportions of IgD-CD27-B cells and plasmablast were significantly higher in anti-MDA5⁺ patients than in anti-ARS⁺ patients. In sharp contrast, effector memory CD8⁺ cells were increased in anti-ARS⁺ patients. In terms of the comparison of clinical features, the strong immune dysregulations of both T and B cell were observed in cases accompanied with malignancy among anti-TIF1 γ patients. Meanwhile, the proportion of plasmablast was correlated with serum level of ferritin which is one of the poor prognostic factors in anti-MDA5⁺ patients. [Conclusions] Immunophenotyping in IIMs revealed the differences among subgroups according to MSAs. These findings clearly showed the heterogeneity of IIMs and indicate different treatment target molecules for these subgroups.

ICW8-2

Serum Fatty Acid Binding Protein 3 (FABP3) levels differentiate active from inactive myositis and correlate with response to therapy

Latika Gupta, Sanjukta Majumder, Amita Aggarwal, Ramnath Misra, Able Lawrence

Sanjay Gandhi PostGraduate Institute of Medical Sciences, Lucknow, India

Conflict of interest: None

[Object] Idiopathic Inflammatory Myositis (IIM) results in significant morbidity, and often mortality. While delayed diagnosis leads to wasted muscles, conventional markers fail to differentiate the reversible component of subclinical inflammation amongst prevalent damage. Fatty Acid Binding Protein 3 (FABP3) is a small cytosolic protein involved in fatty acid transport that is preferentially expressed in slow twitch skeletal muscle fibers. Its selective expression makes it a suitable candidate biomarker to differentiate leaky diseased muscles from those with damage. [Methods] Patients with inflammatory myositis seen between December 2017 to August 2018 were recruited. Those with active infection, pregnancy, renal dysfunction or chronic kidney disease were excluded. Apart from patient and disease variables, activity and damage were assessed using standard IMACS core set measures. Sera were collected at first visit and in those with active disease follow up samples were collected at six months. Those with MDAAT activity score greater than or equal to one were scored as active disease. FABP3 was estimated in sera using ELISA. Non-parametric tests were used for paired and unpaired analysis. [Results] 132 myositis (12 JDM, 55 DM, 19 PM, 21 Overlap and 24 ASS) patients (33 men and 99 women) with median age 38 (24.5-46.0) years and disease duration 0.9 (2.3-5.1) years were included. Mean FABP3 values were higher in those with active (5.73 ng/ml) as compared with inactive (2.92 ng/ml, $p=0.0351$) disease. Of the nine cases followed up for 6 months, levels (Figure) fell with treatment in treatment responders ($n=7$, 14.5 to 7.5 ng/dl, $p=0.03$). FABP3 did not differ between those with different types of myositis or history of polycyclic versus monocyclic course. [Conclusions] Serum FABP3 may be a useful marker of disease activity and response to therapy in inflammatory myositis.

ICW8-3

Inhibition of necroptosis ameliorates in vitro and in vivo models of polymyositis

Mari Kamiya, Fumitaka Mizoguchi, Kimito Kawahata, Hitoshi Kohsaka
Department of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University (TMDU), Tokyo, Japan

Conflict of interest: None

[Object] In polymyositis (PM), CD8⁺ cytotoxic T lymphocytes (CTLs) play assumingly a crucial role in muscle injury. Inhibition of muscle cell death could be a novel therapeutic strategy in PM. The aims of this study are to clarify the mechanisms of CTL-mediated muscle injury and the pattern of cell death of muscle cells. [Methods] OT-I CTLs,

and their mutants lacking perforin 1 or granzyme B were cocultured with myotubes differentiated from C2C12 cells that were retrovirally transduced with the genes encoding MHC class I (H2K^b) and SIINFEKL peptide derived from ovalbumin (H2K^bOVA-myotubes) to discern how muscle cell death is mediated *in vitro* by CTL. C protein induced-myositis (CIM) was used to study the effect of necrostatin-1s (nec1s) on the severity of myositis *in vivo*. Muscle biopsy specimens of PM patients were examined with terminal deoxynucleotidyl transferase nick-end labeling (TUNEL) assay, and histologically for the expression of necroptosis associated proteins. [Results] OT-I CTLs lacking perforin 1 or granzyme B were as cytotoxic to H2K^bOVA-myotubes as wild type OT-I CTLs. Inhibition of Fas ligand by the Fas-Fc chimera protein reduced cytotoxicity of CTLs against the myotubes. The TUNEL assay and time-lapse imaging of cell death visualized by Annexin V and PI revealed that the cell death of the myotubes was non-apoptotic. The CTL-mediated cell death of myotubes was inhibited by nec1s, a necroptosis inhibitor but not by benzyloxycarbonyl-Val-Ala-Asp-fluoromethylketone, an apoptosis inhibitor. Therapeutic administration of nec1s ameliorated CIM. Immunohistological staining of muscle tissue of PM patients revealed the expression of Fas and necroptosis associated proteins including phosphorylated mixed lineage kinase domain like pseudokinase on injured muscle cells. [Conclusions] Necroptosis is involved in muscle cell death of PM. Inhibition of necroptosis should be a novel therapeutic strategy in PM.

ICW8-4

Anti-MDA5 Autoantibody (Ab) Associated Juvenile Dermatomyositis (JDM) constitute a distinct phenotype in North America

Gulnara Mamyrova¹, Takayuki Kishi², Ira N Targoff³, Rodolfo V Curiel¹, Frederick W Miller², Lisa G Rider²

¹Division of Rheumatology, Department of Medicine, George Washington University School of Medicine and Health Sciences, Washington DC, USA, ²Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health, ³Veteran's Affairs Medical Center, University of Oklahoma Health Sciences Center, and Oklahoma Medical Research Foundation

Conflict of interest: None

[Object] To examine frequency and characteristics of anti-MDA5 Ab associated JDM. [Methods] 35 pts with anti-MDA5 Ab associated JDM were compared to those of 157 anti-TIF1, 116 NXP2 and 60 MSA/MAA neg. Myositis Abs were tested by standard immunoprecipitation (IP) and IP-immunoblot. [Results] Anti-MDA5 Abs were identified in 35 (7.7%) pts from a cohort of 453 JDM and JCTM/DM. MDA5 were older at diagnosis vs. TIF1 (8.7 [6.0-13.2] vs. 7.2 [4.5-10.9], $p=0.05$) and vs. NXP2 (8.7 [6.0-13.2] vs. 6.3 [4.5-9.9], $p=0.01$). MDA5 had lower serum CK and aldolase, more frequently weight loss, adenopathy, arthralgia, arthritis, abnormal PFTs, dyspnea, ILD compared to TIF1 and NXP2. The median skeletal, pulmonary, constitutional and overall total clinical system scores at diagnosis were higher in MDA5 ($p<0.0001$). Total number or type of medications received was fewer (4.0 [IQR 3- 6] vs.5.0 [IQR 4- 8], $p=0.02$) and steroid treatment duration was shorter (17.0 [8.1-36.0] vs. 26.3 [14.1-50.5], $p=0.045$) in MDA5 vs. TIF1. MDA5 had fewer flares (46% vs. 70%, $p=0.014$) and shorter time to discontinue steroid therapy (30 mths [IRQ 17-66] vs. 61.0 [IRQ 25.6-134.0], $p=0.007$) vs. TIF1. MDA5 had shorter steroid treatment duration (17.0 mths [8.1-36.0] vs. 27.0 [16.4-48.0], $p=0.04$) vs. NXP2. Multivariable analysis revealed weight loss, arthritis, arthralgia, less frequent dysphagia and less frequent falling episodes were associated with MDA5 vs. anti-TIF1, whereas weight loss, arthritis, and less frequent dysphagia were associated with MDA5 vs. NXP2 and weight loss, arthralgia, arthritis, and periungual capillary changes were associated with MDA5 vs. MSA neg. MDA5 had comparable outcomes with the other groups. [Conclusions] MDA5 Abs are seen in a distinct subset of JDM with frequent arthritis, arthralgia, weight loss, adenopathy, and ILD, but lower serum CK and aldolase. MDA5 have comparable outcomes, but with the ability to discontinue steroids more rapidly and less frequent flares compared to TIF1.

ICW8-5

Myofasia-dominant inflammation is a novel risk factor for rapidly progressive interstitial lung disease in dermatomyositis: a study using whole body MRI

Kohei Karino, Michihiro Kono, Michihito Kono, Nobuya Abe, Yuichiro Fujieda, Masaru Kato, Toshiyuki Bohgaki, Olga Amengual, Kenji Oku, Shinsuke Yasuda, Tatsuya Atsumi

Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Conflict of interest: None

[Object] Rapidly progressive interstitial lung disease (RPILD) is a major cause of death in patients with dermatomyositis (DM). Although clinically amyopathic dermatomyositis (CADM) is one of the risk factors for RPILD, 70% of the patients with CADM do not develop RPILD. Whole-body magnetic resonance imaging (WB-MRI) can detect inflammation of whole muscle and myofascia. In this study, we assessed whether WB-MRI findings are related with RPILD in patients with DM. [Methods] This retrospective study comprised 27 patients with DM who underwent WB-MRI in our hospital. All MRI were performed before the initiation of treatment. Muscular and myofascial signal abnormalities were scored on 42 muscular groups. The ratio of myofascial score to muscular score (myofascia/muscle ratio) was calculated and used to define the relevance of myofascia-dominant inflammation. RPILD was defined as the acute onset and rapid worsening of dyspnea, hypoxemia and radiographic ILD/fibrosis within 1 month. [Results] Of 27 patients, 12 were CADM, and 19 had ILD, including 7 patients with RPILD. All patients including CADM showed abnormal signal intensity in muscle and myofascia (score median: 17 and 26). Muscle scores positively correlated with serum level of creatine kinase ($p<0.01$). The patients with RPILD showed a significantly higher myofascia/muscle ratio compared with the patients without RPILD (2.33 vs 1.41; $p=0.03$). Logistic regression analysis identified myofascia/muscle ratio >1.8 as an independent risk factor for RPILD [odds ratio = 14.6, 95% CI: 1.1, 180.2, $p=0.04$]. [Conclusions] We newly evaluated myofascia-dominant inflammation in patients with dermatomyositis using WB-MRI. Myofascia-dominant inflammation may be a novel risk factor for RPILD.

ICW8-6

Clinical features and outcomes of anti-MDA5 antibody positive patients with idiopathic inflammatory myositis

Huizhong Qiu, Guosheng Wang, Xiaomei Li, Xiangpei Li, Zhu Chen
The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui, 230001, P.R. China

Conflict of interest: None

Object: To detect the positive rate of anti-MDA5 antibody in patients with idiopathic inflammatory myositis (IIM) and to explore the relationship between anti-MDA5 antibody and clinical characteristics. Methods: Serum anti-MDA5 antibody levels from 64 patients collected in Anhui Provincial Hospital from March 2017 to February 2018 were detected by EUROBlotOne Fully Automatic Immunoblot Detection System. According to whether the anti-MDA5 antibody is positive or not, the patients were divided into two groups. The statistical methods used in this study including chi-square test, independent sample t-test, Mann-whitney U test, Kaplan-Meier test. Results: 64 patients can be divided into polymyositis (PM) group, dermatomyositis (DM) group, amyopathic/hypomyopathic dermatomyositis (ADM/HDM) group and other myositis groups, anti-MDA5 antibody positive rate: ADM/HDM group $>$ DM group $>$ PM group (70.6% $>$ 29.0% $>$ 0%, $P<0.05$). The incidence of arthritis, rash, interstitial lung disease (ILD), and fever was higher in patients with anti-MDA5 antibody positive than the negative group ($P=0.006$, 0.001, 0.001, 0.039). The incidence of acute/subacute ILD was significantly higher in patients with anti-MDA5 antibody positive than the negative group ($P=0.005$). Anti-MDA5 antibody positive group showed less muscle inflammation on the MRI than the negative group ($P=0.038$). In the laboratory related indicators, GGT and SF were higher in the anti-MDA5 antibody positive group than the negative group ($P=0.023$, 0.033), CK and LDH were lower than negative group ($P<0.05$, $P=0.021$). Estimated sur-

vival rates in our patients with anti-MDA5 antibody positive were 71.4% and 52.4% at 6 and 12 months, which are significantly lower than the negative group ($P < 0.001$). Conclusions: Anti-MDA5 antibody not only is useful for the diagnosis of ADM/HDM, but also may serve as a serum marker for acute/subacute ILD, mainly NSIP and UIP. Early monitoring of anti-MDA5 antibody in the course of the disease is helpful in predicting the progression of ILD disease, and prognosis.

ICW9-1

Prognosis of Severe Infection Recurrence Based on the Readministration of Biologic Disease Modifying Antirheumatic Drugs Post Treatment of Severe Infection in Rheumatoid Arthritis

Eri Oguro¹, Yuji Yoshida¹, Kentaro Kuzuya¹, Yasutaka Okita¹, Hidetoshi Matsuoka¹, Satoru Teshigawara¹, Maiko Yoshimura¹, Kentaro Isoda¹, Yoshinori Harada¹, Shiro Ohshima¹, Jun Hashimoto¹, Yukihiko Saeki²

¹Department of Rheumatology and Allergology, NHO Osaka Minami Medical Center, ²Department of Clinical Research, NHO Osaka Minami Medical Center

Conflict of interest: None

[Object] There is no consensus regarding the readministration of biological disease modifying antirheumatic drugs (bDMARDs) following treatment for infection. We investigated whether the readministration of bDMARDs following treatment for infection in patients with rheumatoid arthritis (RA) affects infection recurrence. [Methods] The study sample comprised patients with RA who were examined at the Osaka Minami Medical Center between January 2010 and December 2017 and were prescribed bDMARDs. We confirmed whether bDMARDs were re-administered to patients who developed severe infection requiring hospitalization while undergoing treatment with bDMARDs. We divided subjects into a bDMARDs readministration group and discontinuation group. We followed-up with patients over the following 12 months and used logistic regression analysis to investigate the odds ratios for severe infection recurrence owing to the readministration of bDMARDs. [Results] During the study period, bDMARDs were administered to 1,176 patients. Severe infection was observed 164 times in these patients. The severe infection onset rate was 5.73/100 person-years. There were 130 subjects (79.3%) in the bDMARDs readministration group following treatment for severe infection and 34 subjects (20.7%) in the bDMARDs discontinuation group. The severe infection recurrence rate after 12 months was 18.9%, with severe infection recurrence noted in 20 cases (15.4%) in the bDMARDs readministration group, and in 11 cases (32.4%) in the discontinuation group. The adjusted odds ratio for severe infection recurrence within 12 months in the bDMARDs readministration group was 0.46 (95% CI 0.16-1.33, $p = 0.15$). [Conclusions] Although high rate of severe infection recurrence was observed within 12 months in patients who developed a severe infection while being treated with bDMARDs, there was no significant difference in the incidence of severe infection recurrence between the bDMARDs readministration and discontinuation group.

ICW9-2

The disease activity and the use of corticosteroid but not use of biologics are associated with serious infection in rheumatoid arthritis patients -the data from MiRAi cohort-

Yuji Yoshida¹, Shiro Ohshima¹, Eri Oguro¹, Kentaro Kuzuya¹, Yasutaka Okita¹, Hidetoshi Matsuoka¹, Satoru Teshigawara¹, Maiko Yoshimura¹, Kentaro Isoda¹, Yoshinori Harada¹, Shigeyoshi Tsuji¹, Jun Hashimoto², Yukihiko Saeki³

¹Department of Rheumatology and Allergology, National Hospital Organization Osaka Minami Medical Center, ²National Hospital Organization Osaka Minami Medical Center, ³Department of Clinical Research, National Hospital Organization Osaka Minami Medical Center

Conflict of interest: None

[Object] Anti-rheumatic drugs were reported as an risk factors of infections. However, the association between infection and the disease activity and rheumatoid arthritis (RA) progression were controversial. Our aim was to describe serious infection events (SIEs), and investigate the relation between serious infectious risk and RA disease control and anti-

rheumatic drugs in real world patients with RA. [Patients] In total, 8206 patients/year RA outpatients were examined at the Osaka Minami Medical Center in the period from January 2012 to October 2017. The severity of infection was graded according to international criteria. [Results] The cohort contributed to 8206 patient-years of follow-up. There were 251 SIEs in 220 patients, at an average follow-up of 3.7 years. Incidence rate of SIE was 3.0 infections per 100 patient-years. The high disease activity (DAS28 $p < 0.001$, mHAQ $p < 0.01$), joint destruction (Stage $p = 0.02$), sex ($p < 0.01$), age ($p = 0.02$) and the use of corticosteroid ($p < 0.0001$) were associated with SIE. However, the use of biologics (TNF inhibitors, CTLA4-Ig, IL6 inhibitor) were not significantly associated with SIE. [Conclusions] From the data obtained from our cohort, good disease control of RA without the use of corticosteroid were considered very important to reduce serious infections.

ICW9-3

The use of biologic disease-modifying anti-rheumatic drugs does not increase surgical site infection and delayed wound healing after orthopaedic surgeries for rheumatoid arthritis

Yohei Kiso¹, Keiichiro Nishida¹, Masahito Watanabe¹, Minami Matsushashi¹, Shunji Okita¹, Hideki Ohashi¹, Ryuichi Nakahara², Yoshihisa Nasu³, Toshifumi Ozaki¹

¹Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ²Department of Intelligent Orthopaedic System, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ³Department of Medical Materials for Musculoskeletal Reconstruction, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

Conflict of interest: None

[Objective] The aim of the study was to examine whether the use of biologic DMARDs (bDMARDs) is a risk factor of surgical site infection (SSI) and delayed wound healing (DWH) after orthopaedic procedures for rheumatoid arthritis (RA). [Patients and Methods] We investigated incidence of SSI and DWH from medical records of 515 orthopaedic procedures for RA between 2013 and 2017 in our institution. The bDMARDs were stopped pre-operatively based on the half-life of each drug and restarted after removal of stitches according to the 2014 JCR guideline. Risk factors for SSI and DWH were assessed by univariate logistic regression analysis between age, sex, disease duration, pre-operative CRP and DAS28-CRP, BMI, DM, glucocorticoid use, smoke, MTX use, bDMARDs use and surgical procedure. Then, the demographic data of bDMARDs user group and non-user group are matched by Propensity Score (PS) to compare the incidence of SSI and DWH between two groups. [Results] In all cases, SSI and DWH occurred in 7 cases (1.4%) and 17 cases (3.3%), respectively. Two (1.1%) cases of SSI and 9 cases (4.9%) of DWH were recorded among 183 procedures for bDMARDs users. Univariate logistic regression analyses demonstrated that age and foot surgery were associated risk factors for SSI, and age, foot surgery and smoke for DWH. 157 cases were PS-matched for each group of bDMARDs user and non-users. It was confirmed that there was no significant differences in the incidence of SSI and DWH between bDMARDs users and non-users. [Conclusion] In our institution, average 36% of patients who underwent elective orthopaedic surgeries have been treated with bDMARDs at the time of the surgery after 2013. With adequate perioperative discontinuation, the bDMARDs use was not associated with an increased risk of SSI or DWH.

ICW9-4

Safety and efficacy of bDMARDs therapy in RA patients with nontuberculous mycobacteria lung disease (NTM-LD): FIRST registry

Hiroaki Tanaka¹, Kazuhisa Nakano¹, Akio Kawabe¹, Yusuke Miyazaki¹, Satoshi Kubo¹, Shunsuke Fukuyo¹, Shigeru Iwata¹, Shingo Nakayamada¹, Kazuyoshi Saito², Yoshiya Tanaka¹

¹The Department of First Internal Medicine, University of Environmental and Occupational Health, Japan, ²The Department of Rheumatology, Tobata General Hospital

Conflict of interest: None

[Object] The aims of our study were to assess the safety and efficacy

of bDMARDs in RA patients with NTM-LD. [Methods] 2076 RA patients were screened using CT-scan before starting their 1st bDMARDs treatment in our hospital from Apr 2005 to Apr 2018. NTM-LD were diagnosed by culture isolation and when PCR was positive but culture negative, NTM pulmonary colonization were diagnosed. After diagnosis, we consulted the department of respiratory medicine about management of NTM and started bDMARDs for NTM patients with high RA activity despite conventional therapy following IC. The primary endpoint was the proportion of NTM patients achieved LDA (DAS28-ESR<3.2). The secondary endpoint was continuation of bDMARD and the outcome of NTM-LD. [Results] We diagnosed 16 NTM-LD patients and 6 NTM pulmonary colonization patients during screening. Standard regimen (RFP, EB, CAM) was started for 12 patients, macrolides monotherapy for 2 patients and follow-up for 8 patients before starting bDMARDs (ABT 15, ETN 6, TCZ 1). NTM patients were significantly aged (67 vs 60 year old, $p=0.027$) and had long disease duration (141 vs 86 months, $p=0.026$), advanced Steinbrocker stage ($p=0.020$), while DAS28-ESR was equal between 2 groups (5.66 vs 5.68, $p=0.96$). 68% of NTM patients achieved LDA and 77% continued bDMARDs at 1 yr after starting bDMARDs. In 3 NTM patients bDMARDs were discontinued due to adverse event (AE) (LPD, scabies, death unrelated to NTM). Only in one patient who discontinued EB due to AE, NTM-LD worsened and MFLX was added continuing ABT. [Conclusion] CT-Screening before starting bDMARDs was useful to detect NTM-LD. Adequate diagnosis and management for NTM-LD could enable disease control of RA with bDMARDs.

ICW9-5

Cytomegalovirus reactivation during immunosuppressive therapy for rheumatic disease

Kensuke Suga, Aya Nishiwaki, Yosuke Toda, Yoko Yabe, Takayuki Nakamura, Daisuke Kashiwakuma, Shin-ichiro Kagami
Research Center for Allergy and Clinical Immunology, Asahi General Hospital, Chiba, Japan

Conflict of interest: None

[Object] Cytomegalovirus (CMV) reactivation is a life-threatening complication in immunosuppressive therapy. However, risk factors and treatment strategy for CMV reactivation among rheumatic disease are largely unknown. The aim of this study is to investigate risk factors for CMV reactivation and to propose a strategy for managing CMV reactivation in patients receiving immunosuppressive therapy for rheumatic disease. [Methods] We retrospectively analyzed 281 patients treated with immunosuppressive therapy in our department from January 2012 to April 2018. CMV reactivation was defined as positive > 1 CMV-positive cell per two slides (CMV pp65 antigenemia C10/C11). Patients with CMV reactivation were divided into two groups based on the presence of antiviral treatment for clinical symptoms. We determined a cut-off value of CMV-positive cells for the diagnosis of clinical CMV disease. [Results] The mean age was 61.0 ± 16.2 years and 194 (67%) were female. CMV reactivation was observed in 150 cases (53%), and thrombocytopenia was the most common clinical symptom (34 cases, 23%). In a multivariate analysis, CMV reactivation was associated with 4 following factors: lymphocyte counts $<1000/\mu\text{L}$ (OR 3.56 [2.10-6.12], $p<0.01$); total dose of prednisolone (PSL) $>2000\text{mg}$ (OR 1.89 [1.07-3.38], $p=0.03$); complication of interstitial pneumonia (OR 2.87 [1.68-4.98], $p<0.01$); combined use of immunosuppressants (OR 1.88 [1.10-3.22], $p=0.02$). The cut-off level of CMV pp65 antigenemia indicating clinical CMV reactivation was 10 positive cells per two slides by using receiver operating characteristic curve analysis (AUC 0.96, sensitivity 0.90, specificity 0.88). [Conclusions] Lymphocytopenia, total dose of PSL, complication of interstitial pneumonia and combined use of immunosuppressants are risk factors of CMV reactivation. We recommend that CMV pp65 antigenemia of >10 cells per two slides (C10/C11) in patients with rheumatic disease should be treated with antiviral drugs.

ICW9-6

The epidemiology and risk factors of severe herpes simplex virus infection in SLE patients: a nationwide study

Li Tzu-hao^{1,2}, Lai Chien-chih², Chang Yu-sheng³

¹Division of Allergy, Immunology, and Rheumatology, Department of Medicine, Chiayi Branch, Taichung Veterans General Hospital, Taiwan,

²Institute of Clinical Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan, ³Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan

Conflict of interest: None

[Object] Systemic lupus erythematosus (SLE) patients are susceptible to herpes simplex virus (HSV) infection, which is occasional but often leading to overwhelming disease such as encephalitis and keratitis. However, only few attempts have been made at the associated incidence and risk factors. [Methods] We enrolled SLE patients from the Taiwanese National Health Insurance research database between 1997 and 2012. We compared the incidence rate (IR) of severe HSV infection, including viral septicemia, meningoencephalitis, ocular infection, visceral infection and those with complications after infection, with those of non-SLE cohort. We also evaluated the risk factors of severe HSV infection by means of Cox multivariable proportional hazards model. [Results] A total of 122,520 subjects (24,504 SLE patients and 98,016 age- and gender-matched subjects as control group) were analyzed and revealed a significantly higher IR of severe HSV infection in SLE (Incidence rate ratio =3.52, $p<0.001$). Previous skin infection (HR=2.17, $p=0.047$), intravenous steroid pulse therapy (HR=4.48, $p<0.001$), oral daily steroid dose over 7.5mg prednisolone or equivalent (HR=1.60, $p=0.010$) were independent risk factors for severe HSV infection in SLE patients, while age under 18 (HR=0.47, $p=0.021$) was a protective factor. [Conclusions] A higher risk of severe HSV infection was observed in SLE patients. The risk factors for severe HSV infection were age over 18, previous skin infection, intravenous steroid pulse therapy and an oral daily steroid dose over 7.5mg.

ICW10-1

Automatic detection of hand joint region, ankylosis and subluxation in radiographic images using deep learning: development of artificial intelligence-based radiographic evaluation system for bone destruction

Keisuke Izumi^{1,2,3}, Masahiro Hashimoto^{3,4}, Kanata Suzuki^{3,5}, Toshio Endo^{3,5}, Kentaro Doi^{3,6}, Yuki Iwai^{3,6}, Jun Inamo¹, Yuichiro Ota¹, Nobuhiko Kajio¹, Jun Kikuchi¹, Komei Sakata¹, Satoshi Takanashi¹, Chihiro Takahashi¹, Hiroshi Takei¹, Hiroya Tamai¹, Kazuoto Hiramoto¹, Yuko Kaneko¹, Tsutomu Takeuchi^{1,3}

¹Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, ²Division of Connective Tissue Diseases, National Hospital Organization Tokyo Medical Center, ³Medical AI Center, Keio University School of Medicine, ⁴Department of Radiology, Keio University School of Medicine, ⁵Fujitsu Laboratories Ltd., ⁶Fujitsu Ltd.

Conflict of interest: Yes

[Object] Artificial intelligence (AI) techniques including deep learning have been rapidly evolving and have yielded appreciable benefits in many fields in recent years. In rheumatology field, however, these techniques have not been used often. In an early phase of development of an AI-based automatic radiographic evaluating system for bone destruction, we aimed to develop learning-based models to automatically detect hand joint region, ankylosis and subluxation in radiographic images. [Methods] A total of 130 radiographic image sets of both hands were randomly obtained from rheumatoid arthritis patients who had visited our division at Keio University Hospital in 2015. Well-trained rheumatologists determined the boundaries of regions of MP and PIP/IP joints and evaluated the presence of ankylosis and subluxation of each joint in radiographs. These evaluations of hand joints were performed using our developed annotation software tool. In learning phase, joint images were randomly divided into five sets for 5-fold cross validation. As deep learning models, we utilized Single Shot Multibox Detector (SSD) method with ensemble learning for detecting ankylosis and subluxation of MP and PIP/IP joint regions. [Results] Our model showed 100% detection rate of MP and PIP/IP joint regions. As a performance of detecting hand joint ankylosis and subluxation, our model presented precision values of 0.85 and 0.73, recall values of 0.94 and 0.79, and F-measure values of 0.90 and 0.76, respectively. [Conclusions] Deep learning-based models to automatically detect hand joint region, ankylosis and subluxation in radiographic images were developed with relatively small samples, which suggests that the

predictive performance may increase by collecting more training dataset. Next, we are elaborating a plan for a deep learning-based evaluating system for erosion and joint space narrowing.

ICW10-2

Enhanced resting-state functional connectivity of pain processing regions associated with insufficient response to biologics in inflammatory arthritis

Nobuya Abe, Yuichiro Fujieda, Kohei Karino, Michihito Kono, Masaru Kato, Kenji Oku, Toshiyuki Bohgaki, Olga Amengual, Shinsuke Yasuda, Tatsuya Atsumi

Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Conflict of interest: None

[Object] Resting-state functional magnetic resonance imaging (rs-fMRI) studies previously demonstrated abnormal functional connectivity of brain related to chronic pain. However, the association between therapeutic response and abnormal functional connectivity in patients with inflammatory arthritis is still unknown. This study aimed to investigate whether the abnormal functional connectivity could predict poor response to biologics therapy in patients with rheumatoid arthritis (RA) or axial spondyloarthritis (axSpA) using rs-fMRI. [Methods] RA/axSpA patients requiring biologics treatment, underwent rs-fMRI and a clinical evaluation at baseline and 3 months. Disease activity was assessed by simplified disease activity index (SDAI) for RA and the Ankylosing Spondylitis Disease Activity Score (ASDAS) for axSpA. Therapeutic insufficiency was defined as non-fulfillment of SDAI/ASDAS response criteria at 3 months. The network-to-whole brain connectivity were analyzed to evaluate the correlation between the functional connectivity of each network and clinical remission at 3 months. Results were significant on the cluster level with a false discovery rate corrected p value (p-FDR) less than 0.05. [Results] Sixteen patients (11 RA, 5 axSpA, median age 60 years, 77.8% women, biologics naïve 77.2%) were analyzed. SDAI for RA and ASDAS for axSpA at baseline were 15.0 [6.15-21.8] and 2.31 [1.27-3.16], respectively. Administrative biologics included tumor necrosis factor α inhibitors (44%), and 11 patients (68.8%) achieved remission at 3 months. The rs-fMRI analyses revealed that the therapeutic insufficiency correlated with the left post-central gyrus connectivity to the left temporal pole ($r = 0.49$, p-FDR = 0.012). [Conclusion] RA/axSpA patients with persistent disease activity despite biologics therapy would share neurobiologic features of the enhanced association between left post-central gyrus and temporal pole, being potential biomarkers for therapeutic response.

ICW10-3

Lung consolidation and mediastinal lymphadenopathy in patients with early anti-citrullinated protein antibody-positive rheumatoid arthritis

Yushiro Endo, Tomohiro Koga, Shin-ya Kawashiri, Naoki Iwamoto, Kunihiro Ichinose, Mami Tamai, Hideki Nakamura, Tomoki Origuchi, Atsushi Kawakami

Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: None

[Object] Because pulmonary disorder may influence a patient's choice of treatments, it is important for clinicians to determine factors related to pulmonary involvement in rheumatoid arthritis (RA) patients. A previous report showed that patients with early anti-citrullinated protein antibody (ACPA) positive RA have a higher frequency of lung abnormalities than patients with early RA who are ACPA-negative; however, few reports show associations between lung lesions and ACPA-positive RA. We aimed to determine lung field characteristics associated with patients with early RA and ACPA-positivity. [Methods] We enrolled early RA 74 patients between 2014 and 2017 at our institution. All patients underwent power Doppler joint ultrasound and chest computed tomography (CT) within a few months of their first visits to our department. CT findings

were blindly reviewed by two experienced thoracic radiologists who achieved good consensus. We compared clinical profiles, including CT findings, between patients with early RA who were ACPA-negative and ACPA-positive. [Results] CT showed no significant differences in airway lesions. The ACPA-positive group had more findings of consolidation and mediastinal lymphadenopathy than the ACPA-negative group. Multivariate analyses showed that ACPA-positivity was an independent factor predicting consolidation and mediastinal lymphadenopathy in early RA patients. Interestingly, percent consolidation and mediastinal lymphadenopathy were associated with high RA disease activity and smoking history for the ACPA-positive, but not -negative, RA group. [Conclusions] Lung consolidation and mediastinal lymphadenopathy were associated with ACPA production in early RA patients. Lung consolidation detected via CT may be associated with high disease activity in ACPA-positive patients with early RA.

ICW10-4

Impact of Biological Treatment on Left Ventricular Regional Dysfunction in Rheumatoid Arthritis Patients Determined with Global Circumferential and Longitudinal Strain Values using Cardiac Magnetic Resonance Imaging

Isamu Yokoe^{1,2}, Hitomi Haraoka², Atsuma Nishiwaki², Yosuke Nagasawa², Kaita Sugiyama², Yutaka Tanikawa², Masashi Oshima², Marina Hamaguchi², Hiroshi Tsuzuki², Natsumi Ikumi², Takamasa Nozaki², Hiromi Karasawa¹, Takako Shimizu¹, Mitsuhiro Iwata², Noboru Kitamura², Masami Takei²

¹Department of Rheumatology and Internal Medicine, Kyoundo Hospital, Sasaki Institute, Tokyo, Japan, ²Division of Hematology and Rheumatology, Nihon University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] Congestive heart failure (CHF) is a major contributor to morbidity and mortality in patients with rheumatoid arthritis (RA). However, Myocardial disease is typically clinically silent. Feature-tracking (FT) cardiac magnetic resonance (CMR) imaging can be used to assess early left ventricular (LV) dysfunction. This study aimed to assess LV regional function in RA patients and to determine the impact of biological treatment using global circumferential and longitudinal strain values, assessed by FT-CMR. [Methods] RA patients and controls without cardiac symptoms were enrolled, and those with no history and/or clinical findings of cardiovascular disease underwent non-contrast CMR. Patients with RA were administered synthetic disease-modifying antirheumatic drugs (sDMARDs) or biologic DMARDs (bDMARDs). All subjects underwent evaluation of LV regional function, as measured by CMRI. LV global longitudinal peak systolic strain (GLS) and global circumferential peak systolic strain (GCS) were calculated in the 16 LV segments. [Results] We compared 100 RA patients with 30 healthy controls. No statistically significant differences in cardiovascular risk (CV) factors were observed in the characteristics. GCS was significantly reduced by 29% in the RA group compared to controls (p<0.001). Furthermore, GCS was significantly lower by 17% in the sDMARD group than in the bDMARD group (p<0.001). GCS in the RA group was associated with the Disease Activity Score (DAS28). GLS in the RA group was significantly reduced by 15% compared to the control group (p<0.05). GLS was lower by 16% in the sDMARD group than in the bDMARD group. [Conclusions] This prospective study assessed LV regional dysfunction in RA, using global circumferential and longitudinal strain values on CMR. Subclinical LV regional dysfunction of GCS and GLS was prominent in RA patients without cardiac symptoms. Biologic treatment may normalize LV regional dysfunction, associated with a reduction in disease activity.

ICW10-5

Detection of left ventricular regional function in primary Sjögren's syndrome patients without cardiac symptoms, as assessed by feature tracking cardiac magnetic resonance imaging

Atsuma Nishiwaki, Natsumi Ikumi, Hitomi Haraoka, Isamu Yokoe, Yutaka Tanikawa, Masashi Oshima, Marina Hamaguchi, Hiroshi Tsuzuki, Yosuke Nagasawa, Kaita Sugiyama, Hiromi Karasawa, Takamasa Nozaki, Mitsuhiro Iwata, Noboru Kitamura, Masami Takei

Division of Hematology and Rheumatology, Nihon University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] The risk of major cardiovascular (CV) events and the long-term CV outcome in patients with primary Sjögren's syndrome (pSS) remain unclear. Feature-tracking (FT) cardiac magnetic resonance (CMR) imaging can reliably be used to assess myocardial function in patients with early dysfunction. Left ventricular (LV) global longitudinal peak systolic strain (GLS) is prognostic of adverse cardiovascular outcomes. Global circumferential peak systolic strain (GCS) is a predictor of congestive heart failure. We sought to measure GLS and GCS using FT-CMR in pSS patients without cardiac symptoms. [Methods] PSS patients and controls without cardiac symptoms were enrolled. Patients and controls with no history and/or clinical findings of cardiovascular disease, hypertension, diabetes mellitus, or dyslipidemia underwent non-contrast CMR. The Sjögren's syndrome disease activity index (ESSDAI) was determined. [Results] We compared 50 patients with pSS (100% women; age, 53±10 years) with 20 healthy controls (100% women; age, 54±9 years). GCS was significantly reduced in the pSS group compared with that in controls ($p=0.008$). A total of 11 patients (22%) had Raynaud's phenomenon (RP). The mean ESSDAI total score was 5.46 ± 6.21 . The GCS in the RP positive group and the ESSDAI total score ≥ 8 group decreased more than that in the RP negative group and the ESSDAI total score < 8 group ($p=0.009$, $p=0.026$, respectively). Receiver operating characteristic curve analysis showed that GCS reliably detected RP and ESSDAI total score ≥ 8 (area under the curve, 0.75 and 0.71, respectively). GLS was significantly reduced in the pSS group compared with that in controls ($p=0.015$). GLS in the pSS group was not associated with CV risk factors or pSS status such as RP or ESSDAI. [Conclusions] To our knowledge, this is the first prospective study of LV regional dysfunction in pSS and the only study to explore the associations of pSS characteristics with CMR-assessed GCS and GLS.

ICW10-6

The relationship between the hallux valgus angle and the dorsal dislocation of the second metatarsus analyzed through CT scans in Rheumatoid Arthritis patients

Takeomi Nakamura¹, Mitsuyasu Iwasawa¹, Kota Shimomura^{1,2}, Satoru Ohashi¹, Hiroshi Takamura¹, Tetsuro Yasui³, Takumi Matsumoto⁴

¹Department of Orthopedics and Rheumatology, Sagami National Hospital, ²Department of Orthopedics, Sapporo Medical University, ³Department of Orthopedics, Teikyo University Mizonokuchi Hospital, ⁴Department of Orthopedics, The University of Tokyo

Conflict of interest: None

[Objective] There is still some uncertainty regarding the relationship between the hallux valgus (HV) and the dorsal dislocation of the 2nd metatarsus in patients with Rheumatoid Arthritis (RA). Our objective was to elucidate whether there is a significant difference in the pattern of deformity in patients with spread foot as opposed to those without. [Methods] Evaluation included 98 feet of 78 patients - 4 male and 74 female with HV and dislocation of the 2nd metatarsus, averaging 65 years of age. The mean duration of their RA symptoms was 22 years. The Hallux valgus angle (HVA), the 1st-2nd intermetatarsal angle (M1M2), and the 1st-5th intermetatarsal angle (M1M5) were measured on X-rays. The distance between the distal head of the metatarsus and the proximal joint line perpendicular to the axis of the metatarsus were also measured using CT scans in the sagittal plane. It was hypothesized that feet with plasticity had a higher instance of becoming spread foot. The patients were divided into two groups; the 1st where M1M5 was $< 30^\circ$ (23 feet), and the 2nd where M1M5 was $\geq 30^\circ$ (73 feet). The groups were compared using the Pearson Correlation Coefficient (r) of the HVA and the M1M2, and of the HVA and the severity of the dislocation. [Results] Non-spread foot group averages: HVA = 41° M1M2 = 11° M1M5 = 25° Dislocation = 13.5mm. Spread foot group averages: HVA = 48° M1M2 = 15° M1M5 = 37° Dislocation = 14.4mm. The non-spread foot group presented a clear correlation between HVA and M1M2, and HVA and dislocation. ($r = 0.564$ and 0.627 respectively). For the spread foot group, $r = 0.232$ for HVA and M1M2, and 0.284 for HVA and dislocation. [Conclusions] Our study suggested that HV-deformity might influence the dislocation of the 2nd metatarsus in non-spread foot RA patients, perhaps relating to the lack of plasticity of soft tissue. The procedures to correct forefoot deformities in RA patients with lack of plasticity might be challenging due to a possible in-

crease in dislocations.

ICW11-1

Dysfunction of Trim21 promotes aberrant B cell differentiation in systemic lupus erythematosus

Yosuke Kunishita¹, Ryusuke Yoshimi¹, Reikou Kamiyama¹, Daiga Kishimoto¹, Takaaki Komiya¹, Yumiko Sugiyama², Yohei Kirino¹, Hideaki Nakajima¹

¹Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, ²Rheumatic Diseases Center, Yokohama City University Medical Center

Conflict of interest: None

[Background/Purpose] TRIM21 is a member of the tripartite motif family proteins and is one of the autoantigens which react with anti-SS-A antibody (Ab) seen in sera of patients with systemic lupus erythematosus (SLE) and Sjögren's syndrome. TRIM21 has been shown to be involved in cell proliferation and apoptosis in a B-cell cell line. Here we examined the pathological role of TRIM21 in SLE using Trim21-deficient lupus model mice and B cells from SLE patients. [Methods] Trim21-deficient MRL/lpr mice were generated by backcrossing Trim21-deficient C57BL/6 mice to MRL/lpr mice. Urine albumin/creatinine ratio was measured as the urine protein level. Anti-dsDNA and anti-TRIM21 Abs were measured by enzyme-linked immunosorbent assay. CD43-negative resting B cells were isolated from mouse spleens or peripheral blood of SLE patients by magnetic-activated cell sorting and stimulated with several Toll-like receptor (TLR) ligands. The abilities to differentiate into plasmablasts and to product Ab were examined by flow cytometry and cytometer bead array, respectively. [Results] The levels of urine protein and serum anti-dsDNA Ab at 28 weeks of age were significantly higher in Trim21-deficient MRL/lpr mice as compared to wild-type MRL/lpr mice. When we stimulated resting B cells from these mice with TLR ligands for 24 hours, B cells from Trim21-deficient MRL/lpr mice showed significantly higher abilities to differentiate into plasmablasts and to product Ab as compared to wild-type MRL/lpr mice. B cells from SLE patients with seropositivity of anti-TRIM21 Ab also indicated significantly higher ability to differentiate into plasmablasts and to product Ab as compared with SLE patients with seronegativity of anti-TRIM21 Ab or healthy controls. [Conclusion] TRIM21 dysfunction promotes aberrant B cell differentiation and Ab production in SLE. Anti-TRIM21 Ab may be related to the TRIM21 dysfunction.

ICW11-2

Imbalance between Th1 and Th1-Treg-like cells depends on differential regulation of cell metabolism in patients with SLE

Shigeru Iwata, Mingling Zhang, Maiko Hajime, Naoaki Ohkubo, Hiroko Miyata, Yasuyuki Todoroki, Shingo Nakayamada, Yoshiya Tanaka
The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

Conflict of interest: None

[Object] Th1 cells play an important role in SLE. Recently, "immunometabolism" attract much attention. In this study, we examined the involvement of immunometabolism in Th1 cells and its relevance to SLE. [Methods] PBMCs were obtained from healthy controls (HCs) and patients with SLE and analyzed by FACS. In addition, the importance of metabolic change in Th1 cells were assessed in vitro. [Results] Activated effector memory CD4⁺T-bet^{hi} cells in patients with SLE were higher than HCs. The CD4⁺T-bet^{hi} cells showed strong IFN- γ production. mTORC1 is well known as an inducer of aerobic glycolysis. The CD4⁺T-bet^{hi} cells highly expressed p-mTORC1 and was closely related to treatment-resistance in SLE. Therefore, we would examine the effect of mTORC1 inhibitor Rapamycin (Rapa) or glycolysis inhibitor 2DG to such memory mTORC1⁺T-bet^{hi}IFN γ ⁺CD4⁺ cells in vitro. When CD45RA⁺CD4⁺ T cells were isolated from peripheral blood of HCs and stimulated with anti-CD3/CD28 Abs, T-bet expression and IFN- γ production as well as p-mTORC1 expression and aerobic glycolysis were induced. Interestingly, 2DG, but not Rapa, suppressed IFN- γ production and enhanced IL-2 production. Therefore, we hypothesized that 2DG induce Th1-Treg cells as one of Treg cell subsets. As predicted, 2DG induced FoxP3^{hi}T-bet⁺IFN- γ

(Th1-Treg like) cells and suppressed FoxP3⁺T-bet⁺IFN- γ ⁺(Th1 like) cells. Meanwhile, Rapa induced FoxP3^{int}T-bet⁺IFN- γ ⁺ (non-Treg like) cells and did not affect to FoxP3⁺T-bet⁺IFN- γ ⁺(Th1 like) cells. Finally, we examined the involvement of Th1-Treg cells to the pathogenesis of SLE. CD45RA⁺FoxP3^{int}IFN- γ ⁺ (non-Treg) cells were increased, whereas CD45RA⁺FoxP3^{hi}CXCR3⁺T-bet^{hi} (Th1-Treg) cells were decreased in patients with SLE. [Conclusions] These results indicated that activated effector memory Th1 cells were increased while memory Th1-Treg cells were decreased in patients with SLE, and glycolysis inhibitors redressing the imbalance of Th subsets have potential as a new therapeutic strategy.

ICW11-3

Padi4 contributes to the development of mouse model of lupus nephritis via promoting neutrophil infiltration into kidney

Norio Hanata¹, Hirofumi Shoda¹, Hiroaki Hatano¹, Yasuo Nagafuchi¹, Toshihiko Komai¹, Tomohisa Okamura², Kazuhiko Yamamoto³, Keishi Fujio¹

¹Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, ²Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, ³Laboratory for Autoimmune Diseases, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan

Conflict of interest: None

[Object] Roles of *peptidylarginine deiminase 4 (Padi4)* in systemic lupus erythematosus (SLE) remain unclear. The pathological contributions of *Padi4* to SLE were investigated by using *Padi4* knock out (KO) mice. [Methods] Imiquimod (IMQ)-induced lupus model was analyzed in wild type (WT-IMQ) and *Padi4* KO (*Padi4* KO-IMQ) mice. Proteinuria, serum anti-double stranded DNA (anti-dsDNA) antibody titers, the frequencies of immune cells, and the histopathology were evaluated. Neutrophil migration and adhesion were assessed by adoptive transfer and *in vitro* adherence assay. Transcriptome of bone marrow-derived neutrophils was analyzed. [Results] Proteinuria was significantly improved in the *Padi4* KO-IMQ mice, whereas serum anti-dsDNA antibody titers were elevated, and the immune complex depositions in the glomeruli were similarly observed both in the WT-IMQ and the *Padi4* KO-IMQ mice. Notably, neutrophil infiltration was decreased in the kidney of the *Padi4* KO-IMQ mice. Adoptively transferred *Padi4* KO neutrophil showed a decreased infiltration to the kidneys, and the toll like receptor (TLR) 7-primed *Padi4* KO neutrophils showed impaired adhesion to ICAM-1 *in vitro*. The transcriptome analysis demonstrated impaired upregulations of several pathways including p38 mitogen-activated protein kinase (MAPK) in the *Padi4* KO neutrophils. Consistently, TLR 7-primed *Padi4* KO neutrophils demonstrated impaired phosphorylation of p38 MAPK. [Conclusions] These results shed light on the pivotal roles of *Padi4* for neutrophil signaling and infiltration to kidney in the pathogenesis of lupus nephritis. Inhibition of *Padi4* and related signaling pathways would be a novel therapeutic strategy for SLE.

ICW11-4

Activation of caspase-1 in CD16-positive monocyte and correlation with disease activity in systemic lupus erythematosus

Shoichiro Inokuchi¹, Hiroki Mitoma¹, Shotaro Kawano¹, Masahiro Ayano¹, Yasutaka Kimoto², Mitsuteru Akahoshi¹, Yojiro Arinobu¹, Koichi Akashi¹, Takahiko Horiuchi², Hiroaki Niuro³

¹Department of Clinical Immunology and Rheumatology/Infectious Disease, Kyushu University, Fukuoka, Japan, ²Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, ³Department of Medical Education, Faculty of Medical Sciences, Kyushu University, Fukuoka, Japan

Conflict of interest: None

[Object] Inflammasome is a large protein complex which induces activation of caspase-1 (Casp1) and myeloid cells like macrophages are the major cell types equipped with inflammasome. This sense pathogen-associated molecular patterns or endogenous danger signals in cytosol and proteolysis and activation of Casp1 is induced. Activated Casp1 further process pro-interleukin (IL)-1 β and pro-IL-18 into mature forms that are

secreted, followed by inflammation and activation of adaptive immunity. Although elevated IL-1 β and IL-18 in sera have been reported in SLE, cell subsets which undergo inflammasome activation, and the relation between inflammasome activation and clinical features, have been rarely investigated. This study aimed to clarify activated Casp1 in each cell subset in peripheral blood cells at single-cell level and to identify the relation between inflammasome activation and clinical features. [Methods] Activated Casp1 in peripheral monocytes and neutrophils at steady state from SLE, the other autoimmune disease and healthy controls were evaluated by multicolor flow cytometry. The relation between clinical feature and activated Casp1 were analyzed. [Results] In active SLE, activated casp1 was upregulated in monocytes and significantly negatively correlated with serum complement C3 and CH50. A trend of positive correlation between activated Casp1 in monocytes and anti-dsDNA antibody levels was also identified. Activated Casp1 was preferentially expressed in CD16-positive (CD16⁺) monocytes. While activated Casp1 in neutrophils was downregulated in each disease, any correlation between activated Casp1 in neutrophils and clinical features weren't detected. Successful treatment of SLE normalized activated Casp1 in monocytes. [Conclusions] In SLE, CD16⁺monocytes expressed higher activated casp1 compared to healthy controls, and correlation between activated casp1 and disease activity was identified. Targeting inflammasome may be one of the therapeutic strategies of SLE.

ICW11-5

The involvement of mitochondrial activation via glutaminolysis in human B cell differentiation and its relevance to the pathogenesis of SLE

Maiko Hajime¹, Shigeru Iwata¹, Hiroko Miyata¹, Mingzeng Zhang¹, Masataka Torigoe², Shingo Nakayamada¹, Kei Sakata³, Yoshiya Tanaka¹

¹First Department of Internal Medicine, University of Occupational & Environmental Health, Japan, Kitakyushu, ²Department of Endocrinology, Metabolism, Rheumatology and Nephrology, Oita University, Oita, ³Mitsubishi Tanabe Pharma, Yokohama, Japan

Conflict of interest: None

Objective) B cells play a crucial role in SLE. Recently, "Immunometabolism" attract much attention. In this study, we examined the role of mitochondrial function and glutaminolysis in B cell differentiation and its relevance to SLE. Methods) Peripheral blood mononuclear cells were obtained from healthy controls (HCs) and patients with SLE and assessed by FACS. In addition, CD19⁺ cells were isolated from HCs and change of mitochondrial function and glutaminolysis were assessed in the absence of glucose or glutamine, by metformin *in vitro*. Results) Initially, mitochondrial function in B cells from patients with SLE was assessed using DiO6 as a marker of depolarization-activated mitochondrial membrane. CD24⁺DiO6⁺ cells in IgD⁺CD27⁻ memory B cell from patients with SLE were significantly higher than those of HCs. Next, we assessed the role of mitochondrial function and glutaminolysis in human B cell differentiation *in vitro*. Stimulation with CpG (TLR9 ligand) and IFN- α , 1) increased the area of cytoplasm including many expanded mitochondrial cristae with slightly wider and loosely organized intermembrane space in electric microscopy, accompanied with ROS production and DiO6 up-regulation, 2) induced CD27^{hi}CD38^{hi} plasmablasts differentiation and immunoglobulin production. Interestingly, ROS production and DiO6 expression were significantly decreased in the absence of glutamine, leading to inhibition of plasmablasts differentiation and immunoglobulin production. This tendency was not shown in the absence of glucose. Metformin, which is known as AMPK activator, abrogated glutamine uptake, resulting in suppression of ROS production, DiO6 expression, plasmablast differentiation and immunoglobulin production. Conclusion) These results suggest that mitochondrial activation via glutaminolysis may play an important role in the differentiation from IgD⁺CD27⁻ double negative B cells to plasmablasts and production of immunoglobulins in patients with SLE.

ICW11-6

The role of an essential amino acid methionine and its transporter CD98 in human B cell differentiation and its relevance to the pathogenesis of SLE

Mingzeng Zhang, Shigeru Iwata, Maiko Hajime, Naoaki Ohkubo, Kaoru

Yamagata, Shingo Nakayamada, Yoshiya Tanaka
The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: None

B cells play an important role in SLE. Recently, "Immunometabolism" attract much attention. In this study, we examined the involvement of essential amino acids in human B cell differentiation and its relevance to the pathogenesis of SLE. We examined the role of essential amino acids for human B cell differentiation *in vitro*. PBMCs were obtained from healthy controls (HCs) and SLE, and analyzed by FACS. Combined stimulation with BCR, CpG (TLR9 ligand) and IFN- α induced uptake of essential amino acids and plasmablast differentiation, which were more strongly abrogated in the absence of methionine than leucine. Next, we examined the mechanism by which essential amino acids regulate intracellular signaling pathway in B cells. Combined stimulation induced activation of BCR signal and Akt-mTORC1 pathway. As predicted, Akt-mTORC1 pathway was inhibited in the absence of both methionine or leucine. Meanwhile, BCR signal was abrogated in the absence of methionine, but not leucine. Combined stimulation suppressed BACH2 expression, whereas induced PRDM1 and XBP1 expression. EZH2 is well known as transcriptional factor regulating histone modification. We found that EZH2 bind to the promoter region of BACH2 and induced H3K-27me₃, resulting in inhibition of BACH expression. EZH2 expression were abrogated in the absence of methionine. EZH2 inhibitors recovered BACH2 expression and abrogated plasmablast differentiation. Finally, we assessed the expression amino acid transporter CD98/LAT1 and EZH2 in B cells from patient sample. CD98 and EZH2, but not LAT1, in B cells from patients with SLE were highly expressed than those of HCs. EZH2 expression were correlated with CD98 expression in B cells from patients with SLE. These results indicate that essential amino acids methionine play an important role in human B cell differentiation via CD98-BCR/mTORC1-EZH2-BACH2 pathway. Methionine and their signaling pathway might be a potential therapeutic target for SLE.

ICW12-1

The relevance of B cell phenotypic changes to clinical efficacy in patients with SLE-LOOPS registry-

Hiroko Yoshinari, Satoshi Kubo, Shingo Nakayamada, Kazuhisa Nakano, Shigeru Iwata, Kentaro Hanami, Shunsuke Fukuyo, Ippei Miyagawa, Yusuke Miyazaki, Akio Kawabe, Yoshino Inoue, Yoshiya Tanaka
The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: None

[Object] Belimumab (BLM), a human monoclonal antibody neutralizing BAFF, has been approved for SLE treatment. We investigated the clinical efficacy and changes of peripheral immunophenotype by BLM. [Methods] 11 of inactive SLE patients treated with BEL in order to reduce glucocorticoid (GC) dose were enrolled. Primary outcome was dose of GC (PSL equivalents) at 6 months (6M) after treatment with BLM. Peripheral immunophenotypes were evaluated by multicolor flow cytometry. [Results] At baseline, mean age was 37.0 years old, SLEDAI was 4.2, and dose of PSL was 7.4 mg, respectively. Compared to healthy donor, proportion of class switched memory and IgD⁺CD27⁻ (double negative; DN) B cell were increased in spite of inactive SLE. After 6M, SLE activity (SLEDAI 1.8) and dose of GC (PSL 4.6 mg) were significantly decreased and there was no incidence of flare. Regarding immune cell phenotypes, proportions of other immune cell subsets didn't change. However, proportion of Naïve B cell (50.6→24.2%) was notably decreased and that of class switched memory (26.8→44.1%) and DN B cell (10.5→12.1%) were relatively increased compared to baseline. Actual peripheral number of naïve B cell was remarkably decreased by 72%, while that of class switched and DN B cell were not change. This change wasn't observed in SLE patients treated without BLM (adjusted age, sex, SLEDAI and dose of PSL). Moreover, the baseline proportion of naïve B cell was negatively correlated with dose of PSL at 6M after treatment with BLM. [Conclusion] BLM could further reduce dose of GC without flare. Apoptosis of auto-reactive B cells and inhibition of Ig-class switch and Plasmablast (PB) differentiation is considered as the mechanism of BLM. We also suggested that BAFF signal itself was important for naïve

B cell survival *in vivo*. Although it's not clear whether this action regulates the pathogenesis of SLE, memory B cell and PB differentiation might be suppressed by decrease of its source as a long term effect.

ICW12-2

Study on the safety and effectiveness of hydroxychloroquine in patients with systemic lupus erythematosus

Ippei Miyagawa, Kazuhisa Nakano, Shingo Nakayamada, Shigeru Iwata, Kentaro Hanami, Shunsuke Fukuyo, Satoshi Kubo, Yusuke Miyazaki, Akio Kawabe, Yoshino Inoue, Masanobu Ueno, Yoshiya Tanaka
The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: None

[Object] The effectiveness and safety of hydroxychloroquine (HCQ) have not fully been validated in Japanese patients with SLE. [Methods] The primary endpoint was the retention rate up to 1 year in 136 patients with SLE. The secondary endpoints were the changes of SLEDAI, BILAG index and concomitant corticosteroid (CS) dose (mg/day. PSL equivalent) in the remission induction therapy (n=36), CS based maintenance therapy (n=52) and HCQ monotherapy (n=48). [Results] The retention rate as primary endpoint was 80.9 %. In the remission induction therapy, SLEDAI, BILAG index and concomitant CS dose were significantly decreased from 12.9±9.2 to 4.67±6.83, 14.8±10.5 to 4.78±8.39 and 55.8±14.4 to 16.0±20.3, respectively. In the maintenance therapy, SLEDAI and BILAG index were significantly decreased from 4.65±4.6 to 2.94±4.52 and 2.52±4.99 to 1.79±4.94. In the HCQ monotherapy, SLEDAI and BILAG index were significantly decreased from 4.63±3.64 to 2.81±3.60 and 3.15±3.52 to 2.09±3.08. Moreover, exacerbation rate based on the SLEDAI and BILAG was compared between the 1 year before and after induction of HCQ in 76 patients whose clinical course in both 1 year before and after induction of HCQ can be evaluated. Although the reduction rate of concomitant CS was significantly higher during 1 year after induction of HCQ, the disease exacerbation rate based on the SLEDAI and BILAG were significantly lower during 1 year after induction of HCQ. [Conclusions] HCQ, which makes it possible to reduce the concomitant CS and to suppress the exacerbation, can be the mainstay in Japanese patients with SLE.

ICW12-3

Is it important to maintain the high serum trough level in the treatment with tacrolimus for systemic lupus erythematosus?

Takaaki Komiya¹, Yosuke Kunishita¹, Ryusuke Yoshimi¹, Yuki Iizuka¹, Chiharu Hidekawa¹, Masaki Mitsuhashi¹, Natsuki Sakurai¹, Hideto Nagai¹, Naoki Hamada¹, Yutaro Soejima¹, Naomi Tsuchida¹, Daiga Kishimoto¹, Reikou Kamiyama¹, Yohei Kirino¹, Shigeru Ohno², Hideaki Nakajima¹

¹Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, ²Center for Rheumatic Diseases, Yokohama City University Medical Center

Conflict of interest: None

[Object] We have previously reported the relationship between the efficacy and serum trough level of tacrolimus (TAC) in patients with systemic lupus erythematosus (SLE) by the retrospective study. Here we prospectively measured the trough level after a year from the entry of the previous study and examined the disease activity to evaluate the significance of maintaining the trough level of TAC. [Methods] SLE patients who visited our hospital from April 2016 to September 2018 were included in the study. We collected the demographic and clinical parameters at baseline (October, 2017) and at one year (October 2018). We compare the change of SLE disease activity index (SLEDAI) and dose reduction of prednisolone between the patients who maintained high trough levels (> 5 ng/ml) and those who kept low trough levels (≤ 5 ng/ml). [Results] Among forty-nine patients who received TAC, 13 patients maintained the high trough level throughout the year (HT group) and 14 kept the low trough level (LT group). HT group maintained the low disease activity throughout the year, and there was no significant difference between SLEDAI at baseline and at one year (3.2 ± 2.7 vs 2.5 ± 4.3, p = 0.60). Interestingly, SLEDAI in LT group showed the tendency of decrease during

the year (6.9 ± 6.5 vs 4.8 ± 4.3 , $p = 0.28$). The dose of prednisolone was reduced to an equal degree in both groups during one year (7.1 ± 3.9 vs 6.9 ± 4.7 mg/day, $p = 0.90$). [Conclusions] TAC can contribute to maintaining low disease activity in SLE patients, irrespective of its serum trough level.

ICW12-4

Efficacy and safety of hydroxychloroquine (HCQ) at one year in daily clinical practice

Masaru Shimizu, Yuya Kondo, Taihei Nishiyama, Shota Okamoto, Hirofumi Toko, Fumika Honda, Ayako Ohyama, Mizuki Yagishita, Saori Abe, Atsumu Osada, Izumi Kurata, Hiroyuki Takahashi, Masahiro Yokosawa, Hiroto Tsuboi, Isao Matsumoto, Takayuki Sumida
Department of Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

Conflict of interest: None

[Object] To clarify efficacy and safety of HCQ used for SLE patients in clinical practice. [Methods] Cases of SLE treated with HCQ in University of Tsukuba hospital between September 2015 and September 2017 were identified from electrical medical charts. We retrospectively analyzed their 1) baseline characteristics, 2) target lesions, 3) efficacy of HCQ at one year after the treatment, 4) safety profile, and 5) risk factors for drug-induced cutaneous adverse reactions. [Results] 1) Forty-three cases of SLE were treated with HCQ. Thirty-seven cases (86%) were female with a mean age of 39.4 years. The mean disease duration was 10.7 years. Skin involvement was developed in 30 cases (70%), arthritis in 28 cases (65%), hematological abnormalities in 28 cases (65%), and lupus nephritis in 12 cases (28%) during their whole SLE course. Anti-Ro/SSA antibody was positive in 18 cases. 2) HCQ was used to treat skin involvement in 19 cases (44%), arthritis in 14 cases (33%), hematologic abnormalities in nine cases (21%), lupus nephritis in four cases (9%). 3) Skin involvement and arthritis were improved in eight cases (42%) and five cases (36%) respectively at one year. Titers of anti-DNA antibodies were significantly decreased from 27.6 ± 10.3 to 11.0 ± 2.0 . 4) Fourteen cases (33%) experienced adverse events and of these six cases (43%) were drug-induced cutaneous adverse reactions, three cases (21%) diarrhea. Retinal toxicity was not observed. The cumulative continuation rate of HCQ was 72% at one year. [Conclusions] HCQ was effective for skin involvement and arthritis in SLE. The most common adverse event was cutaneous adverse reaction and it was likely that anti-Ro/SSA antibody was a risk factor of HCQ-induced cutaneous skin reaction.

ICW12-6

Do HCQ and MMF improve treatment outcome in patients with SLE? ~from LOOPS registry~

Naoaki Ohkubo, Kazuhisa Nakano, Shigeru Iwata, Kentaro Hanami, Shunsuke Fukuyo, Satoshi Kubo, Ippei Miyagawa, Ayako Yamaguchi, Akio Kawabe, Yusuke Miyazaki, Shingo Nakayamada, Yoshiya Tanaka
The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: None

[Objective] In 2015, HCQ and MMF became available for SLE and lupus nephritis in Japan. Hence the options for SLE treatment have increased. In LOOPS registry, which is a cohort of hospitalized SLE patients in our department, we examined treatment outcome of glucocorticoid (GC) and immunosuppressive therapy before and after August 2015. [Methods] Subjects were SLE patients treated with high dose GC therapy at our hospital from August 2013 to August 2017. We compared the treatment outcome before (60 pts) and after (66 pts) August 2015. The remission was defined as ≥ 4 -point reduction in SELENA-SLEDAI score and no new BILAG A or no more than one new BILAG B domain score compared with the time of hospitalization by reference to SRI-4. The primary endpoint was the remission rate at 12 months. The secondary endpoint was the dose of GC at 12 months. [Results] There was no difference in age, sex, disease duration, SLEDAI score and BILAG score, between the 2 groups. The initial doses of GC were not different between the 2 groups (before/after; 51.4/51.9mg). Trends in the use of immunosuppressive drugs were that HCQ was used in 39 pts (before/after; 0/39), MMF was

used in 21 pts (0/21), IVCY was used in 59 pts (28/31), AZA was used in 7 pts (2/5), and TAC was used in 15 pts (12/3). Although the remission rate was not different between the 2 groups (before/after; 85/88%), the dose of GC at 12 months were tended to be different (before/after; 8.0/7.1mg, $p=0.072$). Therefore, patients who were hospitalized after August 2015 tended to be able to reduce GC. In order to investigate the contribution of each immunosuppressant to accomplish GC reduction to less than 7.5mg, we conducted a logistic analysis. Only HCQ was significantly involved in the outcome ($p=0.018$). [Conclusions] The combined use of HCQ possibly leads to early de-escalation of GC in SLE.

ICW13-1

Complement C9 is highly expressed in synovial fluid of patients with ankylosing spondylitis

Ji-hyun Lee¹, Chang-nam Son¹, Sang-hyon Kim¹, Hye-jin Jeong¹, Jinyeong Chae¹, Ji-min Kim¹, Min-ho Suh², Seong-il Suh², Won-ki Baek², Jin-seol Rhee³, Tae-hwan Kim⁴, Jae-hun Jung⁵, Jong-seo Kim⁶

¹Division of Rheumatology, Department of Internal Medicine, School of Medicine, Keimyung University, Daegu, Korea, ²Department of Microbiology, School of Medicine, Keimyung University, Daegu, Korea, ³Department of Research Affairs, Keimyung University Dongsan Medical Center, Daegu, Korea, ⁴Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, ⁵Department of Applied Chemistry, Institute of Natural Science, Global Center for Pharmaceutical Ingredient Materials, Kyung Hee University, Yongin, Korea, ⁶Center for RNA Research, Institute of Basic Science (IBS), Seoul, Korea

Conflict of interest: None

[Object] Our aim was to identify differentially expressed protein mediators in synovial fluid (SF) of ankylosing spondylitis (AS). [Methods] A Total of 40 SF samples from 10 AS and each 10 controls [Osteoarthritis (OA), Rheumatoid Arthritis (RA), gouty arthritis (Gout)] were collected. Liquid chromatography and tandem mass spectrometry (LC-MS/MS), to identify differentially expressed proteins based on the ratios of the extracted ion current of each protein between the four groups. Among the 9 proteins showing 1.5 fold change, 8 were verified with the exception of the abundant protein Haptoglobin (HP). Matrix metalloproteinase-1 (MMP1) and Matrix metalloproteinase-3 (MMP3) were used as a positive control, and the remaining 6 proteins were subjected to western blot analysis. [Results] We identified 9 proteins that were found to be more than 1.5-fold differentially expressed in SF of AS patients compared to control groups. Proteins such as HP, MMP1, MMP3, Serum amyloid P-component (APCS), Complement factor H-related protein 5 (CFHR5), Fumarylacetoacetase (FAH), Mannose-binding lectin2 (MBL2), Complement component C9 (C9) and Complement C4-A (C4A) were found to be upregulated in the SF of AS patients. CFHR5 and C9 were reported in previous studies with AS serum. APCS was reported in SF as well as serum. However, FAH, C4A and MBL2 were newly discovered through this analysis. We were able to verify the unique expression level of C9 in AS sample using western blot analysis compared to the other three diseases. [Conclusions] We performed quantitatively proteomic profiling of the respective SF sample from 4 diseases, i.e., AS, OA, RA, and GOUT, by LC-MS/MS. The systematic comparative proteomic analysis of the four groups together was carried out for the first time, leading to several differentially expressed proteins in AS. Among them, we expect C9, which expression level was confirmed by western blot analysis and will be further validated by ELISA, can be a potential biomarker for AS.

ICW13-2

Sec16A abnormalities impair antigen presentation and HLA-B27 mediated CD8 T cell immune responses in axial spondyloarthritis

Fanxing Zeng, Nakamura Akihiro, Haroon Nigil
University Health Network

Conflict of interest: None

[Object] HLA-B27 is the strongest genetic risk factor in axial spondyloarthritis (axSpA). A rare mutation of Sec16A was recently identified to be strongly associated HLA-B27 in the development of axSpA in a multiplex family. Sec16A plays an important role in intracellular transport and the assembly of cargo carrier vesicles. In this study, we explore

the functional impact of Sec16A abnormalities on ER-to-Golgi trafficking, HLA-B27 folding and transport, and CD8⁺ T cell mediated immune response. [Methods] B cell lines were generated from the multiplex family members by EBV transformation. For validation, Sec16A in B cell line (C1R-B27) and HeLa cells was knocked out using CRISPR-Cas9. ER-to-Golgi transport efficiency and the assembly of intracellular transport vesicle (COPII) were evaluated. YFP-tagged HLA-B27 was used to investigate the effect of Sec16A abnormalities on HLA-B27 intracellular transport and surface expression. HLA-B27 mediated immune response was assessed by cytotoxic T-lymphocyte assay using HLA-B27 restricted peptide (NP383-391) specific CTL clones. In addition, BioID was carried out to investigate the protein-protein interaction (PPI) of Sec16A variants. [Results] Sec16A abnormalities hindered the assembly of COPII vesicles budding from the ER leading to abnormal intracellular trafficking. Using YFP-tagged HLA-B27, we found that Sec16A abnormalities delayed the intracellular transport of HLA-B27, accumulated HLA-B27 in intracellular vesicles, and impaired HLA-B27 antigen presentation. CTL cytotoxicity was significantly lower in cells with Sec16A abnormalities compared to cells with wild type Sec16A. In the PPI study, we found that Sec16A mutation reduced the affinity of Sec16A to its interactors involved in intracellular trafficking and antigen presentation. [Conclusions] Aberrant Sec16A may contribute to the pathogenesis of axSpA through an imbalance in HLA-B27 transport, folding, peptide binding, antigen presentation and abnormal T cell recognition.

ICW13-3

Incidence of malignancy in patients with ankylosing spondylitis with and without anti-TNF-alpha therapy: a cohort study in North Taiwan

Ming-han Chen^{1,2}, Chang-youh Tsai^{1,2}

¹Division of Allergy- Immunology- Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ²Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan

Conflict of interest: Yes

Objectives: The treatment with tumor necrosis factor- α inhibitors (TNFi) has been authorized for patients with ankylosing spondylitis (AS) for years. However, whether blockade of TNF- α enhances the risk of malignancy in AS patients is unknown. The object of this study is to determine the incidence of malignancy in AS patients with and without anti-TNF- α therapy. **Methods:** AS patients who visited our clinic with greater than 1-year follow-up from 2007 to 2017 were retrospectively reviewed. TNFi were prescribed in AS patients refractory to conventional therapies, defined as treatment with at least two different nonsteroidal anti-inflammatory drugs (NSAIDs) for at least 2 months. We compared rates of incident malignancy in AS patients with and without TNFi. **Results:** We identified 3019 cases and 2174 (72.0%) of them were male. Their mean age at the diagnosis of AS was 27.0 years old. Among them, 389 (12.9%) received TNFi treatment. Fifteen cancers were reported in 46,191 patient-years follow-up. The rates of incident malignancy were 0.62 events/1,000 person-years in the TNFi cohort and 0.28/1,000 person-years in the non-TNFi cohort. After adjustment for age and sex, there was no difference in risk of malignancy for AS patients with TNFi compared to those without TNFi (Hazard ratio 1.071, 95% CI 0.318 to 3.599, $p = 0.912$). **CONCLUSIONS:** The incidence of cancer was not elevated during TNFi therapy compared to alternative therapy in this study, indicating that treatment with TNFi does not increase the risk of malignancy in AS patients.

ICW13-4

The clinical characteristics and treatment conditions of SAPHO syndrome; a single center study of a cohort of 50 cases

Naoki Kondo, Junichi Fujisawa, Naoto Endo

Division of Orthopedic Surgery, Department of Regenerative and Transplant Medicine, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

Conflict of interest: None

[Objective] SAPHO syndrome manifests as bone-joint involvement associated with palmoplantar pustulosis (PPP), pustulous psoriasis, and

severe acne. The aims of this study were to clarify the clinical characteristics including diagnosis and to the treatment status for SAPHO syndrome. [Methods] Fifty consecutive patients (36 females and 14 males) who met the criteria for SAPHO syndrome proposed by Kahn were recruited from January 2015 to December 2017. The mean age was 58 years. The onset patterns, the interval between skin involvement and osteoarticular lesions, the distribution of osteoarticular lesions, and treatment status were examined. [Results] Fifty consecutive patients (36 females and 14 males) who met the criteria for SAPHO syndrome proposed by Kahn were recruited from January 2015 to December 2017. The mean age was 58 years. Six patients had osteoarticular symptoms without skin involvement. Sixty % of the patients had PPP and only 2 % of the patients had psoriasis vulgaris. The interval between skin involvement and osteoarticular lesions was 5.5 years on average (range; - 5 to 29 years). The patients in which skin symptoms preceded was 42 % and the patients who had both symptoms simultaneously was 14 %. Sixty-six % of the patients suffered from pain in the anterior chest wall, followed by peripheral joints (22 %) and sacroiliac joint (18%). Rheumatoid factor was elevated 5 patients (10 %). Related to the treatment status, tonsillectomy was performed in 9 patients. Biotin was treated in 15 patients. Non steroidal anti-inflammatory drugs was treated in 40 (80 %) patients. Conventional synthetic disease modifying anti-rheumatic drugs (DMARDs) was treated in 11 (22 %) patients, followed by biological DMARDs (3 patients, 6 %). [Conclusion] The interval between skin and manifestation of osteoarticular lesions is generally long. Most cases were preceded by skin involvement. However, the attention must be paid for patients who osteoarticular lesions precede.

ICW13-5

Precision medicine using different biological DMARDs based on characteristic phenotypes of peripheral T helper cells in patients with psoriatic arthritis

Ippei Miyagawa, Shingo Nakayamada, Satoshi Kubo, Kazuhisa Nakano, Shigeru Iwata, Yusuke Miyazaki, Hiroko Yoshinari, Kentaro Hanami, Shunsuke Fukuyo, Akio Kawabe, Yoshiya Tanaka

The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: None

[Object] We previously presented the potential of the precision medicine using different biological DMARDs based on characteristic phenotypes of peripheral T helper cells in patients with psoriatic arthritis (PsA). Herein, we validated the usefulness of this strategy for a longer time period, with a greater number of patients. [Methods] Thirty-three patients with PsA underwent bDMARDs therapy selected based on phenotypic differences of peripheral helper T cells. The efficacies of this strategic bDMARDs treatment and the standard bDMARDs treatment administered to the other 38 patients were compared at month 12. [Results] The patients with PsA in the strategic treatment group were classified into the following 4 types based on the peripheral blood analysis: a CXCR3⁺CCR6⁺CD38⁺HLA-DR⁺ activated Th1 cell-predominant type, CXCR3⁺CCR6⁺CD38⁺HLA-DR⁺ activated Th17 cell-predominant type, Th1/Th17-high type, and Th1/Th17-low type. In addition, SDAI was positively correlated with the proportion of activated Th17 cells and activated CD8⁺ cells among activated Th17 cell-increased type. Accordingly, ustekinumab was administered to the activated Th1 cell-predominant patients, secukinumab to the activated Th17 cell-predominant patients, secukinumab or TNF inhibitor to the Th1/Th17-high patients, and TNF inhibitor to the Th1/Th17-low patients. At 12 months of treatment, PASI was significantly decreased in both group (standard: 9.2 \pm 12.7 \rightarrow 3.6 \pm 9.2 strategic treatment: 6.6 \pm 8.7 \rightarrow 1.3 \pm 2.7). SDAI were also significantly decreased at month 12 in both group (standard: 18.3 \pm 12.3 \rightarrow 9.1 \pm 11.0, strategic: 17.7 \pm 10.2 \rightarrow 3.9 \pm 4.0). The rate of low disease activity achievement according to SDAI at month 12 was significantly higher in the strategic bDMARDs treatment group compared with that of the standard bDMARDs treatment group (standard: 65.8 %, strategic: 96.9 %). [Conclusions] The data reported here indicate the potential of precision medicine based on the phenotypic differences in peripheral T helper cells.

ICW14-1

Demonstration of Tissue Resident Memory T Cells in salivary gland in Patients with primary Sjögren's Syndrome

Hui Chu¹, Xiang Yuan¹, Zhen Tan¹, Xu Zheng¹, Xiangpei Li¹, Guosheng Wang¹, Yiping Wang², Xiaomei Li¹

¹Rheumatology and Immunology, The First Affiliated Hospital of University of Science and Technology of China, Hefei, China, ²Westmead Institute for Medical Research, The University of Sydney, Westmead 2145 NSW, Australia.

Conflict of interest: Yes

[Object] Tissue resident memory T cell (Trm) is a novel group of memory T cells with a non-circulating phenotype characterized by expression of CD69 and CD103 and plays a critical role in first-line defense. Effector memory T cell (Tem) and effector T cell (Teff) could be recruited into inflammatory site and transformed into Trm under micro-environment. Our aim is to explore the role of Trm in salivary gland (SG) of patients with primary Sjögren's Syndrome (pSS) in the development of disease. [Methods] 20 pSS patients as the study group and 10 age-matched healthy volunteers as the control group were included in this study. The pSS diagnosis was done according to the International Classification Criteria (2002). The percentage of Tem, Teff and B cells in PBMCs and Trm in SG were detected by flow cytometry. Compare the difference of the percentages of Tem and Teff in patients and controls. Locate Trm and its positional relationship with B cells by Immunohistochemistry and Confocal Laser Scanning Microscopy. Analyze the correlation between B cells in the SG with CD4+Trm, CD8+Trm and serum IgG level respectively. [Results] Compared with the controls, the proportion of Tem (P=0.001) and Teff (P=0.008) in CD4+T cell subsets and the proportion of Tem (P<0.001) and Teff (P<0.001) in CD8+T cell subsets in patients were both significantly increased. Immunohistochemistry showed Trm were present in SG foci and expressed CD69, and Confocal Microscopy showed the CD4+Trm and CD8+Trm respectively and B cells were in close contact with Trm in SG foci. we detected a certain proportion of CD4+Trm and CD8+Trm in patients and the percentage of B cells in SG of patients were both positively correlated with CD4+Trm (r=0.6852; p=0.0031), CD8+Trm (r=0.4603; p=0.0310) and serum IgG level (r=0.4288; p=0.0399). [Conclusions] A small amount of Trm can against infections. As the number increasing, their functional changes contribute to the formation of foci, tissue destruction and disease progression.

ICW14-2

Elevated EPSTI1 promote B cells hyperactivation through NF-KB signaling in patients with Sjögren's syndrome

Jinlei Sun, Haoze Zhang, Chaofeng Lian, Zhilei Chen, Tihong Shao, Suying Liu, Fengchun Zhang, Hua Chen

Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Beijing, China

Conflict of interest: None

[Object] Sjögren's syndrome (SS) is a common systemic autoimmune disease characterized with aberrant B cells activation, which is partially understood. [Methods] We performed whole transcriptome sequencing of B cells from 3 SS patients and 3 Healthy controls (HC). We then confirmed the differential gene expressions in 40 SS patients and 40 HC by quantitative PCR and Western-blot. We further transfected with siRNA targeting candidate genes into B cells and measured the proliferation potential and immunoglobulins secretion. We examined TLR9 signaling to explore the potential molecular mechanism of B cell hyperactivation in SS. [Results] We identified 51 up-regulated and 22 down-regulated differentially expression genes in B cells from SS patients. We confirmed the RNA and protein level of EPSTI1 (Epithelial Stromal Interaction 1) in B cells from 40 SS patients was significantly higher than those from 40 HCs. Comparing with control B cells, EPSTI1-silencing B cells stimulated with CpG (but not anti-IgM) were proliferated less and produced lower level of IgG. we observed the level of p-p65, but not pJNK and (p38MAPK), were decreased in EPSTI1-silencing B cells stimulated with CpG. Consistently, we also found the level of p-p65 was significantly higher in B cells from SS patients than those from HC. Finally, the level of IκBa, a key regulator of p65, was significantly up-regu-

lated in EPSTI1-silencing B cells and B cells from HC. [Conclusions] Elevated EPSTI1 expression in B cells from SS patients promoted TLR9 signaling activation and contributed to the abnormal B cells activation. Mechanistically, EPSTI1 stimulated the phosphorylation of p65, which was likely through the interaction and degradation of IκBa.

ICW14-3

Injection of CD40 DNA vaccine ameliorates the autoimmune pathology of Non-obese Diabetic Mice with Sjögren's Syndrome

Zhou Yingbo¹, Yuan Xiang¹, Qi-kai Wang¹, Guo-sheng Wang¹, Xiang-pei Li¹, Wang Yi-ping², Harris David², Xiao-mei Li¹

¹Department of Rheumatology and Immunology, The First Affiliated Hospital of USTC, University of Science and Technology of China, Hefei, Anhui, China, ²Westmead Institute for Medical Research, University of Sydney, Westmead 2145 NSW, Australia

Conflict of interest: None

Objective: To investigate whether CD40 DNA vaccine could inhibit the immune response and slow the disease progression of Sjögren's syndrome (SS) in non-obese diabetic (NOD) mice. Methods: Female NOD mice were treated with CD40 DNA vaccine, empty vector and normal saline. Serum anti-CD40 antibody was measured by ELISA. Lymphocytes infiltration in the salivary glands was examined by FS calculation. Expression of CD40 and B220 in salivary were also examined with immunohistochemistry. Splenic lymphocyte phenotypes were analyzed by flow cytometry. CD40, IL-1β, TNF-α and IL-6 levels in the salivary glands were detected by PCR. Serum ANA was monitored by immunofluorescence. Results: 1) Compared with the controls, NOD mice treated with CD40 DNA vaccine showed higher levels of anti-CD40 antibody at week 6 and week 10 (P<0.05 and P<0.01, respectively). 2) The expression of CD40 in the salivary glands of NOD mice in CD40 DNA vaccine group was decreased (P<0.05). 3) Infiltration of lymphocytes was inhibited in the salivary glands of mice in the treatment group at week 10. Average weight of wet salivary gland and the ratio of average salivary gland weight to body weight of NOD mice in vaccine group were significantly lower than that in control groups. 4) The expression level of TNF-α and IL-6 in salivary glands were declined (P<0.05 and P<0.05, respectively). 5) The splenic DC and plasma cell populations were reduced and the level of ANA was decreased in the NOD mice with CD40 DNA vaccine treatment. Conclusion: CD40 DNA vaccine ameliorate the pathologic change in NOD mice with SS by downregulation of the expression of proinflammatory cytokines of TNF-α and IL-6, decrease of the percentage of DCs and plasma cells, and suppression of autoimmune inflammation.

ICW14-4

Detection of circulating M3 muscarinic acetylcholine receptor reactive Th17 cells in patients with primary Sjögren's syndrome

Saori Abe, Hiroto Tsuboi, Hanae Kudo, Yuko Ono, Fumika Honda, Izumi Kurata, Mizuki Yagishita, Hiroyuki Takahashi, Masahiro Yokosawa, Yuya Kondo, Isao Matsumoto, Takayuki Sumida

Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: None

[Object] Sjögren's syndrome (SS) is an autoimmune disease which is characterized by lymphocytic infiltration including CD4⁺IL-17 producing helper T (Th17) cells to the lacrimal and salivary glands. We previously detected anti-M3 muscarinic acetylcholine receptor (M3R) antibodies and M3R reactive CD4⁺IFNγ producing helper T (Th1) cells in patients with SS. Moreover, we clarified that M3R reactive Th1 and Th17 cells had pathogenic roles in the development of auto-immune sialadenitis in SS mice model. The purpose of this study was to identify circulating M3R reactive Th17 cells, and to examine the relationship between M3R reactive Th17 cells and clinical features in patients with primary SS (pSS). [Methods] 1) Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood of 9 pSS patients and age gender matched 5 healthy controls (HC). According to their HLA-DRB1 typing, the 20 mer peptides from the full length of M3R, which were highly predicted to bind to HLA molecules, were identified using the immune epitope data-

base website. PBMCs were stimulated with these selected M3R peptides for 39 hours, and IL-17 secretion was detected by IL-17 enzyme-linked immunospot assay (ELISPOT). 2) Clinical features were compared between M3R reactive Th17 cells positive and negative patients with pSS. [Results] 1) 5 of 9 (55.5%) pSS patients, while none of 5 (0%) HC, showed significantly increased IL-17 positive spots against selected M3R peptides stimulation compared with non-stimulation in ELISPOT. 2) Interestingly, 5 pSS patients positive for M3R reactive IL-17 producing spots were significantly older (71.6 ± 8.4 vs 40.0 ± 18.0 years old, $P=0.027$) and had significantly higher ESSDAI score (8.4 ± 4.8 vs 2.0 ± 0.0 , $P=0.031$) than 4 negative patients. [Conclusions] We detected circulating M3R reactive Th17 cells in pSS patients using ELISPOT for the first time. M3R reactive Th17 cells might associate with advanced age and high ESSDAI score in pSS patients.

ICW14-5

Comparison of clinical and pathological characteristics in patients with Eosinophilic granulomatosis with polyangiitis (EGPA) and IgG4-related disease (IgG4-RD)

Ryuichiro Kanda, Satoshi Kubo, Kazuhisa Nakano, Shingo Nakayamada, Shigeru Iwata, Kentaro Hanami, Shunsuke Fukuyo, Ippei Miyagawa, Akio Kawabe, Yusuke Miyazaki, Aya Nawata, Yoshiya Tanaka
The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: None

[Object] There are several similarities between EGPA and IgG4-RD such as high serum IgE levels and allergic background. In this study, we examined clinical and pathological characteristics of both EGPA and IgG4-RD in order to differentiate IgG4-RD mimickers. [Methods] Untreated consecutive patients who were diagnosed with EGPA and IgG4-RD in our department from 2007 to 2018 were enrolled. Immunohistochemistry including IgG4 staining was evaluated in both IgG4-RD and EGPA patients. [Results] 22 EGPA patients and 19 IgG4-RD patients were enrolled. Although the mean age was comparable (EGPA vs IgG4-RD; 59 vs 64 years old), the proportion of female was higher in EGPA (77.3% vs 42.1%). For laboratory tests, the levels of eosinophils (18171.4 vs 378.6 / μ l), CRP (6.5 vs 0.6 mg/dl), sIL-2R (2635.6 vs 1331.4 U/ml), C3 (118.3 vs 80.4 mg/dl), and C4 (24.4 vs 16.2 mg/dl) were significant higher in patients with EGPA. On the other hand, the elevated serum IgG4 (IgG4 >135 mg/dl) was seen in all patients of IgG4-RD (mean 1110.5 mg/dl) and was seen in 95% of EGPA (480.4 mg/dl). In the pathological findings of the skin, paranasal sinus, temporal artery and kidney, lymphoplasmacytic infiltration with infiltrating IgG4-positive plasma cells were seen in 83% of EGPA patients. Especially, in the kidney pathology, two of four patients with EGPA had fibrosis surrounding nest (Bird's eye pattern) and fulfilled the criteria of IgG4-related kidney disease. Namely, most of the EGPA patients met two of three items of IgG4-RD diagnostic criteria. However, EGPA cases have neither mass lesion nor hyperplastic lesion, and could not fulfill IgG4-RD diagnostic criteria completely. [Conclusions] The elevated serum IgG4 and the infiltration of IgG4-positive plasma cells were not specific for IgG4-RD. Therefore, the mass forming in tissue was one of the important clinical manifestations of IgG4-RD. Meanwhile, EGPA were able to have diagnosis of IgG4-related kidney disease which don't have mass lesion.

ICW14-6

Pathologic role of activated SLAMF7+Tfh1 cells in facilitating IgG4 production by B cells in IgG4-related disease

Kazuhiko Higashioka¹, Masahiro Ayano¹, Yasutaka Kimoto², Hiroki Mitoma¹, Mitsuteru Akahoshi¹, Yojiro Arinobu¹, Koichi Akashi¹, Takahiko Horiuchi², Hiroaki Niiro³

¹Department of Medicine and Biosystemic Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, ²Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, ³Department of Medical Education, Kyushu University Graduate School of Medicine Sciences, Fukuoka, Japan

Conflict of interest: None

[Object] IgG4-related disease (IgG4-RD) is a multiorgan inflamma-

tory disease that is characterized by abundant infiltration of IgG4-secreting plasmablasts with storiform fibrosis. Accumulating evidence suggests that follicular helper CD4+ T (Tfh) cells have a critical role in the pathogenesis of IgG4-RD. On the other hand, SLAMF7+CD4+ T cells with cytotoxic potential have recently emerged as an important pathological driver of IgG4-RD. Decreased number of SLAMF7+ CD4+ T cells following rituximab treatment suggests their close interaction with B cells. Relationship between Tfh cells and SLAMF7+ CD4+ T cells, however, still remains elusive. In this study, we have sought to further elucidate a characteristic feature of SLAMF7+ CD4+ T cells in IgG4-RD patients. [Methods] Peripheral blood mononuclear cells were obtained from 21 patients with IgG4-RD and 10 healthy controls (HC). The phenotype of CD4+ T cells was analyzed by flow-cytometry. The frequency of SLAMF7+ cells was evaluated in each CD4+ T cell subset of HC and IgG4-RD patients by the markers such as CD4, CXCR5, CXCR3, CCR6, PD-1 and CD28. Moreover, the correlation between the number of CD4+ T cell subsets and serum IgG4 levels was assessed. [Results] The patients with IgG4-RD enrolled in this study were aged 66 ± 11 years and their titers of serum IgG4 were 372 ± 336 mg/dl. SLAMF7+ cells were almost exclusively confined to activated (PD-1+) subsets of Tfh1 cells (CD4+CXCR5+CXCR3+CCR6-) in IgG4-RD patients. SLAMF7+ Tfh1 cells were CD28 positive and their frequency in IgG4-RD patients was higher than that in HC. Intriguingly enough, positive correlations were only observed between the number of activated SLAMF7+ Tfh1 cells and the titer of serum IgG4. [Conclusions] Taken together, these results suggest that activated SLAMF7+ Tfh1 cells are a critical player in the pathogenesis of IgG4-RD via facilitating IgG4 production by B cells.

ICW15-1

Next-generation sequencing of the whole MEFV gene in Japanese patients with familial Mediterranean fever: A case-control association study

Tomohiro Koga^{1,2}, Kiyoshi Migita³, Yushiro Endo², Remi Sumiyoshi², Fumiaki Nonaka⁴, Shin-ya Kawashiri², Naoki Iwamoto², Kunihiko Ichinose², Mami Tamai², Hideki Nakamura², Tomoki Origuchi², Kazunaga Agematsu⁶, Junya Masumoto⁷, Akihiro Yachie⁸, Katsumi Eguchi⁵, Atsushi Kawakami²

¹Center for Bioinformatics and Molecular Medicine, Nagasaki University Graduate School of Biomedical Sciences, ²Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, ³Department of Rheumatology, Fukushima Medical University School of Medicine, ⁴Department of Rheumatology, Sasebo City General Hospital, ⁵Center for Rheumatic Disease, Sasebo Chuo Hospital, ⁶Department of Infectious Immunology, Shinshu University Graduate School of Medicine, ⁷Department of Pathology, Ehime University Graduate School of Medicine and Proteo-Science Center, ⁸Department of Pediatrics, School of Medicine, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University

Conflict of interest: None

[Object] We aimed to identify the whole nucleotide sequence of the *Mediterranean Fever (MEFV)* gene in familial Mediterranean fever (FMF) and reveal novel single nucleotide polymorphisms (SNPs) associated with the onset of FMF. [Methods] Two hundred SNPs in the whole region of *MEFV*, including promoter regions and intron regions, were genotyped using next-generation sequencing in 266 Japanese patients with FMF and 288 ethnically matched controls. We performed an association analysis using these SNPs to identify genetic variants that predispose to FMF. [Results] We identified the two most significant SNPs [rs28940578; M694I in exon 10, odds ratio (OR) = 153, $p = 2.47 \times 10^{-21}$ and rs3743930; E148Q in exon 2, OR = 1.65, $p < 0.0005$]. Stratified analysis identified rs28940578 as a risk allele in typical FMF. Haplotype AG, defined by rs401298 and rs28940578, was the most significant and prevalent among patients with typical FMF compared with controls (22.4% vs. 0%, respectively; OR = 137, $p = 1.44 \times 10^{-31}$). Haplotype TGT, defined by rs11466018, rs224231, and rs401877, was the most significant among patients with typical FMF without the rs28940578 mutation compared with controls (15.9% vs. 6%, respectively; OR = 12.4, $p = 0.004$). [Conclusions] rs28940578 is associated with the highest risk in typical FMF cases. This is consistent with results from previous studies in Japan. We found novel disease-related SNPs that confer susceptibility

to the onset of FMF among typical FMF without the rs28940578 mutation. There were no relevant SNPs identified in *MEFV* among the atypical FMF group.

ICW15-2

The study of the novel G58V mutation in the TNFRSF1A gene identified in a family with TNF Receptor-Associated Periodic Syndrome (TRAPS)

Shoko Tsuji¹, Tomoyuki Mukai¹, Akiko Nagasu¹, Hiroyasu Hirano¹, Masanori Iseki², Takahiko Horiuchi³, Ryuta Nishikomori⁴, Yoshitaka Morita¹

¹Department of Rheumatology, Kawasaki Medical School, Kurashiki, Japan, ²Department of Immunology and Molecular Genetics, Kawasaki Medical School, Kurashiki, Japan, ³Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, ⁴Department of Pediatrics, Kyoto University Graduate School of Medicine, Kyoto, Japan

Conflict of interest: Yes

[Object] TNF Receptor-Associated Periodic Syndrome (TRAPS) is one of the autoinflammatory diseases. TRAPS is caused by heterozygous mutations in *TNFRSF1A* gene. Although more than 100 *TNFRSF1A* mutations have been reported, only a few mutations such as T50M have been shown as TRAPS mutations. Based on the finding that T50M mutant TNFR1 is accumulated in endoplasmic reticulum (ER), it has been hypothesized that excessive ER stress causes inflammatory responses. Reflecting the mechanism, the cell surface expression of T50M TNFR1 has been shown to be decreased. Recently, we have identified two TRAPS patients with a novel G58V mutation. In this study, we examined the effects of the novel G58V mutation using a cell model by comparing with the T50M mutation and low-penetrant mutations (R92Q, T61I). [Methods] Wild-type (WT) or mutant *TNFRSF1A* (G58V, T50M, R92Q, T61I) constructs were transfected into HEK-293 cells. TNFR1 protein levels were examined by western blotting. The cell surface and intracellular expression levels were determined by flow cytometry. To examine the effect of G58V mutation in the patients, we measured the mitochondrial reactive oxygen species (ROS) in the peripheral blood mononuclear cell (PBMC) of the patients and healthy donors. [Results] Expression levels of the WT and mutant TNFR1 protein were comparable in the whole cell lysates of HEK-293 cells. The cell surface expression of TNFR1 was decreased in the G58V and T50M mutant cells compared to WT TNFR1-transfected cells. In contrast, the R92Q and T61I mutations did not suppress the cell surface expression of TNFR1. PBMCs from TRAPS patients carrying G58V mutation exhibited significantly higher mitochondrial ROS level than that from healthy donors. [Conclusions] The G58V TNFR1 was not expressed on the cell surface, same as the pathogenic T50M mutation. These findings suggest that G58V mutation causes pro-inflammatory status, presumably through the similar mechanisms to the T50M mutation.

ICW15-3

Characteristic features of macrophage activation syndrome in patients with adult Still's disease

Hiroya Tamai, Yuko Kaneko, Tsutomu Takeuchi

Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine

Conflict of interest: None

[Background] Adult Still's Disease (ASD) sometimes develops severe complications such as macrophage activation syndrome (MAS). Although MAS can be fatal, little is known about its clinical courses and relation to initial symptoms, diagnosis and treatment. [Objectives] To clarify characteristic features of MAS in patients with ASD and identify useful factors for optimal strategy to prevent MAS. [Methods] Consecutive ASD patients diagnosed with Yamaguchi's criteria were reviewed retrospectively in our hospital from April 2012 to September 2017. Clinical symptoms, laboratory data and treatment information were collected from their charts and analyzed. [Results] We identified 98 patients with ASD, but 33 patients were excluded from the analyses because of insufficient information at onset, resulting in 65 patients enrolled. The mean age at onset was 45.7 years old and female was 81.5%. Among them, 10 pa-

tients (15.4%) were diagnosed with MAS, with three patients developing MAS before the diagnosis of ASD, five patients after the initiation of glucocorticoid treatment, and two patients at relapse. All patients with MAS were female, and high fever as the first symptom of ASD was more frequent in patients with MAS than those without (70.0% vs 45.5%). MAS after treatment initiation occurred 24.2 days after the initiation of glucocorticoid treatment. The initial dose of prednisolone was 50mg/day in two patients and 30mg/day in three. The development of MAS was rapid with 10-fold increase in transaminase and 14 times increase in ferritin compared to their values at diagnosis. [Conclusions] The incidence of MAS was 15.4% in clinical course of ASD. More than half of MAS occurred after initiation of treatment with a rapid progression.

ICW15-4

Autoinflammation and autoimmunity in Adult-onset Still's disease (AOSD): The relationship between HLA-Class II and MEFV genes in AOSD

Yuya Fujita¹, Hiroshi Furukawa², Jumpei Temmoku¹, Makiko Furuya Yashiro¹, Naoki Matsuoka¹, Tomoyuki Asano¹, Shuzo Sato¹, Hiroko Kobayashi¹, Hiroshi Watanabe¹, Eiji Suzuki³, Tomohiro Koga⁴, Toshimasa Shimizu⁴, Yukitaka Ueki⁵, Katsumi Eguchi⁵, Naoyuki Tsuchiya², Atsushi Kawakami⁴, Kiyoshi Migita¹

¹Department of Rheumatology, Fukushima Medical University School of Medicine, Fukushima, Japan, ²Molecular and Genetic Epidemiology Laboratory, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan, ³Department of Rheumatology, Ohta Nishinouchi General Hospital Foundation, Koriyama, Japan, ⁴Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ⁵Department of Rheumatology, Sasebo Chuo Hospital

Conflict of interest: None

Objective: Adult-onset Still's disease (AOSD) is a genetically-complex inflammatory disease, in which both innate and adaptive mechanisms contribute to the pathogenesis. Recent study revealed an unequivocal genetic association between systemic juvenile idiopathic arthritis and the major histocompatibility region, in particular with the class II allele *HLA-DRB1*11*. In this study, we investigated HLA-Class II and *MEFV* genes, which predispose to either autoimmunity and autoinflammation in Japanese patients with AOSD. **Methods:** *HLA-DRB1*, *DQB1* and *DPB1* alleles were analyzed in 87 Japanese patients with AOSD and 413 Japanese healthy subjects. Genomic DNA samples from the AOSD patients were also genotyped for *MEFV* exons 1, 2, 3, and 10 by direct sequencing. **Results:** We found significant association of *HLA-DRB1*15:01* ($P_c=0.0002$, OR=3.04, 95% CI=1.91-4.84), DR5 serological group ($P_c=0.0006$, OR=2.39, 95% CI=1.49-3.83) and *DQB1*06:02* ($P_c=0.010$, OR=2.54, 95% CI=1.51-4.28) with AOSD, whereas a protective association of *DRB1*09:01* ($P_c=0.0110$, OR=0.34, 95% CI=0.18-0.66). The frequency of *MEFV* mutation was high (56.3%). The predisposing effect of DR5 was confirmed only in patients with AOSD who had *MEFV* variants and not in those without *MEFV* variants. Additionally, DR5 in patients with AOSD were associated with macrophage activation syndrome (MAS) and steroid pulse therapy. **Conclusions:** Polymorphism that alter inflammasome pathway such as *MEFV* can trigger the autoinflammation. Conversely, recent studies demonstrated that genes including HLA affecting unfolded protein. Unfolded protein response (UPR) can contribute to inflammation as well as autoimmunity. We demonstrated that *HLA-DRB1*15:01*, DR5 and *HLA-DQB1*06:02* were significantly associated with AOSD susceptibility. *MEFV* gene, a regulator of inflammasome, also contribute to the development of AOSD. Our data suggests the combined innate and adaptive immune dysfunction lead to Pathogenesis of AOSD.

ICW15-5

Expression of Siglec-10 was decreased on synovial fluid mononuclear cells although increased on peripheral blood mononuclear cells in juvenile idiopathic arthritis patients

Qianzi Zhao, Yang Liu, Pan Zheng, Lawrence Jung
Children's National Medical Center, Washington, DC, USA

Conflict of interest: None

Background/Purpose: Siglec-G (human Siglec-10 homolog) knock-out mice developed increased clinical disease in mouse arthritis model suggesting a role of Siglec-G/10 in pathogenesis of arthritis. Siglec-10 functions as an inhibitory receptor through the interaction between Siglec-10 and CD24. IL-29 has immune-regulation function. In this study, we investigated the expression of Siglec-10 on mononuclear cells (MCs) from synovial fluid (SF) and peripheral blood (PB) of JIA patients and assessed IL-29 as a candidate cytokine produced from the Siglec10-CD24 interaction. **Methods:** The expression of Siglec-10 on PB and SF monocytes was measured by flow cytometry. Flow cytometry sorting was used to isolate monocytes expressing high level of Siglec-10 for culture. Function test of IL-29 mRNA expression was assessed by quantitative real-time reverse transcriptase-polymerase chain reaction. **Results:** The Siglec-10⁺ PBMCs percentage in JIA patients was significantly higher than that in controls. In contrast, Siglec-10⁺ mononuclear cells percentage in synovial fluid was significantly lower than that in PB of JIA patients. One group of CD14^{dim} monocytes in PB expresses high level of Siglec-10 (Mean fluorescent intensity, MFI). Function test showed that those Siglec-10^{hi}CD14^{dim} monocytes from PB of healthy donor had higher IL-29 mRNA transcript after cultured with CD24 fusion protein in vitro compared to controls cultured without CD24 fusion protein. Interestingly, the percentage of this group of Siglec-10^{hi}CD14^{dim} monocytes in PB was higher in JIA patients than in controls, however, the Siglec-10 expression level on those CD14^{dim} monocytes in SF was significantly decreased compared to that in PB of JIA patients. **Conclusion:** Interaction between Siglec-10 on CD14^{dim} monocytes and CD24 may trigger the production of IL-29 which may mediate immunoregulatory function. The reduction of SFMC Siglec10 expression in JIA patients may have contributed to the pathogenesis of JIA.

ICW16-1

Cigarette Smoking at the Time of the Onset of RA Highly Impacts on RF and ACPA Levels in Japanese RA patients; the Study from IORRA and KURAMA Cohorts

Yuki Ishikawa¹, Katsunori Ikari², Motomu Hashimoto³, Koichiro Ohmura⁴, Masao Tanaka³, Hiromu Ito⁵, Atsuo Taniguchi², Hisashi Yamanaka², Tsuneyo Mimori⁴, Chikashi Terao^{6,7,8}

¹Joslin Diabetes Center, Harvard Medical School, ²Institute of Rheumatology, Tokyo, Japan, ³Tokyo Women's Medical University, ⁴Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ⁵Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ⁶Department of Orthopedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ⁷Center for Investigative Medical Sciences, Yokohama, Japan, RIKEN, ⁸Clinical Research Center, Shizuoka General Hospital, Shizuoka, Japan, ⁸Department of Applied Genetics, Shizuoka, Japan, The School of Pharmaceutical Sciences, University of Shizuoka

Conflict of interest: Yes

[Object] We conducted this study to elucidate the impact of cigarette smoking on RF and ACPA levels, which has yet been unclear. [Methods] Totals of 5,694 subjects from IORRA and 545 subjects from KURAMA were enrolled. Their precise smoking status data both before and after the onset of RA were withdrawn from the database. Associations between smoking status and ACPA or RF levels were validated by multiple logistic regression models. The effect of HLA-DRB1 status on the relation above was also explored. [Results] Smoking at the time of onset was an independent risk of high levels of both antibodies, especially RF (≥ 300 IU/mL; OR 2.61, $p=3.2 \times 10^{-19}$, ACPA ≥ 100 AU/mL; OR 1.47, $p=5.5 \times 10^{-7}$) while smoking cessation before onset significantly lowered the risks in comparison with subjects with smoking at onset (RF: OR 0.43, $p=5.2 \times 10^{-7}$, ACPA: OR 0.76, $p=0.010$), suggesting that RF is more sensitive to smoking status than ACPA. The effect sizes of these smoking variables were larger and significant in males than in females. The effect of smoking on high ACPA levels was only observed in the presence of shared epitope (SE, OR 2.09). Also, the effect of smoking on high RF levels was more apparent in the presence of SE than without SE (OR 2.93). Stratifying RA subjects by smoking status did not affect the risks of high levels of autoantibodies in the presence of HLA-DRB1*0901, frequently observed in Japanese and strongly associated with lowering ACPA levels. [Conclusions] Cigarette smoking at the time of RA onset

affects both ACPA and RF levels especially in males, and RF is more sensitive to smoking status than ACPA. The effect is apparent in the presence of SE, indicating an interaction between cigarette smoking and SE in terms of ACPA and RF levels. These data collectively imply a novel potential mechanism of RA pathogenesis.

ICW16-2

Neutrophil Extracellular Trap formation with citrullinated Histone H3 and diminished macrophage efferocytosis play key roles in local anti-citrullinated peptide antibody generation in the lung

Yuko Okamoto^{1,2}, Ashley Visser¹, Nickie Seto³, Mariana J Kaplan³, Michael P Mohning⁴, Stacey M Thomas⁴, William J Janssen⁴, Jill M Norris⁵, Kevin D Deane¹, Michael V Holers¹, Kristen M Demoruelle¹

¹Division of Rheumatology, University of Colorado Denver, Aurora, CO, USA, ²Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan, ³National Institute of Arthritis and Musculoskeletal and Skin Diseases, Systemic Autoimmunity Branch, National Institutes of Health, Bethesda, MD, USA, ⁴Division of Pulmonary Critical Care Medicine, National Jewish Health, Denver, CO, USA, ⁵Department of Epidemiology, Colorado School of Public Health, Aurora, CO, USA

Conflict of interest: None

[Object] We previously reported that anti-citrullinated (cit) peptide antibodies (ACPAs) in the lung associated with Neutrophil Extracellular Trap (NET) remnants in subjects who are At-Risk of developing future RA. Herein, we further characterized neutrophil NET formation and the role of macrophage function in association with ACPA in the lung of these subjects. [Methods] We included 49 subjects At-Risk for RA defined as being without synovitis but At-Risk for RA as first-degree relatives (FDR) of RA patients (N=30) and serum ACPA (+) subjects. Classified RA (N=11), and healthy controls (HC) (N=18) were also included. Serum and induced sputum ACPA were measured using anti-cyclic citrullinated peptide antibody (CCP) ELISA (CCP3.1, Inova). Dissociated sputum cells without stimulation were stained with Hoechst, anti-myeloperoxidase, and anti-cit-H3. Neutrophils that had formed NETs ex vivo were quantitated and characterized by microscopy. Sputum macrophages were incubated with apoptotic Jurkat cells for evaluation of efferocytosis. Separately, in sputum cell-free supernatant, the level of cit-H3-DNA NET remnants, IL-1 β , IL-6, IL-8, IL-10, TNF α , MCP1, MIP1 α , and MIP1 β were measured. [Results] The % of sputum neutrophils forming cit-H3+ NETs ex vivo was significantly higher in At-Risk and RA compared to HC (both $p<0.01$). In At-Risk subjects, sputum anti-CCP levels significantly correlated with % ex vivo cit-H3+ NETs ($r=0.48$, $p<0.01$) and the level of cit-H3-DNA NET remnants ($r=0.80$, $p<0.001$). All sputum cytokine/chemokine levels also significantly correlated with sputum anti-CCP level. Sputum macrophage efferocytosis was decreased in At-Risk and RA compared to HC (both $p<0.01$). [Conclusions] Airway inflammation generating cit-H3 expressing NETs and diminished macrophage efferocytosis may play a role in the development of ACPA in the lung in subjects At-Risk for RA. Additional studies are needed to determine associations with transitions to systemic ACPA and classified RA.

ICW16-3

Follicular Helper T 17 Cell Regulates Autoantibody Hyposialylation via OX40-OX40 Ligand Axis in Experimental Arthritis

Izumi Kurata, Isao Matsumoto, Ayako Ohyama, Atsumu Osada, Yuya Kondo, Hiroto Tsuboi, Takayuki Sumida

Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: None

[Object] Recently, IL-23-Th17 cells axis and hyposialylation of antibodies (Abs) were proved to be linked to the experimental and rheumatoid arthritis. However it remains uncertain how Tfh, including IL-17 producing Tfh (Tfh17), is associated to arthritis and whether it behaves as regulator of Ab hyposialylation. The aim of this study is to explore the relation of Tfh17 and autoantibody hyposialylation in glucose-6-phosphate isomerase (GPI) induced arthritis (GIA). [Methods] 1) Fluctuation of Tfh in draining lymph nodes were analyzed during the arthritis course.

2) Based on a result of above experiment, DCs were stimulated with purified anti-GPI Abs obtained at the arthritis onset (day 7) and resolving phase (day 28). Sialic acid in anti-GPI Abs was quantified by mass spectrometry. Artificial sialic acid removal/supplement was performed *in vitro* and *in vivo*. 3) Expression of *st6gal1*, the responsible enzyme for sialylation, in plasmablasts (PBs) co-cultured with Tfh was measured. OX40-OX40 ligand (OX40L) pathway was blocked with monoclonal Abs. 4) Fluctuation of Tfh17 and its OX40 expression were analyzed. [Results] 1) Tfh was increased and peaked at day 7. 2) DCs produced more proinflammatory cytokines when stimulated with day 7 Abs than with those of day 28. Mass spectrometric analysis revealed significant hyposialylation of day 7 Abs. Sialic-acid-removed Abs became stronger stimulants for DCs and GIA was ameliorated when sialic acid was supplied to mice. 3) Decreased expression of *st6gal1* was observed in differentiated PBs co-cultured with Tfh. OX40-OX40L pathway blocking rescued this decrease. 4) Tfh17 was significantly increased at day 7 and the highest expression of OX40 was observed compared to other Tfh subsets. [Conclusions] Our findings suggested Tfh, especially Tfh17 could have a crucial role in the development of arthritis not only via PB activation, but also via regulation of autoantibody hyposialylation through OX40-OX40L axis in the experimental arthritis.

ICW16-4

Massive *in silico* studies specified UBASH3A (a suppressor of T cell receptor signaling) as a candidate pathogenic factor that is down-regulated in CD4⁺ T cells of patients with rheumatoid arthritis (RA)

Kaoru Yamagata, Shingo Nakayamada, Ippei Miyagawa, Shigeru Iwata, Yoshiya Tanaka

The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: None

[Objective] A variety of *in silico* studies enable us to extract key molecules associated with a pathological condition. Using three databases to study the expression and function of extracted genes based on dys-regulated transcription, we screened a gene susceptible for RA. We next studied a molecular basis to confirm whether a specified molecule is proper as a novel therapeutic target for RA. [Methods] We focus on a gene that overlap via meta-analysis using GWAS, dbSUPER (database of super enhancer (SE) that forms clustered enhancers related to powerful transcription), and BioGPS. CD4⁺ T cells and CD4⁻ cells were separated from PBMC of age-matched healthy donor (HD; n=10) and RA (n=11), and then subjected to qPCR and WB to compare expression level of extracted gene. Effect of alleles at rs1893592 on the expression level was further studied. Immunohistochemistry (IHC) was performed to detect the protein in lymph nodes (LNs) of RA and controls. [Results] 1) *In silico* studies narrowed enormous ranges of genes down to *UBASH3A* gene, encoding a suppressor of T cell receptor (TCR) signaling, whose expression was aberrantly higher in CD4⁺ T cells compared with CD4⁻ cells among HD. Further, pathology-associated SNP in *UBASH3A* gene is located within SE. 2) The mRNA and protein expression of *UBASH3A* significantly decreased in CD4⁺ T cells of RA compared with those of HD. RA patients with AC and CC genotypes at rs1893592, but not AA, showed low level of *UBASH3A* mRNA in CD4⁺ T cells. 3) Clear staining for *UBASH3A* was detected in CD4⁺ T cells of LNs from patients with dermatomyositis, but not with RA. [Conclusions] Integrative analyses find overlapped *UBASH3A* gene specific for cell-type, SE, and RA pathology. Primary expression of *UBASH3A* may be impaired in CD4⁺ T cells of patients with RA. Minor allele C at rs1893592 suppresses expression of *UBASH3A* in CD4⁺ T cells. Down-regulation of *UBASH3A* may lead to aberrant activation of the TCR signaling crucial for RA pathogenesis.

ICW16-5

Prevotella copri from rheumatoid arthritis patients exacerbates collagen-induced arthritis in mice

Takuro Nii^{1,2}, Yuichi Maeda^{1,2}, Masashi Narazaki¹, Atsushi Kumanogoh¹

¹Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University, ²Laboratory of Immune Regulation, Graduate School of Medicine, Osaka University

Conflict of interest: None

[Object] In rheumatoid arthritis (RA), environmental factors such as smoking and periodontal diseases are involved in the disease onset. Among these environmental factors, altered composition of microbiota has been observed in the intestine of early RA patients. We have previously reported that some of RA patients harbored high abundance of *Prevotella copri* (*P. copri*) in the intestine. However, in tropical Asia and Africa, healthy individuals also contained high abundance of *P. copri* in the intestine. Therefore, we tried to analyze whether *P. copri* from RA patients has the ability to induce arthritis. [Methods] Firstly, by using anaerobic culture technique, we isolated *P. copri* from fecal samples of RA patients (RA-*P. copri*) and healthy controls (HC-*P. copri*). We investigated whole genome sequence of RA- and HC-*P. copri* to investigate their genome difference. Second, DBA1 mice in SPF (specific pathogen-free) condition were treated with antibiotics and inoculated RA or HC-*P. copri* for 5 days. After the inoculation, these mice were induced autoimmune arthritis by injection of bovine type II collagen. We evaluated clinical, pathological score in the joints and serum titers of anti-type II collagen antibody. We also analyzed immune cell populations in regional lymph nodes by flow cytometry. [Result] Interestingly, whole genome sequence revealed that RA and HC-*P. copri* were different. RA-*P. copri* has specific region on the genome. We also found the morphological difference between RA- and HC-*P. copri*. RA-*P. copri* inoculated mice had significantly higher arthritis score compared to HC-*P. copri* inoculated mice. In addition, increased serum anti-type II collagen antibody levels were observed in RA-*P. copri* inoculated mice. Moreover, increased Th1 and Th17 cell numbers in popliteal lymph nodes were also observed in RA-*P. copri* inoculated mice. [Conclusion] *P. copri* isolated from RA patients had the strong arthritis-inducing ability via disruption of gut homeostasis.

ICW16-6

Autophagy Promotes Citrullination of Vimentin and Its Interaction with Major Histocompatibility Complex class II in Synovial Fibroblasts

Eri Sugawara, Masaru Kato, Yuki Kudo, Wenshi Lee, Michihito Kono, Yuichiro Fujieda, Toshiyuki Bohgaki, Olga Amengual, Kenji Oku, Shinsuke Yasuda, Tatsuya Atsumi

Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Conflict of interest: None

Objectives: To investigate the role of autophagy in autoimmunity in rheumatoid arthritis (RA) through citrullination of vimentin and its interaction with MHC class II in synovial fibroblasts (SFs). **Methods:** The cell surface expression of MHC class II and B7 costimulatory molecules on SFs was analyzed by flow cytometry after treatment with interferon gamma (IFN- γ). Intracellular citrullinated autoantigens in SFs were analyzed by immunoblotting using serum from anti-citrullinated peptide antibodies (ACPA) positive patient as a primary antibody. SFs were incubated in serum-free medium or treated with proteasome inhibitor MG132 to induce autophagy. An autophagy inhibitor 3-methyladenin (3-MA) was used. Intracellular citrullinated vimentin (cVIM) was evaluated by immunoblotting and immunocytochemistry. The interaction between MHC class II and cVIM was evaluated with co-immunoprecipitation and proximity ligation assay. **Results:** MHC class II, B7-H1, and B7-DC were expressed on SF following treatment with IFN- γ , while B7-H3 was expressed on SF regardless of the presence of IFN- γ . Anti-cVIM positive RA patients' sera recognized 54 kDa protein in SF. By co-immunoprecipitation using anti-vimentin and -citrulline antibodies, the 54 kDa protein recognized by RA sera was revealed to be citrullinated vimentin. Following induction of autophagy by serum-free starvation or proteasome inhibition, intracellular cVIM was increased in SF but the effect was cancelled by the autophagy inhibitor 3-methyladenin. The interaction between MHC class II and cVIM was demonstrated by co-immunoprecipitation. Furthermore, proximity ligation assay revealed that the MHC class II-cVIM interaction significantly increased following induction of autophagy. **Conclusion:** SFs contribute to the autoimmunity in RA through citrullination of vimentin and its interaction with MHC class II promoted by autophagy.

ICW17-1

mTORC1 phosphorylation in CXCR3⁺ memory B cells and its potential as a new mode of action of TNF inhibitors in RA

Shigeru Iwata, Maiko Hajime, Mingling Zhang, Naoaki Ohkubo, Kazuhisa Nakano, Shingo Nakayama, Yoshiya Tanaka
The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

Conflict of interest: None

[Object] B cells play a crucial role in RA. Recently “Immunometabolism” attract much attention, and mTORC1 is well known as a key player of metabolic reprogramming. However, it remained elusive by which mTORC1 involved in the pathogenesis of RA. [Methods] PBMCs were obtained from 32 healthy controls (HCs) and 86 patients with bio-naïve active RA and analyzed by FACS. In addition, we examined the role of mTORC1 for induction of CXCR3 on B cells in vitro. [Results] The ratio of CD19⁺CD27⁺ memory B cells, especially CD19⁺CD27⁺CXCR3⁺ cells were decreased in patients with RA compared to HCs. T-bet is well known as an inducer for CXCR3 in CD4⁺ T cells. However, the level of T-bet expression in CD19⁺ cells was not different between HCs and patients with RA. Meanwhile, the expression of p-mTORC1 in CD19⁺ cells from patients with RA was higher than that of HCs. p-mTORC1 was higher in CD19⁺CD27⁺CXCR3⁺ B cells than CD19⁺CD27⁺CXCR3⁻ B cells. p-mTORC1 expression in CD19⁺CD27⁺CXCR3⁺ cells were correlated with tender joints, swollen joints, disease activity such as DAS28 (CRP), CDAI and SDAI, but not RF and anti-CCP antibodies. We examined the change of the ratio of CD19⁺CD27⁺CXCR3⁺ cells and p-mTORC1 expression before and at 1 year after treatment with biologics (33 patients, TNF inhibitors (TNFi) (n=19), abatacept (ABT) (n=12), tocilizumab (TCZ) (n=2)). The ratio of CD19⁺CD27⁺CXCR3⁺ B cells were recovered and p-mTORC1 expression were decreased in TNFi treatment group, but not in ABT treatment group at 1 year. Finally, we examined the role of mTORC1 for induction of CXCR3 expression on B cells in vitro. Combined stimulation of BCR, CD40L and IFN- γ induced CXCR3 expression on B cells, which were abrogated by mTORC1 inhibitor, Rapamycin. [Conclusions] Taken together, activation of mTORC1 is involved in the accumulation of CXCR3-positive B cells in RA synovium and TNF inhibitors possibly target at this in patients with RA.

ICW17-2

Characteristic increase in fractalkine receptor (CX3CR1)-positive helper T cells in IgG4-related disease (IgG4-RD)

Yoshino Inoue, Satoshi Kubo, Shingo Nakayama, Kazuhisa Nakano, Shigeru Iwata, Kentaro Hanami, Shunsuke Fukuyo, Ipppei Miyagawa, Yusuke Miyazaki, Akio Kawabe, Yoshiya Tanaka
The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: None

[Object] Fractalkine is a chemokine which mediates both cell adhesion and cell migration, and enable inflammatory cells to infiltrate into peripheral tissues effectively. Since the main pathological changes of IgG4-RD include infiltration of lymphocyte and fibrotic changes in affected lesions, we investigated the significance of fractalkine in IgG4-RD. [Methods] Human CD4⁺CX3CR1⁺T cells were induced from naïve CD4⁺T cells under various stimulation, and the characteristics of CX3CR1 expressing cells were analyzed in vitro. The proportion of CX3CR1⁺mononuclear cells in peripheral blood from healthy donor and IgG4-RD patients were analyzed by flow cytometry [Results] Expression of CX3CR1 on CD4⁺T cells was induced by stimulation with TCR and IFN- γ for 5 days and around half of CD4⁺T cells expressed CX3CR1. Compared with CX3CR1⁻T cells, CX3CR1⁺T cells highly expressed both CXCR5 and CXCR3. In addition, CX3CR1⁺T cells expressed Bcl-6 and T-bet, which is a master transcriptional factor of Tfh and Th1 respectively. After stimulation by PMA and ionomycin, CD4⁺CX3CR1⁺T cells produced both IL-21 and IFN- γ . In terms of the proportion of CX3CR1 expression on mononuclear cells in healthy subjects, almost all CD8⁺T cells expressed CX3CR1, while 5% of CD4⁺T cells did. In contrast, B cells did not express CX3CR1. Similarly, in IgG4-RD patients (n=10), CX3CR1 were expressed on CD8⁺T cells, but not on B cells. However, the proportion of CD4⁺CX3CR1⁺T cells in IgG4-RD patients were 12.3%, which

was higher than in healthy subjects (p = 0.01). Furthermore, CD4⁺CX3CR1⁺T cells expressed both CXCR5 and CXCR3 in patients with IgG4-RD. [Conclusions] Our findings suggest that CX3CR1⁺helper T cells have the features of both Th1 and Tfh cells, inducing tissue injury and B cell activation. Moreover, the increased proportion of CD4⁺CX3CR1⁺Th1-Tfh like T cells indicated the possible involvement of this new subset in the pathogenesis and thus fractalkine could be a new therapeutic target for IgG4-RD.

ICW17-3

The CCL22/17-CCR4 axis in macrophage and Treg suppress disease activity in experimental crescentic glomerulonephritis treated with anti-IL-6 receptor antibody

Ryota Sakai^{1,2}, Keiko Yoshimoto³, Katsuya Suzuki³, Tsuneo Kondo², Takahiko Kurasawa², Tsutomu Takeuchi³, Koichi Amano²

¹Department of Microbiology and Immunology, Keio University School of Medicine, ²Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, ³Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine

Conflict of interest: Yes

[Object] We recently reported that the level of CCL22/17, which is a specific ligand of CCR4, is increased in remission patients with ANCA associated vasculitis (AAV) after monotherapy with anti-IL-6 receptor (IL-6R) antibody. To determine the significance of the CCL22/17-CCR4 axis in the experimental model of crescentic glomerulonephritis (GN), which is the main symptom of AAV. [Methods] The GN model was induced by administering rabbit anti-mouse glomerular basement membrane antibodies. The outcome was evaluated by histological assessment and renal function. T cells and macrophages were analyzed by flow cytometry analysis of mononuclear cells that were isolated from the kidney. Disease activity was measured in CCR4-knock out (KO) mice and DEREK (depletion of Tregs by diphtheria toxin) mice, and in mice who received adoptive transfer of wild type (WT)- or CCR4KO-Tregs. CCL22 was dissolved in Medgel and transplanted under the kidney capsule. [Results] Disease activity peaked on day 10 in this model, accompanied by infiltration of Th1/Th17 cells. The proportion of Tregs among CD4⁺ T cells increased to 30%-40% on day 21 and was maintained thereafter. Treg-depletion using DEREK mice aggravated GN symptoms, suggesting that Tregs play an important role in the control and/or tolerance of GN. CCR4-KO mice developed more severe GN compared to WT mice, and the proportion of FoxP3⁺/CD4⁺ cells was significantly decreased in CCR4-KO mice compared to WT mice. Adoptive transfer of WT-Tregs into DEREK mice ameliorated the disease, whereas CCR4-deficient Tregs failed to control GN. Local administration of CCL22 facilitated Treg migration to glomeruli and reduced GN symptoms. Anti-IL-6R antibody treatment ameliorated the disease, upregulated CCL22/17 mRNA in CD11b^{int} CD11c^{int} macrophages and enhanced the accumulation of WT-Tregs, but not of CCR4-deficient Tregs. [Conclusions] Our results suggest that the CCL22/17-CCR4 axis in macrophage and Treg plays a crucial role in the regulation of GN.

ICW17-4

Serum High Type I Interferon is Associated with Active Proliferative Lupus Nephritis in Lupus Patients Accompanied with High Interferon Signature Gene Expression and Plasmacytoid Dendritic Cell Infiltration in Lupus Nephritis Kidney and Leads to Podocyte Damage

Taro Iwamoto^{1,2}, Jessica M Dorschner³, Mark A Jensen², Shanmugapriya Selvaraj⁴, Danielle Vsetecka³, Shreyasee Amin³, Ashima Makol³, Floranne C Ernste³, Thomas Osborn³, Kevin Moder³, Vaidehi R Chowdhary³, Valeria Mezzano⁴, Peter Izmirly⁵, Michael Belmont⁵, Robert M Clancy², Jill P Buyon², Ming Wu⁴, Cynthia A Loomis⁴, Hiroshi Nakajima¹, Timothy B Niewold²

¹Department of Allergy and Clinical Immunology, Chiba University Hospital, ²Colton Center for Autoimmunity, New York University, New York, NY, USA, ³College of Medicine, Mayo Clinic, Rochester, MN, USA, ⁴Department of Pathology, New York University, New York, NY, USA, ⁵Division of Rheumatology, New York University, New York, NY, USA

Conflict of interest: None

[Object] Lupus nephritis (LN) remains one of the most severe organ manifestations in systemic lupus erythematosus (SLE), despite recent advancements in immunosuppressive therapies. High type I interferon (IFN) is a heritable risk for developing SLE, and previous studies have suggested a link between high IFN and lupus nephritis. However, little is known about the relationships between high levels of IFN and the subtypes of LN, and whether IFN plays a critical role in the pathogenesis of LN. [Methods] We studied 221 European-American SLE patients and measured IFN in sera by performing WISH IFN bioassay as described previously. Subtypes of LN were confirmed by renal biopsy review. Serological parameters were measured in the clinical laboratory. mRNA in situ hybridization was performed to detect IFN induced gene (IIG) expression and plasmacytoid dendritic cells in LN kidney biopsies. Real-time PCR was performed to measure gene expressions in human podocyte cell lines. [Results] Proliferative LN was significantly more common among patients with high serum type I IFN compared to patients with low levels of IFN ($p < 0.001$, $OR = 3.0$). Notably, IFN level was significantly higher in active proliferative LN compared to inactive proliferative LN ($p < 0.001$), and these findings were independent of complements and anti-dsDNA antibody levels. mRNA in situ hybridization showed increased expression of IIG accompanying plasmacytoid dendritic cell infiltration in active proliferative LN kidneys. In vitro experiments demonstrated that type I IFN induced gene expressions that are related to apoptosis, cytoskeleton function and pro-inflammatory cell migration in human podocyte cell lines. [Conclusion] Our data support an association between type I IFN and active proliferative lupus nephritis, suggesting that IFN is involved in renal pathogenesis. These data also suggest that IFN could predict renal disease activity or the future risk of developing LN, especially proliferative LN in SLE patients.

ICW17-5

The role of skin tissue in type I interferon regulation and initiation of Systemic Lupus Erythematosus

Antonios Psarras^{1,2}, Adewonuola A Alase^{1,2}, Md Yuzaiful Md Yusoff^{1,2}, Miriam Wittmann^{1,2}, Paul Emery^{1,2}, Edward M Vital^{1,2}

¹Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK, ²NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, UK

Conflict of interest: None

Object Prior to a diagnosis of SLE, there is an At-Risk stage, with ANA and elevated type I IFN (IFN-I) activity with only mild suggestive symptoms not meeting diagnostic criteria. Skin is the most commonly affected organ in SLE. It can be infiltrated by T cells, but keratinocytes and fibroblasts can also produce inflammatory mediators including IFNs. We evaluated skin of At-Risk individuals for IFN-I production compared to healthy controls (HC) and SLE patients. **Methods** Skin biopsies from lesional and non-lesional skin of SLE patients, non-lesional skin of At-Risk individuals and HC were evaluated using in situ hybridisation. IFN-stimulated genes (IFN Score) was measured in skin biopsies and blood using Taqman. Human keratinocytes were cultured and stimulated in vitro; IFN-I expression was measured by qPCR. **Results** IFN Score was increased in At-Risk individuals compared to HC but the fold difference in skin (FD 29.5; 1.3-635.0) was markedly greater than in blood (FD 2.2; 2.0-2.3) suggesting local IFN-I production. Blood IFN Score correlated with active skin but not joint involvement in SLE. Skin biopsies from HC showed no expression of IFN-I. In contrast, active skin lesions from SLE showed diffuse expression of IFNK in the epidermis but not in leucocyte-infiltrating areas. The epidermis of At-Risk individuals also showed diffuse expression of IFNK, but no clinical/histopathological features of inflammation. UV provocation notably enhanced IFNK expression. Keratinocytes from HC ($n=3$), At-Risk individuals ($n=5$) and SLE patients ($n=5$) were cultured and treated with TLR3 or RIG-I stimuli for 24 hours. Keratinocytes from At-Risk and SLE patients showed higher expression of IFNK at baseline; after stimulation the expression of IFNK and IFNB was significantly increased compared to HC. **Conclusions** IFN-I production, a key pathogenic process at the early stage of SLE, is mediated by keratinocytes suggesting that organs such as the skin play an active role in initiating disease.

ICW17-6

Serum levels of TNF- α at 24 hours after the first administration of certolizumab pegol predicts the efficacy of certolizumab pegol at week 12 in TSUBAME study (UMIN0002381) from FIRST registry

Yusuke Miyazaki, Kazuhisa Nakano, Satoshi Kubo, Shingo Nakayama, Shigeru Iwata, Kentaro Hanami, Shunsuke Fukuyo, Ippei Miyagawa, Akio Kawabe, Yoshiya Tanaka

The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan

Conflict of interest: Yes

[Object] To increase the remission rate of rheumatoid arthritis (RA), it is necessary to determine the efficacy of the tumor necrosis factor (TNF) inhibitor as early as possible. Moreover, the response to certolizumab pegol (CZP) at 12 weeks has been reported to predict its long-term efficacy. In this study, we assessed the efficacy of CZP and the relationship between serum TNF- α and IL-6 levels and serum CZP levels and clinical response. [Methods] Eighty-five patients with RA and inadequate response to MTX who received CZP were enrolled. The primary endpoint was change in DAS28 (ESR) at 12 weeks, and secondary endpoints were changes in serum TNF- α , IL-6 and CZP levels at 24 hours after first administration of CZP and the correlation between serum biomarkers and clinical response. [Results] CZP significantly improved DAS28 (ESR) at 12 weeks (baseline and 12w = 5.45 ± 1.25 and 3.35 ± 1.46 , respectively, $p < 0.01$). Serum TNF- α and IL-6 levels were significantly decreased at 24 hours. Serum CZP levels at 24 hours were widely distributed (median $9.4 \mu\text{g/ml}$, range $0.2-31.8 \mu\text{g/ml}$). No correlation was found between TNF- α and IL-6 levels at baseline and clinical response. In univariate analysis, low serum TNF- α and IL-6 levels and high CZP levels at 24 hours after were associated with DAS28 (ESR) remission at 12 weeks. In multivariate analysis, only low serum TNF- α levels at 24 hours were significantly associated with DAS28 (ESR) remission at 12 weeks (OR 0.017, 95%CI 0.003, 0.792). Body mass index and rheumatoid factor did not correlate with serum CZP levels at 24 hours. However, serum TNF- α levels at 24 hours inversely correlated with serum CZP levels at 24 hours ($r = -0.601$, $p < 0.01$) [Conclusions] CZP was effective in cases in which serum CZP levels were rapidly increased and serum TNF- α was strongly neutralized in only one day. These results suggest that low serum TNF- α levels at 24 hours after first administration of CZP may predict the efficacy of CZP.

ICW18-1

The role of Jazf1 in the production of IL-10 in Tr1 cells

Masanori Kono¹, Tomohisa Okamura^{1,2,3}, Mariko Inoue¹, Toshihiko Komai¹, Yukiko Iwasaki¹, Yusuke Takeshima^{1,2}, Shuji Sumitomo¹, Hirofumi Shoda¹, Kazuhiko Yamamoto⁴, Keishi Fujio¹

¹Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, ²Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, ³Max Planck-The University of Tokyo Center for Integrative Inflammation, The University of Tokyo, Tokyo, Japan, ⁴Laboratory for Autoimmune Diseases, Center for Integrative Medical Sciences, RIKEN, Kanagawa, Japan

Conflict of interest: None

[Object] Juxtaposed with another zinc finger gene 1 (JAZF1) gene has been identified as a susceptibility locus for Systemic Lupus Erythematosus (SLE) in GWAS. A recent study revealed that JAZF1 exhibits *cis*-expression quantitative trait locus (eQTL) effect specifically in CD4⁺T cells in SLE patients, indicating that JAZF1 expression in CD4⁺T cells may play an important role in the pathogenesis of SLE. However, the precise role of JAZF1 in autoimmune diseases remains elusive. In this study, we aimed at clarifying the role of Jazf1 in the immune system. [Methods] To evaluate the function of Jazf1-expressing cells, we generated Jazf1-GFP reporter mice. Quantitative RT-PCR was performed on FACS-sorted various types of immune cells from C57BL/6 or Jazf1-GFP mice. Mouse Jazf1 gene was cloned into the pMIG vector and then transduced into MACS-sorted splenic CD4⁺T cells. IL-10 detection in culture supernatants was performed by ELISA. [Results] Among various immune cells, Jazf1 was preferentially expressed in CD4⁺CD25⁺LAG3⁺regulatory T cells (LAG3⁺Tregs) which are equivalent to Tr1 cells characterized by

high levels of interleukin (IL)-10 production. Jazf1-GFP⁺CD4⁺T cells showed elevated expression levels of Lag3 and Egr2, the characteristic genes of LAG3⁺Tregs. Intriguingly, Jazf1 expression was inversely correlated with IL-10 expression at both mRNA and protein levels in LAG3⁺Tregs. As expected, ectopic expression of Jazf1 decreased IL-10 production in CD4⁺T cells under Tr1 differentiation condition. [Conclusions] We previously reported that Egr2-expressing LAG3⁺Tregs ameliorate pathology of lupus-prone mice, and EGR2 is a susceptible gene for SLE. In this study, we revealed that Jazf1 plays a pivotal role in IL-10 production from LAG3⁺Tregs. These findings suggest that JAZF1 is a novel therapeutic target for treating autoimmune diseases, such as SLE. Further studies are needed to evaluate the role of JAZF1 in human LAG3⁺Tregs.

ICW18-2

Antigen-specific Foxp3⁺ Tregs suppress cognate antigen response but not suppress non-cognate antigen response

Yoshihiro Oya¹, Hidekazu Futami¹, Takuya Nakazawa¹, Ryutaro Matsumura¹, Hiroshi Nakajima², Ethan Shevach³

¹Department of Rheumatology, Allergy & Clinical Immunology, National Hospital Organization Chiba-East National Hospital, ²Department of Allergy and Clinical Immunology, Graduate School of Medicine, Chiba University, ³Laboratory of Immunology, Cellular Immunology Section, National Institutes of Health, NIAID

Conflict of interest: None

[Background/Purpose] Suppressive function of Foxp3⁺ T regulatory cells (Tregs) has been established in autoimmune diseases and in allergy. However, how they mediate their suppressive function remains unresolved. To develop Treg therapy, it is needed to understand the biochemical nature and its specificity of suppressor mechanisms in more detail. [Methods] (1): Two antigen-specific naïve effector (Teff) cells from TCR transgenic RAG2^{-/-} mice (OTII Tg mice and SM Tg mice) were transferred to syngenic recipient mice together with APCs pulsed with two antigens and antigen-specific Tregs. Two antigen peptides were pulsed either on distinct APCs or on the same APCs. Splenocytes from the recipient mice were analyzed to determine the Treg suppression on each Teff. (2): APCs pulsed with both peptides were co-cultured with antigen-specific Tregs, and Tregs were depleted out at 18 hours by cell sorting to obtain the suppressed APCs. The stimulatory function of the sorted APCs was determined by co-culture with two TCR Tg Teffs. [Results] (1): In the co-transfer with distinct APCs, Tregs suppressed the cognate antigen specific Teffs, but not the non-cognate antigen specific Teffs. Treg suppressed only the cognate antigen-specific Teffs even when both antigen peptides were pulsed on the same APCs. (2): Teffs were suppressed by the suppressed APCs in the absence of Tregs. Antigen-specificity of the suppression was also maintained by the suppressed APCs. [Conclusions] Under the suppression of Tregs, both the suppressed Teffs and the non-suppressed proliferating Teffs were able to co-exist in the same environment, indicating that APCs are capable of stimulating the non-cognate Teffs even though they suppress the cognate Teffs. These findings suggest that Tregs can mediate antigen-specific suppression through APCs and might shed light on the unresolved issues caused by the unwanted non-specific suppression by the conventional immune-suppressive therapies.

ICW18-3

Distribution of immune-suppressive cells and Toll-like receptors in synovial tissues in the patients with rheumatoid arthritis which were treated by anti-TNF agents

Yuya Takakubo¹, Suran Yang¹, Yuta Suzuki¹, Hiroharu Oki¹, Yasushi Naganuma³, Akiko Sasaki², Kan Sasaki², Hiroshi Orui¹, Michiaki Takagi¹

¹Department of Rehabilitation & Orthopaedic Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan, ²Department of Orthopaedic Surgery, Yamagata Saisei Hospital, ³Department of Orthopaedic Surgery, Yamagata Central Hospital

Conflict of interest: None

[Objectives] The aim of this study was to investigate the immune-inflammatory cells, including Toll-like receptors (TLRs)- equipped cells, in synovial tissue samples from the patients with rheumatoid arthritis (RA)

on anti-TNF agents compared to patients with treatment of conventional synthetic disease-modifying antirheumatic drug (csDMARD). [Methods] Immune-inflammatory cells were evaluated in RA synovitis in patients with anti-TNF group {n=22 (etanercept 16, infliximab 6)} or csDMARD group (n=21) by immunohistochemical and immunofluorescence study. Mean duration of affection by RA of anti-TNF group and csDMARD-group was 8.4 years and 11.4 years, respectively. Period of anti-TNF group was 14 months. Mean CRP level of anti-TNF group and csDMARD-group was 1.4 mg/dl and 2.1 mg/dl and that of DAS28-CRP score (4) of anti-TNF group and csDMARD-group was 4.1 and 4.5 at collecting their samples, respectively. CD3 (T cells), CD20 (B cells), CD68 (macrophages), S-100 (dendritic cells: DC) and TLR1 to 9 immunoreactive cells were counted in at least five x 200 light microscope fields in larger lymphoid infiltrates. The intensity of the inflammation was estimated using the Krenn histopathological grading system (grade 0-3). [Results] The grading scores of synovitis was both 1.6 in each group and correlated best with the T and B cells in the both groups (p<0.05). Interestingly, both T and B cell counts were lower in the anti-TNF than in the csDMARD group (p<0.05). In contrast, the C-reactive protein (CRP) and disease activity score DAS28-CRP did not show clear-cut correlations with the inflammatory grade of the synovitis. Similar numbers of cells immunoreactive for TLR-1 to TLR-9 were found in synovitis in both groups. [Conclusion] Patients clinically responding to anti-TNF agents might still have the potential of moderate/severe local joint inflammation, composed in particular of and possibly driven by the autoinflammatory TLR⁺ cells.

ICW18-4

Inhibitory cytokine synergy of IL-10 and TGF-β3 contributes to humoral immune tolerance mediated by metabolic reprogramming

Toshihiko Komai¹, Tomohisa Okamura^{1,2,3}, Mariko Inoue¹, Kaoru Morita¹, Yukiko Iwasaki¹, Shuji Sumitomo¹, Hirofumi Shoda¹, Kazuhiko Yamamoto^{1,3,4}, Keishi Fujio¹

¹Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, ²Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, Japan, ³Max Planck, Center for Integrative Inflammation, The University of Tokyo, Tokyo, Japan, ⁴Laboratory for Autoimmune Diseases, Center for Integrative Medical Sciences, RIKEN, Kanagawa, Japan

Conflict of interest: Yes

[Object] There is growing evidence that modulation of immunometabolism could be a therapeutic target in systemic lupus erythematosus (SLE). In this study, we assessed the effect of inhibitory cytokine synergy (ICS) of IL-10 and TGF-β3 on B cell metabolic reprogramming and lupus pathologies. [Methods] LPS-stimulated B cells in the presence or absence of IL-10 and/or TGF-β3 were analyzed by RNA sequencing (RNA-seq) and immunoblotting. Oxygen consumption rates (OCR) and extracellular acidification rates (ECAR), as a measure of oxidative phosphorylation and glycolysis respectively, were evaluated by extracellular flux analyser. *In vivo*, the therapeutic effects of pCAGGS-II10, and/or pCAGGS-Tgfb3 plasmid vectors in NP-LPS immunized C57BL/6 mice and imiquimod (IMQ)-treated lupus model mice were assessed. In addition, metabolic signals from NP-LPS immunized mice treated with anti-IL-10 and anti-TGF-β blocking antibody were evaluated by flow cytometer. [Results] RNA-seq and immunoblotting revealed that mammalian target of rapamycin (mTOR) signaling and metabolism pathway were preferentially suppressed in the IL-10/TGF-β3 condition. Intriguingly, both OCR and ECAR were reduced in IL-10/TGF-β3 condition, and enhancement of mTOR signals by MHY1485 counteracted the ICS effects. Simultaneous administration of pCAGGS-II10 and pCAGGS-Tgfb3 inhibited NP-specific and anti-dsDNA antibody production in NP-LPS immunized and IMQ-treated mice, respectively. Further, a combination of anti-IL-10 and anti-TGF-β antibody enhanced NP-specific antibody production with enforced phosphorylation of S6RP and mitochondrial membrane potentials in B cells. [Conclusions] Our findings indicate that ICS contributes to regulate systemic humoral immune responses and lupus pathologies via down-regulation of mTOR signaling and metabolic state in B cells. Fine tuning of immunometabolism mediated by ICS effect might provide novel therapeutic approaches for SLE.

ICW18-5

Modulation of arthritis by type 2 innate lymphoid cells

Yasunori Omata^{1,2}, Georg Schett², Mario Zaiss²

¹Department of Orthopaedic Surgery, The University of Tokyo, ²Department of Internal Medicine 3, Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and Universitätsklinikum Erlangen, Germany

Conflict of interest: None

[Object] Besides many well-characterized cellular and molecular components of innate and adaptive immune system that influence inflammatory processes, recent characterization of innate lymphoid cells (ILC) has revealed an essential role for these populations in the initiation, regulation and resolution of inflammation. ILC2 depend on the transcription factors *GATA3* and *ROR α* and produce the type 2 cytokines IL-4/5/13 upon the activation by IL-25/33. We investigate the role of ILC2 during inflammatory arthritis. [Methods] Human peripheral blood samples collected from patients with rheumatoid arthritis (RA) and healthy controls were analyzed by FACS. Tissue samples (spleen, blood and mesenchymal lymph nodes) from K/BxN serum induced arthritis model (SIA) and collagen induced arthritis (CIA) model were investigated at different time points. Gain (IL-25/33 mini-circle treatment, IL-2/IL-2 antibody complex treatment and adoptive transfer of wild type- or IL-4/13^{-/-} ILC2) and loss (*ROR α* ^{cre}/*GATA3*^{fl/fl} mice and *Tie2*^{cre}/*ROR α* ^{fl/fl} mice) of ILC2 function researches during arthritis were performed to unravel the role of ILC2. [Results] We detected significantly increased ILC2 in blood of RA patients compared to healthy controls. In both SIA and CIA, we detected increased frequencies of ILC2, especially IL-4/13^{+/+}ILC2, at early time points after induction of arthritis. We could highlight the beneficial effects of ILC2 on arthritis severity because experimentally increasing ILC2 numbers attenuated inflammation and joint destruction, whereas genetically reducing ILC2 exacerbated clinical arthritis severities. Adoptive transfer of IL-4/13^{-/-} ILC2 failed to show significant attenuated clinical signs. IL-4/13 competent wild type ILC2 decreased IL-1 β cytokine secretion by macrophages, the main cytokine driving SIA. These data show that ILC2 have immune-regulatory functions in arthritis. [Conclusions] Our data suggests that ILC2 are protective to arthritis.

ICW18-6

B7-H4 inhibits the development of Primary Sjögren's syndrome by regulating Treg differentiation in NOD mice

Xu Zheng¹, Qikai Wang¹, Xiang Yuan¹, Ying-bo Zhou¹, Hui Chu¹, Guosheng Wang¹, Xiang-pei Li¹, Yi-ping Wang², Xiao-mei Li¹

¹Department of Rheumatology and Immunology, The First Affiliated Hospital of USTC, University of Science and Technology of China, Hefei, China, ²Westmead Institute for Medical Research, University of Sydney, Australia

Conflict of interest: None

[Object] B7H4 is a member of the B7/CD28 co-stimulatory/co-inhibitory superfamily. We explored the regulatory mechanism of B7H4 in the pathogenesis of pSS (Primary Sjögren's syndrome) in NOD mice through anti-B7H4mAb or B7H4Ig fusion protein [Methods] 1 Examine B7H4 expression in SGs (salivary glands) of 8 and 15 weeks NOD mice by IHC 2 After anti-B7H4mAb or IgG injected into NOD mice, assess lymphocyte infiltration in SGs by H&E and detect levels of IgG, IgM in sera 3 Detect proinflammatory cytokines, Foxp3 mRNA in SGs and percentage of CD4⁺Foxp3⁺T cells in spleen 4 Detect TGF- β and IL-2 mRNA in SGs. In vitro, SG epithelial cells and naïve CD4⁺T cells co-cultured under Treg-driving conditions in either containing anti-B7H4mAb or IgG 5 B7H4Ig or control Ig were injected into NOD mice. Assess lymphocyte infiltration, cytokines and Foxp3 mRNA in SGs, percentage of CD4⁺Foxp3⁺T cells in spleen [Results] 1 SGs in 15 weeks showed reduced B7H4 expression 2 Anti-B7H4mAb treatment aggravated lymphocyte infiltration in SGs by H&E and significantly increased the levels of IgG, IgM in sera 3 Anti-B7H4mAb treatment showed higher levels of IL-12, IL-1 α , TNF- α mRNA in SGs, however, lower level of Foxp3, IL-10 mRNA in SGs and lower percentage of CD4⁺Foxp3⁺T cells in spleen 4 Anti-B7H4mAb treatment decreased TGF- β and IL-2 mRNA levels in SGs. In vitro, Anti-B7H4mAb inhibited CD4⁺CD25⁺Foxp3⁺T cells production 5 B7H4Ig decreased lymphocyte infiltration and reduced levels

of IL-1 α or TNF- α mRNA, but increased Foxp3 mRNA and IL-10 mRNA level in SGs [Conclusions] Anti-B7H4 mAb inhibited number of Treg and IL-10 production in SGs. Furthermore, anti-B7H4 mAb inhibited the in vitro differentiation of naïve CD4⁺ T cells. Importantly, treatment of NOD mice with B7H4Ig effectively ameliorated pSS, accompanied with decreased level of lymphocyte infiltration in SGs, decreased production of proinflammatory cytokines in SGs. Our findings implicate a protective role of B7H4 on SGEC in the treatment of pSS.

ICW19-1

Rheumatoid Meningitis: Meningeal Biopsy Is Not Essential for Diagnosis

Fawad Aslam¹, Angela Parsons², Marie Grill², Brent P Goodman²

¹Department of Rheumatology, Mayo Clinic, Scottsdale, Arizona, USA.,

²Department of Neurology, Mayo Clinic, Scottsdale, Arizona, USA

Conflict of interest: None

Objectives: Rheumatoid meningitis (RM) is a rare complication of RA. Current clinical practice relies on a meningeal biopsy for diagnosis. Previous reports have emphasized the importance of a biopsy to diagnose RM. Our study aimed to review the clinical history of RM and assess the role of meningeal biopsy in RM patients. **Methods:** An administrative database search was done within the Mayo network from 1990-2017 to identify RM patients for this retrospective study. Patients were only included if RA was diagnosed by a rheumatologist and RM was diagnosed both by a rheumatologist and neurologist. **Results:** Fourteen RM patients were identified. Mean age was 67 years and 57% were males. RA duration was from 0-40 years. None had seronegative disease. RA was controlled in 10/11 (91%) at RM diagnosis. Skin nodules were present in 4/13 (31%) and erosions in 3/10 (30%) patients. Headache, seizure and hemiparesis were the commonest presentations of RM. None had cranial neuropathies. Cerebrospinal fluid cell count and protein levels were abnormal in 11/14 (79%) cases. On MRI, all patients showed enhancement of the pachymeninges, leptomeninges or both: 12/14 (86%) had a frontoparietal pattern. Of the 10 biopsied patients, 90% had nonspecific inflammation. None showed vasculitis or rheumatoid nodules. Infections and IgG4 changes were absent. Corticosteroids, rituximab and methotrexate were used for treatment. 10/12 (83%) patients who underwent repeat MRI showed resolution. The 4 RM patients treated without a biopsy did similarly well. **Conclusion:** RM can present at any time in RA and occurs in well controlled RA. MRI shows fronto-parietal meningeal enhancement. Biopsy is negative for pathognomonic RM features. Those with suspected RM without biopsy do equally well. In contrast to the previous literature, our study shows that clinical evaluation, testing and imaging in RA patients with meningitis, in the absence of atypical features, is sufficient to diagnose RM without a biopsy.

ICW19-2

Screening by CT at the administration of bDMARDs has detected 25 patients with malignancy among 3015 patients with RA, from FIRST registry

Hiroko Miyata¹, Kazuhisa Nakano¹, Shingo Nakayamada¹, Shigeru Iwata¹, Ayako Yamaguchi¹, Shunsuke Fukuyo¹, Satoshi Kubo¹, Ipppei Miyagawa¹, Kazuyoshi Saito², Yoshiya Tanaka¹

¹The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, ²The Internal Department of Tobata General Hospital, Iwakikai, Japan

Conflict of interest: None

[Objectives] To clarify the outcome of RA patients complicated with malignancy. [Methods] 3015 RA patients were screened using CT-scan before starting bDMARDs in our hospital between January 2005 to September 2017. csDMARD-IR RA patients after curative resection of malignancy were considered to start bDMARDs under adequate IC. The primary endpoint was the achievement rate of LDA (DAS28-ESR <3.2) at one year after discovery of malignancy. The secondary endpoints were taken as the patients' background factors at the time of diagnosis of each malignancy. [Results] In the wake of CT scan, malignancy was diagnosed in 25 patients (lung cancer; 12, malignant lymphoma (ML); 4, breast can-

cer; 1, uterine cancer; 1, gallbladder cancer; 1, thyroid cancer; 1, bladder cancer; 1, liposarcoma; 1, kidney cancer; 1, GIST; 1). Four patients with advanced cancer (lung cancer, uterine body cancer, liposarcoma, malignant lymphoma each) received palliative care and the other 21 patients underwent surgery or chemotherapy. The 2-year survival rate was 78.6% (mean observation period: 31.9 months). DAS28-ESR was 5.57 at the time of malignancy diagnosis. 9 cases (36%) achieved LDA after one year. In 9 patients with bDMARD in 11 early cancers, 6 achieved LDA. 2 without bDMARD did not achieve LDA. In 4 cases with advanced malignancy, 2 with ML could maintain LDA with R-CHOP, and a case with thymic cancer/ breast cancer underwent surgery+chemotherapy, treated with low-dose GC + SASP, and shifted with LDA / HDA, respectively. The mean age of RA patients complicated with malignancy was significantly older than those without malignancy (67.9 vs. 61.2, $p = 0.018$). [Conclusion] Screening CT before starting biologics is very important and was useful for detection of early lung cancer in particular. Adequate diagnosis and management for malignancy could enable disease control of RA with bDMARDs.

ICW19-3

Clinical and prognostic characteristics of systemic lupus erythematosus related pseudo-intestinal obstruction in a multi-center cohort study

Liyang Peng, Mengtao Li, Dong Xu, Qian Wang, Jiuliang Zhao, Ziqian Wang, Xiaofeng Zeng

Department of Rheumatology, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Key Laboratory of Rheumatology and Clinical Immunology, Ministry of Education, Beijing, China

Conflict of interest: None

Object This study aimed to explore the clinical features and outcomes of systemic lupus erythematosus related pseudo-intestinal obstruction (SLE-IPO) in a multi-center cohort from China. **Methods** Patients were enrolled from 14 centers to establish a multi-center cohort of SLE-IPO and related data were collected retrospectively. SLE patients with clinical manifestations and image evidence of IPO were included. SLE patients without any gastrointestinal (GI) involvement were recruited as a control group. All-cause death and SLE flare as well as SLE-IPO flare were primary and secondary endpoints. **Results** 220 SLE-IPO patients and 440 SLE patients without GI involvement were included. The time from onset to SLE diagnosis were 4.1 months for SLE-IPO group and 2.0 months for control group. SLE-IPO patients were commonly complicated with smooth muscle dysfunction, including pyeloureterectasis (38.6%), bladder contracture (12.7%), thick gallbladder wall (20.3%) and cholangiectasis (5.3%). SLEDAI score was higher in SLE-IPO group (9.5 ± 6.2 vs. 5.9 ± 6.6 , $p < .001$). SLE-IPO patients also had a larger proportion of specific organ involvement, including nephritis (56.8% vs. 33.2%), hematological involvement (58.2% vs. 47.5%), neuropsychiatric involvement (11.4% vs. 4.3%) and serositis (33.2% vs. 11.4%). SLE-IPO was associated with anti-SSA antibody (OR=2.008, $p < .001$) and anti-rRNP antibody (OR=2.776, $p < .001$). We recorded 18 deaths and 66 flares in SLE-IPO group. Elevation of serum alkaline phosphatase (ALP) or γ -glutamyl transpeptidase (GGT) was the independent risk factor for death (HR=4.163, $p = .020$). Independent risk factor for flare was anti-nucleosome antibody (HR=2.031, $p = .032$). No independent risk factor was found for IPO flare. **Conclusions** SLE-IPO often presents with higher activity and specific organ involvements. Anti-SSA and anti-rRNP antibodies were associated with SLE-IPO. Serum ALP or GGT elevation and anti-nucleosome antibody are potential predictors for death and SLE flare respectively.

ICW19-4

Risk Analysis of Pregnancy Complications in Patients with Connective Tissue Diseases: A Single-center Retrospective Study on Maternal and Fetal Outcomes

Eri Sugawara, Masaru Kato, Yuki Kudo, Wenshi Lee, Michihito Kono, Yuichiro Fujieda, Toshiyuki Bohgaki, Olga Amengual, Kenji Oku, Shinsuke Yasuda, Tatsuya Atsumi

Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University,

Sapporo, Japan

Conflict of interest: None

Objectives: We aimed to evaluate the obstetric complications and the risk factors for these events in pregnant women with connective tissue diseases (CTDs). **Methods:** A single-center retrospective study of women with CTDs at Hokkaido University Hospital between 2007 to 2016 was conducted. Clinical features including general background, autoantibodies, therapies, disease flare, pregnancy complications as well as fetal outcomes were retrospectively collected. The rate of pregnancy complications was compared with the general obstetric population in Japan (GOP) provided by Japan society of obstetrics and gynecology. **Results:** Overall 133 pregnancies in 95 women with CTDs were recorded. Underlying CTDs were systemic erythematosus (SLE) ($n=57$), primary antiphospholipid syndrome (APS) ($n=35$), rheumatoid arthritis ($n=10$) and Other CTDs ($n=31$). Anti-phospholipid antibodies (aPL) in 43 pregnancies (32%), glucocorticoid use in 62 pregnancies (62%), tacrolimus use in 20 pregnancies (15%). There were 24 disease-flare (18%), but no CTD-related death. We recorded 113 live births, 7 abortions, 7 miscarriages and 6 stillbirths. In CTDs, emergency cesarean sections and preterm deliveries appeared significantly more frequent than in GOP (30% vs 12%, $p < .001$, 21% vs 5%, $p < .001$). APS had the highest frequency of preterm deliveries (37%). Birth weight in SLE and APS were significantly lower than GOP (2417 ± 790 (g) and 2207 ± 1030 (g) vs 2853 ± 569 (g), $p < .001$). In pregnancies with SLE, anti-DNA antibody positivity was significantly correlate with the risk of fetal complications (odds ratio 3.475, CI 1.081-11.168, $p = 0.036$) and low complement level represented the risk of maternal complications (odds ratio 3.909, 1.026-14.884, $p = 0.046$). **Conclusion:** Pregnancies with CTDs were at increased risk of having both maternal complications and adverse neonatal outcomes, suggesting that their pregnancies should be closely monitored.

ICW19-5

Mortality and complication of patients with rheumatoid arthritis admitted to intensive care unit in Kyushu University Hospital

Toshifumi Fujiwara^{1,2}, Yukio Akasaki¹, Satoshi Ikemura¹, Junichi Fukushi¹, Yasuharu Nakashima¹

¹Department of Orthopaedic Surgery, Kyushu University Hospital, ²Emergency and Critical Care Center, Kyushu University Hospital

Conflict of interest: None

[Object] The patients with rheumatoid arthritis (RA) are associated with high mortality caused by comorbidity and complication, and are often required the intensive treatment. Severe infections are among the most common causes of their mortality in intensive care unit (ICU). To determine prognostic factors and mortality in patients with RA, including juvenile idiopathic arthritis (JIA), admitted to the ICU in Kyushu University Hospital, we examined the treatments of RA and JIA, comorbidities, complications, the reasons admitted to the ICU, intensive treatments, mortalities within 30 days and 1 year, retrospectively. [Methods] Between January 2010 and March 2018, 53 patients (17 males, 36 females) with RA or JIA staying at the ICU of our institution over 48 hours were included in this study. The admission to the ICU were performed total 59 of times because 5 patients were admitted over twice. The average of age and RA duration at the admission was 66.4 ± 17.7 years (5-96) and 13.5 ± 14.1 years (0-61), respectively, and the average of follow-up duration was 724.4 ± 893.3 days (3-3133). [Results] The reasons for ICU admission included cardiovascular complications (27.1%), infection (28.8%), neurological complications (3.4%), respiratory problem (11.7%), gastrointestinal problems (3.4%), endocrinological cause (3.4%), liver problems (8.5%), kidney problems (6.8%), and others (6.8%). The average of ICU length of stay was 7.0 ± 6.3 days (2-24). The mortality within 30 days was 26.4% (14/53), and 18 of 47 patients (38.3%), excluded 6 patients from 53 patients due to the change of hospital, were dead within a year. APACHEII (19.5 ± 9.4 vs 13.6 ± 5.7) scores and the length of ICU stay (10.1 ± 7.4 vs 4.7 ± 4.6) were significantly differed between the dead and alive group within 1 year. The fatal outcomes within 30 days (7 patients:50%) and 1 year (9 patients:50%) were mainly caused by infection. [Conclusions] Our study has shown the high mortality of RA patients admitted to the ICU.

ICW19-6

The risk factors and prognosis of primary Sjögren's syndrome-associated interstitial lung disease: a multi-center cohort study

Ziwei Liu, Qian Wang, Dong Xu, Mengtao Li, Xiaofeng Zeng
Peking Union Medical College Hospital

Conflict of interest: None

[Object] This study aimed to investigate the risk factors and prognosis of primary Sjögren's syndrome-associated interstitial lung disease (pSS-ILD). [Methods] Baseline clinical manifestations, lab tests, autoantibody, pulmonary function tests (PFT), chest high resolution CT (HRCT), and treatment were retrospectively collected from Peking Union Medical College Hospital and 27 CTD-ILD centers in China. Chest HRCT and PFT were performed to confirm and evaluate ILD. Patients with pSS but without ILD were enrolled as controls. The primary end point was all-cause death, and secondary end point was ILD deterioration, defined as FVC declining $\geq 10\%$ and/or DLCO declining $\geq 15\%$. [Results] This cohort enrolled 258 patients with pSS-ILD, and 88% were female. Mean age was 58.0 ± 10.6 years. In 44.2% of patients, ILD was the initial manifestation of pSS. Most common HRCT pattern was NSIP. FVC was $80.4 \pm 19.8\%$. 1243 pSS patients without ILD were enrolled as controls. Male (OR 2.494, 95%CI 1.166-5.333, $p=0.018$), age of pSS onset (OR 1.066, 95%CI 1.047-1.085, $p<0.001$), and anti-Ro52 antibody (OR 2.797, 95%CI 1.585-4.936, $p<0.001$) were identified as independent risk factors for ILD. In 230 patents with complete survival data, 18 patients died. The 1-, 3-, and 5-year cumulative survival rates were 96.6%, 86.3%, and 79.6%, respectively. Male (HR 4.810, 95%CI 1.271-18.205, $p=0.021$), age (HR 1.079, 95%CI 1.008-1.156, $p=0.033$), and DLCO $<50\%$ (HR 5.762, 95%CI 1.149-28.891, $p=0.028$) were identified as independent prognostic factors. A total of 50 patients entered the ILD deterioration analysis, and 14 deteriorated. Age of ILD onset (OR 1.072, 95%CI 1.012-1.135, $p=0.018$) was identified as predictive factor for ILD deterioration. [Conclusions] This study indicates that pSS patients with male gender, late pSS onset, and anti-Ro52 positivity are recommended to perform chest HRCT and PFT as early screening of ILD. DLCO, as a predictor of survival, should be evaluated at every follow-up visit in patients with pSS-ILD.

ICW20-1

Semaphorins and their involvement in the pathogenesis of autoimmune vasculitis

Masayuki Nishide, Atsushi Kumanogoh
Department of Respiratory Medicine and Clinical Immunology, Osaka University Graduate School of Medicine

Conflict of interest: None

[Object] Semaphorins are intimately associated with the pathogenesis of autoimmune diseases (Nishide and Kumanogoh, Nat Rev Rheumatol. 2018). Recently, we reported an inhibitory function of semaphorin 4D (SEMA4D) in neutrophil activation (Nishide et al. Ann Rheum Dis. 2017). Based on these findings, we aim to clarify how Semaphorin-mediated signaling is involved in the pathogenesis of ANCA-associated vasculitis (AAV). [Methods] In vivo study, we are developing a passive transfer model of acute AAV, using purified antibody or splenocytes taken from MPO-deficient mice immunized with recombinant mouse MPO. The model is evaluated by histological score of kidneys, laboratory findings, and flow cytometry analysis detecting neutrophil extracellular trap (NET) formation. In vitro study, cell transfectants are established by introducing a construct expressing SEMA4D. These transfectants were subjected to proteomics study, immunoprecipitation assay, and reporter cell assay. [Results] In our model, mice exhibit glomeruli vasculitis and their neutrophils show promoted NET formation. In vitro study reveals that SEMA4D is co-expressed with several molecules, including Fc gamma receptors, and be sending intracellular signals through their coupling. [Conclusions] Our data imply that SEMA4D is involved in the primitive innate immune systems such as Fc gamma receptor signals. Although the consistency of experimental settings needs to be improved, our animal models of AAV are useful in further elucidating the unknown pathological mechanisms and therapeutic potentials of semaphorins.

ICW20-2

Transcriptomic analysis can identify decreased DNA methyltransferases expression and is associated with coronary artery lesion formation in Kawasaki disease

Huang Ying-hsien^{1,2}, Kuo Ho-chang^{1,2}

¹Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital, ²Kawasaki Disease Center, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan

Conflict of interest: None

Objectives: Kawasaki disease (KD) is the most common acute coronary vasculitis disease to occur in children. Although we have uncovered global DNA hypomethylation in KD, its underlying cause remains uncertain. In this study, we performed a survey of transcript levels of DNA methyltransferases and demethylases in KD patients. **Methods:** We recruited 145 participants for this study. The chip studies consisted of 18 KD patients that were analyzed before undergoing intravenous immunoglobulin (IVIG) treatment and at least 3 weeks after IVIG treatment, as well as 36 control subjects, using Affymetrix GeneChip Human Transcriptome Array 2.0. An additional study of 91 subjects was performed in order to validate real-time quantitative PCR. **Results:** In our microarray study, the mRNA levels of DNMT1 and DNMT3A were significantly lower while TET2 was higher in acute-stage KD patients compared to the healthy controls. Through PCR validation, we observed that the expression of DNMT1 and TET2 are consistent with the Transcriptome Array 2.0 results. Furthermore, we observed significantly lower DNMT1 mRNA levels following IVIG treatment between those who developed CAL and those who did not. **Conclusion:** Our findings provide an epigenetic study of DNA methyltransferases and demethylases changes and are among the first evidence that transient DNA hypomethylation is induced during KD's acute inflammatory phase.

ICW20-3

Rheumatoid Factor Relates to Characteristic Manifestations in Patients with Eosinophilic Granulomatosis with Polyangiitis

Jun Inamo, Yuko Kaneko, Yuichiro Ota, Tsutomu Takeuchi
Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine

Conflict of interest: None

[Object] To investigate the role of rheumatoid factor (RF) in patients with eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] Consecutive patients who were newly diagnosed with EGPA from August 1998 to January 2018 in Keio University Hospital with RF titre at diagnosis available were enrolled. We divided patients according to the median level of RF titre (75 IU/mL) and compared clinical features between two groups. [Results] Fifteen patients were enrolled in the study. The mean age was 54.5 years old, and 73% were female. Among them, 7 patients were in the RF high titre group (RF ≥ 75 IU/mL) and 8 patients were in the RF low titre group (RF <75 IU/mL). While the Birmingham Vasculitis Activity Score was comparable between the two groups (22.4 vs 19.0, $p=0.451$), the count of eosinophil at diagnosis was significantly higher in RF high titre group than RF low titre group (20207/ μ l vs 5144/ μ l, $p=0.013$). All patients with positive MPO-ANCA were in the RF low titre group. Gastrointestinal and skin lesions were more frequent in the RF high titre group, and parenchymal organ lesions, such as heart and renal organ involvement, were frequent in the RF low titre group. MPO-ANCA titre was significantly correlated with RF titre in the low RF titre group ($r=0.765$, $p=0.027$). [Conclusions] EGPA patients can be classified to two subgroups according to RF titre. Those two subgroups showed different clinical and serological features, suggesting EGPA might be caused by two distinct pathogenesis.

ICW20-4

Endothelial protein C receptor and scavenger receptor class B type 1 are major autoantigens in Takayasu arteritis

Tomoyuki Mutoh, Tsuyoshi Shirai, Hiroshi Fujii, Tomonori Ishii, Hideo Harigae
Department of Hematology and Rheumatology, Tohoku University Graduate School of Medicine

Conflict of interest: None

[Object] Takayasu arteritis (TAK) predominantly affects females in Asia. Although the presence of anti-endothelial cell antibodies (AECAs) have been reported in TAK, it has been difficult to identify autoantigens. We used a serological identification system for autoantigens using a retroviral vector and flow cytometry (SARF), and tried to identify autoantigens in TAK. [Methods] AECA activity against human umbilical vein endothelial cells (HUVEC) was measured and selected as prototype AECA for SARF. Rat myeloma cells expressing HUVEC cDNA library were generated, and stained with prototype AECAs. Then, cells with strong fluorescence were sorted by flow cytometry, and cDNA inserted was analyzed. The frequency and specificity of autoantibodies, and the clinical characteristics were evaluated. [Results] SARF was performed by using nine TAK sera with AECA activities. Four clones which bound to prototype AECA were successfully established by limiting dilution methods. HUVEC cDNA inserted into each clone was analyzed and confirmed that endothelial protein C receptor (EPCR) and scavenger receptor class B type 1 (SR-BI) were novel autoantigens in TAK. Among 51 TAK patients, 15 (33.3%) or 17 (37.3%) patients showed AECA activity against EPCR or SR-BI, respectively. The overlap was observed in 2 patients (3.9%). TAK was classified into 3 subtypes based on the profile of autoantibodies. Anti-EPCR group showed high prevalence of stroke, ulcerative colitis, and type II artery lesion. Anti-SR-BI group presented higher levels of inflammatory markers, type V artery lesion, and older age at onset. Aortic regurgitation (AR) was rare in anti-SR-BI group. Double-negative group presented higher rates of surgery for AR. [Conclusions] EPCR and SR-BI were identified as major autoantigens in TAK. AECAs against EPCR or SR-BI were observed in 66.7% of patients. Autoantibodies against these membrane proteins could be used for classification and management of TAK in clinical practice.

ICW20-5

Tocilizumab Monotherapy for Large Vessel Vasculitis, Results of 104-week Treatment of a Prospective, Single-Center, Open Study

Shuntaro Saito^{1,2}, Ayumi Okuyama², Yusuke Okada², Akiko Shibata², Ryota Sakai^{2,3}, Kentaro Chino², Takahiko Kurasawa², Tsuneo Kondo², Hirofumi Takei², Koichi Amano²

¹Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, ²Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, ³Department of Microbiology and Immunology, Keio University School of Medicine

Conflict of interest: None

[Object] To evaluate the efficacy and safety of tocilizumab (TCZ) monotherapy for Large Vessel Vasculitis (LVV), including Takayasu arteritis (TAK) and Giant cell arteritis (GCA). [Methods] Eleven LVV patients (3 TAK patients and 8 GCA patients) who had been newly diagnosed at our hospital from January 2013 to May 2016 were studied. TCZ (8mg/kg) was administered intravenously every 2 weeks for the first 2 months and every 4 weeks for the next 10 months (total 15 times) without any corticosteroid (CS) or immunosuppressants (IS). Patients were followed for another 1 year after last TCZ administration without any treatment. The efficacy was assessed by clinical symptoms (fever, headache, etc.) and CRP level. Complete and partial response (CR and PR) was defined as disappearance or improvement of all clinical symptoms due to vasculitis and normalization of CRP. Poor clinical response was defined as patients who did not satisfy the criteria of CR/PR/relapse. Relapse of the disease was defined as the worsening or recurrence of clinical symptoms, increase of CRP attributable to activity of vasculitis. [Results] The mean age was 58.9 y/o, the mean disease duration was 3.4 months, mean CRP was 6.0 mg/dl at the diagnose of the LVV. Efficacy of the TCZ monotherapy in active LVV was assessed in 11 patients. Although 1 GCA patient had TCZ withdrawal due to heart failure at week 24, there were no other serious adverse events. Relapse after TCZ cessation was assessed in 10 patients who completed week 52. CR and PR rate were 73%/18% at week 24, and were maintained at week 52. Relapse occurred in 40%, although 60% completed week 104 after TCZ cessation. [Conclusions] This is the first study to show the effectiveness of TCZ monotherapy in LVV patients, which could suggest the crucial role of IL-6 in the pathogenesis of LVV. TCZ monotherapy showed high response rate

as an induction therapy, and some of the patients did not require maintenance therapy after TCZ cessation.

ICW20-6

Poor obstetric outcomes in North Indian women with Takayasu's arteritis

Latika Gupta, Durga Misra, Sakir Ahmed, Avinash Jain, Abhishek Zanwar, Amita Aggarwal, Vikas Agarwal, Able Lawrence, Ramnath Misra

Sanjay Gandhi PostGraduate Institute of Medical Sciences, Lucknow, India

Conflict of interest: None

[Body] Takayasu's arteritis (TA) affects young women in the child-bearing age group. We studied obstetric outcomes in these patients before and after disease onset. [Methods] Women aged more than 18 years with Takayasu's arteritis (ACR 1990 criteria) were included. Demographic data, clinical features, menstrual status, history of conception and maternal and fetal outcomes were recorded from hospital records and telephonic interview. Results are in median and IQR. [Results] In 64 women with TA of age 29 (24-38) years and disease duration 5 (4-10) years, 74 pregnancies had occurred before disease onset in 29 women, while 20 had a total 38 pregnancies after onset of disease. In eight, diagnosis was made during pregnancy. Age at disease onset was 22 (18-30) years. Type 5 disease was the most common (n=32, 59.3%), and equal number of patients had Ishikawa's class I and II disease (n=26, 40.6%). Median ITAS (n=44) was 13 (7-16), DeiTak 12.5 (9-16.75) and TADS 8 (6.5-10). 16 were unmarried of whom 6 did not marry due to disease. 25 patients wanted to get pregnant, of which 8 (30%) did not do so because of her disease. Obstetric outcomes were poorer in pregnancies that occurred after the onset of disease as compared with those prior to it (RR=1.5, p=0.01). Pregnancies after onset of TA carried very high risk of maternal (RR3.9, P<0.001) as well as fetal complications (RR= 2.0, p=0.001). Hypertension was the most common maternal complication (Table 1), and it occurred most often in the last trimester. The baby weight at birth was lower in births after disease (2.3 vs. 3.0, p=0.01). Wong's score greater than or equal to 4 predicted lower birth weight (p=0.04). ITAS scores exhibited moderate correlation with DeiTak (r=0.78) and TADS (r=0.58). ITAS, ITAS-A, DeiTak and TADS could not predict obstetric outcomes. [Conclusions] Women with TA suffer from poor maternal as well as fetal outcomes.

ICW21-1

Integrated bulk and single-cell RNA-sequencing identified disease relevant monocyte subset and key driver inflammatory gene module of systemic sclerosis

Satomi Kobayashi¹, Yasuo Nagafuchi¹, Hirofumi Shoda¹, Mai Okubo¹, Yusuke Sugimori¹, Mineto Ota^{1,2}, Yusuke Takeshima^{1,2}, Yukiko Iwasaki¹, Shuji Sumitomo¹, Tomohisa Okamura^{1,2}, Kazuhiko Yamamoto^{1,3}, Keishi Fujio¹

¹Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, ²Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, ³Center for Integrative Medical Sciences, RIKEN

Conflict of interest: Yes

[Object] This study aimed to elucidate the characteristic transcriptome patterns of peripheral blood immune cells in systemic sclerosis (SSc) and to identify responsible single cells and driver genes of SSc. [Methods] We sorted peripheral blood immune cells from SSc patients and healthy controls (HCs) into 20 cell subsets using flow cytometer, and performed RNA-sequencing (RNA-seq). We performed differentially expressed genes (DEGs) analysis and weighted correlation network analysis (WGCNA) using RNA-seq data of all subsets and found modules of strongly correlated genes. Knowledge-based pathway analysis was performed with Ingenuity Pathway Analysis (IPA). Single-cell RNA-seq of 878 monocytes from SSc patients were performed with ICELL8 system. We defined each cluster signature scores, using marker genes of each single-cell cluster. Bayesian network analysis, not relying on any biological knowledge, was performed to validate key driver genes in SSc. [Results] All subsets showed enhanced inflammatory cytokine signaling. WGCNA

showed that monocyte inflammatory gene module, including *JUNB*, *NFKB1A*, and *CXCL8*, was one of the most characteristic modules in SSc. Single-cell RNA-seq of monocytes from SSc patients revealed that monocytes were divided into 7 clusters. The monocytes in one “inflammatory cluster” characteristically expressed inflammatory module genes. This inflammatory single-cell signature was elevated in bulk monocytes in SSc. Bayesian network analysis validated inflammatory gene module as key upstream driver genes in SSc and identified candidate marker genes. [Conclusions] Monocytes play a crucial role in the pathogenesis of SSc for producing inflammatory cytokines. Disease-relevant monocytes, characterized by high expression of inflammatory module genes might be a novel therapeutic target in SSc.

ICW21-2

Efficacy and safety of botulinum toxin B injection for Raynaud's phenomenon and digital ulcers in patients with systemic sclerosis: single-blind, randomized trial

Sei-ichiro Motegi, Osamu Ishikawa

Department of Dermatology, Gunma University Graduate School of Medicine

Conflict of interest: None

[Object] Patients with systemic scleroderma (SSc) typically develop Raynaud's phenomenon (RP) and persistent digital ischemia and often develop digital ulcers (DUs). Currently, there is no satisfactory treatment for RP and DUs in SSc. We previously reported that botulinum toxin A (BTX-A) injection was effective for the treatment of RP and DUs in SSc patients. However, the efficacy of BTX-B injection has never been examined. The objective was to assess the efficacy and safety of BTX-B for treatment of RP and DUs in SSc patients. [Methods] In the prospective, single-blind, randomized trial, total 45 SSc patients with RP were blinded and randomly divided into 4 groups; no treatment control group, and 3 treatment groups, using 250, 1,000 or 2,000 U of BTX-B injections in the hand with more severe symptoms (UMIN00019985). [Results] Four weeks after injection, the pain/numbness VAS and Raynaud's score (indicating the severity of RP in SSc patients) in the 1,000- and 2,000-U-treated groups were significantly lower than in the control group and 250-U-treated group. These beneficial effects were sustained until 16 weeks after the single injection. At 4 weeks after injection, skin temperature recovery in the 2000-U-treated group was significantly improved. The numbers of DUs in the 1,000- and 2,000-U-treated groups were significantly lower than in the control group. Furthermore, no new DUs developed in the groups treated with 1,000 and 2,000 U for 16 weeks after injection. No systemic or local adverse events were observed in any patients. [Conclusion] We conclude that 1,000 and 2,000 U BTX-B injection significantly suppressed the activity of RP and DUs in SSc patients without any serious adverse events, suggesting that BTX-B might have potential as a long-term preventive and therapeutic agent for RP and DUs in SSc patients. Based on this clinical research result, we are currently doing investigator-initiated clinical trial (A double-blind, randomized, placebo-controlled trial).

ICW21-3

Endothelial ephrin B2 signaling drives protection against pulmonary fibrosis

Brian Wu^{1,2}, Sayaka Nakamura^{1,2}, David Lagares³, Evgeny Rossomacha², Akihiro Nakamura^{1,2}, Poulami Datta², Asrafuzzaman Riyah⁴, Philippe P Monnier⁴, Jianping Wu⁵, Boris Hinz⁶, Mohit Kapoor⁷

¹Departments of Surgery and of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada, ²Division of Genetics and Development, Krembil Research Institute, University Health Network, Toronto, Ontario, Canada, ³Division of Pulmonary and Critical Care Medicine, Fibrosis Research Center and Center for Immunology and Inflammatory Diseases, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA, ⁴Vision Division, Krembil Research Institute, Toronto, Canada, ⁵Department of Medicine, University of Montreal Hospital Research Centre (CRCHUM), Montreal, Québec, Canada, ⁶Laboratory of Tissue Repair and Regeneration, Matrix Dynamics Group, Faculty of Dentistry, University of Toronto, Toronto, Canada

Conflict of interest: None

[Object] Ephrin B2 is a signaling ligand prominently expressed in endothelial cells and has been implicated in driving vasculogenesis and the wound healing response. We have previously shown that ephrin B2 expression in fibroblasts promote myofibroblast activation and migration, which strongly influences the development of fibrosis. Indeed, knock-out of ephrin B2 in fibroblasts was shown to provide partial protection against induced pulmonary fibrosis. We seek to understand the role of endothelial-expressed ephrin B2 in pulmonary fibrosis. [Methods] We have generated endothelial-specific knockouts for ephrin B2 using T₂ promoter for the Cre recombinase system. Genetic knockout is induced through tamoxifen treatment (1 mg/day in 100 μ L corn oil for 5 days) and bleomycin (1.2 U/kg in 50 μ L PBS) is intratracheally instilled to promote the development of pulmonary fibrosis. Mice are sacrificed at 14-days post bleomycin and fibrosis is assessed through histological staining (Masson's Trichrome). [Results] Our conditional ephrin B2 knockout mice were confirmed through biochemical assessment and genotyping. Our endothelial knockout of ephrin B2 provides notable protection against the development of bleomycin-induced pulmonary fibrosis in mice compared to corn oil/PBS treated controls. ImageJ quantification of Masson's Trichrome staining indicated substantial protection against the development of pulmonary fibrosis. [Conclusions] Ephrin B2 in endothelial cell may drive pro-fibrotic processes and the cell-specific knockout appears to drive protection against the development or progression of fibrosis in mouse lungs. Our ongoing studies are assessing whether ephrin B2 is mediated through its receptor ephB4 in fibroblasts and endothelial cells. We anticipate pro-fibrotic character of ephrin B2 may be mediated through eB4 receptor.

ICW21-4

Aryl hydrocarbon receptor signals attenuate lung fibrosis in bleomycin induced mice model for pulmonary fibrosis through increase of regulatory T cells in the lung

Hiroshi Takei^{1,2}, Hidekata Yasuoka^{1,3}, Keiko Yoshimoto^{1,4}, Tsutomu Takeuchi¹

¹Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, ²Center for Arthritis and Rheumatic Diseases, Kawasaki Municipal Kawasaki Hospital, Kawasaki, Japan, ³Division of Rheumatology, Department of Internal Medicine, Fujita Health University School of Medicine, Nagoya, Japan, ⁴Clinical and Translational Research Center, Keio University Hospital, Tokyo, Japan

Conflict of interest: None

[Object] Systemic sclerosis (SSc) is characterized by autoimmunity and systemic fibrosis. Recent reports suggest that aryl hydrocarbon receptor (AhR) signals by various ligands such as tryptophan derivatives can induce immunoreponse including autoimmunity. The aim of this study is to investigate the effect of immunological changes induced by AhR signals can affect the process of fibrosis using the animal model. [Methods] Bleomycin (BLM) was intratracheally administered to C57BL/6 mice at a dose of 0.06 units/body. Either 1 μ g of 5,11-Dihydroindolo [3,2-b] carbazole-6-carboxaldehyde (FICZ), a natural AhR ligand, or vehicle was i.p. injected on day 0, 1 and 2. Mice were sacrificed at week 1 to analyze the infiltrating lung cells using flow cytometry. Pulmonary fibrosis was evaluated at week 3 by histopathology score (Ashcroft score) and the deposition of collagen detected by colorimetric assay. [Results] Flow cytometry analyses revealed more CD4⁺Foxp3⁺ Treg infiltration in the lung of FICZ group at week 1 ($4.1 \times 10^4 \pm 1.0$ vs $2.5 \times 10^4 \pm 0.6$, $p < 0.05$) while IFN γ +CD4⁺ T cells and IL-17A+ γ δ + T cells were reduced ($4.8 \times 10^3 \pm 1.4$ vs $10.3 \times 10^3 \pm 1.9$ and $1.2 \times 10^3 \pm 0.6$ vs $2.7 \times 10^3 \pm 0.5$ respectively, $p < 0.05$). Other subsets such as B cells, NK cells, neutrophils, IL-17A+CD4⁺ T cells and IL-22+CD4⁺ T cells were comparable between two groups. Semi-quantification of lung fibrosis at week 3 evaluated by the Ashcroft score was revealed to be lower in FICZ group compared to vehicle group (2.7 ± 0.8 vs 4.6 ± 0.6 , $p < 0.01$), which was further confirmed by lower lung soluble collagen at week 3 in FICZ group (2042 ± 277 μ g vs 4423 ± 1296 μ g, $p < 0.01$). Furthermore, improvement of lung fibrosis led to better survival during 21 days in FICZ group ($p < 0.05$). [Conclusions] Stimulation of AhR signals attenuated pulmonary fibrosis induced by BLM. Immunological changes induced by AhR stimulations may contribute to ameliorate succeeding fibrotic processes *in vivo*.

ICW21-5

Estimation by nailfold videocapillaroscopy (NVC) is valuable to predict interstitial pneumonitis in patients with SSc

Yurie Sato¹, Satoshi Kubo¹, Kazuhisa Nakano¹, Shingo Nakayamada¹, Yasuyuki Todoroki¹, Shigeru Iwata¹, Kentaro Hanami¹, Shunsuke Fukuyo¹, Akio Kawabe¹, Yusuke Miyazaki¹, Minoru Satoh², Yoshiya Tanaka¹

¹1st Department of Internal Medicine, University of Occupational and Environmental Health, Japan, ²Department of Clinical Nursing, School of Health Sciences, University of Occupational and Environmental Health, Japan

Conflict of interest: None

[Object] Detection of microvascular abnormalities by NVC enables early diagnosis of SSc. However, how these microvascular abnormalities contribute to fibrogenesis is not well known. We investigated the relationship between nailfold capillary changes and interstitial lung disease (ILD) which represents tissue fibrosis in SSc. [Methods] 247 SSc patients were enrolled. Nailfold capillary was evaluated and classified into 4 types of NVC pattern by using NVC (N: Normal, E: Early, A: Active, L: Late). We evaluated ILD quantitatively with using CT scoring method. [Results] The mean age was 64.8 years and the mean disease duration was 7.6 years. The prevalence of ILD was 32.8% and NVC abnormalities was 66.8%. As NVC pattern progress, complication of ILD was increased (Incidence rates of ILD: N 29.1%, E 27.6%, A 33.3%, L 51.4%). There were around 30% of patients who had ILD without NVC abnormalities. Regarding the changes of NVC abnormalities, 62.1% of patients remained unchanged and 22.4% worsened at 1 year. As for ILD, 34.0% improved, 34.0% unchanged and 32.0% worsened in 47 patients who could follow up with CT after 1 year. The changes of ILD were correlated with baseline NVC pattern, 7 patients (58%) who had Active pattern at baseline showed improvement of ILD. Moreover, 43.8% of those cases showed improvement of NVC abnormalities. While, improvement of ILD was only found in 10% of Late pattern. In contrast, improvement of ILD remained in 33.3% of Normal pattern. Consistently, progression of nailfold abnormality was not observed in Normal pattern even ILD worsened. [Conclusions] Most of the cases with advanced capillary abnormality had a higher incidence and the degree of capillary abnormality correlated with treatment response to ILDs. However, ILD and NVC abnormality progressed independently in some cases. These results suggest that the association between fibrosis and microvascular abnormalities is not uniform and NVC may be beneficial to detect such heterogeneity of SSc.

ICW21-6

Incidence And Prognostic Factors For Exacerbation In Patients With Interstitial Pneumonia With Autoimmune Features

Okinori Murata

Division of Pulmonary Medicine, Allergy, and Rheumatology, Department of Internal Medicine, Iwate Medical University School of Medicine

Conflict of interest: None

[Object] Patients with idiopathic interstitial pneumonia (IIP) may have features of connective tissue diseases (CTDs). The term interstitial pneumonia with autoimmune features (IPAF) has been recently proposed for such patients. A few studies have been reported in prevalence of IPAF which was varied from 7.3% to 34.1%. Factors reported to indicate a poor prognosis in IPAF include age, smoking history, decline in %DLCO and presence of a multi-compartment feature within the morphological domain. To date, however, no study has comprehensively described prevalence of IPAF and factors of exacerbation. The aim of study was to identify of prevalence of IPAF in patients with interstitial lung disease (ILD), prognostic factors for exacerbation. [Methods] Of 672 patients who had visited our department between April 2009 and March 2018, 68 patients who diagnosed as IPAF were enrolled. They were divided into two groups, which presented exacerbation and non-exacerbation. Clinical, laboratory and imaging data were collected from medical records and statistically analyzed. [Results] Prevalence of IPAF was 10.1%. Of 68 patients with IPAF, 53% were women and mean age at diagnosis was 64.2 ± 13.8 years old. Mean observation period was 28.8 ± 30.4 months. Exacerbation rate was 25% (n=17). Overall death rate was 5.9% (n=4) and respiratory death rate was 2.9% (n=2). Comparison of characteristics at di-

agnosis between the exacerbation group and non-exacerbation group showed that the exacerbation group had a significantly elevated rate of smoking, KL-6, and SP-D (P=0.012, 0.0064, and 0.029, respectively). [Conclusions] Our large-scale cross-sectional cohort study revealed prevalence of IPAF in patients with ILD and identified three baseline factors associated with exacerbation in the patients with IPAF.

ICW22-1

Functional recovery of Hip Fracture Patients with Rheumatoid Arthritis: Retrospective Analysis using a National Database in Japan

Hiroyuki Okada, Takumi Matsumoto, Yasunori Omata, Jun Hirose, Sakae Tanaka

Department of Orthopaedic Surgery, The University of Tokyo

Conflict of interest: None

[Object] The object of this study was to clarify the prognosis of hip fracture with Rheumatoid Arthritis (RA) with a national database separately divided into femoral neck and trochanteric fractures. [Methods] A total of 71,687 femoral neck fracture patients and 70,196 femoral trochanteric patients without psychotic disorder including dementia were enrolled. They were admitted with ambulance between April 2010 and March 2015. They were dichotomized into two groups: with RA or without RA (non-RA). Baseline demographic information included age, sex, smoking, obesity, and comorbidities. The primary outcome was mortality during hospitalization. The secondary outcome was in-hospital change of Barthel index. Univariable analysis compared outcomes between RA or non-RA group using two-tailed unpaired t-test for continuous variable and chi-square test for discontinuous variable. Multivariable analysis extracted risk factors of mortality and improving factors of Barthel index. [Results] The numbers of RA patients were 1,444 in femoral neck and 1,086 in femoral trochanteric fracture. More femoral neck fracture occurred in RA patients [2.01% vs 1.55%; chi-square test p < 0.001]. Patients in RA group were younger [neck 76.0 years vs 79.1 years; p < 0.001; trochanteric 79.5 years vs 83.1 years; p < 0.001]. In univariable analysis, mortality rate was lower in RA group [neck 2.08% vs 3.26%; p = 0.012; trochanteric 1.84% vs 2.86%; p = 0.045]. Multivariable analysis showed no significant difference in mortality. Barthel index in RA group was better both at admission and at discharge, besides, the improvement was also better. Multivariable linear regression analysis revealed that RA was ADL improving factor in neck fracture [Coefficient 2.29 [95% CI 0.30 to 4.28]]. [Conclusions] The Mortality of hip fracture in RA group was not inferior to non-RA patients. Besides, ADL recovery of neck fracture was better in RA groups. One of the reasons might be loss of ADL with injury was limited in RA group.

ICW22-2

The clinical outcome of MSK unconstrained total elbow arthroplasty in patients with rheumatoid arthritis

Naoki Kondo¹, Katsumitsu Arai², Junichi Fujisawa¹, Naoto Endo¹, Tadamasu Hanyu³

¹Division of Orthopedic Surgery, Department of Regenerative and Transplant Medicine, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan, ²Division of Orthopaedic Surgery, Niigata Prefectural Chuo Hospital, Joetsu, Japan, ³Division of Rheumatology, Nagaoka Red Cross Hospital, Nagaoka, Japan

Conflict of interest: None

[Object] Total elbow arthroplasty (TEA) is a treatment option for destructive and painful unstable elbows in patients with rheumatoid arthritis (RA). We evaluated the clinical outcome of unconstrained total elbow arthroplasty (MNSK system). [Methods] 75 unconstrained TEAs were performed in patients with RA (mean age, 64 years; range, 41-79 years). Total follow up rate was 97 %. Outcome measures included the Japanese Orthopaedic Association functional evaluation score for the elbow joint (JOA score), range of motion, and arc. Bone ingrowth of the humeral component, the incidence of stress shielding around the humeral stem, and incidence of loosening of the ulnar component, complications, and survival rate were investigated. [Results] Mean follow-up was 5.2 (range, 2-11.3) years. The JOA elbow score improved from 42 points preoperatively to 87 points postoperatively (p<0.0001). Each subitem improved

($p < 0.0001$). Flexion improved from 109° to 134° ; the flexion plus extension arc improved from 70° to 108° ($p < 0.0001$). Bone ingrowth of the humeral implant were achieved in all elbows. Stress shielding of the humeral component was detected in 11 elbows (14%); it was significantly higher in 10-mm-diameter and 9-mm-diameter humeral stems than in 8-mm-diameter ones ($p = 0.008$). The ulnar component showed no loosening, except 1 elbow due to infection. Complications were detected in 9 patients (9 elbows, 12 %): periprosthetic infection (3), fracture (4), and dislocation (2). Survival rates were 97% at 5 years and 93% at 10 years postoperatively. [Conclusions] The unconstrained MNSK system for patients with RA showed good outcome in the JOA score and range of motion with a good survival rate. Stress shielding can be avoided by using an 8-mm-diameter humeral stem.

ICW22-3

Proof-of-concept data showing differential effects of ex vivo polarized monocytes/macrophages in a novel human osteoarthritis explant model

Mable Wing Yan Chan^{1,2}, Alejandro Gomez-aristizabal¹, Rajiv Gandhi¹, Wayne Marshall¹, Nizar Mahomed¹, Sowmya Viswanathan^{1,2,3,4}

¹Arthritis Program, University Health Network, Toronto, Canada, ²Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, Canada, ³Cell Therapy Program, University Health Network, Toronto, Canada, ⁴Division of Hematology, Department of Medicine, University of Toronto, Toronto, Canada

Conflict of interest: None

[Object] Monocytes/macrophages (MΦs, as a heterogenous population) are innate immune cells that mediate inflammation and homeostatic tissue repair. We have identified pro-inflammatory MΦs as the major immune infiltrators of osteoarthritic (OA) joints. We aim to understand the role of pro-inflammatory (M1) versus homeostatic (M2) MΦs within OA and propose that modulation of the MΦ populations via *ex vivo* polarized MΦ-based cell therapy will serve as a multimodal treatment that reduces both inflammation and matrix degradation. [Methods] We developed a human explant model using OA cartilage and synovium from total knee replacements that can measure changes in gene expression (qRT-PCR) and extracellular matrix (ECM) catabolism (Safranin-O cartilage histology, cytokine and protease inhibitor levels in medium by immunoassay). CD14⁺ MΦs were isolated from peripheral blood and *ex vivo* polarized into pro-inflammatory (M1, IFN- γ +LPS) and homeostatic (M2, IL-10+TGF- β) MΦs by previously optimized 48 h cytokine protocols. *Ex vivo* polarized MΦs were then co-cultured with explants and samples were harvested at 2- and 7-day. [Results]: Principal component analysis of our OA cartilage gene panel demonstrates differential effects of pro-inflammatory M1 MΦs versus homeostatic M2 MΦs (N=6). Addition of M1 MΦs upregulates catabolic ECM and pro-inflammatory genes and downregulates anabolic genes in OA cartilage. M2 MΦ treatment upregulates anabolic ECM gene expression. Changes in protein levels of soluble TIMP1 mirror gene expression, with 1.5-fold increase in the M2 group and 1.4-fold decrease in the M1 group (N=3). Synovium gene expression was variable (N=4), although addition of M1 MΦs trends upregulation of pro-inflammatory and chemotactic genes. [Conclusions] Polarized MΦs play a significant role in the modulation of the OA inflammatory and degradative microenvironment. Our findings provide proof-of-concept towards using MΦ-based therapy as a novel method for treating OA.

ICW22-4

Knee osteoarthritis and menopausal hormone therapy in postmenopausal women: a nationwide study

Jae Hyun Jung^{1,2}, Gwan Gyu Song^{1,2}, Sung Jae Choi^{1,3}, Bang Cho Hee⁴

¹Korea University College of Medicine, Seoul, Korea, ²Division of Rheumatology, Department of Internal Medicine, Korea University Guro Hospital, Seoul, Korea, ³Division of Rheumatology, Department of Internal Medicine, Korea University Ansan Hospital, Ansan, Gyeonggi, Korea, ⁴Korea University College of Nursing, Seoul, Korea

Conflict of interest: None

[Object] The incidence of osteoarthritis (OA) increases after menopause, and this is related to hormonal changes in women. Estrogen defi-

ciency is known to affect the development of OA, and menopausal hormone therapy (MHT) is suggested to be related to the development of OA. However, the relationship between knee OA and MHT remains controversial. The association between knee OA prevalence and MHT was investigated using large-scale national data. [Methods] Data were collected from 4766 postmenopausal women from the Korea National Health and Nutrition Examination Survey (2009-2012). We included. MHT was defined as regular hormone medication for ≥ 1 year, and demographic and lifestyle variables were compared between the MHT and non-MHT groups. Knee OA was defined according to symptoms and radiographic findings. [Results] In the multiple logistic regression models (adjustment for MHT duration, age, BMI, menarche and menopause age, HTN, DM, alcohol consumption, smoking status, and socioeconomic status), the OA odds ratio was 0.70 for the MHT group (95% confidence interval, 0.50-0.99), compared to the non-MHT group. [Conclusions] The prevalence of knee OA was lower in participants with MHT than in those without MHT.

ICW22-5

Attenuation of Surgically-induced Osteoarthritis (OA) by Inhibition of Autotaxin

Poulami Datta¹, Sayaka Nakamura¹, Evgeny Rossomacha¹, Helal Endisha¹, Carolen Younan¹, Kaushik H Borada¹, Kim Perry¹, Nizar N Mahomed^{1,2,4}, Rajiv Gandhi^{1,2,4}, Jason S Rockel¹, Mohit Kapoor^{1,2,3}

¹Krembil Research Institute, UHN, ²Toronto Western Hospital, ³LMP Department, University of Toronto, ⁴Department of Surgery, University of Toronto

Conflict of interest: None

Objective: Osteoarthritis (OA) is a chronic, progressive joint disease leading to a poor quality of life. Previously, we reported that select Lyso-phosphatidylcholines (lysoPCs) are increased in animal models of OA. We also identified that these particular metabolites may promote OA pathogenesis in an autotaxin (ATX) - dependent manner. ATX is an enzyme responsible for the conversion of lysoPC to the inflammatory mediator lysophosphatidic acid (LPA). Previous studies have also shown that ATX levels in plasma and synovial fluid correlate with the severity of knee osteoarthritis. Thus, we sought to identify if local pharmacological inhibition of ATX can attenuate surgically-induced OA in vivo and its mechanism of action in vitro. **Methods:** 9 week-old mice were subjected to surgically-induced OA. ATX antagonist (PF -8380, Pfizer) was injected intra-articularly in the knee joints at 2nd, 4th, 6th and 8th week of post surgery and subsequent knee joint pathology was evaluated. Primary human chondrocytes were treated with IL-1 β /ATX antagonist, and the expression of catabolic markers was determined. **Results:** Local injection of ATX antagonist reduced the degree of cartilage degeneration in surgically induced OA models compared to saline injected controls. ATX antagonist also reduced the amount of synovitis as compared to controls. Immunohistochemical analysis of mouse knee joints showed decreased expression of catabolic markers (C1-2C and MMP 13) in ATX treated mice compared to control mice. In vitro, ATX antagonist attenuated IL-1 β -induced increases in the expression of MMP13. **Conclusion:** Inhibition of ATX attenuates surgically-induced OA. We are currently investigating the mechanism of action of ATX in attenuating OA. Our data, to date, suggests pre-clinical efficacy of ATX to limit OA progression.

ICW22-6

Analysis of walking functions in patients with rheumatoid arthritis using a wearable device

Masahiro Tada¹, Yutaro Yamada^{2,3}, Koji Mandai^{2,4}, Noriaki Hidaka^{1,2}

¹Department of Orthopaedic Surgery, Osaka City General Hospital, ²Department of Orthopaedic Surgery, Osaka City University Graduate School of Medicine, ³Department of Orthopaedic Surgery, Yodogawa Christian Hospital, ⁴Department of Orthopaedic Surgery, Osaka Social Medical Center Hospital

Conflict of interest: None

[Object] It is unknown how walking is related to disease activity and body composition. The factors related to walking and their relationships with locomotive syndrome were investigated in RA patients using a

wearable device. [Methods] The data from a prospective observational study (CHIKARA study, UMIN000023744) were used. A total of 85 of the 100 RA patients entered and wore an activity meter (HJA-750C; OMRON) for 7 consecutive days. The average daily number of steps, walking exercise (EX) (Mets x Time), and calorie consumption were calculated. The relationships of disease activity, body composition, muscle function, sarcopenia, locomotive syndrome, and frailty were analyzed by uni- and multi-variate analyses. The correlation between the number of steps and locomotive syndrome was examined by receiver operating characteristic (ROC) curve analysis. [Results] The patients' mean age was 65.2 years (women n=67, men n=18), disease duration was 7.7 years, DAS28ESR was 3.12, and the HAQ score was 0.6. Number of steps and walking EX were negatively correlated with MMP3, DAS28ESR, HAQ, locomotive syndrome, and frailty, and positively correlated with leg muscle score, muscle power, muscle speed, grip strength, and walking speed on univariate analysis. In addition, calorie consumption was positively correlated with muscle mass and bone mass. Locomotive syndrome and muscle power were identified as independently associated with the number of steps and walking EX on multivariate analysis. With respect to calorie consumption, only muscle power was identified as an independent factor. When the number of steps was under 3333 on ROC curve analysis, the odds ratio of locomotive syndrome increased 14.4-fold (95%CI: 5.0-41.6) compared with over 3333 ($p < 0.001$). [Conclusions] Locomotive syndrome and muscle power were independently related to the number of steps and walking EX. To prevent locomotive syndrome in RA patients, it was recommended that they exceed 3333 steps per day.

Poster Session

P1-001

A study of information collection concerning rheumatoid arthritis in patients with rheumatoid arthritis -based on the IORRA cohort

Rei Yamaguchi¹, Eiichi Tanaka¹, Eisuke Inoue^{1,2}, Mai Abe¹, Mika Kawano¹, Eri Sugano¹, Naohiro Sugitani^{1,3}, Kumiko Saka¹, Yoko Higuchi¹, Moeko Ochiai¹, Naoki Sugimoto¹, Katsunori Ikari¹, Ayako Nakajima³, Atsuo Taniguchi¹, Hisashi Yamanaka¹

¹Institute of Rheumatology, Tokyo Women's Medical University Hospital, Tokyo, Japan, ²Division of Medical Informatics, St. Marianna University School of Medicine, Kanagawa, Japan, ³Department of Rheumatology, Mie University Graduate School of Medicine, Mie, Japan

Conflict of interest: None

[Object] To examine how rheumatoid arthritis (RA) patients are collecting information and their usefulness. [Methods] The subjects were RA patients who participated in the IORRA in 2017. Based on patient self-reported, the difference in the background of information on RA and the usefulness of information using VAS scale were cross-sectionally evaluated. [Results] A total of 8,026 answers were obtained from 3,470 RA patients (multiple choices allowed). The patient background was 86.8% for women, average age 62.3 years, DAS28 2.55, J-HAQ 0.58, and biologics user 27.2%. The most frequent information sources were medical institutions (doctors, nurses, pharmacists, etc.) (28.9%), television (15.5%), pamphlets distributed at hospital and pharmacy (8.80%), the Internet (8.77%), and newspapers (6.90%). Internet was the most frequent (46.4%) under the age of 40. The average VAS of usefulness was the highest in medical institutions (74.1), followed by television (62.0), pamphlets (59.8), books on RA (53.5), newspapers (49.7), and the Internet (48.2). [Conclusions] RA patients obtained information widely from medical institution and mass media. Especially the reliability of information from medical institutions was high. The information sources were different by patient's age group.

P1-002

Evaluation of factors associated with sarcopenia in patients with rheumatoid arthritis

Takeshi Mochizuki¹, Koichiro Yano², Ryo Hiroshima¹, Katsunori Ikari², Ken Okazaki²

¹Department of Orthopaedic Surgery, Kamagaya General Hospital, ²Department of Orthopaedic Surgery, Tokyo Women's Medical University

Conflict of interest: Yes

[Objective] Rheumatoid arthritis (RA) is a chronic, systemic, and inflammatory disease. This study aimed to identify the prevalence of sarcopenia and factors associated with sarcopenia in RA. [Methods] Overall, 127 patients aged over 65 years with RA were enrolled in the study. Muscle mass was assessed using bioelectrical impedance analysis. Sarcopenia was defined as low muscle mass and low muscle strength in accord with the consensus report of the Asian Working Group for Sarcopenia. Statistical analysis was performed to examine relationship between patient characteristics [age, gender, disease duration, body mass index, disease activity, calf circumference, grip strength, gait speed, HAQ-DI, Mini nutritional assessment (MNA) score, serum albumin, skeletal muscle mass index (SMMI), and bone mass] and sarcopenia. [Results] The prevalence of sarcopenia was 24.4%. The significant related factors by multivariate logistic regression analysis were grip strength ($p=0.003$), MNA score ($p=0.024$), and SMMI ($p=0.004$). [Conclusion] Grip strength, MNA score, and SMMI were associated with sarcopenia. Interventions are required for elderly patients with RA identified as having related factors of sarcopenia to prevent its adverse health consequences.

P1-003

A survey on trends of five years of patients with the elderly patients (aged 75 years or more) with rheumatoid arthritis

Moto Kobayashi¹, Takeshi Kashiwagura², Natsuo Konishi³, Masakazu Urayama⁴, Hiroki Ito⁵, Tsutomu Sakuraba¹, Toshiaki Aizawa⁶, Hidekazu Abe⁷, Norio Suzuki⁸, Keiji Kamo⁹, Hiroshi Aonuma⁴, Yusuke Sugimura¹⁰, Tetsuya Kawano⁶, Masaaki Ogino¹¹, Yoichi Kataoka¹², Hiromi Morita¹³,

Kunitaka Yang¹⁴, Wataru Watanabe¹⁵, Nobuhiro Ishizawa¹⁶, Kazuhiro Shoji¹⁷, Hidetoshi Watanabe¹⁸, Yosuke Iwamoto¹⁹, Naohisa Miyakoshi¹⁹, Yoichi Shimada¹⁹

¹Department of Orthopedic Surgery, Hiraka General Hospital, ²Department of Orthopedic Surgery, Akita City Hospital, ³Department of Orthopedic Surgery, Akita Kousei Medical Center, ⁴Department of Orthopedic Surgery, Ogachi Central Hospital, ⁵Department of Orthopedic Surgery, Noshiro Kousei Medical Center, ⁶Department of Orthopedic Surgery, Kita Akita Municipal Hospital, ⁷Department of Orthopedic Surgery, Ugo Municipal Hospital, ⁸Department of Orthopedic Surgery, Yuri Kumiai General Hospital, ⁹Department of Orthopedic Surgery, Akita Rosai Hospital, ¹⁰Department of Orthopedic Surgery, Nakadori General Hospital, ¹¹Department of Orthopedic Surgery, Koto Kousei Hospital, ¹²Joto Orthopedic Clinic, ¹³Morita Orthopedic Clinic, ¹⁴Yang Orthopedic Clinic, ¹⁵Department of Orthopedic Surgery, Honjo Daiichi Hospital, ¹⁶Department of Orthopedic Surgery, Fujiwara Memorial Hospital, ¹⁷Shoji Orthopedic Clinic, ¹⁸Watanabe Orthopedic Clinic, ¹⁹Department of Orthopedic Surgery, Akita University Graduate School of Medicine

Conflict of interest: None

[Objective] We are active in raising treatment of rheumatoid arthritis (RA) patients and eliminating regional disparity at the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) established in 2010. We extracted the data from AORA registry, examined the trend of RA patients in the last 5 years [METHODS] From the AORA registry from 2013 to 2017, rheumatism patients over 75 years old were investigated. [RESULTS] The proportion of patients aged 75 years or older in the entire AORA registry showed a tendency to increase over the years from 26.3% to 31.0%. The usage rate of MTX was 33.9% to 40.8%, and the average usage amount was 5.1 to 5.6 mg / week, and it showed a somewhat increasing trend over time on a year-to-year basis. The usage rate of steroids was 49.2% to 56.5%, varying from year to year, the average usage amount was around 3.8 mg / day and did not change very much. Regarding bDMARDs, the frequency was 10.1 to 17.7%, which showed an increasing tendency over time. The disease activity indicators had a declining trend over the years since 2013. The HAQ-DI showed no remarkable change. [CONCLUSION] Since the disease activity of older patients with RA after AORA was founded was on a downward trend, the results of the treatment improvement listed as the goal were observed.

P1-004

Big regional differences in drug-use and expenditure in the treatment of rheumatoid arthritis extrapolated from the National Database open data released in 2016-18

Yasuyuki Kamata, Seiji Minota

Rheumatology and Clinical Immunology, Jichi Medical University

Conflict of interest: None

[Object] To clarify whether there are prefecture-to-prefecture differences in drug-use and expenditure in the treatment of RA in Japan by analyzing the National Database open data released between 2016 and 2018 by the Ministry of Health, Labor and Welfare (MHLW). [Methods] Data on MTX and seven biologics that have indication for the treatment of RA were analyzed in this study. There is an assumption that the morbidity of RA is equal throughout Japan at 0.6% of general population. The dosage and cost of drugs for an RA patient were calculated by dividing the total amount of thereof in each prefecture released by MHLW by the estimated number of RA patients. [Results] The maximum regional differences in the prescribed dosage of MTX (mg) and the cost of biologics were 2.7-fold (highest in 445 mg and lowest in 165 mg) and 2.4-fold (highest in 366,000 yen and lowest in 154,000 yen), respectively. In five prefectures, the cost of biologics per RA patient was markedly higher than the national average whereas MTX dose was smaller than that. [Conclusions] There are big prefectural differences in the usage of MTX and biologics in Japan. In order to implement a universal practice of good RA treatment, these data need to be addressed and scrutinized.

P1-005

Survey for AI medical in the Remote medical care for patients with RA or OA

Ryuji Nagamine¹, Weijia Chen¹, Toru Suguro²

¹Center of Artificial Joint and Rheumatism, Fukuoka Tokushukai Medical Center, ²Research Institute of Rheumatology Medical Treatment

Conflict of interest: None

[Object] There are few specialists for RA or OA in remote places and islands. We have a plan of AI medical for the remote medical care in such places. In this study, survey of the patients was performed to clarify the necessity of AI medical. [Methods] The author works in Fukuoka. In one hospital in Ishigaki island, a survey was performed. We provided a questionnaire to 107 patients and got a reply from 71 patients (average age 66.8 years old, 18 cases with RA, 45 cases with OA, etc). Nine patients with RA are taking bDMARD. The contents of the questionnaire were “do they have smartphone?”, “do they need AI?” etc. Number of patients who visited the hospital in Fukuoka to have operation was also assessed. [Results] 23 patients (33%) have smartphones. 58 patients (82%) trust AI medical and 56 patients (79%) will pay for the AI medical. 44 operations including total knee arthroplasty were performed in the past 3 years. The result of the questionnaire revealed the lack of specialists and necessity of AI medical in Ishigaki island. AI medical is useful and convenient for the patients to get information about bDMARD and the follow up of the operations. Japan has so many islands and remote places. [Conclusions] In Ishigaki island, many patients think that AI medical is necessary.

P1-006

Ideal medical collaboration considering patients' movement in rheumatoid arthritis

Hidetoshi Kagawa¹, Ryutaro Yamanaka¹, Masashi Tamaki², Yasuaki Aoki², Hideyuki Okamoto³, Hidekazu Dan⁴, Ken-ichi Sorachi⁵

¹Department of Internal Medicine, Japanese Red Cross Himeji Hospital,

²Department of Orthopedic Surgery, Japanese Red Cross Himeji Hospital,

³Okamoto Internal Medicine Clinic, ⁴Dan Orthopedic Clinic, ⁵Sorachi Internal Medicine Clinic

Conflict of interest: None

[Object] We conducted a questionnaire survey to clarify modifiable factors that regulated patients' movement in rheumatoid arthritis (RA). [Methods] Questionnaire items concerning Jan to Dec 2017 were as follows: the number of patients newly-diagnosed/continuously treated/referred/reversely introduced, and the treatment policy and specific treatment for RA patients. [Results] Among 23 institutions, 14 (hospital 2, clinic 12; internal department 9, orthopedic department 5; specialist 4, non-specialist 10) answered to the questionnaire. A total of 1028 patients were identified and their movement was as follows: 157 newly-diagnosed cases, 130 cases introduced from other institutions, 129 cases introduced to other institutions, and 4 deaths. The strongest factors influencing in every clinical decision regarding patients' introduction for non-specialists was the number of patients experienced. Most non-specialists were concerned about safety management for MTX and lack of experience in use and safety management for biological agents. [Conclusions] Non-specialists exceeding experience of 50 cases possibly provide medical care comparable to a specialist. Close collaboration with a small number of non-specialists interested in rheumatology may improve the gap of regional medical collaboration.

P1-007

Medical care for rheumatoid arthritis at the core hospital without professional rheumatologists in a remote island of Okinawa prefecture

Masashi Momose¹, Mitsuyo Kinjo²

¹Department of Internal Medicine, Okinawa Miyako Hospital, ²Department of Rheumatology, Okinawa Chubu Hospital

Conflict of interest: None

[Object] Miyakojima is a remote island located 290 km far from Okinawa mainland, where 55,000 people reside. Okinawa Miyako Hospital

is the only general hospital, and internists who graduated from residency program in Okinawa Chubu Hospital serve rheumatology care under supervision of specialists. Rheumatology training is incorporated into our 4-year residency program. We aim to describe how specialized care for RA is provided in Miyakojima. [Methods] We investigated the patients prescribed DMARDs from 1/10/2015 to 1/10/2018 by using pharmacy database. [Results] Among 259 patients using DMARDs, 211 RA patients were included after reviewing medical record. The average age was 62.3 year-old and gender ratio was 1:5.8. 161 (76.3%) patients were positive for anti-CCP antibody, 139 positive for RF, and 20 positive for anti-SS-A antibody. 32 patients had RA-ILD, 15 had DM, and 14 had cancer. There are 137 (64.9%) patients using MTX, 100 using SASP, 56 using BUC, and 33 (15.6%) using bDMARDs. During the observation period, 22 patients were hospitalized due to infection. Mortality related to RA is 0%. [Conclusions] Rheumatology training during residency helps young doctors in underserved area provide care for RA patients as well as using bDMARDs in concert with specialists.

P1-008

Association of bDMARDs use with eGFR change in five years in Nin-Ja 2012-2017 cohort

Hiroshi Kajiyama¹, Hisashi Noma², Hirotaka Tsuno³, Atsushi Hashimoto³, Toshihiro Matsui³, Atsushi Kaneko⁴, Shinichiro Tsunoda⁵, Kazuhiro Yokota¹, Yasuto Araki¹, Kojiro Sato¹, Yu Funakubo¹, Kiyoshi Matsui⁷, Koichiro Saisho⁶, Shigeto Tohma⁸, Toshihide Mimura¹

¹Department of Rheumatology and Applied Immunology, Saitama Medical University, ²The Institute of Statistical Mathematics, ³Department of Rheumatology, National Hospital Organization, Sagami National Hospital, ⁴Department of Orthopaedic Surgery and Rheumatology, National Hospital Organization, Nagoya Medical Center, ⁵Department of Rheumatology, Sumitomo Hospital, ⁶Department of Orthopaedic Surgery and Rheumatology, National Hospital Organization, Miyakonojo Medical Center, ⁷Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, ⁸Department of Rheumatology, National Hospital Organization, Tokyo National Hospital

Conflict of interest: None

[Object] The purpose of this study is to test if bDMARDs use is associated with eGFR change. [Methods] Retrospective observational study. Analyzed were 1933 RA cases who were registered to NinJa annually from 2012 to 2017, with 2012 estimated glomerular filtration rate (eGFR) ≥ 60 mL/min/1.73m². Cases with continuous bDMARD use from 2012 to 2015, and from 2014 to 2017 were defined BIO (+), and others were defined BIO (-). Comparative analysis was done with propensity score matching, adjusting 29 background factors in BIO (+) and BIO (-). The outcome were eGFR between 2012 and 2017, and <60 mL/min/1.73m² in 2017, and the continuous outcome was analyzed with linear mixed effects model, and the binary outcome was analyzed with conditional logistic regression. Missing data were complemented with complementary analysis using multiple imputation 200 times. [Results] Propensity-score matched 254 BIO (+) RA cases and 1016 BIO (-) cases showed no significant difference in the continuous outcome and the binary outcome, computed by linear mixed effects model and the conditional logistic regression analysis. [Conclusions] In NinJa 2012-2017 cohort, the evidence showing that bDMARDs use affect five-year eGFR decline in cases with 2012 eGFR ≥ 60 mL/min/1.73m² was not obtained.

P1-009

Clinical characteristics of seronegative arthritis including rheumatoid arthritis

Ichiro Yoshii¹, Tatsumi Chijiwa², Naoya Sawada³

¹Rheumatology and Musculoskeletal Medicine, Yoshii Hospital, ²Department of Rheumatology, Kochi Memorial Hospital, ³Department of Rheumatology, Dohgo Spa Hospital

Conflict of interest: None

[Object] Characteristics of seronegative arthritis were investigated. [Methods] From August 1st, 2010 to July 31, 2018, 884 arthritis patients who were suspected rheumatoid arthritis (RA), were followed up for more than one year. In these, 96 patients were seronegative arthritis with

RF nor ACPA at first consult counted 96, consisted of 31 male and 65 female. Patients who met ACR/EULAR classification criteria (CC); no less than 6 points for 18; 4 and 5 for 71; and less for 7. [Results] A final diagnosis was determined for 41 as RA, while others as non-RA, in these 22 as SpA, 9 as OA, 3 as PMR, 1 as SLE, 1 as PSS, 1 as NTM infection, 16 as unclassified arthritis. In patients who met CC, 15 were RA and 3 were non-RA, while 26 were RA and 52 were non-RA in the other patients. In patients who fulfilled 5 joint points in CC, 15 were RA and 3 were non-RA. All these patients met CC indicative. There is no significant difference in clinical course between RA and non-RA. [Conclusions] In seronegative patients, sensitivity of CC was 83.3%, while specificity was 66.7%. That lacked accuracy, however, it raised to 75% with referring ACR diagnostic criteria 1987. Rheumatologists need to involve diagnostic skills, that should not be cast a spell by CC, and pay great attention to clinical symptoms.

P1-010

Multi center collaboration findings regarding observations at initial diagnosis of rheumatoid arthritis (RA)

Keiko Funahashi¹, Tsukasa Matsubara², Eisuke Shono², Motohiro Oribe², Keisuke Hashimoto², Akira Sagawa², Tamami Yoshitama², Takeshi Mitsuka², Tomohiko Yoshida², Atsuko Imai², Nobuaki Miyake², Kazuyasu Ushio², Tomomaro Izumihara², Tomomi Tsuru², Yosuke Nishioka², Shigeto Kiyokawa², Norihiro Nishimoto²

¹Clinical Research, Matsubara Mayflower Hospital, ²Japanese Clinician's Biologics Research Group

Conflict of interest: None

[Object] There are very few based on observations at the time of initial diagnosis. We performed a retrospective study of the initial diagnoses of patients currently being treated. [Methods] A survey was undertaken at 18 facilities from September to December 2017. Survey items were hematological examination, clinical findings, presence or absence of bone erosion, year of diagnosis, background at the time of diagnosis on 1185 RA patients. [Results] Duration ranged from 0-49 years and average was 6.4 years. The averages of initial diagnostic observations were TJC (28) 4.8, SJC (28) 5.0, PaGA 43.5, PhGA 40.7, CRP 1.4mg/dl, ESR 36mm/h. MMP-3 143ng/ml, and RF 107U/ml. Bone erosion was present at a rate of 31.5% at initial diagnosis. We compared the groups with and without bone erosion, and it was found that it took time to receive a diagnosis. In the group of patients with bone erosion, inflammation markers were higher. However, time of initial diagnosis and bone erosion was not relevant. [Conclusions] As has been reported previously, the cohort study also found that the inflammation markers in patients presenting with bone erosion were higher. The rate of bone erosion has not changed since 2010, the problem would seem to stem from lack of access to specialists.

P1-011

Observations of RA at the time of diagnosis and the effect of patients' treatment history on treatment-a multi-center study

Keiko Funahashi¹, Tsukasa Matsubara², Eisuke Shono², Motohiro Oribe², Keisuke Hashimoto², Akira Sagawa², Tamami Yoshitama², Takeshi Mitsuka², Tomohiko Yoshida², Atsuko Imai², Nobuaki Miyake², Kazuyasu Ushio², Tomomaro Izumihara², Tomomi Tsuru², Yosuke Nishioka², Shigeto Kiyokawa², Norihiro Nishimoto²

¹Clinical Research, Matsubara Mayflower Hospital, ²Japanese Clinician's Biologics Research Group

Conflict of interest: None

[Object] The influence of patient history on the activity level the findings at diagnosis is unclear. It is also unclear whether they influence on treatment. We therefore we compared patient history as well as the state of patients' present treatments and diagnostic findings. [Methods] 1185 patients at 18 facilities who were initial diagnosed with RA were included. Blood examination results, clinical findings, the presence or absence of bone erosion, as well as background factors. In addition, we compared diagnostic findings between GroupB (treated with bDMARDs or tsDMARDs) and GroupC (treated with csDMARDs) [Results] It was found that neither smoking history, gynecological ailments, surgical history, gastrointestinal disorders, periodontal disease history, nor genetic

background had an effect on disease activity at the time of diagnosis. On the other hand, the ratio of patients with erosin in Group B was significantly higher than that of Group C. In addition, the average values of diagnostic indicators was higher in Group B. [Conclusions] RA treatment guidelines take three stages. However as there is evidence of use of bDMARDs and tsDMARDs to early RA, and considering this results, the use of bDMARDs and tsDMARDs to serve early RA should be considered.

P1-012

A study on chronic kidney disease in patients with rheumatoid arthritis

Miki Takata, Tomoya Harada, Ryota Okazaki, Yoshihiro Funaki, Yuriko Sueda, Akira Yamasaki

Division of Medical Oncology and Molecular Respiratory Department of Multidisciplinary Internal Medicine Faculty of Medicine, Tottori University, Yonago, Japan

Conflict of interest: None

[Object] It is known that chronic kidney disease (CKD) is relatively common in patients with RA than that in general adults. To assess renal function is important for RA therapeutic strategy. [Methods] We targeted RA patients who were following for more than 3 months as of 2018. Patients with estimated glomerular filtration rate (eGFR) < 60 ml / min / 1.73 m² for more than 3 months were defined as CKD. Patient background and treatment options were examined. [Results] One hundred and three RA patients were retrospectively analyzed. Among those, 23 (22.3%) were indicated to have CKD. The mean age of patients with CKD was significantly higher than that of without CKD (without CKD: 60.36 ± 1.57 vs with CKD: 73.09 ± 1.94; *p* < 0.0001), and the ratio of male in patients with CKD was significantly higher than that of without CKD (without CKD: male 18.8%, female 81.2% vs with CKD: Male 39.1%, female 60.1%; *p* = 0.0416). MTX was prescribed significantly more to patients without CKD (*p*=0.0001), whereas Tac was prescribed significantly more to CKD patients (*p*=0.0173). [Conclusions] 22.3% of patients with RA were indicated to have CKD. Especially for elderly men, the proportion of CKD was significantly higher, and it was considered to be a group to be careful about RA treatment selection.

P1-013

Characteristics of patients with rheumatoid arthritis and investigation of drug therapy

Takeshi Kuroda¹, Masanori Sudo¹, Sayuri Takamura¹, Shunsuke Sakai¹, Ayako Wakamatsu¹, Hiroe Sato¹, Daisuke Kobayashi¹, Takeshi Nakatsue¹, Yoko Wada¹, Masaaki Nakano², Ichiei Narita¹

¹Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences, ²Department of Medical Technology, School of Health Sciences, Faculty of Medicine, Niigata University

Conflict of interest: None

[Object] We compared data for RA patients between 1991 and 2018 to clarify the clinical features and therapy in the elderly in 2018. [Methods] We evaluated 429 cases of RA in 1991 and 368 cases of RA in 2018 treated in our department. First, the age and sex ratios of the two groups were evaluated. Then, the clinical features of the 129 younger-onset elderly RA (YORA) patients and the 108 elderly-onset RA (EORA) patients in 2018 were assessed. [Results] In 1991 the onset of RA peaked in patients in their 50s and 60s, whereas in 2018 peak occurred in patients in their 60s and 70s. A homogeneity test of the odds ratio of gender between 1991 and 2018 revealed no significant difference. Among 368 patients treated in 2018, polymyalgia was observed in 8 patients over the age of 60 years, and its occurrence was statistically significant (*P*=0.02). AA amyloidosis was observed in only 5 YORA patients. With regard to MTX use, no inter-group difference was observed, but high doses of MTX were not used in the EORA group. Biological agents were used for 23% of the EORA patients and for 38% of the YORA patients, the frequency of abatacept and etanercept use being significant. [Conclusions] The use of medicine appears to be a characteristic feature of care provided for elderly patients with RA.

P1-014

The treatment of patients with elderly-onset rheumatoid arthritis at Hokkaido Medical Center for Rheumatic Diseases

Masato Isobe, Fumihiko Sakamoto, Mihoko Henmi, Akihiro Narita, Yuko Aoki, Hisanori Takamatsu, Akemi Kitano, Toshiyuki Hattori, Norifumi Sawamukai, Takeya Ito, Akio Mitsuzaki, Jun Fukae, Megumi Matsuhashi, Masato Shimizu, Takao Koike, Kazuhide Tanimura
Hokkaido Medical Center for Rheumatic Diseases

Conflict of interest: None

[Object] With the increase in the elderly population, opportunities to treat elderly-onset rheumatoid arthritis (EORA) cases are increasing. We investigated EORA cases at our hospital. [Methods] We compared the characteristics, disease activity, and clinical course of 83 patients of untreated RA who started treatment in September 2017 to September 2018 at our hospital, and classified it into a group under 60 years old (non-EORA group) and a group aged over 60 years (EORA group). [Results] Of the 83 non-treated RA cases (average age 59.0 years old (20 to 91 years old), male 21: female 62) visited our hospital, 45 patients (54.2%) in the non-EORA group and 38 (45.8%), and 15 patients (18.1%) were over 75 years old. Disease activity was significantly higher in the EORA group. There was no significant difference in the duration of disease between the two groups, the Steinbrocker stage classification, the seronegative RA occupation rate, and the MTX usage rate. The bDMARD usage rate was high in the EORA group (*p*=0.035). [Conclusions] EORA group accounted for less than half of cases of untreated RA at our hospital. In the EORA group, the inflammatory response, disease activity, and the use rate of bDMARDs were high. MTX was also actively used even for elderly people.

P1-015

Development of a nationwide database of JIA: CoNinJa (Children's version of NinJa)

Toshihiro Matsui¹, Kosuke Shabana², Shigeto Tohma³, Masaaki Mori⁴

¹Department of Rheumatology, National Hospital Organization Sagami-hara National Hospital, ²Department of Pediatrics, Osaka Medical College, ³National Hospital Organization Tokyo National Hospital, ⁴Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, National University Corporation Tokyo Medical and Dental University

Conflict of interest: Yes

[Object] To conduct a large-scale, continuous and long-term investigation on clinical practice and prognosis concerning patients with juvenile idiopathic arthritis (JIA), this study aims to construct a nation-wide JIA database: CoNinJa (Children's version of NinJa), which has the same platform as a nation-wide adult RA database: NinJa (National Database of Rheumatic Diseases in Japan). [Methods/Results] In addition to all the items collected in NinJa, the items necessary for the evaluation of JIA were covered. Unlike NinJa, CoNinJa added findings and disease type at the onset, past history of medications and complications. Patients with all disease types of JIA regardless of current age were registered in CoNinJa. We made the data of CoNinJa possible to be took over to NinJa. We decided to collect data once a year. In the first year (2006), 15 facilities were participated and 714 cases (202 systemic JIA, 223 oligoarticular JIA, 93 RF (-) polyarticular JIA, 146 RF (+) polyarticular JIA, and 36 enthesitis-related JIA) were registered in CoNinJa. [Conclusions] CoNinJa was developed and started operation. We will collect data continuously and clarify the actual condition and problems of JIA practice in Japan; and investigate the long-term prognosis of JIA by taking over to NinJa.

P1-016

The relationship of distal interphalangeal (DIP) joint involvement with high disease activity status in rheumatoid arthritis (RA) - Analysis based on NinJa2017 database using Nishiyama's Joint index vector

Takahiro Mizuuchi¹, Tetsuji Sawada¹, Susumu Nishiyama², Mayu Tago¹, Koichiro Tahara¹, Eri Kato¹, Hiroaki Mori¹, Haeru Hayashi¹, Toshihiro Matsui³, Shigeto Tohma⁴

¹Department of Rheumatology, Tokyo Medical University Hospital Shinjuku Japan, ²Rheumatic Disease Center, Kurashiki Medical Center, Kura-

shiki, Japan, ³Department of Rheumatology, NHO Sagamihara Hospital Sagamihara Japan, ⁴NHO Tokyo Hospital Kiyose Japan

Conflict of interest: None

[Object] To analyze the relationship of DIP joint involvement (DIP+) with disease activity and affected joint distribution in RA. [Method] We used the data of adult-onset RA patients registered in *NinJa2017* with DAS28-CRP were available (n=12716). In addition to clinical parameters, Nishiyama's joint index vector (x, y, z) (Rheumatol Int, 2012, J Big Data, 2018) was used for analysis. [Results] Prevalence of symptomatic (tenderness and/or swelling) DIP+ of both 2nd to 5th DIP joints was 1.6%. which was lower than that of other hand joints. DIP+ was not related to disease duration, CRP, or RF and ACPA titers, while it was numerically more prevalent in women. Mean age was significantly lower in DIP+ patients. On the other hand, in addition to TJC, SJC, DAS28-CRP, mHAQ, upper and lower joint indices (x and y) were significantly higher in DIP+ patients than those without. Large joint predominance index (z), was negative in DIP+ patients. The limitation of the present study includes lack of radiographic information. [Conclusion] We have clearly demonstrated that DIP involvement was significantly associated with high disease activity and small-joint predominance, albeit infrequently. We consider that it is necessary to pay more attention to DIP symptoms in active RA patients.

P1-017

Shift of the discordance of global assessment (GA) of rheumatoid arthritis (RA) disease activity between RA patients (PGA) and their physicians (PhGA) - Analysis based on NinJa 2015-2017 database and Nishiyama's joint index vector

Yusuke Yamamoto¹, Tetsuji Sawada¹, Susumu Nishiyama², Mayu Tago¹, Koichiro Tahara¹, Eri Kato¹, Hiroaki Mori¹, Haeru Hayashi¹, Toshihiro Matsui³, Shigeto Tohma⁴

¹Department of Rheumatology, Tokyo Medical University Hospital, ²Rheumatic Disease Center, Kurashiki Medical Center, ³Department of Rheumatology, NHO Sagamihara Hospital, ⁴NHO Tokyo Hospital

Conflict of interest: None

[Purpose] We have previously demonstrated that PGA-PhGA discordance was significantly related to pain VAS, functional impairment (mHAQ), and large-joint involvement. The aim of the present study is to investigate the factors causing persistent PGA-PhGA discordance. [Methods] We used the data of 3876 patients with RA who were registered in both *NinJa2015* and *NinJa2017*, and whose DAS28-CRP data were available. PGA-PhGA was defined as PGA minus PhGA. Nishiyama's joint index vector V (x, y, z) was included for analyzing the factors related to persistent PGA-PhGA discordance. [Results] In *NinJa2015*, it was demonstrated that PGA-PhGA was increased by pain and mHAQ, while it was decreased by CRP, x, y, and z. Regarding PGA-PhGA over two-year period, PGA-PhGA of *NinJa2015* and that of *NinJa2017* were significantly correlated, and 50% of the RA patients whose PGA-PhGA were 3 and above in *NinJa2015* were still discordant in *NinJa2017*. PGA-PhGA in *NinJa2017* was increased by pain, mHAQ, and PGA-PhGA discordance in 2015, while it was decreased by CRP and x index. [Conclusion] PGA-PhGA discordance can be persistent. RA care providers should pay attention to pain and functional impairment to share common disease recognition with their RA patients.

P1-018

The cause of death of rheumatoid arthritis patients who died in our hospital

Atsushi Kondo, Ayuko Sogabe, Naoya Sawada, Yosuke Murata, Akihiro Yamada, Kazuo Jouyama, Kenichiro Matoba, Yasuaki Okuda, Makoto Onishi, Kiyoshi Takasugi
Dohgo Spa Hospital, Matsuyama, Japan

Conflict of interest: None

[Object] Rheumatoid arthritis (RA) patients with joint deformity or with high disease activity has dramatically decreased because of the appearance of biological products. There are many patients in our hospital

who are forced to stay in hospital or who have been examined for many years due to RA. We investigated the causes of death, age, etc. of patients who died in our hospital. [Methods] We collected all patients who died in our hospital during the 10 years from January 2008 to September 2018, and extracted RA patients among them, examined by a medical record about age, RA disease duration and cause of death. [Results] During this period, the number of patients who died at our hospital was 168, among which 112 RA patients had RA. The mean age at the time of death of RA patients was 82.2 ± 7.3 years, age of onset was 55.0 ± 16.9 years, and the mean disease duration until death was 27.2 ± 15.6 years. The most common cause of death is 35 cases (31%) of pneumonia, 12 cases (11%) of heart failure, 9 cases (8%) of septicemia, and 8 cases (7%) of senility. [Conclusions] In most cases, disease activity of rheumatoid arthritis was low, and the age of death was not different from that of healthy people regardless of age of onset and duration of disease.

P1-019

The role of SH3BP2 in rheumatoid arthritis and systemic lupus erythematosus murine models

Kyoko Kawahara, Tomoyuki Mukai, Akiko Nagasu, Shoko Tsuji, Yoshitaka Morita

Department of Rheumatology, Kawasaki Medical School

Conflict of interest: Yes

[Object] The adaptor protein SH3BP2 is widely expressed in immune cells and controls intracellular signaling pathways. In this study, we investigated the role of SH3BP2 in rheumatoid arthritis and systemic lupus erythematosus murine models. [Method] SH3BP2-deficient mice were backcrossed onto DBA/1 background. SH3BP2-deficient mice were immunized against bovine type II collagen (CII), and the development of arthritis was observed. Serum anti-CII antibody levels were determined. The response of the lymph node cells to the CII were analyzed. Next, for the lupus model, we used Fas-lpr mice, which possess impaired Fas signaling. SH3BP2-deficient Fas-lpr mice were created, and then serum anti-dsDNA antibody of the mice were determined at 32-week old. [Result] In the arthritis model, SH3BP2 deficiency suppressed the induction of arthritis, accompanying with the decreased anti-CII antibody. The response of lymph node cells to CII was not altered. In the lupus model, the development of the anti-dsDNA antibody was significantly decreased by SH3BP2 deficiency. [Conclusion] SH3BP2 deficiency suppressed the development of the disease-associated antibodies. SH3BP2 could be a potential therapeutic target for autoimmune diseases.

P1-020

Increased Interferon alpha production by monocytes associated with enhanced STING pathway in systemic lupus erythematosus

Go Murayama^{1,2}, Asako Chiba², Ayako Makiyama^{1,2}, Ken Yamaji¹, Naoto Tamura¹, Sachiko Miyake²

¹Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan, ²Department of Immunology, Juntendo University School of Medicine, Tokyo, Japan

Conflict of interest: None

<Background> We reported that the proportion of IFN α producing monocytes stimulated with STING agonist was significantly increased in SLE patients. In this study, we investigated STING-signaling pathway in SLE. <Methods> Peripheral blood mononuclear cells (PBMCs) from SLE patients and healthy controls (HCs) were stimulated with a STING agonist, 2'3'-cGAMP, and the proportion of IFN α positive cells was investigated by intracellular cytokine staining and flow cytometry. After pretreatment with or without IFN α for 24 hours, IFN α production and localization of STING in monocytes from HCs were assessed. <Results> The frequency of IFN α ⁺ monocytes in SLE was positively correlated with SLEDAI. The expression of STING was increased and co-localization of STING and TBK1 was enhanced in monocytes from SLE patients. Pretreatment with IFN α enhanced IFN α production by monocytes stimulated with 2'3'-cGAMP and co-localization of STING with TBK1. <Conclusions> IFN α is known to be playing an important role in the pathogenesis of SLE. We found enhanced IFN α production by lupus monocytes was partially due to increased expression of STING and co-localization of

STING and TBK1. We also demonstrated that exposure to IFN α enhanced co-localization of STING and TBK1.

P1-021

Tofacitinib inhibits granulocyte-macrophage colony-stimulating factor-induced NLRP3 inflammasome activation in human neutrophils
Jumpei Temmoku¹, Makiko Furuya Yashiro¹, Yuya Fujita¹, Naoki Matsuoka¹, Tomoyuki Asano¹, Shuzo Sato¹, Eiji Suzuki², Hiroko Kobayashi¹, Hiroshi Watanabe¹, Kiyoshi Migita¹

¹Department of Rheumatology, Fukushima Medical University School of Medicine, ²Department of Rheumatology, Ohta Nishinouchi Hospital

Conflict of interest: None

[Object] GM-CSF has emerged as a crucial cytokine that activates myeloid cells to initiate tissue inflammation. The molecular actions of GM-CSF against innate immunity are poorly characterized. We investigated the in vitro effects of GM-CSF on the activation of human myeloid lineages, neutrophils. [Methods] Human neutrophils were stimulated with GM-CSF in the presence or absence of tofacitinib. The cellular supernatants were analyzed for interleukin-1 beta (IL-1 β) and caspase-1 by ELISA methods. JAK2/STAT3 activation in neutrophils was assessed by Western blot using phospho-specific antibodies. [Results] Stimulation with GM-CSF alone, was shown to increase the release of IL-1 β and cleaved caspase-1 (p20) from human neutrophils. Tofacitinib, which inhibits GM-CSF-induced JAK2-mediated signal transduction, completely abrogated GM-CSF-induced IL-1 β secretion. GM-CSF stimulation also induced NLRP3 protein expression in neutrophils, which was abrogated by tofacitinib. [Conclusions] These results indicate that GM-CSF signaling induces NLRP3 inflammasome activation. This process can be blocked by tofacitinib, which interferes with JAK2/STAT3 signaling pathways. Our data suggest that JAK inhibitors have the potential to block the GM-CSF-mediated inflammasome activation.

P1-022

CDK4/6 activity stabilizes AP-1 components c-Jun and Fra1, and regulates AP-1 transcriptional activity in rheumatoid arthritis synovial fibroblasts

Tadashi Hosoya, Tetsuya Saito, Yasuhiro Tagawa, Akio Yamamoto, Kimito Kawahata, Nobuyuki Miyasaka, Hitoshi Kohsaka
Department of Rheumatology, Tokyo Medical and Dental University (TMDU), Tokyo, Japan

Conflict of interest: None

[Object] Rheumatoid arthritis (RA) synovial fibroblasts (RASFs) are the main source of matrix metalloproteinases (MMPs). This study was designed to discern the underlying mechanisms in the regulation of MMPs by the cyclin-dependent kinase (CDK) 4/6. [Methods] CDK4/6 activity was inhibited or enhanced with a small-molecule CDK4/6 inhibitor (CDKI) or gene transduction. Expression of inflammatory mediators was evaluated at the protein and transcription levels. Binding of the nuclear extracts to TRE, AP-1 targeted sequence, was assessed. Protein expression was evaluated with or without MG132 as a proteasome-inhibitor. [Results] CDKI inhibited the transcription of the MMP-1 and MMP-3 genes, which contain the TRE sequence in their promoter and decreased the amount of nuclear proteins binding to the TRE sequence. Among the AP-1 binding proteins, the c-Jun and Fra1 proteins were decreased when CDK4/6 activity was inhibited and increased when CDK4/6 activity was enhanced. CDK4/6 protected both of the proteins from proteasome-dependent degradation. [Conclusions] CDK4/6 stabilized c-Jun and Fra1 proteins and regulated the transcriptional activity of AP-1. CDKI would provide anti-inflammatory effects in inflammatory diseases including RA by the selective down-regulation of c-Jun and Fra1.

P1-023

Immunohistochemical staining of the lip tissues from Sjögren syndrome patients with the monoclonal anti-Ro52 autoantibody obtained using the ISAAC system

Maiko Okumura^{1,2}, Hirofumi Taki¹, Koichiro Shinoda², Hiroyuki Hounoki², Reina Tsuda², Kazuyuki Tobe²

¹Rheumatology, Internal Medicine, Takaoka-saiseikai Hospital, ²The First Department of Internal Medicine, University of Toyama

Conflict of interest: None

[Object] Ro52 is a protein in cytoplasm. Ro52 specific autoantibody (anti-Ro52 autoantibody) appear in the sera of connective tissue diseases (CTDs) patients. Some reported the relationship of anti-Ro52 autoantibody with the CTDs and it is suspected that Ro52 and Ro52 specific autoantibody relate to CTDs. Immunohistochemical analysis using human monoclonal anti-Ro52 autoantibodies obtained from CTD patients showed the portality of Ro52 and suspected the relationship with CTDs. [Methods] We obtained 12 human monoclonal anti-Ro52 autoantibodies from 4 CTD patients (European J Immunol. 2018;48 (10):1717-1727) using ISSAC system (Nat Med. 2009 Sep;15 (9):1088-92). We stained the lip tissues of Sjögren syndrome (SS) patients and healthy donors, using the human monoclonal anti-Ro52 autoantibody. [Results] In immunohistochemical analysis of lip tissues of 5 SS patients and 5 healthy donors, cytoplasm of acinar cell and ductal epithelium of SS lip tissues were stained by human monoclonal anti-Ro52 autoantibody. It was reported that ductal epithelium of SS lip tissues were stained by monoclonal anti-Ro52 autoantibody producing hybridoma (Clin Exp Immunol. 2014;177:244-252). [Conclusions] Immunohistochemical analysis suggested that Ro52 appear in injured tissues and seem to be related to CTDs.

P1-024

CCL11 is involved in cell migration in rheumatoid arthritis

Kuninobu Wakabayashi¹, Takeo Isozaki¹, Masahiro Hosonuma¹, Airi Nishimi¹, Shinichiro Nishimi¹, Sho Ishii¹, Yuzo Ikari¹, Takahiro Tokunaga¹, Hidekazu Furuya¹, Katsunori Inagaki², Tsuyoshi Kasama¹

¹Division of Rheumatology, Department of Medicine, Showa University School of Medicine, ²Department of Orthopedics, Showa University School of Medicine

Conflict of interest: None

[Object] The aim of this study is to investigate the expression and the function of CCL11 in fibroblast like synoviocyte (FLS) of rheumatoid arthritis (RA). [Methods] We measured the levels of CCL11, TNF- α , MCP-1, MIP-1 α and RANTES in synovial fluids (SFs) from the patients with RA using ELISA. After TNF- α stimulation, the protein expression levels of CCL11, MCP-1, MIP-1 α and RANTES in the culture medium were measured by ELISA. To confirm the role of CCL11 in cell migration, FLS were stimulated with CCL11 and were allowed to migrate through uncoated transwell chambers. Finally, to block the expression of CCL11, FLS were transfected with siRNA against CCL11, and we demonstrated migration assay and expression analysis. [Results] The levels of CCL11 in SFs from the patients with RA were positively correlated with the levels of TNF- α , MCP-1 and MIP-1 α . The secretion of MCP-1, MIP-1 α and RANTES in RA FLS conditioned medium were increased by TNF- α stimulation. CCL11 stimulated cells were significantly higher efficient at migration than unstimulated cells. CCL11 siRNA treatment decreased the secretion of MCP-1 in TNF- α treated RA FLS conditioned medium and the RA FLS migration. [Conclusions] These data show that CCL11 is involved in cell migration in RA.

P1-025

Dissociation of arthritis symptoms and pain-related behavior in experimental arthritis

Yohsuke Oto^{1,2}, Takayuki Matsushita^{1,2}, Masayuki Yoshiga¹, Kazuhiro Otani¹, Kentaro Noda¹, Daitaro Kurosaka¹

¹Division of Rheumatology, Department of Internal Medicine, The Jikei University School of Medicine, ²Center for Neuroscience of Pain, The Jikei University School of Medicine

Conflict of interest: None

[Object] Rheumatoid arthritis (RA) patients are suffering from pain, even in optimal control of inflammatory disease, as revealed with recent studies showing a low correlation between the pain intensity and objective measures of inflammation. To clarify this mechanism, we developed

novel methods to evaluate pain-related spontaneous voluntary behavior in RA model. [Methods] Collagen-induced arthritis (CIA) was induced in mice and spontaneous behavior was examined. In voluntary wheel running test, mice were single-housed in home cage with running wheels to count rotation numbers. In thermal preference test, mice were allowed to freely explore between plates with elevating (25–49°C) and fixed temperature (25°C), and the ratio of staying on elevating plate were calculated. Tofacitinib was administered subcutaneously by osmotic pump. [Results] In voluntary wheel running test, CIA decreased the rotation numbers. In thermal preference test, CIA preferred staying on median temperature region (32–43°C). These behavioral indices significantly correlated with arthritis score, which were eliminated by tofacitinib treatment despite improvement of the arthritis score. [Conclusions] By tofacitinib treatment, transient dissociation between pain-related behavior and arthritis score were observed in CIA.

P1-026

Interferon-gamma-producing ability of NK cells in adult-onset Still's disease

Yasuhiro Shimojima, Dai Kishida, Yoshiki Sekijima
Division of Neurology and Rheumatology, Department of Internal Medicine, Shinshu University School of Medicine

Conflict of interest: None

[Object] We investigated interferon- γ (IFN- γ)-producing ability in circulating natural killer (NK) cells from patients with adult-onset Still's disease (AOSD). [Methods] Twenty patients in the acute phase of AOSD (acute AOSD), 7 of the 20 patients after treatment, and 11 healthy controls (HC) were employed. NK cells and their IFN- γ expression levels were analyzed by flow cytometry. The cytokine receptors of interleukin (IL)-12, IL-15, and IL-18 on NK cells were also evaluated. [Results] The frequency of NK cells was significantly lower in acute AOSD than in HC. IFN- γ expression in NK cells was significantly increased and was improved after treatment. However, IFN- γ expression in NK cells revealed an inverse correlation with serum ferritin levels. Expression of IL-12 and IL-15 receptors on NK cells was significantly increased in acute AOSD, whereas that of IL-18 receptor indicated no significant difference between three groups. [Conclusions] The ability of IFN- γ production in NK cells may be correlatively inhibited dependent on a disease activity; meanwhile, upregulation of IL-12 and IL-15 receptors on NK cells may compensate for promoting IFN- γ production in acute AOSD.

P1-027

Anti-Fractalkine Monoclonal Antibody Suppresses Joint Destruction by Inhibiting Migration of Osteoclast Precursors and Inducing Synovial Cell Death in Collagen-Induced Arthritis Model Mice

Kana Negishi-Hoshino, Tomoya Nakatani, Yoshikazu Kuboi, Wataru Ikeda, Naoto Ishii, Nobuyuki Yasuda, Toshio Imai
KAN Research Institute, Inc.

Conflict of interest: None

[Object] The purpose of this study is to elucidate the roles of the fractalkine (FKN)-CX3CR1 axis in the collagen-induced arthritis (CIA) mice. [Methods] The arthritis score was monitored, and joint destruction was evaluated by histology. The mRNA levels in the affected joints were assessed by quantitative RT-PCR. Osteoclast precursors (OCPs) were transferred to CIA mice to evaluate the migration of OCPs into the synovium. Apoptosis of fibroblast-like synovocyte (FLS) was measured by histology. [Results] Anti-mouse FKN (mFKN) mAb significantly improved synovitis and joint destruction with marked reduction of *Tnf* and *Il6* mRNA expression in the joints. Anti-mFKN mAb strongly inhibited the OCP migration into the synovium, whereas etanercept or tofacitinib had no significant effects. OCPs derived from CX3CR1 knock out mice also markedly decreased the migration to the synovium compared with OCPs derived from wild type mice. Apoptosis of FLS in the synovium was significantly induced after the single administration of anti-mFKN mAb. [Conclusions] FKN-CX3CR1 axis could directly regulate the OCP migration and the FLS survival. Inhibition of FKN-CX3CR1 axis could be an attractive new therapeutic option for the treatment of both joint destruction and synovitis in rheumatoid arthritis patients.

P1-028

The roles of JAK/STAT pathway in the pathogenesis of HTLV-1-positive rheumatoid arthritis

Yumi Kariya, Kunihiko Umekita, Takeshi Kawaguchi, Motohiro Matsuda, Shunichi Miyauchi, Ichiro Takajo, Akihiko Okayama
Department of Internal Medicine, Rheumatology, Infectious Diseases and Laboratory Medicine, Faculty of Medicine, University of Miyazaki Japan

Conflict of interest: None

[Object] We investigated the role of JAK/STAT pathway in modification mechanism of RA (Rheumatoid arthritis) condition resulting from HTLV-1 (Human T-cell leukemia virus type 1) infection. [Methods] In HTLV-1 infected cell lines (MT2B, MT2J) and HTLV-1 not infected T cell line (Jurkat), treated with Tofacitinib (Tof), cell proliferation analyzed and expression mRNA of IL-6 and IFN γ were measured using real-time quantitative PCR. Phosphorylation of STAT in MT2B and MT2J was assessed by immunoblot. In RASF (RA synovial fibroblasts) cultured with each cell lines and treated with Tof, expression mRNA and protein level of IL-6 and CXCL10 were measured using real-time quantitative PCR and ELISA. [Results] Tof suppressed cell proliferation, mRNA expression and production of IL-6 and IFN γ in MT2B and MT2J dose dependent manner, but not in Jurkat. Phosphorylation of STAT was inhibited by Tof. In RASF cultured with MT2B and MT2J, Tof reduced IL-6 and CXCL10 level dose dependent manner. [Conclusions] Our findings demonstrated that activated JAK/STAT pathway is important for proliferation and production of inflammatory cytokines of HTLV-1 infected cell. Therefore Tof has potential to be effective for treatment of HTLV-1 positive RA regulating activation of HTLV-1 infected cell and RASF.

P1-029

Fas ligand influences the gene expressions of various key molecules in rheumatoid synovial fibroblasts

Koji Fukuda¹, Yasushi Miura^{1,2}, Toshihisa Maeda¹, Shinya Hayashi¹, Ryosuke Kuroda¹

¹Department of Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan, ²Division of Orthopedic Science, Department of Rehabilitation Science, Kobe University Graduate School of Health Sciences, Kobe, Japan

Conflict of interest: None

[Object] Fas ligand (FasL) is a member of tumor necrosis factor superfamily (TNFSF6) and reported to be involved in synovial hyperplasia of rheumatoid arthritis (RA). Apoptosis through Fas/FasL pathway of RA synovial cells was inhibited by pro-inflammatory cytokines present within the synovium. In this study, we investigated the gene expression profiles regulated by FasL in rheumatoid synovial fibroblasts (RA-FLS) to reveal the mechanism how FasL is involved in the pathogenesis of RA. [Methods] RA-FLS were incubated with FasL for 12h. Gene expressions were detected by microarray assay. [Results] The most upregulated 3 genes by FasL were dual specificity phosphatase 6 (DUSP6), epiregulin (EREG) and interleukin11 (IL-11). DUSP6 regulates CD4+ T-cell activation and differentiation. EREG associates with the development of cytokine-induced arthritis. IL-11 decreases the pro-inflammatory cytokines. The most downregulated 3 genes were angiopoietin-like 7 (ANGPTL7), protein inhibitor of activated STAT2 (PIAS2) and growth differentiation factor 5 (GDF5). ANGPTL7 promotes pro-inflammatory responses. PIAS proteins inhibit the activated STAT. GDF5 is associated with joint destruction of RA. [Conclusions] FasL regulates the expression of various genes in RA-FLS and may affect the pathogenesis of RA.

P1-030

Roles of histone acetyltransferases and transcriptional factor ROR alpha/REV-ERB alpha against TNF alpha-induced CCL2 expression in RA-FLSs

Ikumi Okumura¹, Kohsuke Yoshida¹, Kenta Kaneshiro¹, Koto Uchida¹, Arisa Yaekura¹, Yuto Oketani¹, Kanta Morii¹, Koji Tateishi², Yasuhiro Terashima², Yoshiko Kawasaki³, Nao Shibamura⁴, Yoshitada Sakai⁵, Akira Hashiramoto^{1,3}

¹Department of Biophysics, Division of Clinical of Immunology, Kobe University Graduate School of Health Sciences, Kobe, Japan, ²Depart-

ment of Orthopedic Surgery, Kohnan Kakogawa Hospital, Kakogawa, Japan, ³Department of Rheumatology, Kobe Kaisei Hospital, Kobe, Japan, ⁴Department of Orthopedic Surgery, Kobe Kaisei Hospital, Kobe, Japan, ⁵Department of Rehabilitation Science, Kobe University Graduate School of Medicine, Kobe, Japan

Conflict of interest: None

[Object] We have reported that TNF α induced expressions of clock gene *Bmal1* through transcriptional activator *Rora* and repressor *Rev-erb α* in RA fibroblast-like synoviocytes (RA-FLSs) and that histone acetyltransferases CBP and p300 were involved in this process. In the present study, we focused on chemokine CCL2, regulated by ROR α and REV-ERB α as well as Bmal1, to investigate the effect of histone acetyltransferases on TNF α -induced CCL2 expression in RA-FLSs. [Methods] RA-FLSs were pretreated with ROR α antagonist SR1001 (20 μ M), REV-ERB α agonist GSK4112 (20 μ M) or CBP/p300 inhibitor C646 (25 μ M) for 1 h and then stimulated with TNF α (10ng/ml). Likewise, small interfering RNA (siRNA) of both *CBP* and *p300* were introduced into RA-FLSs, and stimulated with TNF α . Thereafter, intracellular CCL2 mRNA and culture supernatant CCL2 were analyzed by qPCR and ELISA, respectively. [Results] TNF α -induced CCL2 expression was further inhibited by simultaneous treatment with both SR1001 and GSK4112, as compared with solo treatment of each agents. Further, CCL2 expressions were also suppressed by treatment with C646, and silencing of both CBP and p300 genes. [Conclusions] We newly found that TNF α induced expression of CCL2 through ROR α and REV-ERB α , which was associated with CBP/p300 in RA-FLSs.

P1-031

The nociceptive pain control in the hypothalamo-neurohypophysial/spinal pathway in the carrageenan induced arthritis rats

Makoto Kawasaki¹, Haruki Nishimura¹, Yasuhito Motojima¹, Takanori Matsuura¹, Hitoshi Suzuki¹, Yoshiaki Yamanaka¹, Hideo Ohnishi¹, Yoichi Ueta²

¹Department of Orthopedic Surgery, University of Occupational and Environmental Health, ²Department of Physiology, University of Occupational and Environmental Health

Conflict of interest: None

[Object] We evaluated the neurological reaction in the hypothalamo-neurohypophysial and hypothalamo-spinal pathway using the knee arthritis model rats. [Methods] Adult male Wistar rats were used. The right knee arthritis was induced by intra-articular injection of 100 μ L of 3 % carrageenan. Carrageenan-treated rats were perfused at 3, 6, and 12 hours after injection for immunohistochemistry. Furthermore, Carrageenan-treated rats were decapitated 2 and 6 hours after injection for *in situ* hybridization and collecting blood samples. [Results] The number of the Fos-LI positive cells in lamina I-II of the dorsal spinal cord, paraventricular nucleus and supraoptic nucleus was counted. The number of them in all regions were significantly increased in the arthritis rats. In addition, all of the plasma oxytocin (OXT), vasopressin (AVP) and corticosterone were significantly increased in the arthritis rats. Furthermore, all of expression levels of OXT mRNA, AVP mRNA and corticotropin-releasing hormone mRNA in the hypothalamus and proopiomelanocortin mRNA in the anterior pituitary were significantly increased in the arthritis rats. [Conclusions] The hypothalamo-neurohypophysial and hypothalamo-spinal pathway were activated by the nociceptive stress of knee arthritis.

P1-032

A disintegrin and metalloprotease -17 is involved proliferation of rheumatoid arthritis osteoblasts

Hidekazu Furuya, Takeo Isozaki, Shinichiro Nishimi, Airi Nishimi, Sho Ishii, Takahiro Tokunaga, Yuzo Ikari, Kuninobu Wakabayashi, Tsuyoshi Kasama

Division of Rheumatology, Department of Medicine, Showa University School of Medicine

Conflict of interest: None

[Object] We have previously reported ADAM-17 is expressed in

rheumatoid arthritis (RA) synovial fluids and synovial tissues. The purpose of this study was to clarify the role of ADAM-17 in bone destruction of RA. Here, we examine the role of ADAM-17 in proliferation of RA osteoblast (HOB). [Methods] To examine the expression of ADAM-17 in RA-HOB, RA-HOB were stimulated with concentration adjusted TNF- α at 24 hours and measured using ELISA. To determine ADAM-17 expression in RA-HOB lysate, western blotting (WB) was also performed. To confirm the presence of ADAM-17 on RA osteoblasts, immunostaining was performed. Finally, in order to examine the role of ADAM-17 in osteoblasts growth, cell proliferation assay was performed. [Results] ADAM-17 was expressed in TNF- α stimulated RA-HOB conditioned medium, which was significantly higher compared to non-stimulated RA-HOB conditioned medium. We also found that ADAM-17 expression in RA-HOB by using immunostaining and WB. Using siRNA assay, ADAM-17 in RA-HOB was suppressed. In the osteoblast deficient in ADAM-17, the proliferation ability of the cell was decreased by 13%. [Conclusions] In this study, we showed the role of ADAM-17 in RA-HOB proliferation, suggesting the possibility that it plays an important role in bone destruction in RA.

P1-033

IL-6 induces the resistance for apoptosis-induction via circadian clock gene *Hlf* in synovial cells

Yuto Oketani¹, Koto Uchida¹, Kohjin Suzuki¹, Kenta Kaneshiro¹, Kanta Morii¹, Arisa Yaekura¹, Ikumi Okumura¹, Kohsuke Yoshida¹, Yoshiko Kawasaki², Koji Tateishi³, Yasuhiro Terashima^{1,3}, Nao Shibamura⁴, Yoshitada Sakai⁵, Akira Hashiramoto¹

¹Department of Biophysics, Division of Clinical of Immunology, Kobe University Graduate School of Health Sciences, Kobe, Japan, ²Department of Rheumatology, Kobe Kaisei Hospital, Kobe, Japan, ³Department of Orthopaedic Surgery/ Rheumatology, Kohnan Kakogawa Hospital, Kakogawa, Japan, ⁴Department of Orthopaedic Surgery, Kobe Kaisei Hospital, Kobe, Japan, ⁵Department of Rehabilitation Science, Kobe University Graduate School of Medicine

Conflict of interest: None

[Object] Interleukin-6 (IL-6) is responsible for the pathogenesis of rheumatoid arthritis (RA), however, the detailed mechanism how it effects on synovial hyperplasia remains unclear. We've reported the relation between the growth activity of RA fibroblast-like synoviocytes (RA-FLS) and clock genes. In this study, we explored the effect of IL-6 on dexamethasone (DEX)-induced apoptosis of RA-FLS. [Methods] Synovial cells were treated with or without DEX (10,100,300,500 μ M:24 hr) and examined cellular viabilities by WST-8. Synovial cells were treated with or without IL-6/sIL-6R (100 ng/ml:48 hr) and DEX (10 μ M:24 hr) to examine cellular viabilities by WST-8, expressions of PARP by western blotting and *Hlf/Tef/Dbp/Bik* by qPCR. [Results] DEX decreased cell viabilities dose-dependently, which was disturbed by IL-6/sIL-6R pretreatment. IL-6/sIL-6R inhibited cleavages of PARP, and suppressed the expressions of circadian transcriptional factor *Hlf* and pro-apoptotic factor *Bik*. [Conclusions] Results suggested that IL-6 induces the resistance for apoptosis via clock genes in RA-FLS.

P1-034

Analysis of inflammatory cytokine levels produced from M1/M2 macrophages in AOSD

Hideto Nagai¹, Yohei Kirino¹, Hiroto Nakano¹, Ryusuke Yoshimi¹, Yosuke Kunishita¹, Naomi Tsuchida¹, Naoki Hamada¹, Yutaro Soejima¹, Takaaki Komiya¹, Reikou Kamiyama², Daiga Kishimoto², Natsuki Sakurai², Masaki Mitsuhashi², Yuki Iizuka², Chiharu Hidekawa², Yuji Yoshioka⁴, Yumiko Sugiyama³, Kouji Kobayashi³, Takeaki Uehara⁵, Shigeru Ohno³, Shohei Nagaoka⁴, Hideaki Nakajima^{1,2}

¹Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan, ²Department of Hematology and Clinical Immunology, Yokohama City University School of Medicine, ³Rheumatic Diseases Center, Yokohama City University Medical Center, ⁴Department of Rheumatology, Yokohama Minami Kyousai Hospital, ⁵Department of Rheumatology, Chigasaki Municipal Hospital

Conflict of interest: None

[Object] Adult-onset Still's disease (AOSD) is an auto-inflammatory disease primarily caused by macrophage (M Φ) activation. M Φ can be categorized into inflammatory M1 or anti-inflammatory M2 subsets, but these functions in AOSD remain unknown. We here investigated cytokine productions in polarized macrophages from AOSD. [Methods] Monocytes separated from pre-treatment, remission AOSD patients and healthy donors (HCs) were stimulated with GM-CSF or M-CSF for 9 days. After 9-day culture, some of them were stimulated with toll-like receptor (TLR) ligands such as LPS, poly (I:C) and imiquimod. Levels of 13 inflammatory cytokines were simultaneously measured using a cytokine bead array. [Results] 16 AOSD (6 men, 10 female, mean age; 49.3 (man), 59.7 (female)) and 11 HCs participated. All patients fulfilled Yamaguchi's criteria. The mo-Pouchot score ranged from 0 to 8 (mean \pm SD;1.8 \pm 2.6). We found that IL-1b, IL-6, IL-18, IL-23, TNFa levels in supernatants M1 or M2-cultured dish from AOSD were statistically lower compared to HCs. M2 produced more IL-6 compared with M1. In patients in remission, cytokine production levels recovered to normal. [Conclusions] The multiple inflammatory cytokine productions of M1/M2 M Φ were significantly lower than HCs. Further research is needed for finding the reason.

P1-035

Histopathological changes of synovial tissue in rheumatoid arthritis patients treated with TNF inhibitors

Yoshinori Takashima¹, Koji Fukuda¹, Shinya Hayashi¹, Tomoyuki Kamenaga¹, Ryosuke Kuroda¹, Marowa Hashimoto³, Keiko Funahashi^{2,3}, Tsukasa Matsubara^{2,3}

¹Department of Orthopedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan, ²Matsubara Mayflower Hospital, Kato, Japan, ³Research Institute of Joint Disease, Kobe, Japan

Conflict of interest: None

[Object] Tumor necrosis factor (TNF)- α is one of pro-inflammatory cytokines that play an important role in pathogenesis of rheumatoid arthritis (RA). TNF inhibitors have been suggested to induce apoptosis in TNF-producing cells resulting in suppression of synovitis. In this study, we demonstrated the distribution of apoptosis cells in synovium obtained from treated RA patients histologically to reveal the action site of TNF inhibitor. [Methods] Synovial tissues were obtained from 20 RA patients, including 3 patients treated with TNF inhibitors. The sections were stained by hematoxylin and eosin (HE), or TdT-mediated dUTP nick end labeling (TUNEL). [Results] In the sections stained with HE, the formation of discoid fibrosis and the other characteristic changes were found in sublining layers of RA synovium treated with TNF inhibitors. In the sections with TUNEL stain, apoptosis of lining cells around the discoid fibrosis was detected. [Conclusions] In this study, we demonstrated the apoptosis of lining cells around the discoid fibrosis. These results indicated that TNF inhibitors might induce apoptosis of synovial cells (especially lining cells) leading to suppress RA synovitis.

P1-036

The effect of ACPA derived from RA patient's B cell in the activation of osteoclastogenesis

Kazuhisa Ouhara¹, Syuichi Munenaga¹, Shintaro Hirata², Eiji Sugiyama², Hidemi Kurihara¹

¹Department of Periodontal Medicine, Hiroshima University, Graduate School of Biomedical & Sciences, ²Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital

Conflict of interest: None

[Object] Rheumatoid arthritis (RA) is the autoimmune and chronic disease caused by the genetic and environmental factors. The pathogenesis of RA is the increase of citrullinated protein and anti-cyclic citrullinated peptide antibody (ACPA). However, the effect of ACPA in the progression of joint disruption is still unclear. In this study, to clarify the mechanism of RA pathogenesis by increasing ACPA, CCP1-Ab generated from RA patient's B cell was applied into RA model mouse. [Methods] RA model mouse was established by injecting of laminarin to induce joint inflammation. At the same time, CCP1-Ab or control antibody was applied intravenously. After 6 weeks of CCP1-Ab application, arthritis score of joint, IL-6 level in serum and joint, microCT analysis were per-

formed. Bone marrow mononuclear cell (BMC) was also cultured in the presence of CCP1-Ab with sRANKL and M-CSF to determine the osteoclastogenesis. [Results] The severe joint swelling was observed in the addition of CCP1-Ab in mouse model. The increase of arthritis score, IL-6, and bone resorption were observed. The activation of osteoclastogenesis was also shown in the presence of CCP1-Ab. [Conclusion] The possibility of the involvement of ACPA in the progression of RA in mouse model was observed.

P1-037

Novel multiple heterozygous NUDT15 variants caused an azathiopurine-induced severe alopecia, tongue ulcer and leukopenia in a systemic lupus erythematosus patient: Case report

Mizuna Otsuka, Tomohiro Koga, Remi Sumiyoshi, Momoko Okamoto, Yushiro Endo, Sosuke Tsuji, Ayuko Takatani, Toshimasa Shimizu, Takashi Igawa, Shin-ya Kawashiri, Naoki Iwamoto, Kunihiro Ichinose, Mami Tamai, Hideki Nakamura, Tomoki Origuchi, Atsushi Kawakami
Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: None

Serious adverse events of treatment with AZA are leukopenia and alopecia. Recent studies have shown that *NUDT15* R139C was strongly associated with thiopurine-induced leukopenia among Asian populations. A 57-years-old Japanese man presented a tongue ulcer and slight fever 4 weeks after the introduction of AZA for the treatment of SLE. He was admitted to our department since laboratory data showed severe neutropenia and high level of CRP. After admission, we stopped AZA and initiated daily injection of G-CSF, but his tongue ulcer was not improved, and neutropenia had been sustained for 3 weeks. In addition, although alopecia of the patient was not clear at admission, it progressed a total alopecia 3 weeks after admission. A genetic analysis revealed multiple heterozygous mutations in exon 3 of the *NUDT15* gene (R139Y). Homozygous mutation of R139C in the *NUDT15* gene is known to result in severe neutropenia and total alopecia similar to this case, but with heterozygous mutation of R139C, a clinical course is relatively mild. This case suggests that genetic testing of *NUDT15* is useful for predicting the severity of AZA adverse events and that *NUDT15* R139Y heterozygous mutations associated with higher AZA-induced toxicity than a *NUDT15* R139C heterozygous mutation.

P1-038

Factors that correlate with creatinine cystatin-C ratio

Ichiro Yoshii¹, Tatsumi Chijiwa², Naoya Sawada³

¹Rheumatology and Musculoskeletal Medicine, Yoshii Hospital, ²Department of Rheumatology, Kochi Memorial Hospital, ³Department of Rheumatology, Dohgo Spa Hospital

Conflict of interest: None

[Object] Relationships between creatinine cystatin-C ratio (C/C ratio), that is estimated reflection of muscular power, and other factors were evaluated statistically. [Methods] From May to September 2018, C/C ratio was measured from 426 subjects. Relationship between C/C ratio and age, sex, body mass index (BMI), cystatin-C (CysC), creatinine kinase (CK), red blood cells (RBC), bone mineral density in lumbar spine and femoral neck (BMD-LS and BMD-FN), suffering rheumatoid arthritis (RA), Barthel Index (BI), were evaluated statistically with single mode linear regression analysis. Statistical significance was set within 1%. [Results] Aging, being female, and CysC correlated significantly with C/C ratio negatively, while CK, RA, BI score, and BMD-FN demonstrated positive correlation. Influence of aging is more evident in female than in male. BMI and BMD-LS demonstrated no significant correlations. [Conclusions] C/C ratio is suggested that reflects muscle volume. This index is also suggested the correlation with activities of daily living. BMD demonstrated significant correlation with C/C ratio in femur, but not in lumbar spine, where is influenced by other factors predominantly. From these results, C/C ratio candidates as one index for reflection of RA treatment effects.

P1-039

Attempt of optimal use of infliximab by Remicheck Q

Hidekazu Futami, Kazuyuki Ishijima, Keiko Umemiya, Yoshihiro Oya, Takuya Nakazawa, Ryutaro Matsumura
Center of Rheumatology, Allergy and Clinical Immunology, National Hospital Organization Chiba East National Hospital

Conflict of interest: None

[Object and Methods] During the treatment of infliximab, for the case requiring reexamination of therapy due to ineffectiveness, we performed Remicheck Q, and examined the results of the examination of those cases and clarified whether it was effective for selection of therapy. [Results] For 18 patients receiving infliximab, the Remicheck Q inspection was carried out. A positive result was obtained at 85% in 12 cases of rheumatoid arthritis, 3 cases of Behcet's disease, 2 cases of psoriatic arthritis, 1 case of ankylosing spondylitis disease. There were also 5 cases using biosimilars, and in cases with clinical effect, all cases were positive. Among the eight patients with insufficient clinical effect, 5 cases were positive in Remicheck Q, 3 cases required switching to other biological products. Three cases of Remicheck Q negative, 2 cases became positive for Remicheck Q by increasing infliximab. [Conclusions] Remicheck Q examination for patients receiving infliximab is thought to provide valuable information for treatment changes, especially for ineffective cases. Although it had insurance problems, it was suggested that it is a useful test for biosimilar usage cases.

P1-040

The diagnostic utility of IgG rheumatoid factor (IgG-RF) and anti-agalactosyl IgG antibody (CA-RF) in rheumatoid arthritis (RA)

Moemi Miyazaki, Kenshi Inoue, Naofumi Dobashi, Kenta Misaki
Department of Rheumatology, Kita-Harima Medical Center

Conflict of interest: None

Object: Serum RF and anti-cyclic citrullinated peptide antibody (ACPA) are commonly applied to diagnose RA. However, there's no established diagnostic marker for seronegative RA. Here, we investigated the utility of serum IgG-RF and CA-RF in the clinical situation of diagnosis of RA. Methods: We retrospectively analyzed 202 patients who visited Rheumatology department at our medical center due to arthralgia. Serum IgG-RF and CA-RF were measured between April and September 2016 as their first visit examination. ROC analysis was performed to evaluate the sensitivity, specificity and cut-off value of these two markers. 2010 ACR/EULAR-RA classification criteria was adapted to diagnose RA. Results: Two-hundred two patients (M: 66, F: 136, mean age: 60.8 years old) were included in this study, and 60 patients (29.7 %) were diagnosed as RA. Sensitivity and specificity of IgG-RF and CA-RF were Sen: 70.0 %. Spe: 73.2 % (PPV: 52.5 %, NPV: 85.2 %) and Sen: 73.3 %. Spe: 81.7 % (PPV: 62.9 %, NPV: 87.9 %) respectively. AUCs and cut-off values of IgG-RF and CA-RF were AUC: 0.740, cut-off: 1.85 and AUC: 0.817, cut-off: 16.1 AU/mL respectively. Conclusions: Serum IgG-RF and CA-RF could be useful markers as an adjunct to the diagnosis of RA as mentioned above.

P1-041

Anti-citrullinated protein antibodies are low affinity and cross-reactive

Akihisa Haraguchi¹, Hisakata Yamada^{1,2}, Masakazu Kondo², Toshifumi Fujiwara¹, Takahide Sakuragi¹, Tomoko Tsutsui¹, Yasuharu Nakashima¹
¹Kyushu University, ²Kondo Clinic of Rheumatology and Orthopaedic Surgery

Conflict of interest: None

[Object] Anti-citrullinated protein antibodies (ACPAs) are specifically produced in rheumatoid arthritis (RA). It has been reported that avidity of some ACPAs are lower than that of foreign antigen-specific antibodies, but it is unclear whether 1) low avidity is common to all ACPAs, 2) low avidity is a general feature of autoantibodies, or 3) the differences in affinity associates with cross-reactivity among ACPAs. To address these issues, we measured affinity of various antibodies including ACPAs and

other autoantibodies. [Methods] Antibodies in the serum from RA patients were detected by ELISA. Binding avidity was measured by adding NaSCN to the assay. Cross-reactivity was measured by pre-incubation of the serum with the competitor peptides. [Results] All ACPAs, including anti-CCP, and anti-citrullinated fibrinogen (cFib), a-enorase (cEno), and histone H3 (cHis), were low avidity compared to antibodies against foreign antigens, whereas other autoantibodies, including anti-SS-A and TPO antibodies, were comparably high avidity. There was a cross-reactivity among ACPAs in most cases, and the binding to cEno was overwhelming [Conclusions] Self tolerance might not be the reason for the low avidity of ACPAs. A relationship between avidity and cross-reactivity of ACPAs was suggested.

P1-042

Serum cystatin C is associated with older age, TAC use, higher ESR but not with DAS28 in RA patients with normal eGFR

Shuzo Yoshida¹, Yuko Kimura¹, Akitoshi Machida², Nobuhisa Shibahara³
¹Department of Immuno-Rheumatology Center, Arisawa General Hospital, Hirakata, Osaka, Japan, ²Department of Orthopedic Surgery, Arisawa General Hospital, Hirakata, Osaka, Japan, ³Department of Urology, Arisawa General Hospital, Hirakata, Osaka, Japan

Conflict of interest: None

[Object] To evaluate the association of serum cystatin C (CyS-C) with disease activity in RA patients with normal eGFR. [Methods] We retrospectively assessed the association of CyS-C with patient background and disease activity including CRP, ESR, and DAS28 in RA patients with normal eGFR. [Results] One hundred patients with RA were evaluated. Sixty-nine patients were normal eGFR (eGFR >60 mL/min/1.73 m²). In the patients with normal eGFR, the mean age was 65.8±13.1 years, mean disease duration was 9.3±9.6 years, and mean DAS28-CRP was 2.61±1.38. Forty-one patients administered MTX, 12 patients TAC, and 20 patients PSL. Thirty-three patients were elevated CyS-C. CyS-C elevated group significantly older age, higher CRP, higher ESR. However, no differences were observed between elevated CyS-C group and normal CyS-C groups in DAS28-CRP. In multiple logistic regression analysis, older age, higher ESR, and TAC use was identified as independent predictors of factors for elevated CyS-C. [Conclusions] The results of this study indicated that older age, TAC use, and higher ESR associated with elevated serum CyS-C in RA patients with normal eGFR.

P1-043

Measurement of human high affinity immunoglobulin gamma Fc receptor I (FCGR1A) concentrations in serum and plasma and comparison with neutrophil CD64 by flow cytometry in patients with infection

Akiko Komiya¹, Akito Tominaga², Kako Kodama², Takuya Kakutani², Koichiro Horie², Shinichi Nogi², Kanako Iwata³, Hirota Tsuno², Hideki Ogihara², Tatsuoh Ikenaka⁴, Takahiro Nunokawa^{2,5}, Atsushi Hashimoto², Shigeto Tohma⁶, Toshihiro Matsui^{1,2}

¹Department of Clinical Laboratory, National Hospital Organization Sagami-hara National Hospital, Kanagawa, Japan, ²Department of Rheumatology, National Hospital Organization Sagami-hara National Hospital, ³Department of Rheumatology, Clinical Research Center for Allergy and Rheumatology, National Hospital Organization Sagami-hara National Hospital, ⁴Department of Rehabilitation, National Hospital Organization Sagami-hara National Hospital, ⁵Department of Emergency, National Hospital Organization Sagami-hara National Hospital, ⁶National Hospital Organization Tokyo National Hospital

Conflict of interest: None

[Object] Recent studies have shown that quantifying CD64 (Fc gamma RI) on neutrophils by flow cytometer is a useful diagnostic marker of infection. On the other hand, the establishment of a serological diagnostic test is also desired for ease of sample storing. In this study, we investigated the serum and plasma levels of Human high affinity immunoglobulin gamma Fc receptor I (FCGR1A) in patients with infection to determine the usefulness for detecting infectious disease. [Methods] FCGR1A were detected in the sera and plasma using ELISA kit from patients with infection before treatment with antibiotics. We also measured neutrophil

CD64 expression quantitatively by flow cytometry. Cut-off point for CD64 positivity was 2000 molecules/cell as defined in our previous study. Correlation was evaluated by Spearman's rank correlation coefficient testing. [Results] The expression level of neutrophils CD64 from 66 patients with infection in active phase was 5540.3 ± 427.88 molecules/cell (mean \pm SEM). Correlation of CD64 expression on neutrophils with serum CD64 was -0.1764 ($p = 0.1565$) and -0.1645 with plasma CD64 ($p = 0.1869$). [Conclusions] In this study, there is no statistical correlation between CD64 on neutrophils and CD64 in sera and plasma in patients with infection.

P1-044

How could the change of medication affect preoperative blood examination in patients with rheumatoid arthritis planning surgical treatment of lower limb ?

Ryo Okabayashi¹, Motohiro Suzuki¹, Tetsuya Ichikawa³, Tetsuyuki Nagafusa⁴, Eiji Torikai², Shigeyuki Miyamoto³, Yukihiro Matsuyama¹

¹Department of Orthopedics, Hamamatsu University School of Medicine,

²Department of Orthopedics, Iwata City Hospital, ³Department of Orthopedics, Narita Kinen Hospital, ⁴Department of Rehabilitation, Hamamatsu University School of Medicine, ⁵Department of Orthopedics, Kikugawa City Hospital

Conflict of interest: None

[Object] Medication for rheumatoid arthritis (RA) has been changed drastically after appearance of methotrexate (MTX) and biologics (Bio). The purpose of this study is to investigate the effect of medication such as MTX and Bio for the blood examination data in RA patients especially planning surgical treatment of lower limb. [Methods] During 1990 to 2017, 63 patients underwent total knee arthroplasty or forefoot arthroplasty. We classified this period into 4 subgroups (group A: before 1999 that MTX was not permitted in Japan, group B: 1999 to 2002 that MTX was permitted and Bio was not permitted, group C: 2002 to 2010 that the first stage of Bio, group D: 2010 to 2017 that the second stage of Bio). We evaluated the preoperative datum of laboratory findings such as 1 hour-ESR, AST, ALT, BUN, creatinine, total protein, albumin, and CRP. [Results] Mean ESR (mm/h) was lower in group D than in group A and B (A: 65.8, B: 61.2, C: 40.1, D: 29.7). Mean CRP (mg/dl) was significantly lower in group B, C and D than in group A (A: 4.24, B: 1.2, C: 0.95, D: 0.4). There were no differences of other data items in these groups. [Conclusions] We can perform surgical treatment such as TKA and/or forefoot arthroplasty in well controlled inflammatory condition of RA since post-marketing of MTX.

P1-045

A temporal artery ultrasonography image of the giant cell-related arteritis and histologic examination

Yukie Saito¹, Yuji Uzawa², Yuji Yoshioka², Daisuke Kanai², Akiko Suda², Shohei Nagaoka²

¹Yokohamaminamikyousai Hospital, ²Yokohamaminamikyousai Hospital

Conflict of interest: None

[Object] The giant cell-related arteritis (GCA) features the permeation of the many nuclei giant cell pathologically and is the disease that inflammation happens in all layers characteristics. It enforced sonography (US) and examined US image and the biopsy result of the case that enforced superficial temporal artery biopsy. [Method] I met a temporal arteritis classification standard of ACR in 1990 and examined a medical record base in 13 cases that carried out temporal artery US and neither biopsy with collagenosis rheumatism internal medicine by December, 2017 from January, 2015. I estimated having adventitial vascular wall thickening or not as an inner media and compared the wall thickening part of US with the biopsy result. [Result] Five men, average age 77.9 ± 8.6 years old, inspection from mean CRP 15.3 ± 8.0 mg/dl, mean ESR 91.1 ± 26.5 mm/hr, the onset was an average of 31.0 days. I examined the factor which affected the positive rate, but there was not the meaningful item. [Conclusion] The thickening of the vascular wall accepted it in all cases by the temporal artery biopsy, but was not able to detect 2 cases (15%) of those in US. In US, the possibility with the case that sensitivity was insufficient of vascular wall thickening views was suggested for a

GCA diagnosis.

P1-046

Anti-interleukin-10 antibody in systemic lupus erythematosus

Marina Uchida, Seido Ooka, Kanako Suzuki, Yutaka Goto, Hisae Fujimoto, Kana Ishimori, Hiromi Matsushita, Kimito Kawahata
St. Marianna University School of Medicine

Conflict of interest: None

[Object] Cytokines contribute to various manifestations of systemic lupus erythematosus (SLE). Although antibodies against cytokines are known to be present in SLE, there have been few studies which have determined the presence of anti-IL-10 antibody. Therefore, we assayed anti-IL-10 antibody in SLE and examined the clinical significance. [Methods] We performed a retrospective study of 80 Japanese patients with SLE. Sixteen scleroderma patients, 19 rheumatoid arthritis (RA) patients, 23 Behcet's disease patients, and 23 healthy subjects were selected as control groups. Clinical information was abstracted from medical records. Anti-IL-10 antibody level was determined with an enzyme-linked immunosorbent assay. [Results] Fourteen patients with SLE were found to be anti-IL-10 antibody-positive. Absorbance was significantly higher in serum from patients with SLE and RA than in healthy individuals. In SLE, patients with low complement values were significantly more common in the antibody-positive group. Serum IgG levels were significantly higher in the antibody-positive group. [Conclusions] The present study found that anti-IL-10 antibody is present in SLE and related to clinical parameters. These results suggest that anti-IL-10 antibody may be involved in part of the disease process of SLE.

P1-047

Study on synovitis and enthesitis of distal phalange using joint ultrasonography in patients with finger pain or stiffness

Shigenori Tamaki¹, Takashi Kato², Motokazu Kai³, Kunikazu Ogawa³, Hisaji Oshima⁴, Ikuko Tanaka¹

¹Nagoya Rheumatology Clinic. Nagoya, Japan, ²Department of Radiology, National Center for Geriatrics and Gerontology, Obu, Japan, ³Mie Rheumatology Clinic. Suzuka, Japan, ⁴Department of Connective Tissue Disease. Tokyo, Japan, Tokyo Medical Center

Conflict of interest: None

[Object] Since enthesitis of distal phalange often accompanies tendinitis and manifests symptoms such as finger stiffness and pain, it is necessary to distinguish from rheumatoid arthritis (RA). We observed all distal phalanges in joint US and prospectively studied the utility of US in differentiating between synovitis and enthesitis. [Methods] 130 patients with finger symptoms (50.9 ± 4.2 years old) who showed no RA change by X-ray were examined. All spine and sacroiliac joint X-ray was further evaluated with 50 inflammatory back pain cases. [Results] Enthesitis was found in 67% of all cases and was significantly higher than 52% of synovitis ($p = 0.016$). RF was positive in 32% of enthesitis, 37% in synovitis, ACPA was positive in 25% of enthesitis and 32% in synovitis. In 50 cases spine and sacroiliac joint X-ray was taken, paraspinal bone formation was found in 60% and sacroiliac joint findings according to the ankylosing spondylitis (AS) New York Criteria were found at 66%. [Conclusions] In cases finger stiffness and pain, enthesitis of distal phalange was observed more frequently than synovitis. There was the possibility of spondyloarthritis including AS, and it was considered that US examination including the distal phalange was necessary.

P1-048

Study of disease assessment for rheumatoid arthritis based on joint ultrasonography

Mihoko Henmi, Akihiro Narita, Atsuhiko Sugimura, Fumihiko Sakamoto, Yuko Aoki, Akemi Kitano, Takeya Ito, Toshiyuki Hattori, Norifumi Sawamukai, Masato Isobe, Jun Fukae, Megumi Matsushashi, Akio Mitsuzaki, Masato Shimizu, Kazuhide Tanimura, Takao Koike
Hokkaido Medical Center for Rheumatic Diseases, Sapporo, Japan

Conflict of interest: None

[Object] Several studies reported about different methods of disease assessment for rheumatoid arthritis (RA) based on joint ultrasonography (US), however, there has been no standard method. In a recent report, the OMERACT-EULAR-Ultrasound Task Force published data on the Global OMERACT-EULAR Synovitis Score (GLOESS) which was combination of semi-quantitative gray scale (GS) and power Doppler (PD) scoring for 2-5MCP joints. We compared performance of our US-22joints with GLOESS. [Methods] We studied 1870 joints of 85 patients with RA. Our US-22joints method targeted 1-5MCP, 1-5PIP and wrist joints. We evaluated each joint according to semi-quantitative GS, PD scores and quantitative measurement of synovial vascularity (Vs) then calculated sum of each score for 22 joints. The GLOESS was calculated according to the previous report (D'Agostino et al. *ARD* 75, 2016). [Results] There showed significant relationship between GLOESS and US-22joints (GS, PD and Vs). There were low relationship between DAS28-CRP and GLOESS also US-22joints. [Conclusions] Our results revealed that there was significant relationship between GLOESS and US-22joints. Our US-22joints could be as useful as GLOESS to assess disease activity of RA.

P1-049

Evaluation of Direction of Probe in Ultrasound Sonography of 1st and 5th Metatarsal Phalangeal Joints in Patients with Rheumatoid Arthritis

Hiroko Minamoto¹, Yuji Hirano², Daisuke Kihira²

¹Department of Clinical Laboratory, Toyohashi Municipal Hospital, ²Department of Rheumatology, Toyohashi Municipal Hospital

Conflict of interest: None

[Object] Ultrasound sonography (US) is important in examination of rheumatoid arthritis (RA). Although decreasing of examination joints can save time, risk of missing pulse dopplar (PD) or bone erosion (ERO) should be considered. This study evaluated direction of probe in US examination on 1st and 5th MTP joints in RA patients. [Methods] 120 RA patients in whom US were performed from Jan-Aug in 2018 were used in this study. Detection rates of PD and ERO in 1st and 5th MTO joints were compared. [Results] Patients characteristics: 88 female and 62 male. Mean age was 60.9 years old. RA duration was 7.5 years. Meas DAS28-CRP was 2.8. Mean mHAQ was 0.35. Detection rates of PD: Positive in 16.3% at 1st MTP and 15.8% at 5th MTP from the saggital view. Positive in 13.8% at 1st MTP and 11.7% at 5th MTP from the side view. Detection of ERO: Positive in 1.3% at 1st MTP and 1.3% at 5th MTP from the saggital view. Positive in 10.4% at 1st MTP and 15.4% at 5th MTP from the side view. [Conclusions] Although there were not so much differences in detection rates of PD between the saggital view and the side view, there were differences in detection rates of ERO.

P1-050

Validation of a novel automatic software for evaluating sonographic synovitis in rheumatoid arthritis

Kei Ikeda¹, Yuki Matsumoto², Takahiro Sugiyama¹, Manami Kato¹, Tadamichi Kasuya¹, Takashi Kumagai¹, Kazumasa Suzuki¹, Hiroki Furuya¹, Masashi Fukuda¹, Aiko Saku¹, Sohei Makita¹, Takashi Itoh¹, Mieko Yamagata³, Shunsuke Furuta¹, Hiroshi Nakajima¹

¹Department of Allergy and Clinical Immunology, Chiba University Hospital, ²Corporate R&D Headquarters, KONICA MINOLTA, INC., ³Department of Rheumatology, National Hospital Organization Shimoshizu National Hospital

Conflict of interest: Yes

[Objective] We aimed to validate the accuracy and utility of a novel automatic software in evaluating sonographic synovitis. [Methods] We recruited 20 rheumatoid arthritis (RA) patients who underwent ultrasound for evaluating synovitis. We scanned the PIP joints, MCP joints, midcarpal joint, radiocarpal joint, and distal radioulnar joint, bilaterally, and stored the image representing the most severe synovitis in each joint region. We evaluated these stored images by semiquantitative grading (0-3) and a novel automatic software for gray-scale (GS) synovial hypertrophy and synovial power Doppler (PD) signals and analyzed their correlations. [Results] 15 patients were women with mean age 65.0 year-old, mean disease duration 6.1 years, mean SDAI 19.7, mean total GS score 39.9,

and mean total PD 10.6. Correlation coefficients between GS score and software-based synovial hypertrophy area were 0.67 for the PIP joints, 0.70 for the MCP joints, and 0.76 for the wrist joints, whereas those between PD score and software-based ratio of synovial PD signal area were 0.84 for the PIP joints, 0.79 for the MCP joints, and 0.69 for the wrist joints. [Conclusions] Automatic evaluation of synovitis by a novel software correlated well with conventional semiquantitative evaluation in active RA.

P1-051

Ultrasonographic evaluation of the toe joint in patients with rheumatoid arthritis

Atsushi Nagata¹, Yasuhide Kanayama², Hitomi Nagasaka¹

¹Department of Clinical Technology, Toyota Kosei Hospital, Toyota Japan, ²Department of Orthopedic Surgery and Rheumatology, Toyota Kosei Hospital, Toyota Japan

Conflict of interest: None

[purpose] Examine an existence views rate of the toe joint in the joint echo in the rheumatic. [Object] I intended for 150 cases that enforced an echo in a diagnosis of RA or a disease activity evaluation purpose during from April to June in 2018. [Methods] I followed «joint echo imaging law guidelines» with 36 places of 32 joints of both sides MCP, PIP, wrist, MTP and evaluated GS, PD in grade 0-3. In 150, I examined The following items about 115 cases that enforced an echo for 35 diagnosis purposes, disease activity evaluation purpose. (1) Existence views rate of 26 GS, PD every each joint which led to a diagnosis of RA in 35 (if there are views, I define $GS \geq 2$, $PD \geq 1$) (2) 115 if there are views [Results] patient background, 37 men, woman 113, average age were 60.9 years old. (1) $GS \geq 2$ MCP11 (42.3%), PIP9 (34.6%), wrist18 (69.2%), MTP21 (80.8%), $PD \geq 1$ MCP9 (34.6%), PIP7 (26.9%), wrist17 (65.4%), MTP12 (46.2%). (2) $GS \geq 2$ MCP47 (40.9%), PIP33 (28.7%), wrist62 (53.9%), MTP105 (91.3%), $PD \geq 1$ MCP42 (36.5%), PIP24 (20.9%), wrist74 (64.3%), MTP36 (31.3%). [Conclusions] It was 26 cases that led to a diagnosis of RA in the echo of the diagnosis purpose, and it was high, and, as for the PD incidence of the toe joint, it was thought that the observation of the toe joint was useful following a wrist.

P1-052

Analysis of subclinical synovitis by re-palpation after ultrasonography in patients with rheumatoid arthritis in clinical remission

Jun Ishizaki¹, Takuya Matsumoto¹, Koichiro Suemori¹, Eiji Sada², Katsuto Takenaka¹, Hitoshi Hasegawa¹

¹Department of Hematology, Clinical Immunology, and Infectious Diseases, Ehime University Graduate School of Medicine, Toon, Ehime, Japan, ²Department of Medical Technology, Ehime Prefectural University of Health Sciences

Conflict of interest: None

[Object] We examine whether subclinical synovitis is palpable by re-palpation after ultrasonography (US), and the differences in clinical significance between the palpable and non-palpable synovitis groups are analyzed. [Methods] In 55 patients archived in clinical remission, bilateral hand and finger joints were scanned using US, imaging the dorsal surface. Only each number of subclinical synovitis in three areas including the wrist (the radial, median and ulna side; 6 sites), the MCP and the first IP and 2-5th PIP joint was presented to the attending physician and palpation was performed. The Grey scale (GS) and power Doppler (PD) graded on a semi-quantitative scale (0-3) and the presence of spontaneous pain and joint destruction were compared in 2 groups. [Results] 18 patients (32.7%) had subclinical synovitis in 38 sites. 17 sites (44.7%, wrist 9/20, MCP 6/16, IP 2/2) were palpable by re-palpation after US. Synovitis with high GS grade was easy to palpate (G1: 3/11, G2: 10/22, G3: 4/5), but there was no difference by PD grade. There was no significant difference in the presence of spontaneous pain and bone erosion in 2 groups. [Conclusions] Our analysis suggested that about half of the subclinical synovitis found using US in remission patients is observable with palpation.

P1-053

Power Doppler ultrasound findings in Löfgren syndrome

Tomohisa Uchida¹, Keita Fujikawa¹, Akinari Mizokami¹, Atsushi Kawakami²

¹Department of Rheumatology, Japan Community Healthcare Organization, Isahaya General Hospital, Isahaya, Japan, ²Unit of Translational Medicine, Department of Immunology and Rheumatology, Unit of Advanced Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: None

Background: Löfgren syndrome is an acute form of sarcoidosis, which is characterized by a triad of arthritis, bilateral hilar lymphadenopathy (BHL), and erythema nodosum (EN). The prevalence of the syndrome is extremely rare in Japan. We evaluated our case by power Doppler ultrasound (PDUS) and compared the findings with previous reports. **Case report:** A 62 years-old female suffering from arthralgia of knee and ankle joints with EN-like rash and swelling of lower extremities was admitted to our hospital. The serum levels of ACE and lysozyme were elevated and BHL was identified on chest CT. FDG uptake in hilar lymph nodes and periarticular tissue was shown on PET-CT. In PDUS, the presence of subcutaneous edema with PD signals and slightly tenosynovitis was determined, and joint effusion of knee and ankle joints without synovitis was detected. Cutaneous biopsy supported EN and lung and lymph node biopsy revealed non-necrotic granuloma. She was diagnosed with Löfgren syndrome. Her symptoms improved after NSAID treatment. **Result:** PDUS findings in the present case were compatible with previous reports. **Conclusion:** In Löfgren syndrome, the PDUS findings of periarticular arthritis due to subcutaneous edema with hyperperfusion and tenosynovitis without synovitis will facilitate the diagnosis.

P1-054

A case of immune-mediated meningococcal arthritis with tenosynovitis confirmed by using joint ultrasonography

Hiroki Ikai, Hiroyuki Yoshida, Tatsuya Arai, Yoshihiro Nakamura, Fumiya Kitamura, Tsuyoshi Watanabe, Mari Yamamoto, Yukari Murai, Waka Kokuryo, Koji Takasugi, Naoho Takizawa, Yoshiro Fujita
Department of Rheumatology, Chubu-Rosai Hospital

Conflict of interest: None

A 20-year old woman had sore throat 2 weeks before her visit. She then developed fever and arthralgia from a day before admission. During the course, headache and dysuria, and urinary frequency did not appear. On examination, the temperature was 38.3°C. The both side of hand joints, elbow joints, and feet joints were erythematous and warm, and movement and palpation of these joints caused pain. The laboratory test showed leukocytosis of 11200 /mm³, normal serum creatinine and urinalysis, normal liver function tests, and CRP level was 7.37 mg/dl. Both blood and synovial cultures were negative. *Neisseria meningitidis* grew in pharyngeal culture. By using ultrasonography, we confirmed tenosynovitis of both hands. Treatment with ceftriaxone and NSAIDs led to improvement of arthritis and cutaneous lesions within one week with normalization of CRP level. Discussion Meningococcal arthritis has been described as a direct result of bacteremia or as a result of immune mediated mechanism that related to immune complex. (Medicine (2017)96:29) We diagnosed this case as immune-mediated arthritis because of no isolation of *N meningitidis* from blood nor synovial fluid and the onset after the course of pharyngitis. We report ultrasound findings of meningococcal arthritis here.

P1-055

The affected area and functional disorder among rheumatoid arthritis

Daisuke Ikuma, Naoki Sawa, Hiroki Mizuno, Akinari Sekine, Masahiro Kawada, Rikako Hiramatsu, Eiko Hasegawa, Noriko Hayami, Masayuki Yamanouchi, Tatsuya Suwabe, Junichi Hoshino, Kenmei Takaichi, Yoshifumi Ubara
Department of Rheumatology and Applied Immunology, Toranomon Hospital

Conflict of interest: None

[Object] To analyze the affected area associated with functional disorder among rheumatoid arthritis (RA). [Methods] We retrospectively studied 21 patients who had ultrasonography from July 2017 to Dec. 2017. We compared Health Assessment Questionnaire (HAQ) between patients with >1 power doppler (PD) in wrist extensor tendons, 1stMCP joints and wrist joints. [Results] There were no significant differences in HAQ between the patients with >1 PD in wrist extensor tendons and not ($P=0.39$). Moreover there were no significant differences in HAQ between the patients with >1 PD in 1stMCP joint and not ($P=0.37$). There were no significant differences in HAQ between the patients with >1 PD in wrist joint and not ($P=0.21$). [Conclusions] the affected area detected by ultrasonography were not associated with HAQ.

P1-056

Comparison of hand joint / shoulder joint echo findings and clinical features of tumor associated syndrome in our hospital

Shoichi Nawachi, Kazuya Matsumoto, Reika Hayashi, Ryutaro Yamanaka, Hidetoshi Kagawa
Department of Nephrology and Rheumatology, Japanese Red Cross Society Himeji Hospital

Conflict of interest: None

[Background] Differentiation between paraneoplastic syndromes (PRS) and rheumatoid arthritis (RA) / polymyalgia rheumatica (PMR) is sometimes difficult. There are few reports mentioning PRS. We examined the joint echo findings obtained in 5 cases of PRS while comparing with the clinical features. [Methods] Between April 2015 and September 2018, we investigate and examine five patients which shows significant findings (synovitis, bursitis and biceps tendon attachment flame) with joint echo and whose malignant tumors is found later. Regarding RA, we evaluate synovial membranes of both hands and fingers joints by grayscale (GS) and power doppler (PD). [Results] We obtained data of 5 patients (male / female: 3/2) and average age is 63.6 years [54, 82]. All of them, RF and anti-CCP antibody are negative. There is no significant difference in the site of arthritis. Four patients have already treated with PSL 5 mg/day or more before the first visit. Two patients diagnose with RA in our department and intervene therapeutically. Background disease of PRS is lung cancer in 3 cases and malignant lymphoma in 2 cases. All of them are advanced cancers of Stage III to IV. [Conclusion] It is difficult to distinguish between PRS and RA / PMR only by echocardiography.

P1-057

Pathology of residual synovitis and potential of controlling their inflammation in rheumatoid arthritis (preliminary report)

Jun Fukae¹, Akemi Kitano¹, Akihiro Narita¹, Mihoko Henmi¹, Fumihiko Sakamoto¹, Yuko Aoki¹, Masato Isobe¹, Norifumi Sawamukai¹, Toshiyuki Hattori¹, Akio Mitsuzaki¹, Takeya Ito¹, Masato Shimizu¹, Megumi Matsuhashi¹, Tamotsu Kamishima², Kazuhide Tanimura¹, Takao Koike¹
¹Hokkaido Medical Center for Rheumatic Diseases, ²Faculty of Health Sciences, Hokkaido University

Conflict of interest: None

[Background] Residual synovitis (R-synovitis) still remain in rheumatoid arthritis (RA) despite clinical remission. R-synovitis have risk of joint structural destruction and lead to generalized disease relapse in near future. We used imaging technologies and studied active synovitis and reported that osteitis strongly had relation to R-synovitis. We further observe sequential change of active-synovitis with osteitis and study that whether anti-rheumatic therapy + denosumab suppress change to R-synovitis or not. [Methods] We study patients with active RA and compare patients treated with DMARDs and DMARDs + denosumab. Clinical examination, joint magnetic resonance imaging and ultrasonography are performed sequentially. Metacarpophalangeal, proximal interphalangeal and wrist joints are observational targets. [Preliminary results] 13 patients were entered the study and ongoing (age 47-75, F/M=12/1, DAS28=median 5.4). [Discussion] In the previous report, we reported active synovitis + osteitis significantly lead to R-synovitis. Denosumab that suppress osteoclasts might control osteitis and then suppress change

to R-synovitis. We focused on synovitis-osteitis and continue the study.

P1-058

Photoacoustic imaging of synovium in rheumatoid arthritis

Koichi Murata^{1,2}, Moritoshi Furu^{1,2}, Hiromu Ito², Motomu Hashimoto^{1,3}, Masao Tanaka^{1,3}, Kohei Nishitani^{1,2}, Kosaku Murakami³, Tsuneyo Mimori³, Shuichi Matsuda²

¹Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ²Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ³Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Conflict of interest: Yes

[Object] Photoacoustic imaging is an emerging imaging modality based on photoacoustic effect. Image reconstruction of a photoacoustic wave emitted by absorption of light energy by nanosecond pulsed laser enables to visualize a blood vessel with high spatial selectivity. We have developed a new photoacoustic imaging device (PAI - 05) which is superior to existing ones at resolution of 0.2 mm in 3D image and will show the results of imaging of RA patients. [Methods] We used the wavelength of the laser light being 797 nm. Hands of six RA patients with finger joint pain or swelling (age: 50-83 years, 5 females, disease duration: 0.5 - 40 years, Stage: 1-4, DAS 28 (ESR): 2.1-6.4) were visualized. Results were compared with serological examination, disease activity, and ultrasound images. [Results] Regarding the superficial palmar artery, high resolution images was obtained. Regarding the deep part, the synovial membrane beneath the extensor tendon was poorly visualized, but a blood vessel image, which could be detected by ultrasound in a certain degree or more, was obtained in the area that was not obstructed by extensor tendons.

P1-059

Dynamic Contrast Enhanced Magnetic Resonance Imaging of Hand and Foot is Beneficial Diagnostic Tool in Rheumatoid Arthritis Diagnosis

Minami Matsuhashi¹, Ryuichi Nakahara², Masahito Watanabe¹, Shunji Okita¹, Yohei Kiso¹, Yoshihisa Nasu³, Keiichiro Nishida¹, Toshifumi Ozaki¹

¹Department of Orthopaedic Surgery Dentistry and Pharmaceutical Sciences, Okayama University, Okayama, Japan, ²Department of Intelligent Orthopaedic System, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Okayama, Japan, ³Department of Medical Materials for Musculoskeletal Reconstruction, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Okayama, Japan

Conflict of interest: None

[Object] The purpose of this study is to investigate the usefulness of our new MRI protocol evaluating bilateral hands and feet with one test. [Methods] First, we took T1-weighted (T1W), T2W, and after injection of dynamic and 3D dynamic scanning of hands with the head first prone position. Then, a patient was changed position to foot first supine, 3D dynamic and T1W of feet was taken. Retrospectively, we investigated 30 cases with undifferentiated arthritis (UA) who underwent our MRI protocol. 16 cases were diagnosed to be rheumatoid arthritis (RA), and 14 cases to be non-RA. The MRI findings including synovitis, tenosynovitis, and bone marrow edema were evaluated, and the prevalence of findings was compared between two groups. [Results] Synovitis in both hands and feet were detected in 75% patients of RA group (only in hands; 13% only in feet; 6%). In non-RA group, the proportion of them 43%, 0%, 7%. In RA group, five of seven patients who didn't fulfill the ACR/EULAR RA classification criteria showed significant MRI findings of feet. These MRI findings helped to start rheumatic treatment at early stage. [Conclusions] In this study, 81.8% of RA patients showed positive MRI findings in both hands and feet. Our MRI protocol can be a beneficial tool for diagnostic screening of rheumatic UA.

P1-060

Predictors of improved MRI findings in rheumatoid arthritis patients one year after treating with TNF inhibitors

Yasuhiro Kubota

Kubota Orthopedics and Rheumatology Clinic, Toyota, Aichi, Japan

Conflict of interest: None

[Object] This study aimed to examine the predictors of rheumatoid arthritis patients whose MRI findings improved one year after treating with TNF inhibitors. [Subjects] Subjects were 14 patients. Mean age was 50.3 years. TNF inhibitors used were: adalimumab (n=6), golimumab (n=6), etanercept (n=1), and infliximab BS (n=1). [Methods] Hand MRI were performed before and one year after treating with TNF inhibitors. Bone erosion, joint space narrowing (JSN), bone marrow edema, synovitis, and tenosynovitis were scored by RAMRIS. Those who had total MRI scores that improved by $\geq 20\%$ were assigned to the improvement group (group I), and the remaining patients were assigned to the non-improvement group (group N). Age, disease duration, stage, and baseline MRI score were assessed for both groups. [Results] The group I consisted of 7 patients with a mean disease duration of 31.4 months. The group N consisted of 7 patients with a mean disease duration of 79.6 months. Baseline MRI scores in the group I vs. the group N were as follows: mean bone erosion: 8.4 vs. 14.3, JSN: 4 vs. 31.4, bone marrow edema: 5.7 vs. 13.6, synovitis: 8.0 vs. 6.9, and tenosynovitis: 7.6 vs. 8.0. [Conclusions] The group I had low scores for baseline total MRI and JSN scores, and tended to have a shorter disease duration.

P1-061

Three cases which could evaluate disease activity of large vasculitis with DWIBS

Hidetoshi Matsuoka¹, Yuji Yoshida¹, Eri Oguro¹, Kentaro Kuzuya¹, Yasutaka Okita¹, Satoru Teshigawara¹, Maiko Yoshimura¹, Kentaro Isoda¹, Yoshinori Harada¹, Shiro Ohshima¹, Jun Hashimoto¹, Yukihiko Saeki²

¹Department of Rheumatology & Allergology, NHO Osaka-Minami Medical Center, ²Department of Clinical Research, NHO Osaka-Minami Medical Center

Conflict of interest: None

Large vasculitis is diagnosed from symptoms, blood tests, image findings. To prevent complications such as visual loss of giant cell arteritis and vasoconstriction / occlusion of Takayasu arteritis, diagnosis at an early stage and image inspection for detection of vascular stenosis / occlusion / dilation and aneurysm is very important. Although contrast CT is a useful test, it has problems of radiation exposure and contrast medium. The imaging range is limited for MRI and ultrasound. DWIBS is a whole body MRI using a diffusion weighted image in the imaging method announced in 2004. It is an examination spreading in the area of malignant tumor and it is reported that finding similar to FDG - PET can be obtained in the tumor area, and whole - body screening is possible without cheap, no exposure, no drug administration. We report three cases in which DWIBS was useful for evaluation and activity evaluation of large-scale vasculitis at our hospital and follow-up follow-up.

P1-062

Association between bone marrow lesion in preoperative knee MRI of patient undergoing total knee arthroplasty and symptom and function of the knee joint

Daisuke Hamada, Tomohiro Goto, Koichi Sairyo

Department of Orthopedics, Tokushima University Graduate School

Conflict of interest: None

[Object] Bone marrow lesion (BML) is observed as ill-defined hypointensity area in T1 weighted images and hyperintensity area in STIR or fat suppressed T2 weighted images of the MRI. The association between BML and knee pain has been reported. However, the number of studies that examined the extent of BML and symptom and function of the knee before total knee arthroplasty is still limited. The purpose of this study is to examine the association between BML in preoperative MRI of

the patient undergoing total knee arthroplasty and the symptom and function of the knee joint. [Methods] Eighty-two knees in 64 patients who underwent TKA and was performed preoperative MRI since 2014 was included. The extent of BML is scored using MRI Osteoarthritis Knee Score (MOAKS). The knee symptom and function were evaluated using 2011 Knee Society Score (KSS). The correlation between BML score and each item of the KSS was examined. [Results] BML score was correlated with the objective evaluation score that indicated preoperative alignment and range of motion. No significant correlation was found in other KSS items. [Conclusions] Unexpectedly, there was no correlation between symptom and BML score and significant correlation was found between objective evaluation and BML score.

P1-063

Usefulness of high-resolution magnetic resonance vessel wall imaging for diagnosis of cerebral vasculitis in SLE

Mayuko Fukushima, Shunichi Fujita, Takahiko Akagi, Hiroshi Sawachika, Tomoyuki Mukai, Yoshitaka Morita
Department of Rheumatology, Kawasaki Medical School, Kurashiki, Japan

Conflict of interest: None

A 62-year-old man was referred to our clinic with lower leg edema and abdominal pain. He presented with nephrotic-range proteinuria, and a renal biopsy revealed lupus nephritis of the membranous type. Antinuclear antibody and anti-DNA antibody were positive, but antiphospholipid antibody was negative. Abdominal computed tomography also indicated mesenteric panniculitis. He started to receive prednisolone (50 mg/day) and mycophenolate mofetil (1000 mg/day). These treatments improved abdominal pain, while sudden onset of dysarthria was developed on the 10th day. Brain magnetic resonance imaging (MRI) showed acute cerebral infarction, and then he started to take anticoagulant and antiplatelet agents. Despite these treatments, he developed repeated recurrences of cerebral infarction on the 11th and 12th days. High-resolution magnetic resonance vessel wall imaging revealed intracranial arterial wall thickening with vessel wall contrast enhancement. A diagnosis of cerebral vasculitis in SLE was made. Steroid pulse therapy and intravenous cyclophosphamide therapy were performed, but he died of brainstem infarction on the 27th day. Clinical significance: The vessel wall MRI techniques may contribute to early diagnostic assessment of cerebral vasculitis in SLE, and improve patient outcomes.

P1-064

Two cases of atlantoaxial synovitis

Tetsushi Aita¹, Susumu Nishiyama¹, Yasuhiko Yoshinaga¹, Shoji Miyawaki¹, Hiroki Kishimoto²
¹Rheumatic Disease Center, Kurashiki Medical Center, Kurashiki, Okayama, Japan, ²Department of Orthopedic Surgery, Kurashiki Medical Center, Kurashiki, Okayama, Japan

Conflict of interest: None

Cervical spine involvement is a common complication of rheumatoid arthritis (RA), and it involves disease duration and disease activity. Some cases were reported that seronegative RA with rheumatoid pannus at C1-C2 at disease onset. Case1: A 38-year-old women with a history of rheumatoid arthritis in her twenties was referred to our department with a chief complaint of cervical pain for two months. She had no peripheral joint symptoms at this time and RF/ACPA were negative. But cervical MRI showed synovitis around the odontoid process. Infliximab was initiated because prednisolone and methotrexate were not effective and her symptom gradually disappeared. Case2: A 81-year-old women had complained cervical pain for two months. There is no sign of peripheral arthritis and RF/ACPA were negative. But cervical MRI/CT showed odontoid process inflammatory pannus and erosions. We diagnosed with atlantoaxial synovitis. Methotrexate was not effective and golimumab was started. Precise cervical evaluation of plain radiographs is often difficult. Indeed, MRI demonstrates early synovitis. When synovitis was confirmed, aggressive treatment from early stage is necessary because resultant deformities may cause neurologic deficits, such as cervical myelopathy, paresis, and even sudden death.

P1-065

Evaluation of radiological changes of distal interphalangeal joint in patients with rheumatoid arthritis

Satoshi Ikemura, Junichi Fukushi, Yukio Akasaki, Toshifumi Fujiwara, Yasuharu Nakashima
Department of Orthopaedic Surgery, Graduate School of Medical Sciences, Kyushu University

Conflict of interest: Yes

[Object] The purposes of this study were to evaluate the frequency of the radiological changes of DIP joint, and to determine the factors associated with its changes. [Methods] This study reviewed 49 RA patients. The changes of metacarpophalangeal (MP), thumb interphalangeal (IP), and proximal interphalangeal (PIP) joints as well as DIP joint, were investigated with comparison between initial and final hand radiographs. Clinically, the duration of disease, disease activity (DAS28-CRP), therapeutic drugs were investigated. [Results] Radiological changes of DIP joint were observed in 4 patients (8.2%). In the radiological DIP change positive group, the rate of presence of radiological rheumatic changes of MP and PIP joints were significantly higher than those in the radiological DIP change negative group ($P < 0.05$). The mean DAS28-CRP (3.91) in the radiological DIP change positive group was significantly higher than that (2.28) in the radiological DIP change negative group ($P < 0.05$). [Conclusions] Radiological rheumatic changes of DIP joint were observed in 4 patients (8.2%) during the course of disease. The results of this study indicate that disease activity relates to radiological rheumatic changes of DIP joint as well as other common sites of deformity, such as MP and PIP joints.

P1-066

The development of the automatic measurement of joint space distance of the metacarpophalangeal joint of the rheumatoid arthritis patient by the super-resolution image processing. Second report: Edge abstraction by mask processing by GraphCut

Koji Funahashi¹, Tadahiro Natsume¹, Ken Ikuta¹, Katsushi Koyama², Kiyomi Koike², Junichiro Hagita², Naoki Fukaya³
¹Department of Orthopedic Surgery, Kariya Toyota General Hospital, ²Department of Nephrology and Rheumatology, Kariya Toyota General Hospital, ³Habirisu Hitotsugi

Conflict of interest: None

[Background] We reported that the measurement of joint space distance (JSD) using the curve fitting method and super-resolution image processing for detecting the radiographic progression. [Object] To develop the algorithm of automatic measurement of JSD for the purpose of saving the time. [Methods] We prepared bilateral 2nd -5th metacarpophalangeal (MCP) joint X-ray images of rheumatoid arthritis patients. Edge extraction was performed by GraphCut which is a tool on Matlab, measurement JSD by the curve fitting method were performed automatically. We compared the difference between automatic measurement and manual operation. [Results] In 29 joints of 40 joints (72.5%) in both 2nd -5th finger MCP joint, the difference of measurement value between automation and manual operation was less than 0.1mm. In 30 joints of 40 joints, (80.0%) it was less than 0.2mm. In index and middle finger, 18 joints (90.0%) were less than 0.1mm. All joints were less than 0.2mm. In ring and little finger, 11 joints (55.0%), 12 joints (60.0%) were respectively. [Conclusions] We tried the automation of the measurement of the JSD. We developed the method that the measurement value was calculated in several seconds automatically.

P1-067

Carpal bone cysts resembling erosions are relatively common findings

Atsushi Moriya¹, Hiroshi Tanaka¹, Eiichi Shiigi¹, Hiroki Yamagata¹, Yasuhiro Tani²
¹Yamaguchi Prefectural Grand Medical Center, ²Nagato General Hospital

Conflict of interest: None

[Object] To investigate the prevalence and distributing features of

carpal bone cysts. [Methods] We analyzed 156 CTs on carpal bones of patients with distal radius fractures (a mean age of 63 years). Patients with carpal bone fracture or prior arthralgia were excluded from this study. Cystic alterations on CTs were evaluated separately in each carpal bone in the sagittal, coronal and transverse planes. A carpal bone cyst was defined as a sharply margined intraosseous radiolucent lesion (usually larger than 2 mm in size). [Results] CTs showed carpal bone cysts in 72 (46%) out of 156 subjects. Altogether, 121 carpal bone cysts were found in the 1404 carpal bones evaluated (4 in the trapezium, 10 in the trapezoid, 21 in the capitate 5 in the hamate, 24 in the scaphoid, 35 in the lunate, 21 in the triquetrum, and 1 in the pisiform). Cystic alterations were found more often in the older subjects. [Conclusions] The distribution and frequency of cystic alterations as detected by CTs in carpal bones were identified. Cystic lesions were found frequently seen in the capitate, scaphoid, lunate and triquetrum, which also frequently show bone erosions in rheumatoid arthritis. These finding of the present study may be considered when distinguishing arthritic joints from normal joints.

P1-068

Mid-term efficacy and prevention of knee joint destruction of Infliximab in rheumatoid patients

Masaaki Usui¹, Kazuo Fujiwara¹, Shinji Narazaki¹, Hiroshi Wakabayashi²
¹Okayama City Hospital, Okayama, Japan, ²Okayama City Hospital, Okayama, Japan

Conflict of interest: None

[Object] Mid-term efficacy and prevention for knee joint destruction of Infliximab (IFX) in rheumatoid patients for the knee joint destruction of infliximab was examined. [Methods] In the patients who introduced IFX for RA from June, 2004 to August, 2009, radiographic appearance of both knee joints standing position in 22-patients having a knee joint symptom was studied. The dosage start age was an average of 54.3 years old. Larsen Grade0/1/2/3/4/5 at the time of the dosage start was 2, 23, 8, 7, 2, 2 knees each. [Results] Larsen Grade0/1/2/3/4/5 in 2014 was 2, 20, 11, 7, 2, 2 knees each. Progress of Grade was seen in 5 knees, but the improvement such as open sizes of joint space was seen in 8 knees. Larsen Grade0/1/2/3/4/5 in 2018 was 1, 17, 11, 9, 4, 31 knees each. Progress of Grade was seen in 14 knees, and 1 knee of Grade3 became Grade4, and TKA was enforced. [Conclusions] Improvement of the radiographic appearance was seen in the short term, but a progress of Grade was not avoided in the mid-and-long term by the IFX dosage.

P1-069

Predictors of radiographic progression in patients with rheumatoid arthritis by using magnetic resonance imaging and ultrasound

Ayuko Takatani¹, Mami Tamai¹, Nozomi Oki², Yoshikazu Nakashima¹, Mizuna Otsuka¹, Momoko Okamoto¹, Yushiro Endo¹, Sosuke Tsuji¹, Toshimasa Shimizu¹, Remi Sumiyoshi¹, Tomohiro Koga¹, Shin-ya Kawashiri¹, Naoki Iwamoto¹, Takashi Igawa¹, Kunihiro Ichinose¹, Kazuhiko Arima³, Hideki Nakamura¹, Tomoki Origuchi¹, Masataka Uetani², Atsushi Kawakami³

¹Nagasaki University Graduate School of Biomedical Sciences, Department of Immunology and Rheumatology, Nagasaki, Japan, ²Nagasaki University Graduate School of Biomedical Sciences, Department of Radiological Sciences, Nagasaki, Japan, ³Nagasaki University Graduate School of Biomedical Sciences, Department of Public Health, Nagasaki, Japan

Conflict of interest: None

[Object] To clarify the predictors of radiographic progression in patients with rheumatoid arthritis. [Methods] Forty four patients with RA were enrolled and observed for 12 months. They were evaluated by using US synovitis score, semi-quantitative exam by grey-scale and power Doppler (PD) every 3 months. MRI and radiograph were done every 6 months. Synovitis, bone marrow edema and bone erosion were assessed by the Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS). Radiographic progression was defined as Δ Genant-modified Sharp score (GSS) >0.5 . After univariate analysis, multivariate analysis was performed to establish the predictors for radiographic pro-

gression. [Results] Median of disease duration was 8.5 months and that of DAS28-CRP was 4.18 at baseline. Radiographic progression was found in 14 patients. A univariate analysis showed radiographic joint space narrowing score and RAMRIS synovitis scores, bone marrow edema score and erosion score at baseline were associated with radiographic progression. Multivariate analysis revealed RAMRIS bone marrow edema score and CRP at baseline were predictors of radiographic progression. [Conclusions] Our findings suggest MRI bone marrow edema score and CRP at baseline were useful to predict radiographic progression.

P1-070

Accuracy assessment of metacarpophalangeal joint space and bone microstructure measurements on HR-pQCT imaging

Nozomi Oki¹, Ko Chiba², Kounosuke Watanabe², Masataka Uetani¹, Makoto Osaki², Naoki Iwamoto³, Atsushi Kawakami³

¹Department of Radiological Science, Nagasaki University Graduate School of Biomedical Sciences, ²Department of Orthopaedic Surgery, Nagasaki University Graduate School of Biomedical Sciences, ³Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: None

[Object] The purpose of this study is to evaluate the accuracy of metacarpophalangeal (MCP) joint space and bone microstructure measurements on HR-pQCT imaging. [Methods] A total of 30 MCP joints in 16 healthy controls were scanned by HR-pQCT repeatedly three times. A dedicated software was used for measurements of the joint space and bone microstructural parameters of the MCP joints. According to the image quality grading, HR-pQCT images were classified into two groups with or without grade 4. Reproducibility of the three measurements was evaluated by RMS%CV (Root Mean Square% Coefficient of Variance) and compared in the two groups. [Results] The RMS%CV of without grade 4 group and with grade 4 group were joint space width (JSW) mean 1.79%, 1.92%, JSW minimum 4.88%, 8.29%, JSW. maximum 1.84%, 1.04%, JSW. Asymmetry 4.6%, 10.66%, joint space volume 1.35%, 1.36%, vBMD 0.62%, 2.03%, BV/TV 0.81%, 2.28%, Tb. Th 0.51%, 0.78%, Tb. Sp 2.15%, 4.71%, SMI 2.58%, 6.88%, Conn.D 1.42%, 6.14%, respectively. [Conclusions] The accuracy of joint space and bone microstructure measurements using HR-pQCT was sufficient by obtaining images with less motion artifact. This technique is thought to be applicable to longitudinal studies of inflammatory joint diseases such as rheumatoid arthritis.

P1-071

A case of the submandibular tumor which occurred in a patient with Sjogren's syndrome/scleroderma. The importance of follow-up study by ultrasonography

Kaori Yanagawa¹, Sayaka Ueno¹, Koichiro Ohmura², Yukiko Komano¹, Ikuko Masuda¹

¹Center for Rheumatic Diseases, Jujo Takeda Rehabilitation Hospital, ²Department of Rheumatology and Clinical Immunology, Kyoto University

Conflict of interest: None

A 70 years-old woman who had been diagnosed as limited type scleroderma and Sjogren syndrome, developed left submandibular swelling. Ultrasonography showed a 4cm of left submandibular gland tumor. After continuing the swelling of area one year later, ultrasonography revealed that tumor had a tendency to increase in size. Contrast MRI and CT showed tumor was solid and lobular with gadolinium enhancement, unlike benign pleomorphic adenoma or Warthin's tumor. For the purpose of treatment and diagnosis, surgery to remove all tumor was performed. The tumor were somewhat malignant findings which is reaching widespread to deep-layer of the gland with strong adhesion. The pathologic diagnosis was the MALT lymphoma secondary to sialoadenitis associated with Sjogren's syndrome, in acknowledgment of LEL (lymphoepithelial lesion) with many irregular-shaped lymphocytes colonization. Immunostaining of that lesion showed that the plasma cells of 100% of IgG4/IgG ratios lay scattered to LEL surrounding tissue, suggested IgG4-RD co-ex-

isted in that lesion. (Even though the serum IgG4 level has never been high). When it is associated with a parotid swelling for Sjogren's syndrome, it is necessary to be closely followed-up by ultrasonography with a suspect of malignant lymphoma.

P1-072

A case of Budd-Chiari syndrome associated with systemic lupus erythematosus (SLE) and anti-phospholipid antibody syndrome (APS), whose clinical course was followed-up by abdominal ultrasonography (AUS)

Sayaka Ueno¹, Koichiro Ohmura², Kaori Yanagawa¹, Yukiko Komano¹, Ikuko Masuda¹

¹Center for Rheumatic Diseases, Jujo Takeda Rehabilitation Hospital, Kyoto, Japan, ²Department of Rheumatology and Clinical Immunology, Kyoto University

Conflict of interest: None

[Case] 62 years old female was diagnosed with SLE and APS by having episodes of thrombosis of deep vein in 1973 and inferior vena cava (IVC) in 1974. In 2011, abdominal CT and MRI pointed out a severe stenosis of IVC, leading to the diagnosis of Budd-Chiari syndrome. The case had been followed up by AUS thereafter. In 2013, AUS showed a hepatosplenomegaly, small amount of ascites, and localized coarsening of liver S6,7. In 2016, coarsening spread throughout liver, however, no other changes were detected. She had right hypochondriac pain in 2017, AUS showed a 90 mm of hepatocellular carcinoma (HCC) protruding out of S6,7. Although she was referred to a specialist, she eventually died due to intraperitoneal rupture of HCC. [Discussion] Disease activity of the primary diseases were in remission. Hepatobiliary enzyme was within the normal range, HBV and HCV were negative throughout the observation period. However, portal hypertension due to IVC obstruction lasted for a long time, and hepatic roughness localized in 2013 spread to the whole liver in 2016. Retrospectively, hepatic fibrosis had clearly progressed, and the risk of developing HCC was high. Further tests by other modalities such as MRI and the earlier referral to a specialist should have been considered.

P1-073

A study of appropriate biologics (Bio) for elderly rheumatoid arthritis (RA) patients

Yasuo Inoue¹, Kae Takagi², Junji Chiba¹

¹Department of Orthopaedic Surgery, Tokyo Women's Medical University Medical Center East, ²Department of Internal Medicine, Tokyo Women's Medical University Medical Center East

Conflict of interest: None

[Object] The aim of this study is to clarify which specific Bio are appropriate for elderly RA patients by comparing Bio for both groups. [Methods] Of 238 patients of RA treated with Bio were divided into two groups by age. 145 patients under 64 years old were grouped as Group Y (GY). 93 patients over 65 years old were grouped as Group O (GO). The efficacy of each Bio in the two groups was compared based on the change of 0 to 6 months in disease activity, Δ DAS (CRP), and the degree of functional improvement, Δ HAAQ. The persistency and the number of consecutive days of each Bio, and complications developed after the Bio administration were compared in both groups. [Results] The top three Bio with highest persistency in GO were tocilizumab, infliximab and etanercept. Abatacept was initiated to the patients with the longest disease duration and the highest average age, and the persistency in both groups were almost equal. [Conclusions] In addition, the effectiveness of each Bio was not significantly different in both groups. However, since the persistency of each Bio recognizes the difference between the two groups, the treatment by the Bio for elderly RA is necessary to examine characteristics of each Bio.

P1-074

Comparison of molecular targeted therapy for rheumatoid arthritis patients - Seronegative VS Seropositive -

Satoshi Baba, Rina Okita, Ruriko Kuratani, Rumiko Miyagi, Shinichiro

Tsunoda

Division of Rheumatology, Sumitomo Hospital, Osaka, Japan

Conflict of interest: None

[Object] Seronegative rheumatoid arthritis still has many unknown points. We compare Seropositive RA (SPRA) and Seronegative RA (SNRA), and show the difference in reactivity to molecular targeted therapy. [Methods] From March 2016 to October 2018, 66 patients who initiated molecular targeting drugs newly in our hospital were classified into SPRA group and SNRA group, and clinical evaluation (DAS 28, CDAI, SDAI) were compared. [Results] There were 39 patients with SPRA (Tocilizumab <TCZ>:9, Etanercept <ETN>: 3, Abatacept <ABT>:8, Certolizumab pegol <CZP>:13, Tofacitinib <TOFA>:6), 27 patients with SNRA (TCZ:6, Sarilumab <SARI>:2, ETN:3, ABT:2, CZP:10, Infliximab <IFX>:1, TOFA:1, Baricitinib <BARI>:2). There was no significant difference in the decrease of CDAI at 6 months ($p = 0.35$). In addition, we compared decrease of DAS28 and SDAI score at 6 months for drugs other than IL-6 inhibitors. There was no significant difference in the reduction of the DAS28 score ($p = 0.22$), but the SDAI score was significantly lower in the SNRA group than in the SPRA group (SN: -23.4 VS SP: -15.5, $p = 0.032$). [Conclusions] The therapeutic effect of molecular targeted drugs on SNRA may be better than SPRA.

P1-075

A research of cases in which more than 10 years have passed since the start of biological drug treatment in rheumatoid arthritis patients

Daisuke Kihira, Yuji Hirano, Yukiyoshi Oishi

Department of Rheumatology, Toyohashi Municipal Hospital

Conflict of interest: None

[Object] To investigate the long-term outcome of rheumatoid arthritis (RA) patients who have been in the treatment for 10 years or more from the start of Bio. [Methods] We surveyed 74 patients with RA who were treated more than 10 years as of December 2017 from start of Bio. We divided patients into two groups, 41 patients who continued Bio for 10 years or more and 33 cases who discontinued. Cases in which Bio were changed were analyzed as continuation group. The two groups were compared statistically. [Results] All patient characteristics: average age 58.3 years, mean disease duration 11.4 years, average DAS28-CRP 5.47. Total continuation rate was 83.8% at 3 years, 71.6% at 5 years, 55.4% at 10 years. The Bio continuation group was significantly better in DAS28-CRP, SDAI, mHAQ, MMP3, CRP than the Bio discontinuation group at last. Comparison of the two groups at the time of start of Bio showed that age, body weight (BW), PSL administration rate, MTX administration rate and mHAQ showed a significant difference in univariate analysis. DM cases were present only in the discontinuation group. In multivariate analysis, significant difference was observed in BW and PSL administration rate. [Conclusions] It was suggested that the long-term persistence rate of Bio was affected by BW, administration of PSL, and DM.

P1-076

Biologic treatment in elderly patients with rheumatoid arthritis

Hideki Takagi, Masayuki Watanabe

Orthopedic Surgery, Nagoya Central Hospital

Conflict of interest: None

(Object) The aging of patients with rheumatoid arthritis (RA) is progressing in Japan. However, there are few reports on the use of biological products for elderly patients over 75 years old. We examined the outcome of treatment with biologic agents for elderly RA patients aged over 75 years. (Methods) We investigated the patient background at the time of introduction, introduced drugs, adverse events and outcome in 9 patients who introduced biological products in RA patients over 75 years old. (Results) Introduced drugs were abatacept 3, infliximab 2, adalimumab 1, tocilizumab 1, certolizumab-pegol 1, golimumab 1. The age at the time of administration was 75 to 87 years old (median 76 years old), the administration period was 2 months to 11 years (median 3 years 6 months), and only 3 cases were able to continue until the investigation. The reasons for discontinuation were all 6 cases of adverse events, of which 2

cases of lung cancer, 2 cases of bacterial pneumonia, 1 case of pneumocystis pneumonia, and 1 case of heart failure. (Conclusions) As a result of administering biologic products to elderly patients aged over 75 years, two-thirds cases were discontinued due to adverse events, and it was confirmed again that extreme caution was required for the occurrence of side effects.

P1-077

The comparative effect of TNF inhibitors, Tocilizumab (TCZ) and Methotrexate (MTX) on diabetic control in patients with Rheumatoid arthritis (RA)

Kei Fujioka, Saori Inui, Tomofumi Takeda, Ichiro Mori, Tatsuo Ishizuka
Center of General Internal Medicine and Rheumatology, Gifu Municipal Hospital, Gifu, Japan

Conflict of interest: None

[Object] To determine the comparative effects of anti-rheumatic medications (TNFi, TCZ, and MTX) on glucose tolerance [Methods] We identified 30 RA patients complicated with glucose intolerance ($HbA1c \geq 5.6$) at our hospital from May 2013 to October 2017, and treated with as follows; TNFi + MTX group (10 cases: IFX 1 case, ETN 5 cases, GLM 4 cases), MTX alone group, and TCZ ± MTX group (10 cases) had been registered. We have compared the changes of HbA1c levels, body weight and DAS 28-ESR before and after treatments for 6 and 12 months. We analyzed these results with paired and unpaired *t* test using JMP12.2.0. [Results] Each group showed significant improvement of DAS 28-ESR after treatment for 6 and 12 months ($P < 0.05$). The mean reduction in HbA1c showed a significantly decreases in the TCZ ± MTX group after treatment for 6 ($P < 0.01$) and 12 months ($P < 0.01$), and MTX alone group for 12 months ($P < 0.05$). There were no significant differences in body weight between an each group. [Conclusions] In this study, The TCZ showed a significant improvement in the glucose tolerance than TNFi. Although MTX have the improvement of glucose tolerance, these effects was attenuated in combination with TNF.

P1-078

Ultrasonographic evaluation of Tocilizumab and TNF antagonist therapy in patients with rheumatoid arthritis

Yasuhide Kanayama¹, Atsushi Nagata², Hitomi Nagasaka²

¹Department of Orthopaedic Surgery and Rheumatology, Toyota Kosei Hospital, Toyota, Japan, ²Department of Clinical Technology, Toyota Kosei Hospital, Toyota, Japan

Conflict of interest: None

[Objectives] To evaluate the clinical efficacy of Tocilizumab (TNF) and TNF antagonist (TNF) therapy in patients with rheumatoid arthritis (RA) using ultrasonography (US). [Methods] We used TCZ and TNF treated 26 and 33 RA patients more than 24 weeks. We evaluated the improvement of gray scale (GS) and power doppler (PD) score from baseline to week 24. [Results] In the patients receiving TCZ ($n=26$) and TNF ($n=33$), the mean age was 58.6 vs 55.0 years old ($p=0.216$), disease duration was 7.9 vs 5.1 years ($p=0.516$), the mean MTX dose was 11.7 vs 10.8 mg/w ($p=0.404$), the rate of ACPA positive was 85% vs 85% ($p=0.980$), DAS28-ESR was 5.33 vs 4.78 ($p=0.052$), GS score was 21.2 vs 17.3 ($p=0.197$) and PD score was 12.6 vs 9.0 ($p=0.233$). The respective changes in GS and PD score after 4 weeks were as follows: GS: -2.0 vs -3.9 ($p=0.612$) and PD: -2.5 vs -1.3 ($p=0.322$). The respective changes in GS and PD score after 12 weeks were as follows: GS: -6.7 vs -5.2 ($p=0.396$) and PD: -5.5 vs -2.6 ($p=0.150$). The respective changes in GS and PD score after 24 weeks were as follows: GS: -11.4 vs -7.9 ($p=0.171$) and PD: -8.4 vs -4.7 ($p=0.140$). [Conclusion] The present study provides evidence supporting the TCZ and TNF therapy improved not only the disease activity not also the inflammatory synovitis.

P1-079

The examination of the efficacy of biologics (Bio) after switching from TNF-inhibitors (TNF-i) in rheumatoid arthritis (RA) patients

Misuzu Fujimori¹, Koji Takasugi¹, Kazuhiko Ezawa¹, Ryozo Harada², Wataru Yamamoto³, Masamitsu Natsumeda⁴, Keiichiro Nishida⁵

¹Department of Internal Medicine, Kurashiki Sweet Hospital Rheumatic Disease Center, Kurashiki, Japan, ²Department of Orthopedics, Kurashiki Sweet Hospital Rheumatic Disease Center, Kurashiki, Japan, ³Department of Health Information Management, Kurashiki Sweet Hospital, Kurashiki, Japan, ⁴Department of Internal Medicine, Mabi Memorial Hospital Rheumatic Disease Center, Kurashiki, Japan, ⁵Department of Orthopedics, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Conflict of interest: None

[Object] We compare the efficacy of TNF-i v.s. abatacept (ABT) v.s. tocilizumab (TCZ) with insufficient response to first TNF-i on RA treatment. [Methods] 80 RA patients were changed their treatment from TNF-i to other Bio (another TNF-i: 28 cases, ABT: 29 cases, TCZ: 23 cases) through Jan 2014 to Dec 2017 in our hospital. We compared their background, clinical response (DAS28, CDAI and SDAI) and retention rate at 6 and 12 months, between these 3 groups. [Results] No significant association was found in any backgrounds and retention rates between 3 groups. Δ DAS, Δ CDAI and Δ SDAI at 6 months were higher score in TCZ group than them in ABT group. There were 12 cases in TNF-i group, 7 cases in ABT group and 12 cases in TCZ group which showed good or moderate response in DAS28 at 6 months. In the comparison of the background among these DAS responders, ABT group were significantly older than TNF-i group, and RF-positive cases were more in TCZ group than them in TNF-i group. [Conclusions] Our study suggested that ABT may be effective in older patients and non-TNF-i may be more effective in RF-positive patients after switching of first TNF-i.

P1-080

The efficacy of bDMARDs therapy in elderly-onset rheumatoid arthritis

Kiichiro Ando, Hiroaki Sakai

Department of Orthopaedic Surgery, Chuno Kosei Hospital

Conflict of interest: None

[Object] To evaluate the efficacy in biologic disease-modifying anti-rheumatic drugs (bDMARDs) therapy [Methods] This study comprised 7 patients with EORA. Patients received tocilizumab, abatacept, golimumab and adalimumab therapy with or without methotrexate for 6 months. The outcomes were assessed with the disease activity during 6 months study period, using the 28-joint Disease Activity Score based on the erythrocyte sedimentation rate (DAS28 ESR) and Clinical Disease Activity Index (CDAI). [Results] DAS28ESR (from 3.7 to 2.4) and CDAI (from 5.5 to 3.0) decreased significantly from baseline to Week 24. DAS-28ESR Remission achieved in 6 cases at Week 24. Tocilizumab monotherapy was also effective with RA patients of in adequate response to other bDMARDs therapy. The retention rate of tocilizumab at 24 weeks was 100%. The average dose of methotrexate tapered from 6.5mg to 3.5mg. The average dose of glucocorticoid also tapered from 5.0mg to 4.0mg. [Conclusions] These results suggested that bDMARDs therapy is effective in patients with EORA.

P1-081

Consideration of Biologics for Elderly onset rheumatoid arthritis

Mio Matsuura, Yuichiro Takami

Department of Rheumatology, Kinan Hospital

Conflict of interest: None

[Object] We introduced Biologics to elderly patients with rheumatoid arthritis (RA) and examined the effectiveness and safety of them at our hospital and two related hospitals. [Methods] We targeted 100 RA patients aged 75 or older who are treated with the Biologics from April 2013 to October 2018 at the above three hospitals. [Results] The mean age was 81 ± 0.5 , mean disease duration was 7.9 ± 1.0 , 68 women (68%). Among them, infectious complications that required hospitalization were 3 cases. That was 2.03 cases / 100 persons-year. Of these cases, 49 cases were in which the efficacy evaluation of more than 6 months could be analyzed. We used HAQ and DAS28 ESR to an index of effectiveness. The results was $HAQ 1.59 \pm 0.13$ (at the time of introduction= 1) / $0.68 \pm$

0.12 (after 6 months=[2]) and DAS 28-ESR 4.94 ± 0.16 ([1]) / 3.00 ± 0.22 ([2]). 39 cases (79.6%) had restrictions on physical function with HAQ > 0.5 at the time of introduction. After 6 months, it decreased to 21 cases (43%). [Conclusions] The effectiveness and safety of biologics can be expected in elderly people.

P1-082

Clinical evaluation of abatacept and golimumab in patients with rheumatoid arthritis in our department

Yuji Akiyama^{1,2}, Takuma Wada², Mayuko Takamatsu Sakamoto², Takashi Maruyama², Yoshihiro Yoshida², Kazuhiro Yokota², Noritsune Kozu³, Hiroshi Kajiyama², Yasuto Araki², Kojiro Sato², Yu Funakubo², Toshihide Mimura²

¹Division of Rheumatology, Department of Internal Medicine, Ogawa Red Cross Hospital, Saitama, Japan, ²Department of Rheumatology and Applied Immunology, Saitama Medical University, Saitama, Japan, ³Department of Orthopedics, Kouzu Clinic, Chiba, Japan

Conflict of interest: Yes

[Object] To investigate the efficacy and the adherence of abatacept (ABT) and golimumab (GLM) in RA patients. [Patients] ABT/GLM; 26 (5 males, mean 63.1 yo, mean disease duration 9.7 y) / 25 (3 males, 66.1 yo, 11.1 y), MTX; 16 (5 mg/w) / 17 (5.52), PSL; 19 (4.73mg/day) / 13 (1.94). Bio-naïve: 6/11. [Methods] Efficacy of ABT and GLM was evaluated by DAS28-ESR4, CDAI and SDAI for 156 weeks. [Results] 1) Mean DAS28 at the baseline (ABT/GLM): 5.87/5.80, CDAI 25.47/23.42, SDAI 28.64/27.48. The disease activity was significantly decreased in both groups. As time went by, the ratio of LDA + remission increased significantly until 24 weeks and maintained until 208 weeks in both groups. No significant difference in both groups. 2) The adherence rate; more than 80% (ABT/GLM) at W52, 69.2%/60% at W104, 61.5%/40.0% at W156 and 46.2%/36.0% at W208. No significant difference in both groups. 3) HAQ-DI was significantly improved after 12 weeks in ABT. 4) Both levels of CRP and MMP-3 were significantly reduced in GLM after 12 weeks, while the only CRP level in ABT after 52 weeks. 5) Drop-out reasons (ABT/GLM); inadequate response 5/7, cancer 1/1, organizing pneumonia 0/1, pneumonia 1/1, EBV reactivation 1/1, remission 1/0 and so on. [Conclusions] The efficacy and the adherence of ABT and GLM were similar.

P1-083

Biological treatments in the elderly patients with rheumatoid arthritis

Seiko Yamazaki¹, Nobuo Matsui²

¹Yamasaki Orthopedic Rheumatology Clinic, ²Nagoya City General Rehabilitation Center Affiliated Hospital

Conflict of interest: None

[Object] The purpose of our study was to assess and compare the effects and safety of biological treatments in elderly patients with RA. [Methods] From February 20th to September 30th, subjects were 12 RA patients (4 males, 8 females) aged over 65 years who used biological agents, average age 73.9 years (66 to 81 years old), Nine elderly onset aged over 60 years, average disease duration 15.5 years, ACPA positive 9 cases, INF 1 case · TCZ 3 cases · GLM 7 cases · ABT 1 case, 5 cases switching from other bDMARDs. The evaluation of disease activity by DAS 28 ESR, SDAI, MTX dosage, and extended of bDMARDs administration period were examined. [Results] As a result of comparing before and after the biological treatments, DAS 28 ESR improved from 5.28 to 3.09 and SDAI improved from 27.86 to 8.26. The dose of MTX was reduced from an average of 8.6 to 6.3 mg/w, and the administration interval was extended in two cases of GLM. Transient liver function disorder was observed in 2 patients with GLM. In 2 cases of TCZ and GLM, administration was discontinued for economic reason. MTX combination was discontinued in 2 cases of GLM. [Conclusions] An effective treatment was obtained for elderly RA patients by careful selection of adaptive cases and appropriate biological drugs.

P1-084

Safety and effectiveness of certolizumab pegol in patients with rheumatoid arthritis in real-life settings: Final 24-week results of post-marketing surveillance

Hideto Kameda¹, Keiichiro Nishida², Toshihiro Nanki³, Shigeki Momohara^{4,5}

¹Division of Rheumatology, Department of Internal Medicine, Toho University Ohashi Medical Center, ²Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ³Division of Rheumatology, Department of Internal Medicine, School of Medicine, Toho University, ⁴Hakkeikai Incorporated Medical Institution, ⁵Department of Orthopaedic Surgery, Keio University

Conflict of interest: Yes

[Object] Safety and efficacy of certolizumab pegol (CZP) was evaluated in a real-world setting in Japanese patients (pts) with rheumatoid arthritis using post-marketing surveillance data. [Methods] Adverse events (AEs) observed during the 24-week (wk) CZP treatment period were recorded. Disease activity was evaluated using DAS28-ESR at baseline, Wk12, Wk24 and withdrawal. [Results] 3727 pts were enrolled; safety/efficacy were evaluated in 3647/1807 pts. Total CZP exposure was 1679.8 pt-years. AEs were reported in 24.7% pts, adverse drug reactions (ADRs) in 14.6%. The only ADR reported in >1% pts was rash. Selected serious ADRs of interest included infections (n=111; 3.0%), tuberculosis (6; 0.2%), allergic reactions (9; 0.2%), interstitial lung disease (17; 0.5%), heart failure (2; 0.1%), malignancy (8; 0.2%), hepatic failure (7; 0.2%). No autoimmune diseases, demyelinated diseases or pan-cytopenia were reported. There were 9 deaths, 3 drug-related. From baseline to last observation DAS28-ESR reduced from 4.76 ± 1.36 to 3.43 ± 1.48 and response rates of EULAR Good response and Good or Moderate response were 34.9% and 66.6% respectively. [Conclusions] CZP efficacy was confirmed in the real-world. No new safety signals were identified, and the safety profile was consistent with the class.

P1-085

Effectiveness of early introduction of Certolizumab pegol in the treatment of elderly onset rheumatoid arthritis

Eriko Hasegawa^{1,2}, Satoshi Ito¹, Yoichi Kurosawa^{1,2}, Shinji Taniguchi¹, Asami Abe¹, Hiroshi Otani¹, Kiyoshi Nakazono¹, Akira Murasawa¹, Ichie Narita², Hajime Ishikawa¹

¹Department of Rheumatology, Niigata Rheumatic Center, Shibataishi Niigata, Japan, ²Division of Clinical Nephrology and Rheumatology, Niigata University Medical and Dental Hospital, Niigata Niigata, Japan

Conflict of interest: None

[Object] Elderly onset rheumatoid arthritis (EORA) often develops with high disease activity. Comorbidities are associated with intolerance to the treatment. Certolizumab pegol (CZP) for early RA patients was shown to be effective in C-OPERA study, but the evidence in elderly patients is limited. We aimed to investigate the effectiveness of early induction of CZP in EORA. [Methods] We retrospectively analyzed the date obtained from consecutive 12 EORA patients who started treatment with CZP within 3 months after the induction of conventional synthetic disease modifying anti-rheumatic drugs. [Results] Disease duration of RA at the time of induction of CZP was 3.1 ± 1.6 months. The duration from introduction of csDMARDs was 19.1 ± 11.8 days. Interstitial pneumonia was accompanied in 1 patient, chronic kidney disease in 5 patients and diabetes mellitus in 4 patients. After 4 weeks of treatment, DAS28-ESR (5.8 ± 1.1 vs. 3.0 ± 1.3 , $p=0.002$) and HAQ-DI (1.6 ± 0.9 vs. 0.5 ± 0.6 , $p=0.002$) were significantly decreased. No infection was occurred during the observational period. [Conclusions] Early introduction of CZP was effective in ameliorating disease activity and activity of daily life among elderly patients. Further investigation is needed to assess efficacy and safety.

P1-086

Clinical effect of certolizumab pegol in patients with rheumatoid arthritis from data registered in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA)

Yusuke Sugimura^{1,2}, Takeshi Kashiwagura², Natsuo Konishi², Masakazu Urayama², Hiroki Ito², Moto Kobayashi², Takayuki Tani², Tsutomu Sakuraba², Toshiaki Aizawa², Hidekazu Abe², Norio Suzuki², Keiji Kamo², Hiroshi Aonuma², Tetsuya Kawano², Yosuke Iwamoto², Naohisa Miyakoshi³, Yoichi Shimada³

¹Department of Orthopedic Surgery, Nakadori General Hospital, Akita, Japan, ²Akita Orthopedic Group on Rheumatoid Arthritis, ³Department of Orthopedic Surgery, Akita University Graduate School of Medicine

Conflict of interest: None

[Objectives] To analyze the efficacy of certolizumab pegol (CZP) in patients with rheumatoid arthritis (RA). [Patients and Methods] Among the Akita orthopedic group on rheumatoid arthritis (AORA), twenty-three patients were followed up for at least 52 weeks of treatment with CZP. We evaluated persistence rate, DAS28-CRP and reasons for discontinuing at 52 weeks. [Results] The patient characteristics were as follows: there were 6 males and 17 females, mean age was 61.3 years and mean disease duration was 12.1 years. Nine patients were biologics-naïve, while 14 were biologics-switched. MTX had been administered to 19 patients (82%), mean dose was 8 mg/week, PSL to 16 patients (70%), mean dose was 4 mg/day and csDMARD to 5 patients (22%). Thirteen patients (57%) were administered continuously in 52 weeks. At 0, 4, 12, 24 and 52 weeks after initiation, the mean DAS28-CRP were respectively 4.36, 3.63, 3.45, 3.43 and 3.41. The reasons for discontinuing were insufficient effect in 9 cases (naïve; 2), switch; 7) and remission in 1 case. [Conclusion] Persistence rate of CZP at 52 weeks was 57%.

P1-087

Clinical Feature of our RA Patients with Golimumab < What is the surrogating marker of effectiveness? How will be the failure case of GLM? >

Hiroshi Hori¹, Tsuyoshi Kobashigawa², Toru Yago², Eri Watanabe², Hiroki Yabe², Chihiro Terai², Shigeru Kotake²

¹General Medicine, Jichi Saitama Medical Center, ²Department of Rheumatology, Jichi Saitama Medical Center

Conflict of interest: None

[Object] To identify predictive factors in RA patients with effective GLM treatment. [Methods] All RA patients using GLM in our hospital between January 2011 and July 2018 were included. We investigated age, gender, concomitant DMARDs, doses of GLM, SJC, TJC, CRP and the effectiveness after switching from GLM, retrospectively. And we assessed the factors of effectiveness using GLM and features of agents after GLM therapy. [Results] We analyzed 44 patients (36 females) whose median age was 65 years old. Thirteen patients (30%) were ineffective GLM therapy. Mean CRP level in the patients with effective GLM therapy (1.9mg/dL) was lower than the patients with ineffective (3.7mg/dL) GLM treatment, significantly (p=0.02). TJC in patients with effective GLM therapy (2.2) was lower than that with ineffective (5.8), significantly (P<0.05). Ten patients (91%) switched to TCZ treatment in our patients of ineffective GLM therapy. The rate treatment continuation with TCZ was significantly higher than that without TCZ (p=0.03). [Conclusions] In our study, the patients with the high level of TJC or CRP tended to be the GLM failure, and almost those cases were switched to TCZ treatment, continuity.

P1-088

Effectiveness and safety of golimumab in rheumatoid arthritis patients over 75 years of age

Yoichi Kurosawa^{1,2}, Satoshi Ito¹, Eriko Hasegawa^{1,2}, Daisuke Kobayashi^{1,2}, Shinji Taniguchi¹, Asami Abe¹, Hiroshi Otani¹, Kiyoshi Nakazono¹, Akira Murasawa¹, Ichiei Narita², Hajime Ishikawa¹

¹Department of Rheumatology, Niigata Rheumatic Center, Niigata, Japan, ²Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences

Conflict of interest: None

[Object] We examined the efficacy and safety of golimumab (GLM) in elderly patients with rheumatoid arthritis over 75 years old. [Methods] We investigated the continuation rate and the frequency of infectious diseases in 168 patients who were introduced GLM in our hospital. [Results] There were 56 cases in which GLM was introduced in over 75 years old, and 112 cases in under 74 years old. GLM was discontinued in 2 cases (3.6%) due to infection, 1 case (1.8%) due to malignancy, and 1 case due to lumbago over 75 years old. Under 74 years old, GLM was discontinued in 2 cases (1.8%) due to infection, 2 cases (1.8%) due to malignancy, 2 cases (1.8%) due to psoriasis, and 1 case (1.8%) had developed multiple sclerosis. Thirty-two patients (57%) were over 75 years old and 76 (68%) were under 74 years old who were able to continue administration for 52 weeks. There was no difference in disease activity and steroid dosage at the beginning of GLM administration. Evaluation at 1 year after the treatment showed improvement in disease activity. [Conclusions] The elderly patients aged over 75 years had a slight increased incidence of infection and a low continuation rate compared to those under 74 years old, whereas generally good treatment effect could be obtained.

P1-089

Prediction of efficacy of each biologics based on serum IL-6 concentration

Mitsuhiro Iwahashi¹, Kazuyuki Yoshizaki², Hirofumi Watanabe¹, Shuntaro Miyoshi¹, Rie Sasaki¹, Jiro Yamana¹, Seizo Yamana¹

¹Division of Rheumatology, Higashihiroshima Memorial Hospital, ²Department of Biomolecular Science and Regulation, The Institute of Scientific and Industrial Research, Osaka University

Conflict of interest: Yes

[Objectives] TNF α and IL-6 are inflammatory cytokines that play important role in RA and are strongly correlated with disease activity. Serum level of TNF α and IL-6 prediction suggest the efficacy of different biologics might be predictable. [Methods] 135 RA patients who have started either IFX, ETN, ADA or TCZ at our site and have assessed DAS28 after 6 months of treatment. Using patients' pretreatment serum, we measured TNF α and IL-6 and categorized into 3 groups; Low IL-6 (2.6-16.7 pg/mL), moderate IL-6 (16.8-74.3 pg/mL), high IL-6 (78.1-5797.4 pg/mL). [Results] Tender joint count, swollen joint count, ESR, DAS28-ESR, CRP, RF in each group (low: moderate: high IL-6) is 4.3: 7.5: 6.0, 3.5: 6.5: 7.0, 27.8: 51.1: 62.0, 4.3: 5.4: 5.5, 0.9: 3.3: 3.4, 57.1: 122.3: 311.0 respectively. In all parameter, moderate IL-6 group presents more severe disease activity than low IL-6 group. But there is no significant difference between moderate IL-6 and high IL-6 group, except RF. Ratio achieving remission defined as "DAS28-ESR<2.6" in each group by TNF inhibitor was 60.7%: 64.7%: 30.0%, ratio achieving remission by TCZ was 70.5%: 60.7%: 60.0%. [Discussions] Compared to TNF inhibitor, decrease in efficacy was not shown in patients treated with TCZ, even in the high IL-6 group.

P1-090

Tocilizumab treatment is more effective for patients with rapid progression of joint erosion

Shinya Hayashi¹, Tsukasa Matsubara², Koji Fukuda¹, Keiko Funahashi³, Marowa Hashimoto³, Tomoyuki Kamenaga¹, Yoshinori Takashima¹, Ryosuke Kuroda¹

¹Kobe University Graduate School of Medicine, ²Matsubara Mayflower Hospital, ³Research Institute of Joint Disease

Conflict of interest: None

[Object] The purpose of this study is to investigate efficacy of tocilizumab treatment for RA patients with joint destruction. [Methods] Thirty-one patients with RA were eligible to participate. Radiographical parameters including total sharp score (TSS)/ year, erosion score/ year, joint space narrowing score (JSS)/ year and clinical parameters at initial time and 1 year after tocilizumab introduction including MMP3, mHAQ, ESR, CRP, CDAI. Correlations between the TSS/year, JSS/year, or erosion/year and MMP3, mHAQ, ESR, CRP, or CDAI were examined by Pearson's chi-square test. In all cases, p < 0.05 was considered significant.

[Results] We did not find any significant difference between TSS/year, JSS/year and clinical parameters. However, we only found significant negative-correlation between erosion score and delta CDAI (CDAI at initial time -CDAI at 1 year after tocilizumab introduction) ($r = -0.53$, $p = 0.015$). This result indicated joint erosion score at initial time was associated with improvement of CDAI. [Conclusions] Our finding suggested that tocilizumab treatment may be more effective for RA patients associated with progressive joint erosion.

P1-091

IL-6 plays a critical role in the continuity of joint inflammation in RA

Yasuhiko Hirabayashi

Department of Rheumatology, Hikarigaoka Spellman Hospital

Conflict of interest: None

[Object] To clarify the role of IL-6 in the continuity of joint inflammation in RA. [Methods] Tocilizumab (TCZ) was used to interfere with IL-6 signaling in inflammatory joints of RA. The efficacy was evaluated by DAS28ESR and CRP in 296 (female 254) patients with RA who had received TCZ not less than 84 days between May 28, 2008 and August 31, 2018. [Results] Mean patient age was 58.2 years and mean disease duration 9.1 years. DAS28-ESR was 4.50 ± 1.34 (mean \pm SD) initially, falling to 2.60 ± 1.19 after 1 month, to 1.72 ± 0.88 after 3 months and to 1.48 ± 0.80 after 1 year. It was less than 1.50 until 10 years later. Swollen joint count (SJC) was 4.17 ± 3.83 initially, falling to 0.45 ± 1.02 after 1 month and to 0.17 ± 0.66 after 6 months. It was less than 0.50 until 10 years later. CRP was 1.54 ± 2.10 mg/dl initially and it was less than 0.20 for 10 years thereafter. No "no response" was shown by EULAR response criteria. These indicate that arthritis was almost completely ameliorated by TCZ irrespective of baseline characteristics. [Conclusions] TCZ was effective against arthritis in all patients, indicating that IL-6 is essential for the continuity of joint inflammation in RA. Thus, perfect blockade of IL-6 signaling in inflammatory joints is key to complete remission of RA.

P1-092

Cases of strongly positive (>1000 U/mL) anti-cyclic citrullinated peptide antibodies in rheumatoid arthritis patients significantly decreased after infliximab treatment

Hiroshi Yokoyama

Yokoyama Orthopedic Clinic, Nishinomiya, Hyogo, Japan

Conflict of interest: None

ACPA testing is useful in the diagnosis of RA. We report two cases of RA patients who presented with highly abnormal ACPA titers and that were significantly decreased after infliximab (IFX) treatment. Case 1: A 71-year-old woman developed polyarthritis in December 2015. At her first visit, she was diagnosed with RA, ACPA 1263.6 U/mL and was administered MTX. Treatment with IFX started in March 2016, and her symptoms began to improve and in July 2018, ACPA decreased to 161.0 U/mL, respectively. Case 2: A 52-year-old woman developed arthritis in October 2013. She received MTX at another hospital, but was in poor control due to hepatic impairment, and visited our clinic in June 2015. At her first visit, she was administered ETN without MTX; however, due to inadequate efficacy, ETN was switched to ABT in July 2017. ABT alone and in combination with MTX provided limited improvements with no abnormalities in hepatic function. In December 2017, her treatment was switched to IFX, when with ACPA 4138.8 U/mL. IFX was administered every 4 weeks and her symptoms were alleviated. In April 2018, and ACPA were sharply decreased 710.0 U/mL, respectively, in August. Conclusion: Improvements in clinical symptoms and significant decreases in ACPA levels were observed in patients treated with IFX.

P1-093

CKD with the MTX-LPD past

Takao Kubota

Division of Rheumatology and Nephrology, Japan Self Defense Forces Central Hospital

Conflict of interest: None

[Object] To clarify the characteristics of CKD with the MTX-LPD past RA patients. [Methods] Six RA patients who developed MTX-LPD were investigated in this study. We compared the clinical and laboratory parameters of patients who achieved regression of LPD by MTX withdrawal and evaluated the clinical course of CKD thereafter. [Results] Four patients achieved regression of LPD by MTX withdrawal. Three patients received biological agents after LPD, and demonstrated an improved disease activity of RA and persistent remission of LPD, whereas only one patient experienced renal dysfunction after MTX-cessation. [Conclusions] Careful CKD management is needed with MTX-LPD past RA patients.

P1-094

Methotrexate tapering pattern over two years of adalimumab and high-dose methotrexate combo therapy (≥ 12 mg/week) for patients with rheumatoid arthritis: post-hoc analysis of HAWK Study 104-week data

Yoshiya Tanaka¹, Tsuneyo Mimori², Hisashi Yamanaka³, Naomi Sunaga⁴, Kazuo Morita⁴, Junko Kimura⁴, Tsutomu Takeuchi⁵

¹The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, School of Medicine, ²Department of Rheumatology and Clinical Immunology, Kyoto University Graduate School of Medicine, ³Institute of Rheumatology, Tokyo Women's Medical University, ⁴AbbVie GK, Tokyo, Japan, ⁵Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine

Conflict of interest: Yes

[Object] To investigate the extent of methotrexate (MTX) dose reduction over 2 years in patients with rheumatoid arthritis (RA) who commenced treatment with MTX and adalimumab (ADA). [Methods] Using data from the HAWK study, MTX dosage patterns were analyzed in patients with early RA (≤ 2 years) and DAS28-CRP > 3.2 .^{1,2} Where both the baseline and 104-week data points were available, average DAS28-CRP values were calculated to evaluate the relationship between final MTX dose and effectiveness. [Results] Among the 130 patients in the effectiveness analysis set with DAS28-CRP data at 104 weeks, the proportion of patients receiving MTX at a dose of $< 8 / 8-10 / 10-12 / \geq 12$ mg/week at 104 weeks was 10% / 20% / 15% / 55%, respectively. The mean DAS28-CRP at 104 weeks was 1.31 / 1.54 / 1.62 / 1.62, respectively, and the mean change from baseline was 3.36 / 3.06 / 2.88 / 2.93, respectively. No significant differences in change from baseline were observed between groups (paired t-test: $p = 0.5385$). [Conclusions] At 104 weeks, around 30% of patients could reduce MTX dose below 10mg without a negative impact on disease activity.

P1-095

Infliximab dose adjustment can improve the clinical outcomes of rheumatoid arthritis patients by RemicheckQ

Yuji Nozaki, Yasuaki Hirooka, Chisato Ashida, Daisuke Tomita, Akinori Okada, Asuka Inoue, Koji Kinoshita, Masanori Funachi, Itaru Matsumura

Department of Hematology and Rheumatology, Kindai University Faculty of Medicine

Conflict of interest: None

[Object] We evaluated the clinical responses of 42 patients with rheumatoid arthritis (RA) undergoing continuous or dose-adjusted infliximab treatment over 12 months. [Methods] Patients have not done the RemicheckQ test and received the 3 mg/kg infliximab continuously (R-; $n = 30$), and received the dose adjustment of infliximab (3 mg/kg and 6 mg/kg) from week 14 (R+; $n = 12$) based on the RemicheckQ test. The retention rate and clinical response were determined at month 12. [Results] R+ and R- groups retention rates at week 54 were 91.7% and 71.7%, and the groups' remission disease activity in the DAS28 were 80% and 31.3%, respectively. Δ DAS28 score at 12 months was significantly decreased in the R+ group. [Conclusions] In an assessment of adequate RemicheckQ test, the RA patients who did not respond to the initial dose of infliximab showed improved clinical responses after a dose adjustment

of infliximab.

P1-096

The Clinical Efficacy of Certolizumab Pegol (CZP) in Rheumatoid Arthritis (RA) : A Multicenter Retrospective Study (The Second Report)

Akira Furusaki¹, Akira Sagawa¹, Yoshiharu Amasaki², Atsushi Noguchi², Kazuo Matsui², Izumi Yasuda³, Kiminori Hasegawa⁴, Satoko Nakamura⁵
¹Sagawa Akira Rheumatology Clinic, ²Department of Rheumatology, Tonan Hospital, ³Internal Medicine, Yagi Orthopaedic Hospital, ⁴Department of Rheumatology, Sapporo Yamanoue Hospital, ⁵Department of Rheumatology, Hokkaido Orthopaedic Memorial Hospital

Conflict of interest: None

[Object] We investigate efficacy and the drug survival of CZP in RA in daily clinical practice in Sapporo. [Methods] We conducted a retrospective survey of the medical records of patients who started CZP until April 2018. [Results] 62 patients (53 women) were evaluated. Baseline characteristics of the patients mean age 53.1 years, mean disease duration 11.2 years, mean CZP use 3.06 years, MTX use 85.5%, mean MTX dosage 7.8mg/week, PSL use 56.6%, mean PSL dosage 2.2mg/day, Bio-naïve 27.4%, DAS28-ESR 4.63±0.18, SDAI 20.9±1.3. At Week 24, the remission rate of DAS28 and SDAI were 24.2% and 16.1% respectively. Of 37 patients who have, reached moderate response (MR) at 12 weeks, 22 had sustained remission or low disease activity until last observation. However, of 9 patients who had not reached MR at 12 weeks, only one attained the target. The drug survival rate of CZP after 1 and 3 years was 86.5%, and 51.5% (log-rank test). The improvement of MMP-3 at 4 weeks was predictive for the continuation of CZP (P=0.036) (Cox proportional hazards model analysis). [Conclusions] The study revealed the clinical efficacy of CZP in daily clinical practice. The improvement of MMP-3 at 4 weeks and the treatment response at 12 weeks might be predictive of the effectiveness and the survival of CZP.

P1-097

Safety and therapeutic effect predictive factors of golimumab for Juntendo University hospital aged rheumatoid arthritis patients

Nagachika Sugisaki, Kurisu Tada, Yoshiyuki Abe, Michihiro Ogasawara, Ran Matsudaira, Ken Yamaji, Naoto Tamura
Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] We examined the clinical effect and safety of senior patients at Golimumab (GLM) for administered rheumatoid arthritis (RA) patients. [Methods] All of 73 patients were started to receive subcutaneous injections every 4 weeks of GLM. And we analyzed on safety, continuation rate and side effects at the less than 65 years or over 65 years group. [Results] DAS28 remission patients (score<2.3) at week 52 was 56.1%. The mean score of DAS28 at baseline, 52 were 4.03±1.38, 2.47±1.10. Remission group were disease duration until initiation of administration was short, the degree of progress of joint destruction was low, methotrexate (MTX) concomitant dose was high, and steroid combined dose was low. In comparison between young people and the elderly, there was no difference in disease duration, stage, class until initiation of administration, there was no advantage in CRP/mHAQ/DAS 28 CRP at 52 weeks. And there was significant frequency of occurrence of serious adverse events. [Conclusions] GLM administration is validity from the administration early, we showed also high continuation rate after 52 weeks, also high DAS28-CRP remission achievement rate. In addition, it was suggested that administration for elderly people is as safe as young patient.

P1-098

The analysis of effect and safety in the combination therapy of Abatacept and Tacrolimus for RA

Tomoya Nakajima¹, Yoshikazu Fujikawa², Yumiko Nobuhara¹, Takashi Nakazawa¹

¹Osaka Saiseikai Nakatsu Hospital, ²Kobe University Hospital

Conflict of interest: None

[Background] Both Abatacept (ABT) and Tacrolimus (Tac) are DMARDs which have similar mechanism of action against T cells. Whether both drugs should be used together in RA treatment is unclear. [Object] To reveal the effect and safety in the combination therapy of ABT and Tac ('ORE-Tacro'). [Methods] We extracted the RA patients prescribed with 'ORE-Tacro' from October 2017 to September 2018, and analyzed DAS28-CRP and the adverse events. [Results] In 14 patients except 2 of Tac self-discontinuation, 7 patients achieved moderate EULAR response. Then, six patients with Tac followed by ABT were analyzed, and the effects of Tac could not predict the therapeutic outcome of ABT. 'ORE-Tacro' failure due to severe adverse event was only one event in the patient with pneumonia (6.6 events/100 person-year). This incidence was equivalent to that of Japanese post-marketing surveillance of abatacept. [Conclusions] It was proved that 'ORE-Tacro' can be effective in spite of similar mechanism of action. There could be no increase of adverse event, so this combination therapy can be a promising treatment option. However, the patients' predictive factors for 'ORE-Tacro' remain unclear in our study.

P1-099

Empirical Exposure-Response Modeling of Sarilumab in Japanese and Non-Japanese RA Patients

Hideto Kameda¹, Christine Xu², Kazuteru Wada³, Owen Hagino⁴, Anne Paccaly⁵, Hubert Van Hoogstraten², Yoshiya Tanaka⁶

¹Division of Rheumatology, Department of Internal Medicine, School of Medicine, Toho University, ²Sanofi Genzyme, ³Sanofi K.K., ⁴Sanofi, ⁵Regeneron Pharmaceuticals, Inc., ⁶The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: Yes

[Object] To evaluate sarilumab exposure-response (E-R) relationships for pharmacodynamic (PD) biomarkers, efficacy and safety endpoints in Japanese vs non-Japanese patients with RA. [Methods] The Japanese Phase 3 KAKEHASI study (NCT02293902) data were evaluated against pooled data from the global (non-Japanese) MOBILITY (NCT01061736 Part B) and TARGET (NCT01709578) studies. Patients received placebo or sarilumab (150 or 200mg SC q2w) plus conventional synthetic DMARDs. [Results] Exposure-response relationships between functional sarilumab trough concentrations and PD biomarkers (C-reactive protein, serum amyloid A), efficacy parameters (ACR20/50/70, DAS28-CRP), and safety parameter (absolute neutrophil count) were assessed at Week 24. Consistent E-R relationships supported extrapolation of efficacy and safety results from non-Japanese to Japanese patients. PD biomarkers, efficacy and safety assessments were similar between Japanese patients and non-Japanese patients with body weight <60kg, and ≥60kg to <100kg. [Conclusions] These empirical E-R analyses support the approved dosage of sarilumab (200mg q2w SC) in Japan. [Acknowledgments] Study funding and editorial support (Vicki Cronin, Adelphi Communications Ltd) were provided by Sanofi and Regeneron Pharmaceuticals, Inc.

P1-100

Early phase biologic therapy in patients with elderly-onset rheumatoid arthritis (after the age of 80)

Ikuko Onishi, Kentaro Susaki, Yoshihiro Akashi, Satoshi Tohdo, Masayuki Inoo, Noriyuki Kurata
Utazu Hospital

Conflict of interest: None

[Object] Early phase EORA patients should be treated using the treat-to-target strategy, although low disease activity is the realistic goal due to their co-morbidities, patient factors and drug-related risks. Biologics therapy could be a choice of treatment. We treated 16 early phase of EORA patients (≥80 years) with biologics and analyzed clinical, biological, immunogenetic data. [Methods] 16 patient (man:5, woman 11, 83.9±2.9 years old), disease duration: 1.95±1.4month. No one was treated with MTX, 10 patients were treated with PSL (mean 5.9mg). 6 patients had pulmonary disease. 7 patients had diabetes. 8 patients were treated

with abatacept, 8 patients were treated with Golimumab. [Results] Baseline disease mean activity were DAS44-CRP4.5, SDAI 24.2, HAQ1.84. After 3 month, mean activity were improved to DAS44-CRP2.5, SDAI 6.1, HAQ1.58. 2 patients werewithdrawed. One of them got Pneumocystis jirovecii. 8 of 10 patients could taper or stop of PSL. [Conclusions] Biologics treatments in early phase of EORA are useful even after the age of 80. We may prevent progression to irreversible geriatric syndromes, patients with EORA. While we must take care of the risk of serious infection.

P1-101

The comparison of time until 1st biologic introduction with elderly onset rheumatoid arthritis (ERA) and non-elderly onset rheumatoid arthritis (NRA)

Noriyuki Namura, Kazuya Kamada, Takafumi Hagiwara
Department of Rheumatology, Takarazuka City Hospital

Conflict of interest: None

[Object] In ERA patients, most of them develop acutely, and have high acute response from their onset. And we often experience that their function level is suddenly affected. It is important to recover their function immediately with treat to target strategy. We examined the difference in the time until 1stbiologic introduction from ERA and NRA. [Method] We examined 229 RA patient in our hospital. We defined the onset RA 60 years or older as ERA and the others as NRA. The number of biological preparation user of them, ERA was 31 cases, and NRA was 29 cases. We analyzed both group using background factors and thier time until 1stbiologic introduction. [Results] We found that the period until 1stbiologic introduction for ERA was statically significantly shorter than NRA. Regarding their background factors, their CRP have a statically significant difference. But we could find no difference in their gender, ESR, RF, ACPA, mHAQ, DAS28ESR, SDAI at their 1stvisit. In the regression analysis, we showed negative correlation in the onset age and time until 1stbiologic introduction ($p < 0.01$). [Conclusions] In ERA who might have high acute phase response, we showed the time until 1stbiologic introduction is shorter than NRA. But, there was no significant difference in clinical background both groups.

P1-102

Clinical features of our hospital with or without MTX in rheumatoid arthritis treatment

Keina Yomono¹, Ken Nagahata¹, Shuhei Hattori¹, Kei Shimogori², Shotaro Suzuki¹, Seiji Takenouchi¹, Lisa Hirahara¹, Ritsuko Yokochi¹, Noboru Hagino¹
¹Division of Hematology and Rheumatology, Teikyo Chiba Medical Center, ²Jyouban Hospital

Conflict of interest: None

[Object] We cross-sectionally investigated the characteristics of RA patients without MTX treatment, compared with the ones with MTX. [Methods] Single-center cross-sectional study was performed, and 312 RA outpatients were analyzed. Patients with or without MTX group were compared about their clinical features and current treatments. [Results] In total, 213 patients were analyzed (non-MTX group $n=106$; MTX group $n=206$). Non-MTX group patients' median age at analysis was 73 (range 66-79) years old. Anti-CCP antibody positivity rate was 81.1%, Glucocorticoid (GC) use was 54.7%, median GC dosage was 4 (range 2.5-5) mg/day. bDMARDs were used in 34.9% of non-MTX group. The reasons for not using MTX are (1) significant adverse reaction (30.1%), (2) clinically-significant lung disease in (27.3%) and others. In the group with MTX, the median age at analysis was 64 years (range 56-72), and the anti-CCP antibody positivity rate was 71.8%. GC is used in 22.3%, median dosage was 2.5 (range 2-4) mg/day. bDMARDs were used in 33.9%. The median dose of MTX was 10 (range 8-12) mg/week. [Conclusions] In our study, MTX avoidance in RA treatment was associated with more systemic GC use. No difference was seen in the prescription rate and selection of bDMARDs.

P1-103

Understanding of methotrexate (MTX) in patients with rheumatoid arthritis (RA) treated with MTX and their health literacy (HL)

Teruhisa Azuma

Department of General Internal Medicine, Shirakawa Kosei General Hospital

Conflict of interest: None

[Object] To describe understanding of MTX in RA patients and their HL [Methods] Corss-sectional study using original questionnaire and HLS-EU-Q16 in single institute [Results] 50 RA patients (women 86%) were enrolled. Understanding of why and when to take MTX and folate was high, however, understanding of when to stop MTX was low. Proportion of low HLS (≤ 33) was 60%. [Conclusions] We need to enhance understand of when to stop MTX, incorporating to education tool considering their HL.

P1-104

Overall Treatment (Tx) Satisfaction in Rheumatoid Arthritis Patients (pts) in Low Disease Activity (LDA) or Remission (REM) and Their Treating Physicians (phys): A Cross-sectional Survey

Yuko Kaneko¹, Masayo Sato², Zhihong Cai², Minako Sato²

¹Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, ²Eli Lilly Japan K.K.

Conflict of interest: Yes

[Object] To assess if there is a discordance in overall Tx satisfaction between pts and phys. [Methods] A multi-center (Jp), non-interventional, cross-sectional observational study with phys and their pts (LDA or REM) was conducted. Using a structured survey questionnaire, anonymous data on Tx satisfaction and relevant information were collected from both subjects separately. [Results] At 15 sites, 204 pts and 38 treating phys were enrolled and 202 pairs were concordance-evaluable. Mean age of pts was 64.7 yr, proportion of female was 67.3% and mean disease duration was 12.3 yr. For 2-level (satisfied or unsatisfied) assessment of Tx satisfaction, 195 pts from self-evaluation (96.5%) and 190 pts evaluated by phys (94.1%) answered 'satisfied' with high level of concordance (184 pairs, 91.1%). As for communication between pts and phys, a shared Tx decision was made in more than 90% of the pairs. The most popular answer about the most important Tx goal was different between pts ('Have a social life without worrying') and phys ('Prevent joint damage, deformity, and joint swelling'). [Conclusion] Tx satisfaction was high in both subjects. Some differences were observed in detailed questions of Tx outcomes and the most important goal.

P1-105

Actual conditions of drug prescription with a risk of falling for rheumatoid arthritis patients

Kosuke Sakurai^{1,2}, Nobuyuki Yajima¹, Masahiro Hosonuma¹, Tomoki Hayashi¹, Mika Hatano¹, Mayu Saito¹, Nao Oguro¹, Yoko Miura¹, Ryo Yanai¹, Sakiko Isojima¹, Ryo Takahashi¹, Yusuke Miwa¹

¹Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan, ²Pharmacy of Showa University Hospital

Conflict of interest: None

[Object] There is a report describing a high risk of falling for rheumatoid arthritis (RA) patients. But incidents have not been evaluated by concomitant drug as a risk factor. The study aims to investigate actual conditions how often drugs with a risk of falling could be prescribed for RA patients. [Methods] The study targeted RA patients who visited Department of Rheumatology at Showa University Hospital in 2017. We selected the patients who received a prescription for drugs with a risk of falling. We set 4 categories of drugs with a risk of falling; sedatives/hypnotics, antidepressants, antipsychotics and benzodiazepines (BZDs). [Results] 116 patients received a prescription for drugs with a risk of falling. The breakdown of the prescriptions was 83 for sedatives/hypnotics, 13 for antidepressants, 4 for antipsychotics, and 38 for BZDs. For the 4 categories of drugs, there were 95 patients for the prescription of 1 drug, 14

patients for the prescription of 2 type drugs, and 7 patients for the prescription of more than 3 type drugs. 5 out of 116 patients were periodically visiting the hospital specifically for mental/nervous system disorder. [Conclusions] Drugs with a risk of falling were prescribed 12% of the RA patients. Since those drugs may possibly increase a risk of falling.

P1-106

Cost and effectiveness analysis of DMARDs therapy (annual report from Ninja 2017)-the cost of DMARDs increase again and the cost-effectiveness decreased-

Yasuo Suenaga¹, Shunsuke Mori¹, Toshihiro Matsui², Shigeto Tohma³

¹Department of Rheumatology, Beppu Medical Center, NHO, Oita, Japan, ²Department of Rheumatology, National Hospital Organization Sagami-hara National Hospital, ³National Hospital Organization Tokyo National Hospital

Conflict of interest: Yes

[Objectives] To evaluate the balance between the clinical effects of recent anti-rheumatic treatment and its cost [Method] The Data from RA patients registered in the large cohort database (NinJa) in 2002-2017 was analyzed. They included clinical indices and dosage of DMARDs. The annual cost-effectiveness calculated from them. [Results] All averages of clinical indices were decreasing constantly, but more slowly in 2016-2017. The annual cost of DMARDs was about 500,000 yen / patient in 2017, 20,000 yen higher than the cost in 2016. The rate of the cost of biologics was 71.4 % and decreased in 3 years. However, the usage rates of GLM and JAK inhibitors increased. Their annual costs /patient were higher than other DMARDs. ([The rate of the number of low activity patients to that of high activity patients] / cost) were increasing since 2009 and exceeded the level in 2003 (pre-bio-era in Japan), but decreased in 2017. [Conclusion] The NHI price revision led to the stop of increase of the DMARDs' cost in 2014. And it continued without the price revision in 2016. We expected that the cost of DMARDs might have hit the ceiling. Contrary to our expectation, it increased again in 2017. The increase of the usage of GLM and JAK might be involved with that augmentation.

P1-107

Cessation of Adalimumab after complete remission

Sho Sendo, Yoshikazu Fujikawa, Takumi Nagamoto, Yuzuru Yamamoto, Yoshihide Ichise, Hirota Yamada, Ikuko Naka, Yo Ueda, Takaichi Okano, Kengo Akashi, Akira Onishi, Jun Saegusa, Akio Morinobu
Rheumatology and Clinical Immunology, Kobe University Hospital

Conflict of interest: None

[Objectives] To elucidate the course after stopping adalimumab (ADA) because of achieving complete remission (CR) in rheumatoid arthritis (RA) patients. [Methods] We retrospectively analyzed the course of 11 RA patients after stopping ADA. [Results] Baseline characteristics of 11 patients were following; age:60.1±12.8y.o, male/female:1/10, RF:62 (26-177), ACPA:47.4 (6.8-163.6), Class:1.6±0.5, stage:2.0±0.9, duration from diagnosis to stating ADA:52 (20-140) months (M), duration of using ADA:30 (16-37) M, MTX using rate:100%, MTX dose:6.2±2.3mg/wk, GC using rate:27.3%, GC dose:0 (0-0.86) mg/day and DAS28CRP:1.5±0.42. Four patients (36.4%) restarted ADA; relapsed group (RG), and the others sustained cessation of ADA; non-relapsed group (nRG). The duration of stopping ADA was 5.0±3.0M in RG and 76.2±11.2M in nRG. There was no difference between RG and nRG in RF, ACPA, Class, stage, duration from diagnosis to stating ADA, DAS-28CRP and GC dose. RG tended to be longer duration of using ADA (RG:49.8±32.3M, nRG:23.7±9.9M, p=0.071), and tended to be higher MTX dose at the point of stopping ADA (RG:8.0±2.8mg/wk, nRG:5.1±2.5mg/wk, p=0.056). [Conclusion] More than 70% patients who achieved CR could stop ADA for a long duration, while most of the RG needed to restart ADA within 6 M after stopping it.

P1-108

Significance of Measurement of Remi-check Q in RA Patients Treated with Infliximab in Extended Interval Method - Possibility of Indication to Drug Holiday -

Toshiyuki Kitaori, Haruki Takagi, Kazutaka Takatsuka, Hiroko Morise, Tomoya Kotani, Akinori Murakami
Fukui Red Cross Hospital

Conflict of interest: None

[Object] The clinical significance of REMI check-Q (RQ, LDI Medicine Corporation, Tokyo Japan) measurement in RA patients treated with long term administration of IFX at extended dosing interval was clarified. [Methods] The concentration of IFX was measured by RQ in 28 RA patients treated with this agent for at least 2 years, and positive rate was evaluated. The patients were divided into RQ positive group and negative group and group comparison was performed. The comparison between groups divided by administration interval to 8-9w (standard) and 10-12 w (extended) groups were also performed. [Results] The RQ positive rate was 50% (14/28 cases). No significant difference was observed in backgrounds between positive and negative groups. RQ was positive in 66.7% (10/15 cases) of standard group and 30.8% (4/13 cases) of extended group, whereas DAS28-ESR was 2.82 and 2.29, respectively. [Conclusions] In extended group 9 patients had negative RQ results, reducing the overall positive rate. Unexpectedly, however, all of them maintained the activity status of REM or LDA. It is inferable from our experiences that drug holiday of IFX may be achieved successfully in some patients whose disease activity stay good even after RQ turn negative along with extended administration interval.

P1-109

Efficacy and clinical significance of shortening the duration of subcutaneous injection of Tocilizumab

Tamami Yoshitama
Yoshitama Clinic for Rheumatic Diseases

Conflict of interest: None

[Objective] To shorten the administration interval of Tocilizumab (TCZ) subcutaneous injection and evaluate its effectiveness and clinical significance. [Methods] Out of 185 subjects who introduced TCZ from June 2008 to August 2018 in our hospital, 29 subjects changed from intravenous drip infusion to subcutaneous injection and 83 cases started with subcutaneous injection were targeted. We shortened the administration period for 11 cases in which low disease activity could not be achieved by CDAI evaluation at 3 months after the start of TCZ subcutaneous injection and evaluated prospectively for DAS, CDAI, HAQ, joint ultrasound examination 3 months later. Patients who failed to confirm the efficacy were changed to other DMARDs and evaluated the effectiveness after 3 months. [Results] Six cases were able to be judged effective in the CDAI evaluation and confirm improvements by joint ultrasonography at 3 months after shortening the administration period. The medicines were changed from TCZ to Adalimumab, Golimumab, Tofacitinib, and Balicitinib for invalid cases and the efficacy was confirmed in either case. [Conclusions] It was suggested that discrimination of effective cases for shortening TCZ administration period has significance in achieving T2T.

P1-110

A questionnaire survey for patients treated by tocilizumab at our hospital

Akinori Murakami, Haruki Takagi, Kazutaka Takatsuka, Toshiyuki Kitaori, Hiroko Morise, Tomoya Kotani
Department of Orthopaedic Surgery, Fukui Red Cross Hospital

Conflict of interest: None

[Object] We performed a questionnaire survey whether patients treated with tocilizumab (TCZ) evaluated intravenous route (IV) and whether they wanted to switch to subcutaneous route (SC). [Methods] 28 patients (6 males and 22 females) currently treated with TCZ-IV for rheumatoid arthritis in our hospital were asked. [Results] Dissatisfaction points were outpatient time (71%) and treatment cost (43%). 7 patients (25%) wanted

to switch to SC. A reason of the choice of SC was shortening of outpatient time (57%). Reasons of the choice to keep IV were reassurance for infusion in the hospital (70%) and fear of auto-injection (35%). In patients dissatisfied with cost, there was significantly more hope of IV interval extension than SC transition. We expected that patients who had history of other medication SC had anticipated less resistance to SC, but there was no significant. [Conclusions] As in past reports, many patients didn't want to switch to SC. It is considered that the cause is that we didn't adequately inform patients that SC was cheaper due to body weight and that if the previous SC drug form was syringe type, patients felt fear of SC. We need to explain the device improvement and the reduction of cost sufficiently and suggest a treatment method suitable for patients.

P1-111

Steroids or bDMARDs? Patients' choice

Runa Minami^{1,2}, Naoki Nishijima², Kazuma Sawabe¹, Masato Araki¹
¹Misugikai Otokoyama Hospital, ²Tango Central Hospital

Conflict of interest: None

[Object] With the advent of biologic drugs and methotrexate, disease activity can be well controlled in Rheumatoid Arthritis. However, because bDMARDs are expensive, we sometimes use them under the dosage recommended in package inserts. [Methods] 219 patients who regularly visit our hospital in 2018 for RA treatment was analyzed. We collected the patients' data of sex, age, dosage of bDMARDs, MTX, csDMARDs and steroid. [Results] Average age of the patients were 68 (30-97), 163 female and 56 male. 80 were treated with bDMARDs. 23 of 32 treated with ETN were treated with low dose. 16 of 24 treated with ABT were treated with low dose. 11 treated with GLM and 8 treated with TCZ were prescribed as indicated in package inserts. 91 were treated with prednisolone and 35 were prescribed more than 5mg/day. 19 of 35 were not treated with bDMARDs. 7 of 35 were treated with bDMARDs but low dose. [Conclusions] Steroids sometimes cause side effects such as osteoporosis and infection, and recommended to discontinue in 6 months or use lower dose than 5mg/day. However, more than 16% of patients of RA were prescribed more than 5mg/day and 74% of them were not treated with bDMARDs or with low dose. We conclude that 12% of patients of RA chose steroids rather than bDMARD by economical reason.

P1-112

Investigation of surgical treatment during treatment of rheumatoid arthritis (RA) in our hospital

Kota Azuma, Makoto Terada, Yuko Kashiwara, Yuka Hyodo, Shiori Hiroumi
Itami City Hospital

Conflict of interest: None

Objective: Considering the risk of perioperative infection and wound healing, it is desirable to withdraw anti-RA drugs, but exacerbation of joint symptoms due to discontinuation is also expected. Methods: We studied postoperative infections in 119 RA patients who underwent surgical treatment at our hospital. Male 19, female 100. At the perioperative period, oral DMARDs were continued, the biological preparation was discontinued. Results: There were 3 cases of infections after surgery, osteomyelitis, suppurative spondylitis, tibialis muscle abscess. Both improve with antibiotic treatment. Two cases were steroid users, in one case abatacept, three cases MTX 4 to 8 mg were used. Discussion: According to the guidelines of the Japanese Rheumatology Association, MTX is recommended not to increase the risk of complications if it is 12 mg/week or less, continuation of the perioperative period is recommended. On the other hand, a certain rest period is required for biological products before and after the perioperative period. Although we could not point out obvious infectious disease risk factors in this study, we believe the risk of infectious diseases is infinitely low according to the guidelines. We will report on literature on the study of 119 cases this time and report it.

P1-113

Rheumatoid arthritis with progression of joint destruction although C-reactive protein (CRP) negative persisted by using methotrexate (MTX) : A case report

Masashi Morishige, Manabu Yamamoto, Koji Yoshida
Department of Orthopaedic Surgery, JCHO Tokuyama Central Hospital

Conflict of interest: None

[Case report] A 62-year-old man persisting arthralgia for about 10 months had swell and tenderness of the right index finger PIP joint, left knee joint and bilateral 2nd-5th toe MTP joints. Laboratory data revealed CRP was negative (<0.02mg/dl), but RF and ACPA were high (RA:1920IU/ml) (ACPA:229U/ml). In X-ray, erosion was observed in the hand and foot joints, the modified total sharp score (mTSS) was 22 pts. MTX was started with the diagnosis of RA, but the joint swelling and pain persisted (despite negative CRP). Half a year later, biological disease-modifying anti-rheumatic drugs (bDMARDs) was considered, but denied due to economics. For 7 years joint destruction had progressed despite negative CRP and mTSS increased to 129 pts. [Discussion] CRP is thought to be negative for RA with no or low IL-6 production. It is reported MTX reduce IL-6 but does not affect TNF and TNF has low correlation with IL-6. Although TNF inhibitor is effective in the MTX ineffective case, but it was difficult to use bDMARDs in this case. It should be changed or added to other synthetic DMARDs (sDMARDs). [Clinical significance] There are no clear criteria for the selection of DMARDs in the MTX ineffective case. This case suggested which DMARDs should be used in the MTX ineffective case.

P1-114

Clinical effectiveness and safety of Etanercept Biosimilar

Takashi Mitsuhashi^{1,2}, Kenji Mannami¹, Makoto Mannami¹
¹Mannami Orthopedic Surgery, ²Kyoto Ohara Memorial Hospital

Conflict of interest: None

[Object] To evaluate the clinical effectiveness and safety of Etanercept Biosimilar (ETN-BS) [Methods] Since May 2018, ETN-BS has been administered to 10 patients with RA in our clinic. The patients were 2 men and 8 women with a mean age of 64.4 years. Of the patients, 20% concomitantly used MTX; 3 were biologic-naive patients previously treated with csDMARDs, and 7 were switched from other biologic agents (2 from etanercept, 2 from golimumab, 2 from certolizumab, and 1 from abatacept). The effectiveness and safety of ETN-BS were evaluated using the 28-item Disease Activity Scale (DAS28) and simplified disease activity index (SDAI) over time. [Results] The mean DAS28 and SDAI scores at the initiation of ETN-BS (week 0) were 3.56 and 19.3, respectively. At week 12, the mean DAS28 and SDAI scores were 2.74 and 8.04, respectively. One patient without combination use of MTX developed an adverse reaction (eruption) to ETN-BS and discontinued its use 2 months after treatment initiation. [Conclusions] Although further follow-up was necessary, use of ETN-BS resulted in decreased disease activity and remission induction as indicated by the decrease in DAS28 and SDAI scores to 2.74 and 8.40, respectively. ETN-BS may be a promising treatment option with respect to medical economics.

P1-115

Efficacy and safety of Golimumab in the elderly patient with rheumatoid arthritis

Koei Oh^{1,2,3}, Yasuo Inoue³, Kae Takagi⁴, Katsunori Ikari^{1,2}, Junji Chiba³, Hisashi Yamanaka¹, Ken Okazaki²

¹Institute of Rheumatology, Tokyo Women's Medical University, ²Department of Orthopedics, Tokyo Women's Medical University, ³Department of Orthopedics and Rheumatology, Tokyo Women's Medical University Medical Center East, ⁴Department of Internal Medicine, Tokyo Women's Medical University Medical Center East

Conflict of interest: None

[Object] The proportion of elderly RA is growing as a result of the increasing aging population. It is not well-known how their complications and comorbidities have influence on the elderly RA receiving bio-

logics. Thus, we evaluated golimumab (GLM) efficacy and safety up to 3 years in the elderly RA. [Methods] We divided 120 cases into two groups: group O (GO); 49 cases ≥ 65 y/o, group Y (GY); 71 cases < 65 y/o. Patient's demographics, disease activity, functional assessment, medications, rates of efficacy and persistency were statically assessed between GO and GY. [Results] Initial DAS28 (CRP) in GO (4.9 ± 1.05) was higher than GY (4.16 ± 1.01) respectively. EULAR good and moderate response were: 64.5% (GO), 66.2% (GY) at week 12, and 67.2% (GO) 66.2% (GY) at week 52. The remission rate of DAS28 (CRP) were: 33.7% (GO) 34.6% (GY) at week 52, and 32.8% (GO) 34.6% (GY) at week 156. The continuation rate were 78.2% (GO) 79.8% (GY) at week 52, and 67.8% (GO) 65.9% (GY) at week 156. The reason of discontinuation were 4 cases of serious adverse events (AE), 3 cases of insufficient effectiveness and 6 cases of second failure. [Conclusions] GLM had an effect on the elderly RA as much as the young RA. Special attention should be required for the elderly RA.

P1-116

Efficacy of iguratimod plus TNF inhibitor in rheumatoid arthritis patients who MTX cannot use

Toshiaki Miyamoto, Kenji Yamazaki, Ryuhei Ishihara
Internal Medicine and Rheumatology, Seirei Hamamatsu General Hospital

Conflict of interest: Yes

Objective Iguratimod (IGU) was approved in June 2012 and recommended by guideline 2014 in the treatment of rheumatoid arthritis (RA). Although there have been efficacy of monotherapy and concomitant MTX in clinical trials, however, there have been no reports of concomitant biologic DMARDs (Bio). Therefore, we investigated efficacy of IGU+Bio therapy in RA patients who had MTX intolerance at the author's institution. **Methods** Subjects were 9 patients who had MTX intolerance from June 2015 to July 2018. Previous treatment Bio. was ADA. Baseline characteristics were Mean age 61.3 years, mean duration of illness 94.0 months, corticosteroid use 11.1% (mean 3.0 mg/day). The course of DAS28, SDAI, CDAI and remission rates were analyzed. **Results** Mean DAS28-CRP, SDAI, CDAI were decreased trend from the initiation of IGU treatment at 24 weeks ($3.29 \rightarrow 2.55$, $15.3 \rightarrow 8.58$, $14.5 \rightarrow 7.74$) and at 52 weeks ($3.29 \rightarrow 2.44$, $15.3 \rightarrow 8.24$, $14.5 \rightarrow 7.34$). Remission rates of DAS28-CRP, SDAI, CDAI were 50%, 50%, 50% at 24 weeks and 60%, 60%, 60% at 52 weeks. **Conclusion** IGU+Bio might be a new RA treatment option for aiming remission in patients who had MTX intolerance.

P1-117

A case report of rheumatoid arthritis who had appeared lung tuberculosis after baricitinib administration despite negative result of interferon gamma release assay

Ichiro Yoshii
Rheumatology and Musculoskeletal Medicine, Yoshii Hospital

Conflict of interest: None

[Purpose] We have experienced one rheumatoid arthritis (RA) patient who appeared lung tuberculosis (TB) after baricitinib (BAR) administration despite negative pre-screening result of interferon gamma release assay (IGRA). [Case Presentation] Eighty-four-year-old man consulted with two-year-history of RA. At first consult, his SDAI was 13.0, and started MTX from 6 mg per week, and gradually increased to 12 mg. His disease activity was so high that his SDAI had increased up to 36.4 when MTX was tapered. 4 mg BAR was administered, with no anti-TB drug due to negative result of IGRA. His SDAI had been settled so rapidly that remission attained at six weeks. Fatigue emerged six months later, and chest X-ray showed TB findings with Grade 5 in Gaffky scale. He had admitted for TB treat. Gaffky have been settled to Grade 0, despite fatigue and appetite loss remained. SDAI maintained remission with 7.5 mg PSL, however somnolence and appetite loss continued. [Discussion] BAR inhibits JAK1 and JAK2, that blocks signaling pathway of many cytokines. It blocks inflammation, despite also blocks interferon gamma and then suppresses type 3 allergic reaction. Emergence of TB must be cared. [Clinical Significance] We need to take extreme care for TB when BAR

is administered even IGRA showed negative.

P1-118

A case of severe and prolonged agranulocytosis induced by salilumab

Midori Kitayama¹, Ayaka Inoue¹, Hiroaki Nakagawa¹, Takuro Maeda¹, Noriaki Yo¹, Chihiro Tanaka¹, Takashi Yamane¹, Rimi Iwamoto², Yasuhiro Terashima³

¹Department of Rheumatology, Kakogawa Central City Hospital, ²Department of Pharmacy, Kakogawa Central City Hospital, ³Department of Rheumatology, Konan Kakogawa Hospital

Conflict of interest: None

A 78-year-old woman was diagnosed as RF/ACPA positive RA. Cs-DMARDs were started but high disease activity remained. Abatacept was administered, but failed after 2 months, so she had received salilumab (at the time WBC count 6080/ μ L). She came to ER a few hours after injection, complaining of shivering high fever, and was hospitalized. On the next day, a blood exam showed WBC 830/ μ L (Neu11%), and then she was transferred to our hospital. We started G-CSF and antibiotics followed by febrile neutropenia. On day 5, we stopped first treatment since WBC count rose to 4200/ μ L (Neu40.9%). On day 9, WBC count decreased to 1980/ μ L (Neu18%), so we restarted G-CSF until day 11. We need G-CSF administration again on day 16 because of neutropenia, but after that, WBC count recovered steadily to range before salilumab injection. IL-6 is an important mediator for RA and to inhibit IL-6 would make improvement in disease activity. The process of agranulocytosis caused by IL-6 inhibitors is not unclear. The frequency of agranulocytosis is less than 0.1% in tocilizumab and 0.6% (1/161 cases) in salilumab. It happens the next day of tocilizumab administration and it takes 1-2 weeks to get improvement in WBC count. This case indicates we need careful intervention for neutropenia induced by salilumab.

P1-119

A case of lung-tuberculosis (TB) in a patient of rheumatoid arthritis long after the initial treatment for the latent tuberculosis infection (LTBI)

Satoko Nakamura¹, Kiminori Hasegawa²
¹Department of Rheumatology, Hokkaido Orthopaedic Memorial Hospital, Sapporo, Japan, ²Department of Rheumatology, Sapporo Yamanoue Hospital, Sapporo, Japan

Conflict of interest: None

[Case] A 77-year-old female was diagnosed as dermatomyositis (DM) on 2015 followed by treated with steroid pulse therapy and MTX at the previous hospital. INH was co-administered for her LTBI for 6 months, because of her history of pulmonary TB during childhood. On January 2018, she developed RA, therefore Tocilizumab was started without LTBI treatment. In August 2018 she was admitted to our hospital for further evaluation. Her chest-X ray for screening on admission showed a fine grainy shadow, subsequent sputum showed the presence of tubercle bacillus, leading to the diagnosis of pulmonary TB. [Clinical significance] Since the screening methods such as IGRA as well as the treatment of LTBI was established, the clinical guideline had recommended the biologic agents should be administered concomitant with LTBI treatment for 6-9 months in case of the previous infection of TB. However we have no answers regarding to the questions such as "How long the effectiveness of initial LTBI treatment is persistent?" "In the case of bio-switch, should we perform re-treatment for LTBI?" In this context, this case clearly highlights the clinical caveat for TB, as reconsidering the necessity of LTBI re-treatment and the importance of sharing the medical information between medical facilities.

P1-120

When RA Patients treated with MTX admitted by infection, we should start Leucovolin rescue

Akihiko Mukai¹, Megumi Matsueda¹, Mayumi Kawaguchi²
¹Department of Rheumatology, Coop-Osaka Hospital, ²Internal Medicine, Mimihara General Hospital

Conflict of interest: None

[Object] Methotrexate (MTX) has been used for many years in patients with rheumatoid arthritis (RA). We experienced cases of RA patients treated with MTX who were admitted with infection and cytopenia. We investigated how severe infections are related to the cytopenia of MTX. [Methods] Among RA patients treated with MTX, admitted with infectious disease since 2014 were studied. We retrospectively investigated the diagnosis of infection and renal function, protein albumin, blood cell count, edema, dehydration and drug therapy before and after hospitalization. [Results] 21 cases were studied. M:F 1: 3. Age 73 ±13 years old. 11 pneumonia, 4 pyelonephritis, 2 cholecystitis, 2 tuberculosis, 2 others. Cytopenia was confirmed in 6 cases, and pancytopenia was 4, rescued with leucovorin. Cytopenic cases were elder, lower protein albuminemia, decreased renal function. Some cases developed into cytopenia after hospitalization or MTX doses <4 mg. [Discussion] Pancytopenia caused by MTX is a risky condition. In this study, 20% (4/21 cases) patients suffered from severe infection among RA using MTX were not rare. [Conclusions] RA patients who are using MTX are hospitalized for infection, we should not only discontinue of MTX, and also start leucovorin rescue.

P1-121

Clinical study of MTX-LPD developed during RA treatment

Masahiro Kondo¹, Yohko Murakawa¹, Tomoko Sugiura², Mayuko Moriyama¹, Manabu Honda¹

¹Faculty of Medicine, Department of Rheumatology, Shimane University, ²Sugiura Clinic

Conflict of interest: None

Objective Occurrence of MTX-LPD in RA patients has been reported. Causative or predictive factors of it remained to be unknown. **Method** Clinical characteristics of 21 MTX-LPD patients treated in our hospital or Hamada medical center were analyzed retrospectively. **Results** Average prescription period, average maximum dosage and average total prescription dosage of MTX were 5.9 yrs (2-12.7), 11.3 mg/wk (4-16) and 2453 mg (394-4726), respectively. Six of 10 cases who were examined EBV were positive. Pathologically 6 of 12 cases showed DLBCL. DAS28-ESR score were under LDA in 10 cases. In ten, peripheral blood lymphocyte counts (PBLC) decreased at onset of LPD compared with 6 month before onset, especially in EBV positive ones. LPD in 8 cases were improved with the cessation of MTX, however 2 of them recurred thereafter accompanied with decrease in PBLC. Unfortunately, 4 cases were dead. **Conclusions** Accumulative amounts or taking periods of MTX seem to be irrelevant to LPD onset in our cases, because LPD occurred in some of them treated with a small amount or in a relatively short period of MTX. PBLC decrease was observed at onset and relapse of LPD, particularly in EBV-positive ones. The decrease in PBLC might be involved in the onset and be useful for prediction of MTX-LPD onset.

P1-122

Analysis of 15 cases of methotrexate related lymphoproliferative disease (MTX-LPD) in our hospital

Junki Hiura¹, Ayumi Uchino¹, Toshiyuki Ota², Shuji Nagano¹

¹Department of Rheumatology, Iizuka Hospital, Fukuoka, Japan, ²Center for Rheumatology, Iizuka Hospital, Fukuoka, Japan

Conflict of interest: None

[Object] To clarify the clinical characteristics of MTX-LPD in rheumatoid arthritis (RA) patients. [Methods] The 15 MTX-LPD patients (12 females, 3 males) who received RA treatment at our hospital between January 2012 and September 2018 were selected. We analyzed about background, clinical course and treatment of RA after development of LPD. [Results] The mean age and RA duration at LPD diagnosis were 66.3 and 11.1 years, respectively. The mean MTX dose was 6.9 mg/week, total dose was 1926 mg, and used period were 6.1 years. The pathological type was composed of 10 diffuse large b-cell lymphoma (DLBCL), 2 T cell lymphoma, 1 follicular lymphoma, 1 MALT lymphoma, 1 EBV-LPD respectively. 4 of 15 cases were improved naturally, and 1 case was being observed after MTX stopping. 9 cases were need to chemotherapy. 2 cas-

es were relapsed and 1 case died. 1 of 15 case died before chemotherapy. 2 cases of death were both DLBCL. 6 cases were received sulaosulfapyridine (SASP), after development of LPD, tocilizumab (TCZ) was used in other 3 cases, 4 cases were drug free. [Conclusions] As previously reported, it was suggested that DLBCL histological type was related to poor survival. RA treatment after development of LPD was mainly performed by SASP, and TCZ was tended to be chosen as bDMARDs.

P1-123

The analysis of the treatment in 21 RA patients with methotrexate associated lymphoproliferative disorders (MTX-LPD)

Kazuya Kamada, Noriyuki Namura, Takafumi Hagiwara
Department of Rheumatology, Takarazuka City Hospital

Conflict of interest: None

{Purpose} Because reports and analysis of RA treatment with MTX-LPD are insufficient, as for the rheumatic treatment before and after the MTX-LPD onset, we cannot yet have conviction. {Methods} In our facility, we investigated 21 RA patients who developed MTX-LPD between 2010 and 2017. And we retrospectively examined RA disease activity from their medical record. {Results} After stopping of MTX treatment, as for 14 of 21 MTX-LPD patients, their MTX-LPD resulted in spontaneously regression. But others needed chemotherapy (cTx) for their treatment. The average time to RA treatment resumption from MTX-LPD onset of cTx (-) and cTx (+) were 30 days and 450 days respectively. The change of RA disease activity in 12 months before and after MTX-LPD onset (-12M/ 0M/+12M) were 6.3/6.6/11.9 for CDAI, 0.6/3.9/1.9 for CRP (mg/dL), 93/94/123 for MMP-3 (ng/mL) and 320/144/7 for RF (U/mL). In 14 of 21 cases, they needed biologic therapy, and the time to biologics introduction from MTX-LPD onset of cTx (-) and cTx (+) were 350 days and 1127 days respectively. {Conclusions} Our analysis suggested that RA disease activity became gradually worsen after MTX-LPD onset. Biologic agent is often required with many cases of MTX-LPD by a restriction of the csDMARDs use.

P1-124

Two cases of patients with rheumatoid arthritis who had cancers diagnosed by screening CT scan of lung before administration of biological DMARDs

Yuji Joyo¹, Yohei Kawaguchi¹, Yusuke Oguri¹, Hiroto Mitsui¹, Gen Kuroyanagi¹, Yuko Nagaya²

¹Department of Orthopaedic Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, ²Department of Joint Surgery for Rheumatic Diseases, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Conflict of interest: None

[Objective] We report the two cases of patients with rheumatoid arthritis (RA) who had cancer diagnosed by screening CT scan of lung before administration of biological DMARDs (bDMARDs) in our hospital between April 2017 and May 2018. [Case 1] A 77-year-old woman developed RA at age of 75 years and had been treated with methotrexate (MTX), prednisolone (PSL) and tacrolimus, however her arthralgia had gradually worsened. The CT scan of lung revealed the breast cancer. After radical mastectomy, low diseases activity of RA is maintained without introduction of bDMARD. [Case 2] An 83-year-old woman with early onset RA had treated with MTX and PSL for a year. However, her disease activity remained high. Screening CT scan revealed lung metastasis of pancreatic cancer. MTX was ceased. She died in a month after diagnosis of pancreatic cancer. [Discussion] The number of elderly patients with RA treated with bDMARDs is increasing. Since aging is a risk factor of malignant tumors, we must be aware of various types of cancer in the treatment of elderly RA patients. Screening CT before administration of bDMARDs is useful for detection of not only interstitial pneumonia and tuberculosis but also cancer.

P1-125

A study on the effect of renal dysfunction in RA

Kazuhiro Fukuoka, Chinatsu Hyodo, Yoshinori Komagata, Shinya

Kaname
Department of Nephrology and Collagen Disease, Kyorin University
School of Medicine

Conflict of interest: None

[Object] we tried to clarify the relationship between rheumatoid arthritis (RA) treatment and renal function. [Methods] We classified each case of CKD by eGFR at the initiation of treatment in RA patients who had been treated in our hospital after 2014. In addition, retrospective studies were conducted on the relationship between the use of medications such as glucocorticoid (GC), NSAIDs, csDMARDs, bDMARDs and eGFR. We also observed the dose reduction effects of bDMARDs in MTX, tacrolimus, bucillamine treating groups. [Results] In our study, the incidence of CKD was equivalent to the general population and tended to increase with age. In the case of impaired renal function, the amount of MTX dosages was small, and there was a tendency to be used in combination with other drugs. In addition, the combined use of bDMARDs, GC usage and MTX dose reduction effect were observed (20% and 15%, respectively). [Conclusions] In some RA cases, serum creatinine level was found lower because their muscle volume is relatively low, and these made reduce the average eGFR data in a whole cases. Renal dysfunction in RA is responsible for limiting the range of use of therapeutic agents. In these cases, treatment using bDMARDs in combination was considered to be useful.

P1-126

Organizing pneumonia in rheumatoid arthritis patients treated with anti-tumor necrosis factor biologics: A case series

Akira Okamoto¹, Tetsuji Kawamura², Rinko Katsuda², Yasutaka Ohnishi², Kohei Miyake², Akiko Kitagawa¹

¹Department of Rheumatology, National Hospital Organization Himeji Medical Center, ²Respiratory Medicine, National Hospital Organization Himeji Medical Center

Conflict of interest: None

[Background] Organizing pneumonia (OP) induced by treatment with anti-TNF biologics in rheumatoid arthritis (RA) patients is rare. Herein, we report four such cases. [Case 1] A 76-year-old male. OP was treated with high-dose prednisone (PSL), showing improvement. Subsequently, he was treated with PSL, methotrexate (MTX), and certolizumab pegol (CZP) for uncontrolled arthritis. OP relapsed 56 days after initiation of CZP. [Case 2] A 58-year-old female. OP was treated with high-dose PSL, showing improvement. Subsequently, she was treated with PSL, MTX, and etanercept (ETN). OP relapsed 525 days after initiation of ETN. [Case 3] A 78-year-old male treated with PSL, MTX, and ETN. OP occurred 31 days after initiation of ETN. Treatment with ETN was discontinued and switched to ABT [A1]. Although OP improved, arthralgia continued. ABT was switched to golimumab (GLM). OP relapsed 32 days after initiation of GLM. [Case 4] A 69-year-old female reported cough and arthralgia and was diagnosed with RA complicated by OP. She received PSL and MTX. Although OP improved, arthritis continued and CZP was initiated. OP relapsed 392 days after initiation of CZP. [Conclusion] Physicians should closely monitor patients for the occurrence of OP after treatment with anti-TNF biologics.

P1-127

Nivolumab-induced recurrence of rheumatoid arthritis in a patient with advanced metastasis of gastric adenocarcinoma

Masataka Nishikawa¹, Atsushi Goshima², Hajime Owaki²

¹Department of Rheumatology, Japan Community Healthcare Organization Osaka Hospital, ²Department of Orthopaedic Surgery, Japan Community Healthcare Organization Osaka Hospital

Conflict of interest: None

[Case] 63 years-old male. He had developed rheumatoid arthritis (RA) at the age of 46 years. His remission had been maintained with methotrexate (MTX) at 8mg/week, and tacrolimus at 1.5mg/day. He underwent the surgery for gastric adenocarcinoma and received chemotherapy (CTx) at the age of 55 years. Although the medication for RA was

discontinued, another 5 years remission maintained. Although he redeveloped RA at the age of 60 years, he achieved remission again with MTX. He discontinued MTX again because of CTx for peritoneal metastasis at the age of 61 years. Prednisolone (PSL) 5mg/day was administered for the side effect of CTx and another 2 years RA remission was maintained. Nivolumab was administered at the age of 63 years, because of advanced peritoneal metastasis. After 2nd administration, his RA symptoms were worsened (TJC: 3, SJC: 6, CRP 4.92mg/dL, VAS 77mm, DAS28-CRP 5.31). The increase of PSL (10mg/day) was selected, because of terminal status of his life. Although RA symptoms were improved, he was dead 3 month later. [Clinical significance] Nivolumab inhibits the interaction between PD-1 and PD-L1 thus inhibiting the cancer immune escape pathway. This case teaches the rheumatic side effects of immunotherapy in the treatment of cancer, especially in patients with RA.

P1-128

Unique seasonal change in number of bDMARDs initiation observed from NDB analyses

Fumihiko Ando¹, Katsuhiko Takabayashi^{1,2}, Takahiro Suzuki¹, Hideki Hanaoka³

¹Division of Medical Informatics., Chiba University Hospital, Chiba, Japan, ²Department of Internal Medicine., Sanwa Hospital, Matsudo, Japan, ³Clinical Research Center, Chiba University Hospital, Chiba, Japan

Conflict of interest: None

[Object] To analyze initiation numbers of bDMARDs to rheumatoid arthritis patients. [Method] We analyzed 51,018,706 claimed data over seven years for patients treated with biological disease-modifying anti-rheumatic drugs (bDMARDs). 205,906 patients with rheumatoid arthritis (RA) were treated with bDMARDs at least once during these seven years from big claim data. [Result] We noted an apparent seasonal change in number of bDMARDs initiation. It shows a sine curve shape, with the highest months from June to August and the lowest in December and January in every year. It was also observed from each drug, or each prefecture. [Conclusion] From NDB analysis we noted seasonal sine curve change in number of bDMARDs initiation

P1-129

Problems of treatment with rheumatoid arthritis at cases of medical lawsuit

Kentaro Doe, Kazuhisa Nozawa, Souichiro Nakano, Kentaro Minowa, Ken Yamaji, Naoto Tamura

Department of Rheumatology, Juntendo University School of Medicine

Conflict of interest: None

[Background and methods] Treatment of rheumatoid arthritis has progressed rapidly in these days, but there is risk of emerging medical lawsuit due to adverse effects of drugs. So we examined the problems in medical lawsuit and referred them to their clinical guidelines and the attached documents with drugs. [Methods] We analyzed the problems at the cases of medical lawsuit. [Results] There are many problems about lack of informed consent about adverse effects to patients in the case of lawsuit. Doctors must get latest information about adverse effects from the attached documents and medical literatures and give the informed consent to the patients before the induction of the treatment. In addition, we must take care about onset and worsening in not only interstitial pneumonia, liver damage, kidney damage, cytopenia, HBV, HCV, tuberculosis and fungus infection, but also varicella, measles, disseminated herpes zoster, intestinal diverticulum and psoriasis. There is a lost case in medical lawsuit for doctor in the patient with disseminated herpes zoster induced by steroid therapy. [Conclusion] It is very important to give informed consent to patients about predictable adverse effects of the treatment from latest drug information in the attached documents.

P1-130

Factors related to fatigue in patients with rheumatoid arthritis

Yoshio Nagayama

Nagayama Rheumatology Orthopaedics, Sakai, Japan

Conflict of interest: None

[Object] To evaluate factors related to fatigue in patients with RA. [Methods] We examined 305 RA patients who were evaluated the fatigue using FACIT-F. We divided into a low fatigue group (L) with 36 points or more and a high fatigue group (H) with 35 points or less. We examined a cross-sectional study on the relationship between each factor such as age, gender, disease duration, Steinbrocker classification, RA disease activity, medication, Hb, HADS-D, HADS-A. [Results] There were 166 cases in group L and 139 cases in group H. The age was 63.1 in group L, 68.5 in group H ($P<0.01$), Class was 1.64 in group L, 1.90 in group H ($P<0.01$), DAS28-CRP was 1.67 in group L, 2.20 in group H ($P<0.01$), SDAI was 3.98 in group L, 7.35 in group H ($P<0.01$), MTX dosage was 7.59 in group L, 5.97 in group H ($P<0.01$), Use of biologics was 21.6% in group L, 34.5% in group H ($P=0.01$), Hb was 12.7 in group L, 12.2 in group H ($P<0.01$), HADS-D was 3.28 in group L, 8.21 in group H ($P<0.01$), HADS-A was 3.96 in group L, 7.58 in group H ($P<0.01$), there were significant differences. In multiple logistic regression analysis, high HADS-D and high HADS-A were extracted as independent risk factors. [Conclusions] Depression and Anxiety were risk factors for fatigue in patients with rheumatoid arthritis.

P1-131

Current status of late-elderly rheumatoid arthritis patients treated by biological agents (comparing the situation of care insurance service)

Hitoshi Tada¹, Yuko Fujiwara²

¹Internal Medicine, Haradoi Hospital, Fukuoka, Japan, ²Department of Orthopedics, Haradoi Hospital, Fukuoka, Japan

Conflict of interest: None

[Object] Continuing treatment of patients with rheumatoid arthritis (RA) until the terminal stage is a problem for the future. We report the outcome of late-elderly RA patients who were introduced biological agents (Bio) because of high disease activity with or without care insurance services. [Methods] Since 2005, 28 RA patients with late-elderly who are 75 years of age or older at our hospital were treated with Bio. Of 7 patients (R patients) were received care insurance services. We compared the period of treatment and complications of 7 patients with the 21 patients (NR patients) who were not received care insurance services. [Results] Average of age at the start of Bio therapy, R patients was 78.5 (71-86), and NR patients was 75.2 (64-88), average treatment period was 72.4 months (24-159 median 49.3), and 65.0 months (5-161, median 42.0), respectively. In R patients, there were 3 deaths due to complication, in NR patients, there were 8 deaths, respectively. [Conclusions] Our data showed that late-elderly RA patients can be continued Bio therapy with care insurance service and can be receive almost same treatment as outpatients. Cooperation between medical care and nursing care is essential for the community-based integrated care systems.

P1-132

Survey of Attitude for Member of Team Medical Care for Rheumatoid Arthritis

Kanako Shimura, Miho Tachihara, Setsuko Tajima, Yukie Saio
Department of Rheumatology, Toho Hospital

Conflict of interest: None

Purpose: We set up medical care team for Rheumatoid Arthritis on September, 2017. We surveyed attitude of team members by questionnaire. Eligible person: Team member (exclude MD): 27 person, 12 types of occupation. Methods: On A: May, B: July, and C: September of 2019, we surveyed attitude of team members by questionnaire on a five point scale, and evaluated the average by 6 ranks. Results: Result of B was similar to A. But attitude of members on C was changed in comparison to A as follows. Rank up: Skill up of myself. No change: Understanding of boss and hospital, Number of staff, information of seminar, further understanding by another occupation, cooperation between hospital and clinic, cooperation between hospital and outpatient pharmacy, length and frequency of team conference, and observation of another hospital. 1 rank down: worthwhile of job, understanding by another occupation, motiva-

tion to prepare plan, understanding to another occupation, and motivation to admit seminar. 2 ranks down: Motivation to participate in team, inform importance of team, participation and presentation at meetings. Conclusions: Although the member's attitude to improve their skill went up, the attitude was not connected with motivation to participate and to give presentation at the meeting.

P1-133

Treatment strategy for super elderly rheumatoid arthritis patient

Ichiro Yoshii¹, Tatsumi Chijiwa², Naoya Sawada³

¹Rheumatology and Musculoskeletal Medicine, Yoshii Hospital, ²Department of Rheumatology, Kochi Memorial Hospital, ³Department of Rheumatology, Dohgo Spa Hospital

Conflict of interest: None

[Object] Number of aged rheumatoid arthritis (RA) patient is increasing partly due to social population ageing. We would think treatment strategy for RA patient who is older than 75-year-old in reviewing our cases, retrospectively. [Methods] We picked up 576 RA patients who were treated for more than three years, who configured 151men and 425 women, and average age at first consult was 65.1. Patients were divided according to age when disease activity recorded minimum (min-DAS), as less than 65, 65 to 74, and no less than 75. Mean values of as 28-joints disease activity score with C-reactive protein (DAS28-CRP) at first consult, when clinical remission was attained, at min-DAS, and after min-DAS, and patients' clinical background, administration ratio and dose of methotrexate and glucocorticoid steroid (GCS), biological agent administration (BIO) ratio were compared in the three groups statistically with ANOVA. [Results] No statistical difference demonstrated in all parameters, except of GCS administration ratio at min-DAS. That demonstrated significantly higher in the group no younger than 75 than the other two groups, while it turned the same after min-DAS. [Conclusions] It is suggested that aiming clinical remission is the right treatment strategy even for super elderly RA patient.

P1-134

Drug therapy for patients with rheumatoid arthritis at JCHO Yugawara Hospital

Takuo Juji¹, Ichiro Nakamura^{1,2}, Naohiro Izawa¹, Akihiro Uchio¹, Takumi Matsumoto⁴, Jinju Nishino⁴, Katsumi Ito³, Sakae Tanaka⁴

¹Department of Rheumatology, Yugawara Hospital, Japan Community Health Care Organization, Kanagawa, Japan, ²Faculty of Medical Science for Health, Teikyo Heisei University, Tokyo, Japan, ³Department of Rheumatology, Heisei Yokohama Hospital, Kanagawa, Japan, ⁴Department of Orthopaedic Surgery, Faculty of Medicine, The University of Tokyo, Tokyo, Japan

Conflict of interest: None

[Object] Treatment of rheumatoid arthritis (RA) is progressing year by year. Control of disease activity has been improved by the approval of methotrexate (MTX) and the introduction of biologic agents. In this study, we investigated the drug therapy of patients with rheumatoid arthritis in our hospital. [Methods] We examined the rheumatic drugs used for RA patients treated at our hospital. [Results] There were 407 RA patients treated at our hospital, 336 women, 71 males, average 68.1 years of age. In the use of csDMARDs, 250 cases of MTX, 77 cases of salazosulfapyridine, 65 cases of bucillamine, 48 cases of iguratimod, 35 cases of tacrolimus, 13 cases of leflunomide and 4 cases of gold sodium thiomalate. The combined number of csDMARDs was 0 - 4, with an average of 1.3. Dose of MTX was 1 to 11 mg/week, 5.1 mg/week on average, and combined use of folic acid was 66 cases. Use of glucocorticoid were 150 cases, 0.5 to 10mg/day in conversion of prednisolone, and an average of 3.4 mg/day. The use of biological agents was 135 out of 407 patients, 43 cases of etanercept, 31 cases of abatacept, 26 cases of tocilizumab, 16 cases of infliximab, 15 cases of golimumab and 4 cases of adalimumab. [Conclusions] We investigated the contents of drug treatment of RA patients treated in our hospital.

P1-135

Safety of abatacept under the multi-disciplinary approach for the treatment of elderly people with rheumatoid arthritis

Satomi Kashiwaya, Sanae Kawahara, Mika Ogawa, Sachiko Kojima, Yuka Tashiro, Hiroshi Ito, Hironari Hanaoka, Hidehiro Yamada
Medical Center for Rheumatic Diseases, Seirei Yokohama Hospital

Conflict of interest: None

To assess the safety of abatacept (ABT) under our multi-disciplinary approach for the treatment of elderly people with rheumatoid arthritis (RA). In 2016 we established the co-laborative medical team for rheumatic diseases, consisting of pharmacists, care nurses and rheumatologists. We retrospectively reviewed the medical charts of the consecutive 151 RA patients who were introduced with ABT from 2016 until March 2018. Tolerability and serious adverse events of ABT was compared between elderly group (age 75 or older) and control group (age less than 75). Mean age of the elderly (n=66) and the control (n=85) was 81 and 64, with male ratio of 17% and 20%, respectively. MTX was co-administered in the elderly less commonly with less doses than the control. Concomitant prednisolone was used in about 40% of both groups with similar initial doses. The 2-years event-free survival of ABT was 54% in the elderly and 63% in the control (p=0.29). Cumulative severe adverse event rate and cumulative rate of insufficient efficacy was similar between groups (p=0.12, p=0.72). Severe infection occurred in 2 elders (2.70/100 person-year). Our multi-disciplinary approach for the treatment of elderly RA with ABT seemed working. Further work is needed to reduce treatment-related co-morbidities.

P1-136

Relevance of biologics for the long-term effects and patient satisfaction in the elderly on set rheumatoid arthritis

Kosaku Oda, Ikuyo Noguchi
Department of Orthopedic Surgery, Takatsuki Red Cross Hospital Osaka Japan

Conflict of interest: None

(Object) Treatment for EORA needs with various complications and polypharmacy. Efficacy of T2T improved by practicing safety management. On the other hand, effectiveness of the patient's own satisfaction is left. Therefore, we examined the relationship between long-term effect and patient satisfaction with Abatacept and Golimumab for EORA. (Method) We randomly extracted EORA aged 65years older during the 3years from 2015 to 2018. Examined the background, disease activity, HAQ transition, patient satisfaction survey of the ABT and the GLM group. (Result) Group A 10 pts 75.6 ±7.0y, Group G 9 pts 73.2 ±4.0 y were the same background. eGFR, the dose of MTX, DAS-CRP showed a declining in both groups significantly. In HAQ maintained 36 months later. No liver and kidney disease exacerbations and serious infection were observed in both groups. (Conclusion) By actively interposing treatment including BIO in EORA with high disease activity, it controls HAQ and leads to prolongation of healthy life. However, long-term effectiveness and patient satisfaction do not necessarily agree with each other, and efforts to further improve patient satisfaction by communicating with patients through team including nurses are necessary.

P1-137

A practice report of the educational hospitalization program by the multidisciplinary team for patient with Rheumatoid Arthritis in our hospital and consideration from questionnaire

Ryuhei Ishihara, Kenji Yamazaki, Toshiaki Miyamoto
Seirei Hamamatsu General Hospital

Conflict of interest: None

[Object] We grasp the shortcoming of outpatient care of rheumatoid arthritis (RA) in educational hospitalization. [Methods] Our hospital perform the educational program for patients with doctors, nurses, pharmacists, occupational therapists, medical social workers. The study include 7 patients in May - September 2018. We conducted a questionnaire about the problem for each individual and evaluate understanding of each as-

pect of RA (disease, treatment, care, nutrition, rehabilitation, welfare system) by Visual analogue scale. Statistical analyses were performed using Kruskal-Wallis tests, Bonferoni-adjusted Wilcoxon ranks test. [Results] There is not a statistical difference between understandings each aspect of rheumatoid arthritis care at the time of admission (p=0.6). Multiple comparison showed a tendency to have a poor understanding of welfare system than disease understanding, albeit not statistically significant (p=0.015). There was a significant improvement in the understanding of each aspect at the time of discharge. There was no uniform answer for future worries, so it was considered that custom-built program was necessary for each. [Conclusions] Insufficient element has no tendency for each patient, so we need to deal with patients individually not only uniformly.

P1-138

Perioperative complications after spine surgery and joint surgery in patients with rheumatoid arthritis during biologic agent therapy

Taketoshi Kushida¹, Norihiro Ichikawa¹, Takanori Saito¹, Yoshio Ozaki², Yonsu Son²

¹Department of Orthopaedic Surgery, Kansai Medical University Hospital, ²Department of Rheumatology and Clinical Immunology, Kansai Medical University Hospital

Conflict of interest: None

[Object] The aim of this study was to evaluate the risk factors of biologic agents for rheumatoid arthritis (RA) during perioperative complications after spine surgery. [Methods] We analyzed the perioperative complications after spine surgery in 65 patients treated with biologic agents from January 2006 through December 2016 at our hospital. They were divided into 3 groups (22 patients treated with spine surgery, 28 patients treated with TKA and 15 patients treated with THA) [Results] In this study, there were one deep infection in TKA group and one postoperative hematoma in spine group. [Conclusions] Many patients treated with biologic agents had no complication during perioperative period. However, we always have to pay attention to serious complications.

P1-139

Effects of low intensity pulsed ultrasound on bone healing after metatarsal shortening offset osteotomy

Shoichi Kaneshiro, Hideki Tsuboi
Department of Orthopaedic Surgery, Japan Organization of Occupational Health and Safety, Osaka Rosai Hospital

Conflict of interest: None

[Object] We evaluated effects of LIPUS on bone healing after metatarsal shortening offset osteotomy (MSO). [Methods] We enrolled consecutive 122 toes of 34 female patients (Pts) who underwent MSO for RA or hallux valgus (HV). 64 toes of 17 Pts from July without LIPUS treatment (C group; RA 15, HV 2) were compared with 58 toes of 17 Pts with LIPUS treatment (L group; RA 11, HV 6). The corrected metatarsal heads were fixed with K-wires for 2 weeks (Ws). After removal of the K-wires, full weight-bearing was allowed with fitting of an arch support. At 4 days after surgery, we began LIPUS treatments and continued the application for 12 Ws postoperatively. We assessed clinically JSSF standard rating system, and radiographically the osteotomy site to determine the time to callus formation and union using x-rays. [Results] JSSF lesser toes scale significantly improved postoperatively from 43.4 to 83.9 in the C group, and from 44.2 to 87.1 in the L group. The time to callus formation was 9.6 Ws in the C group, and 8.2 Ws in the L group. There were no significant differences between groups. The time to union was 15.2 Ws in the C group, and 12.8 Ws in the L group. There was a significant difference. [Conclusions] Our results indicate that LIPUS accelerated bone healing after we performed MSO.

P1-140

The Short-term Result of 3D-porous Continuum Cementless Cup for RA

Masashi Tsuchida^{1,2}, Atsushi Kusaba^{1,2}

¹Zama General Hospital, ²Department of Orthopaedic, Showa University

Conflict of interest: None

[Object] Bone quality of RA is insufficient. Recently 3D porous cementless cup has been introduced and used for RA in our institute. The aim of this study is to evaluate the short term result of 3D porous Continuum cementless cup. [Methods] The use of Continuum cup for RA started from 2014 and 11 joints of 9 patients were undergone cementless total hip arthroplasty. Among them, clinical and radiological evaluation were performed. [Results] JOA score was improved from 41 to 95 at the last follow up period. All cup was stable and no intra- and postoperative complication was occurred. Initial gap was detected on 1 joint and completely filled at the last follow up period. [Conclusions] The short term result of 3D porous Continuum cup for RA is satisfactory with adequate initial stability even porotic bone. Although further investigation is essential, the cup could obtain long-term stability because of 3D porous surface structure.

P1-141

A case of using tocilizumab for rheumatoid arthritis difficult to manage pain while waiting conversion surgery

Tetsuo Watanabe¹, Hiroshi Fujinaga¹, Hideyuki Kitahara^{1,3}, Hiroaki Hikami^{1,4}, Kozo Takahashi²

¹Japanese Oriental Medicine and Rheumatology, Toyama Prefectural Central Hospital, ²Department of Clinical Laboratory, Toyama Prefectural Central Hospital, ³Department of Japanese Oriental Medicine, Faculty of Medicine, University of Toyama, ⁴Shikino Care Center

Conflict of interest: None

[Introduction] Recent progress of chemotherapy make conversion surgery (CS) safe and effective for initially unresectable patients. However, the report is rare about rheumatoid arthritis (RA) of uncontrollable disease activity while waiting CS. [Case] A 65 years old female with RA under remission with infliximab (IFX) was diagnosed as pancreatic hilar cancer. IFX and methotrexate were stopped, and laparoscopic gastric jejunal bypass surgery was performed. After 11 courses of GEM/nab-PTX therapy, it was regarded as an indication for CS. Polyarthralgia appeared, at her age of 67, at 3 weeks after the end of chemotherapy. Combined with preoperative radiotherapy, DAS28-ESR was reached at 6.84 since intravenous dexamethasone palmitate, loxoprofen, igranimod, salazosulfapyridine, 15mg of prednisolone (PSL) and tramadol were ineffective. After tocilizumab (TCZ) subcutaneous injection was started, pain was improved the following week, PSL were tapered, and TCZ was stopped due to remission with the second administration. There was no relapse of pain for 26 days after last TCZ and she went into pancreaticoduodenectomy. [Conclusion] This case suggested the efficacy of using TCZ for the patient of RA with difficulty of pain relief during CS preoperative term.

P1-142

Conservative treatment of broad skin necrosis after total knee arthroplasty at rheumatoid arthritis patient. A case report

Shigeru Hioki¹, Daisuke Nozawa²

¹Department of Orthopedic Surgery, Tsukuba Central Hospital, ²Department of Orthopedic Surgery Faculty of Medicine, University of Tsukuba

Conflict of interest: None

[Object] Skin necrosis is serious complication after total knee arthroplasty, especially in rheumatoid arthritis patient. Usually, muscle flap is first choice for the treatment of broad skin necrosis, but conservative treatment is another option. [Methods] A 78-year-old woman, who developed rheumatoid arthritis of the mutilance type at 65 years old, achieved total knee arthroplasty on her left knee. Wound necrosis, the size was 4 by 5 centimeter, was revealed at 3 weeks after the surgery. Two consecutive skin flap surgeries were ended in failure, skin necrosis got to larger (3.5 by 9 centimeter). The patient didn't want another operation. Afterward she received conservative treatment for 1 year until achieved epithelialization. [Results] Broad skin necrosis could achieve epithelialization with conservative treatment for 1 year. [Conclusions] This case suggests that a long term conservative treatment can be an optional therapy

py for broad skin necrosis after total knee arthroplasty.

P1-143

Conservative treatment for patella fractures after total knee arthroplasty: two case reports

Takeshi Yoshikawa, Midori Tono

Department of Orthopaedic Surgery, Kagawa Prefectural Central Hospital

Conflict of interest: None

(Purpose) We report two cases of patellar fractures after total knee arthroplasty (TKA) that was treated successfully with conservative methods. (Case1) A 75-year-old woman was operated with PS-type TKA for osteoarthritis of her left knee. 2 months after operation, displaced patellar fracture (Keating classification type-2B) was detected accidentally by the X-ray of the schedule. In spite of displaced fracture, we tried conservative treatment for that fracture. 10 months later, she had no pain, no extensor lag, no complications. (Case2) A 70-year old woman was operated with PS-type TKA for rheumatoid arthritis of her right knee. 1 month after operation, she was diagnosed as a displaced patellar fracture (Keating classification type-2B). Same as case1, we treated conservatively, and we got a good result three months later. (Conclusion) Patellar fractures after TKA, even if displaced fracture, associated with an intact extensor mechanism and a stable implant were treated successfully with nonoperative means. On the other hand, operation for this fracture was reported to be associated with a high rate of complication and reoperation.

P1-144

Changes in walking ability following forefoot reconstruction for patients with rheumatoid arthritis

Hyunho Lee^{1,2}, Hajime Ishikawa¹, Asami Abe¹, Shinji Taniguchi¹, Tomonori Sakamoto¹, Yoichi Kurosawa¹, Eriko Hasegawa¹, Chinatsu Takai¹, Daisuke Kobayashi¹, Hiroshi Otani¹, Satoshi Ito¹, Shu Saito², Kiyoshi Nakazono¹, Akira Murasawa¹

¹Department of Rheumatology, Niigata Rheumatic Center, ²Department of Orthopaedic Surgery, Nihon University School of Medicine

Conflict of interest: None

[Objectives] To clarify changes in plantar pressure and walking ability after rheumatoid forefoot reconstruction [Methods] 74 feet in 55 patients were evaluated. Patients were divided into two groups: group Sw, 59 feet treated by Swanson implant arthroplasty for the 1st MTP; group No, 15 feet treated by arthrodesis for the 1st IP or nothing at the 1st MTP. Most patients were treated by shortening oblique osteotomy at the 2nd to 5th metatarsal neck. Peak plantar pressure and TUG, gait speed, stride and cadence for walking ability were measured just before surgery and at 1 year after surgery. [Results] Peak pressure at the 1st IP, 2nd and 3rd MTP decreased, MM and LM increased in group Sw significantly. Preoperative peak pressure at the 1st IP in group Sw was significantly lower than that in group No, and it decreased more postoperatively. TUG decreased, gait speed and stride increased significantly in both groups. There was no significant differences in walking ability between two groups. Moderate positive correlation between preoperative peak pressure at the 2nd MTP and walking ability was found. [Conclusion] The patients whose walking ability was maintained highly with forefoot deformity might need early surgical intervention.

P1-145

Comparison of the First Metatarsal Shortening osteotomy and the scarf osteotomy by Short-term results for Forefoot Deformities of Rheumatoid arthritis

Kenta Makabe¹, Yoshio Uchida¹, Kenichi Shimane¹, Yuichi Nagase², Takuji Nishikawa¹

¹Department of Rheumatology, Tokyo Metropolitan Bokutoh Hospital, Tokyo, Japan, ²Department of Rheumatology, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan

Conflict of interest: None

[Object] We compare short-term postoperative results of the first

metatarsal shortening osteotomy and the Scarf osteotomy, for forefoot deformities of rheumatoid arthritis (RA). In addition, in each group, we divided into two, older than 70 years and those with less. [Methods] Twenty-two feet of 18 cases are group A, underwent the first metatarsal shortening osteotomy between September 2013 and January 2018, and 26 feet of 21 cases are group B, underwent the Scarf osteotomy between April 2015 and May 2018. We checked AP view of weight-bearing radiographs at pre-operation and at final follow-up. Clinical evaluation included the JSSF RA foot ankle scale and the SAFE-Q at final follow-up. [Results] The mean follow-up period was 44 and 26 months. HV angle improved from 36.1 degrees to 10.6 degrees, and 45.0 to 17.7 degrees. SAFE-Q was generally comparable each other. Nine feet in Group A and 15 feet in Group B were over 70 years of age, but there was no significant difference in each of the outcomes compared with those under 70 years. [Conclusions] There was no statistically difference in these osteotomies. Preoperative HV angle is larger in group B, Scarf osteotomy is useful for severe Hallux valgus in RA patients. In addition, both osteotomies are useful for older people aged 70 years.

P1-146

Results of joint-preserving procedures by a modified Mann method of the first metatarsal by concomitant use of metatarsal bone shortening for the treatment of hallux valgus in rheumatoid patients

Daichi Mukunoki¹, Keita Nagira¹, Masako Hayashibara¹, Chikako Takeda¹, Hideki Nagashima¹, Hiroshi Hagino²

¹Department of Orthopedics, Tottori University Hospital, Yonago, Tottori, Japan, ²Department of Health Sciences, Tottori University School of Medicine, Yonago, Tottori, Japan

Conflict of interest: None

[Object] This study aimed to evaluate joint-preserving surgery by a modified Mann method by concomitant use of metatarsal bone shortening for the treatment of hallux valgus in rheumatoid patients. [Methods] Radiographic outcome in terms of hallux valgus angle (HVA), metatarsal1-metatarsal2 angle (M1M2 A), metatarsal1-metatarsal5 angle (M1M5 A) were investigated after an average of 4 years postoperatively. The change in HVA at 5 degrees or more postoperatively was defined as an exacerbation group. Between the improvement group and the exacerbation group, Various parameters were examined. [Results] Mean age of the patients was 62.8years (8 females) and mean disease duration of RA was 17.4 years. The mean preoperative HVA, M1M2 A, and M1M5 A were 42.7 degrees, 15.2 degrees, and 31.7 degrees respectively. The mean HVA, M1M2 A, and M1M5 A at the last investigation were 9.8 degrees, 5.1 degrees, and 19.9 degrees respectively. Deviation of the seed bone showed a tendency of maladaptation in the exacerbation group. [Conclusions] Mann's modified method with concomitant use of first metatarsal shortening osteotomy corrects HV angle well. By performing rotation correction with the first metatarsal bones, there is a possibility of preventing hallux valgus postoperative recurrence.

P1-147

Evaluation of adductor hallucis tendon transfer using a suture anchor with metatarsal osteotomy for hallux valgus deformity of rheumatoid arthritis

Taro Yoshioka^{1,2}, Kosuke Ishizaka¹, Eigo Kikuchi², Takahiro Okai²

¹Department of Orthopaedics, Kawakita General Hospital, ²Center for Rheumatology and Joint Surgery, Kawakita General Hospital

Conflict of interest: None

[Object] We evaluated the results of seven cases of adductor hallucis tendon transfer using a suture anchor with metatarsal osteotomy for hallux valgus deformity in patients with rheumatoid arthritis (RA). [Methods] From September 2017, six patients involving seven cases were treated. RA disease activity was in remission in all patients. Metatarsal osteotomy for corrective hallux valgus was performed. A distal osteotomy using modified Mitchel method was performed in six of the seven cases. Proximal osteotomy was performed by using the modified Mann method in one case. The adductor hallucis tendon was released on the lateral side of the base of the proximal phalanx of the great toe and was attached to the lateral side of the metatarsal head by using suture anchor. As a clinical

outcome, the hallux valgus angle (HVA), M1M2 angle (M1M2A), and JSSF hallux scale score were measured at preoperatively and 6 months postoperatively. [Results] The HVA, M1M2A, and JSSF hallux scale score were significantly improved postoperatively. No patient complained of residual pain. [Conclusions] Adductor hallucis tendon transfer using a suture anchor with metatarsal osteotomy for hallux valgus deformity of RA was found to be a useful surgical technique.

P1-148

Shot-term results of proximal closing-wedge osteotomy of the first metatarsal in rheumatoid arthritis

Ryo Tanaka, Haruhiko Akiyama

Department of Orthopaedics, Gifu University School of Medicine

Conflict of interest: None

[Object] However there are various operative procedures for forefoot deformities, a large number of first-metatarsal osteotomies have difficulties in correcting the rotational deformities and adjusting the shortened quantity of the metatarsal bone. The aim of this study is to assess the results of proximal closing-wedge osteotomy for patients with rheumatoid arthritis (RA) in our institution. [Methods] From January 2016 through April 2018, 6 feet were treated this procedure. Subjective, functional, and radiographic outcome were assessed. [Results] The mean Japanese Society for Surgery of the Foot hallux scale improved from preoperative level of 42.0 to 92.5 postoperatively. The average hallux valgus and intermetatarsal angles improved from 43.6° preoperatively to 17.3° postoperatively, and 17.7° to 6.0°, respectively. To assess the repositioning of pronation deformity of the first metatarsal, the medial sesamoid was measured according to the measurement system proposed by Hardy and Clapham. All foot was classified as grade VII preoperatively and 3 of these were grade IV or lower at the latest follow-up. [Conclusions] Proximal closing-wedge osteotomy of the first metatarsal was beneficial for correcting forefoot deformities in RA over the shot term.

P1-149

Tenotomy of Tibialis anterior muscle tendon caused by it being exposed after Total ankle arthroplasty in rheumatoid arthritis patients: reports of three cases

Takaaki Noguchi¹, Shigeyoshi Tsuji¹, Makoto Hirao², Kosuke Ebina², Hideki Tsuboi³, Shosuke Akita¹, Jun Hashimoto¹

¹Department of Orthopaedics, Osaka Minami Medical Center, ²Department of Orthopaedics, Osaka University Graduate School of Medicine, ³Department of Orthopaedics, Osaka Rosai Hospital

Conflict of interest: None

[Purpose] Exposure of TA by wound healing trouble after TAA in RA patients is one of the serious complications. We examined the postoperative process about 3 patients who resected TA immediately after exposure of TA. [Method] 3 patients underwent TAA through an anterior approach in RA. We examined ROM and muscle strength of ankle, wound healing period and walking start time after tenotomy. [Results] We operated tenotomy within 3 days after exposure of TA. Patients started to walk in 14 days and wound healing was recognized in 21 days after surgery. Drop foot was not seen and there is no difference between pre- and post-operative dorsiflexion power of ankle. In addition, the change was not seen in ROM after tenotomy. [Discussion] It has been reported that there are 10-30% of complications associated with wound healing after TAA. Especially in RA, wound healing trouble risk is increased. Not only it takes several months for healing by the conservative therapy and causes reduction of the ADL, but also is accompanied by the risk of the deep infection once when TA is exposed. Drop foot and decreasing dorsiflexion power of ankle was not seen because it was tightly inserted implant in TAA. If TA is exposed by wound healing trouble after TAA, tenotomy of TA is an effective therapeutic method.

P1-150

Medium to long-term Clinical and Radiographic Outcome of a Total Ankle Arthroplasty in Patients with Rheumatoid Arthritis

Hiroshi Takasu, Hidetoshi Tsushima, Kenjiro Fujimura, Satoshi Kamura,

Hisaaki Miyahara
Department of Orthopedics, National Hospital Organization Kyushu
Medical Center, Fukuoka, Japan

Conflict of interest: None

[Object] We report the medium to long-term outcome of a total ankle arthroplasty (TAA) in patients with rheumatoid arthritis (RA) in our hospital. [Method] Between 2009 to 2016, we performed TAA in 11 patients with RA (1 man and 10 women, mean age was 64.7 years old), using FINE total ankle system. The mean follow-up duration was 60 (range, 18-114) months. Outcomes were evaluated with the preoperative and postoperative range of motion (ROM), the Japanese Society for Surgery of the Foot (JSSF) scale score and a postoperative self-administered foot-evaluation questionnaire (SAFE-Q), the angle of varus and valgus of ankles, the angle between of the placement of the implant and the complications. [Results] The preoperative ROM (plantar/dorsal flexion) was $16.5^{\circ} \pm 12.9^{\circ} / 4.0^{\circ} \pm 4.6^{\circ}$, and the postoperative ROM was $21.4^{\circ} \pm 7.7^{\circ} / 7.7^{\circ} \pm 4.1^{\circ}$. The angle of the placement of the implant was $0.1^{\circ} \pm 4.05^{\circ}$. The three patients fractured the medial malleolus. The three patients had loosening of the implant, however, they didn't need to have re-operation, such as the re-replacement of implant, or the arthrodesis. [Conclusions] The medium to long-term clinical outcomes for the TAA in our hospital were found to be satisfactory.

P1-151

Characteristics of rheumatoid arthritis patient who underwent total knee arthroplasty-comparisons before and after appearance of biological DMARDs

Ryuta Sakurai, Kenjiro Fujimura, Hidetoshi Tsushima, Satoshi Kamura, Takashi Komatsu, Hisaaki Miyahara
Orthopedics/Rheumatology, National Hospital Kyusyu Medical Center

Conflict of interest: None

Objectives: It is reported the number of total knee arthroplasty (TKA) in rheumatoid arthritis (RA) patients is decreasing. This change might cause by the usage of biological DMARDs. We investigated the characteristics of RA patients who will lead to TKA. Methods: We divided RA patients into two groups (group A and group B). Group A included the patients who underwent TKA from 1998 to 2002, and group B included from 2013 to 2017. We investigated disease modified anti-rheumatic drugs (DMARDs), mean age, disease duration, C-reactive protein (CRP) and radiographic changes. Result: DMARDs usage and mean age was significantly increased and CRP was significantly decreased in after group. Disease duration was not changed. The number of patient with joint space narrowing and osteophytes were not significantly changed but bone destruction and bone cyst were significantly decreased in group B. Conclusions: After the appearance of biological DMARDs, RA is better controlled from the perspective of CRP, the existence of Larsen classification, bone destruction and bone cyst in X-ray. However, we found less changes the point of osteophyte and narrowing of joint space.

P1-152

A comparison of prevalence of osteoporosis between in rheumatoid arthritis patients and osteoarthritis patients with total knee replacement

Hidenori Tanigawa¹, Ayano Hayashi², So Nomoto¹
¹Department of Orthopedic Surgery, Saiseikai Yokohamashi Tobu Hospital, ²Department of Nursing, Saiseikai Yokohamashi Tobu Hospital

Conflict of interest: None

[Object] More than 80000 total knee arthroplasties (TKAs) are performed in a year for osteoarthritis (OA) patients or rheumatoid arthritis (RA) patients. A complication of osteoporosis can increase the risk of postoperative fractures or implant loosening. An OLS (Osteoporosis Liaison Service) team encourages the patients to take a bone density examination for early diagnose of osteoporosis. In this study, we compared the prevalence of osteoporosis in RA patients with that in OA patients. [Methods] The subjects are 20 RA patients undergoing TKA from January 2015 to April 2018, and 119 OA patients undergoing TKA in 2017. A

bone density examination was performed before surgery. [Results] The result in RA patients was following: Osteoporosis 35%, Bone loss 60%, Normal: 5%, whereas the result in OA patients was following: Osteoporosis 19.3%, Bone loss 58%, Normal: 22.7%. The T score in RA patients (-2.24) was significantly decreased compared to that in OA patients (-1.59). [Conclusions] The prevalence of osteoporosis is higher in the RA patients compared with OA patients. It is reported that ten percent of patients would experience falls within a year after the surgery, and a fall decreases the patients' ADL. A bone density examination to RA patients undergoing TKA is recommended.

P1-153

Factors affecting the postoperative patients' satisfaction of total knee arthroplasty in rheumatoid arthritis

Atsuo Uefuji, Natsuko Nakagawa, Toshihiko Harada
Hyogo Prefectural Kakogawa Medical Center

Conflict of interest: Yes

[Object] Total knee arthroplasty (TKA) is considered to be good treatment. Though, some patients continues complains. The purpose of this study was to show the preoperative factors affecting postoperative patient satisfaction of TKA in rheumatoid arthritis (RA) patients. [Methods] 17 knees of 16 patients (2 male and 14 female with mean age of 67.0 ± 8.6 years old) with RA, undergoing primary TKA, were included in this study. Patients were assessed using patients' expectation part of the 2011 Knee Society Score. The consideration items were age, duration of RA, functional class score of American College of Rheumatology, surgery history of hip or knee arthroplasty, image of Femoro Tibial angle in standing position Xp, image of Patella Tilt in lying position CT, and serum CRP score at the time of TKA. [Results] Younger than 70 years old patients showed better postoperative expectation scores compared to older patients. Patients with lower than 10 degree Patella Tilt, showed better scores compared to patients with higher degree. There were no significant differences in other items. [Conclusions] Patients with high age and patients with high degree Patella Tilt showed worse outcomes. We should increase clinical cases and do more considerations for those patients.

P1-154

Evaluation of the effect of Total Knee Arthroplasty to functional analysis in rheumatoid arthritis patients

Kenya Terabe, Daihei Kida, Yosuke Hattori, Shotaro Mori, Tomotaro Sato, Atsushi Kaneko
National Hospital Organization Nagoya Medical Center

Conflict of interest: None

[Object] In this study, we evaluate the efficacy of Total Knee Arthroplasty (TKA) to functional analysis in rheumatoid arthritis patients. [Methods] 70 patients (Pts) who underwent TKA were included in this study. 5 patients were man and 65 were woman. The baseline mean age and duration of RA were 66.2 ± 11.1 years, 18.3 ± 12.4 years respectively. Efficacy was evaluated based on mHAQ and SDAI comparing with pre and post 1 year TKA. We investigated factors that relate with improvement of mHAQ. [Results] Average of mHAQ improved 0.9 ± 0.6 at baseline to 0.8 ± 0.6 at 1 year after TKA. mHAQ was improved in 27 Pts, no change in 28 Pts, worsened in 15 Pts. Average of SDAI and MMP-3 significantly improved 12.2 ± 7.3 to 9.3 ± 8.3 , 229.9 ± 278.0 to 119.9 ± 156.2 , respectively. mHAQ was improved in 27 Pts (R group) and was not improved in 43 Pts (N group). The decrease of SDAI (Δ SDAI) in R group is significantly higher than that in N group (R group: -5.5 ± 6.7 , N group: -1.5 ± 6.1 $p < 0.05$). In addition, There was a significantly correlation with Δ mHAQ and Δ SDAI ($r = 0.324$ $p < 0.01$). [Conclusions] In this study, improvement of mHAQ after TKA surgery relate with that of SDAI. These results suggested that improvement of mHAQ after TKA surgery needs to that of disease activity.

P1-155

Improvement of Locomotive syndrome score 25 after total knee arthroplasty

Kensuke Koyama^{1,2}, Yoshihiro Takayama^{1,2}, Hiroataka Haro^{1,2}

¹Department of Orthopaedic Surgery, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, ²Center for Clinical Immunology and Rheumatology, University of Yamanashi

Conflict of interest: None

[Object] There were few reports on locomotive syndrome score 25 (LSS25) related to surgical intervention. The purpose of this study was to examine the relationship between total knee arthroplasty (TKA) and improvement of locomotive syndrome score. [Methods] Fifty four patients (OA:45, RA:9) underwent primary unilateral TKA and got consent before surgery were included. Using LSS25 before and 6 months of TKA, we examined the degree of improvement of LSS25. Furthermore, in order to find preoperative factors to satisfy locomotive syndrome degree 2 (LSS25<16 points), logistic regression analysis was performed. [Results] LSS25 was significantly improved from preoperative 46 points to 25.6 points after 6 months. Five patients satisfied the locomotive syndrome degree 2 before TKA, but increased 20 cases in 6 months after surgery. Male, preoperative LSS25 were the relative factors for satisfying the locomotive syndrome degree 2 in 6 months after TKA ($p<0.05$). [Conclusions] Multiple factors such as osteoporosis and spinal disease were affected to LSS25, but it was suggested that unilateral TKA improves in the short time.

P1-156

The effect of stress steroid on the total hip and knee arthroplasty in rheumatoid arthritis

Sumito Kawamura¹, Daisuke Kawamura², Koji Suzuki³

¹Department of Orthopaedic Surgery, Kobayashi Hospital, ²Department of Orthopaedics, Kawamura Orthopaedics, ³Department of Orthopaedic Surgery, Hokkaido Orthopaedic Memorial Hospital

Conflict of interest: None

[Object] The purpose of this study is to elucidate the effect of stress steroid on total knee and hip arthroplasty in rheumatoid arthritis. [Methods] Among the RA patients, thirty-five of TKA (total knee arthroplasty) and ten of THA (total hip arthroplasty) patients were examined. All patients were injected intravenously of prednisolone (20mg) an hour prior to the surgery. Control group was chosen on the OA (osteoarthritis) patients with age, sex, and BMI matched. Post-operative blood sugar, nausea, vomiting, infection, venous thromboembolism was examined. [Results] Average blood sugar was significantly increased from 96.8mg/dl to 138.5mg/dl. Post-operative nausea/vomiting was significantly decreased on the steroid group. The rate of other adverse events was not significantly different. [Conclusions] Preoperative injection of high dose prednisolone was effective to decrease post-operative nausea/vomiting.

P1-157

Comparison of post result of total knee arthroplasty for osteoarthritis and rheumatoid arthritis

Manabu Yamada, Arata Nakajima, Shiho Nakano, Keiichiro Yamamoto, Keita Koyama, Shinji Taniguchi, Hiroshi Takahashi, Masato Sonobe, Koichi Nakagawa

Department of Orthopedics, Toho University Medical Center Sakura Hospital

Conflict of interest: None

[Object] To consider the relationship between osteoarthritis (OA) and rheumatoid arthritis (RA) with FINE total knee arthroplasty (TKA) in our hospital after postoperative patient patient-based Outcome. [Methods] Primary TKA 145 patients 169 knees from August 2013 to July 2016, OA 131 patients 153 Knees, RA 14 patients 16 Knees, FINE Knee CR is utilized, the average age at the time of surgery was 72.3 years, OA 72.7 years, RA 68.5 years, 34 males consisting of 31 cases of OA and 3 cases of RA and 135 females consisting of 122 cases of OA and 13 cases of RA, The average BMI was 26.8, OA 27.2, RA 23.8, and the follow-up period was 13.3 months on average. Surgery was performed by Measured resection in all cases, osteotomy was performed according to the ordinary method, and the implant was placed after balancing soft tissue. We examined the relation of Japanese version KOOS as a patient-based outcome.

[Results] For statistical analysis, the Mann-Whitney test was used, and $p<0.05$ was regarded as significant difference. We compared KOOS as OA and RA post TKA results, but no significant difference was observed. [Conclusions] It is necessary to increase the number of cases and follow up survey in the middle and long term.

P1-158

A study on the pathogenesis of valgus knee in patients with rheumatoid arthritis

Masato Sonobe¹, Arata Nakajima¹, Takashi Nakamura², Hiroshi Takahashi¹, Shinji Taniguchi¹, Manabu Yamada¹, Keita Koyama¹, Keiichiro Yamamoto¹, Shiho Nakano¹, Toru Suguro³, Koichi Nakagawa¹

¹Department of Orthopaedic Surgery, Toho University Sakura Medical Center, ²Department of Orthopaedic Surgery, Toho University Omori Medical Center, ³Japan Research Institute of Artificial Joint

Conflict of interest: None

Objective: To investigate the pathogenesis of valgus knee in patients with rheumatoid arthritis. **Methods:** The study included 83 knees in 66 patients who underwent primary TKA between June 2010 and March 2018 at our hospital. Patients included 6 men and 60 women, with the average onset of RA was at 53.1 years and the average duration of RA was 14.5 years. They were classified into two groups (valgus, neutral + varus) by femoro-tibial angle. We investigated the following as risk factors: onset of RA, gender, BMI, duration of RA, medication, disease activity, RF, ACPA, osteoporosis, mL DFA (mechanical lateral distal femoral angle), MPTA (medial proximal tibial angle). We compared these risk factors between the valgus and another groups. **Results:** A univariate analysis demonstrated that there was a significant difference in duration of RA, mL DFA, and MPTA between the two groups. A multivariate logistic regression analysis demonstrated that there was a significant difference in MPTA between the two groups. **Conclusions:** This study suggested that longer duration of RA, smaller mL DFA, and bigger MPTA were risk factors of valgus knee in patients with rheumatoid arthritis.

P1-159

Assessment of the results of total knee arthroplasties in patients with rheumatoid arthritis using the Knee Injury and Osteoarthritis Outcome Score (KOOS)

Masashi Naito¹, Yuichi Nagase¹, Sakae Tanaka²

¹Department of Rheumatology, Tokyo Metropolitan Tama Medical Center, ²Department of Orthopaedic Surgery, The University of Tokyo Hospital

Conflict of interest: None

[Object] The Knee Injury and Osteoarthritis Outcome Score (KOOS) is a knee-specific patient-reported outcome measure. The object of the present study was to assess the results of total knee arthroplasties in patients with rheumatoid arthritis using the KOOS. [Methods] We performed 18 total knee arthroplasties on patients with rheumatoid arthritis and evaluated the results using the KOOS in one year after surgery. [Results] Symptoms and Stiffness, Pain, Daily living, Sports/Recreation and QOL subtotal scores were all significantly improved after surgery. Sports/Recreation score was lower both before and after surgery compared with other scores, suggesting that patients with established RA have difficulties in playing sports or in recreational activities. Additionally, we investigated items of ascending and descending stair before and after surgery and patients with RA who underwent TKA still have some difficulties in terms of those items. [Conclusions] The subdomain scores of KOOS were improved after TKA in patients with RA. However, these data indicated that established RA have still difficulties in playing sports or in recreational activities after TKA.

P1-160

Motional analysis of RA wrist after Sauvé-Kapandji procedure- In association with smoothness of articulation -

Yusuke Yamamoto, Hisashi Ohki, Makoto Kitade, Yuya Izubuchi, Akihiko Matsumine

Department of Orthopaedics and Rehabilitation Medicine Faculty of

Conflict of interest: None

[Object] Sauvé-Kapandji procedure (SK) is one of typical surgical treatments. We performed motion analysis of wrist joint of the patients after SK procedure and evaluated the smoothness of the joint movement. [Methods] The subjects were 7 females, 10 hands undergone SK procedure (SK-RA). Steinbrocker's classification was Stag III 2 cases, Stage IV 8 cases. The control group consisted of 8 RA patients, 8 hands (RA), and 3 healthy volunteer, 6 hands (HV). A biaxial electric angle meter was used to measure the wrist joint angle. For data analysis, two channels of analog amplifier and analysis software were used. We calculated the jerk in each movement of palmar-dorsi flexion, ulnar-radial deviation and darts slow motion. In the SK-RA, X-ray measurement of the wrist joint was performed. We compared the three groups. [Results] In the SK - RA, the range of motion was smaller than that of the HV group. Compared to the RA, the movable axis and the angular jerk of the SK-RA tended to approach the HV. The angular jerk in the SK-RA did not depend on the joint morphology. [Conclusions] The wrist stabilizes after SK procedure, and it was suggested that the function improvement could be expected regardless of the joint destruction and the joint morphology.

P1-161

Insufficiency fracture of the diaphyseal radius after Sauve-Kapandji procedure in a rheumatoid arthritis patient

Takahiro Iwata, Mitsuru Saito

Department of Orthopaedic Surgery, Takayama Red Cross Hospital

Conflict of interest: None

[Case report] We report a case of insufficiency fracture of the diaphyseal radius after Sauve-Kapandji (S-K) procedure in a rheumatoid arthritis (RA) patient. A 79-year-old woman had been mediated with methotrexate and etanercept. She had undergone S-K procedure of the left wrist combined with synovectomy and tendon transfer, due to extensor tendon rupture of little finger. Bone density of femoral neck was 51% of the young adult mean and administered denosumab. Although she had not experienced any recent trauma, she presented with left forearm pain 9 months postoperatively. Radiographs showed transverse fracture of the diaphyseal radius. We performed open reduction and internal fixation (ORIF) with a locking plate. We treated with low intensity pulsed ultrasound (LIPUS). The fracture healed within 7 months. This case represents the first description of presentation with diaphyseal radius fracture after the S-K procedure in a RA patient treated by ORIF and LIPUS. We considered mechanical stress resulting from the absence of ulnar support, osteoporotic bone, and high activities of daily living under biological agent as contributory factors. Orthopaedic surgeons should be aware that insufficiency fracture after the S-K procedure could occur at the diaphyseal radius in RA patients.

P1-162

Conservative treatment for distal radius fractures in rheumatoid arthritis patients

Rika Kakutani¹, Takahiro Nezu², Tadamasu Hanyu²

¹Department of Orthopedic Surgery, Nagaoka Red Cross Hospital, ²Department of Rheumatology, Nagaoka Red Cross Hospital

Conflict of interest: None

[Purpose] We researched differences in treatment outcome of distal radius fractures, and whether it affected RA treatment. [Object and Methods] Six cases 6 hands, excluded Smith fractures, volar/dorsal Barton fractures and comminuted fractures from 11 RA patients who injured the distal radial bone fracture were followed at our hospital between 2016 and June 2018. All cases were almost good RA condition. No cases used biological preparation. PSL was used in 2 cases. Normal patients, excluded the cases onset RA after injury and under 60 year old were 71 cases. All cases were performed closed reduction and evaluated reduction position of X-ray. Type of fracture, could not achieved categories of closed reduction, CRP and condition of RA before and after injury were researched. [Results] The cases completed conservative treatment in RA

group were 4 cases and normal group were 35 cases. There was not the significant difference. In RA group, fracture healing was not delayed and RA condition was not worse during treatment of fractures. [Conclusions] At good controlled RA patient, the results of the bone fracture treatment was not inferior compared to normal patients. RA condition was not worse during treated fracture.

P1-163

A case of negative pressure closure therapy was effective for several times surgical wound dehiscence after artificial elbow joint replacement surgery

Naoko Koenuma^{1,2}, Yu Sakuma^{1,2}, Koichiro Yano^{1,2}, Katsunori Ikari^{1,2}, Ken Okazaki¹

¹Department of Orthopedic Surgery, Tokyo Women's Medical University,

²Department of Orthopedic Surgery, Institute of Rheumatology, Tokyo Women's Medical University

Conflict of interest: None

[Introduction] There are an increasing of patients taking anticoagulant medicine with rheumatoid arthritis (RA). Occasionally we annoyed the troubles of wounds after surgery in such patients. We reported that the negative pressure wound therapy (NPWT) was effective for delayed wound healing after artificial elbow joint replacement (TEA). [Case] A 75-year-old female, she is treated to RA with PSL, MTX, and ETN. And she takes the warfarin, as she had the coronary artery bypass grafting. We operated for TEA with heparinization. 2 months later she had a dislocation of the TEA, we operated for aponeurosis suture with taking warfarin. 4 days after, the wound was completely opened and the inside of the wound was full of hematoma. We had the debridement and suture the wound several times, the wound was closed with moisturizing therapy. But the TEA was dislocation again, so we performed re-replacement surgery. After surgery, the wound was dehiscence. We set NPWT with Instillation and Dwelling (NPWTi-d) after debridement. 2 weeks after, the wound was closed. [Conclusions] We think that the delayed wound healing is caused by soft vulnerability due to PSL, bleeding due to anticoagulant and bacterial infection. We suggest that we can controlled the environment without bacteria using NPWTi-d.

P1-164

Clinical study of revision total elbow arthroplasty in rheumatoid arthritis

Hajime Yamanaka¹, Hiroshi Tamai¹, Tatsuya Kobayashi¹, Taisei Kawamoto²

¹Department of Orthopaedic Surgery, National Hospital Organization Shimoshizu Hospital, ²Department of Orthopaedic Surgery, Matsudo City Medical General Hospital

Conflict of interest: None

[Object] To investigate the results of revision total elbow arthroplasty (TEA) in patients with rheumatoid arthritis (RA). [Methods] 3 revision TEAs with 2 patients were performed due to implants loosening. We investigated the clinical course and the factors of causes of loosening (C.L). [Results] 1st patient with FINE ELBOW (F-E), loosening of ulnar component was onset at 1 year 5 months after primary operation (P.O). Revision TEA was done with using a metal sack at 1 year 7 month from P.O. The C.L were thought the insufficiency of cementing (I.C) and of ability of fixation on all poly. component. 2nd patient with Coonrad-Morrey loosening of humeral component was onset at 2 year 10 months after P.O. Revision TEA was done at 3 year 3 month from P.O to replace a new implant using impaction bone grafting. The C.L were thought the I.C and overlord to humeral implant due to lumbar spondylosis. 3rd patient, the other side of 1st patient, with F-E, loosening of humeral component was onset at 4 year 1 months after P.O. Revision TEA was done with long stem implant at 11 year 11 month from P.O. The C.L were the I.C and overlord to humeral implant due to lumbar fracture. [Conclusions] The causes of revision TEA were thought due to I. Ci and overlord to implant due to lumbar diseases.

P1-165

Evaluation of complications of total elbow arthroplasty for Rheumatoid arthritis

Satoshi Kamura, Hidetoshi Tsushima, Kenjiro Fujimura, Koji Sakuraba, Hisaaki Miyahara, Takashi Komatsu, Ryuta Sakurai, Hiroshi Takasu
Department of Orthopaedic Surgery and Rheumatology, National Hospital Organization Kyushu Medical Center

Conflict of interest: None

[Object] We presented that Total elbow arthroplasty (TEA) is a reliable treatment for severe rheumatoid arthritis (RA) of the elbow previously. The study also showed a relatively high occurrence of complication in TEA. The purpose of this study was to assess the risks of those complications, especially periprosthetic fractures. [Methods] The objects were 29 RA patients (34 elbows) treated using TEA in our center between 2009 and 2018. [Results] The mean age and disease duration of them was 66.4 and 27.9 years respectively. The semi-constrained, cemented prosthesis was used for all case. Results: The post-operative complications occurred in 12 patients, fracture in seven patients (20.6%) and ulnar nerve disorder in five patients (14.7%). Neither surgical site infection and soft tissue disorder were observed in the serial. The mean age of patients with and without fracture was 70.1 and 65.4 respectively and the mean disease duration was 34.3 and 26.2 years respectively. [Conclusions] Our study may reveal that fracture after TEA tend to occur in elderly people with bone fragility. It suggested that making decision of surgical indication carefully and treatment for osteoporosis were important in TEA for RA.

P1-166

A case of rheumatoid arthritis with severe metallosis of ulnar component after K-ELBOW total elbow arthroplasty

Takeshi Oguchi, Toki Takemoto, Sakurako Yoshino, Shiro Urata
Department of Rheumatology and Orthopaedic Surgery, Anjo Kosei Hospital, Aichi, Japan

Conflict of interest: None

[Introduction] K-ELBOW total elbow arthroplasty (TEA) has been used in patients with rheumatoid arthritis (RA) for relief of pain or improvement of elbow function in Japan since 2005, however we experienced a case of revision surgery due to severe metallosis of ulnar component. [Case report] A 72-year old female with a 29-year history of RA was underwent right K-ELBOW TEA eight years ago. Her preoperative right elbow range of motion (ROM) was from 45 to 125 degree, JOA score was 47, and her left elbow was almost ankylosing. Although ADL improved markedly after TEA, synovial fluid punctured from her joint showed black after 7 years. We diagnosed as metallosis and a revision surgery was performed. Intraoperative findings showed implant failure of the ulnar component with severe metallosis in the soft tissues around the prosthesis. No findings of loosening of both implants, only ulnar component was revised with long stem. At 1 year after revision, ROM of the elbow was from 45 to 140 degrees. JOA score was improved from 83 points preoperatively to 88 points postoperatively. [Conclusions] We need attention to TEA complications associated with malrotation of ulnar component. The case report emphasizes that the indications for surface replaced type TEA should be carefully considered.

P1-167

Surgical outcome of linked total elbow arthroplasty

Tomoya Kotani, Haruki Takagi, Kazutaka Takatsuka, Toshiyuki Kitaori, Hiroko Morise, Akinori Murakami
Fukui Red Cross Hospital

Conflict of interest: None

[Object] We discussed about TEA implant failure in our hospital. [Methods] Between 2003 and 2018, we performed 9 linked TEA. There were 8 rheumatoid arthritis cases and 1 osteoarthritis case. Mean follow-up time was 6.6 years. [Results] Our used implant were Coonrad-Morrey (n=3), Discovery (n=5) and SOLAR (n=1). Revision cases were 3 cases (Discovery only). The follow-up time of revision cases was mean 3.3

years (range:2-5 years). The complications of revision cases were radiographic loosening and bone defect. Their humeral stems were implanted for flexed position. 2 patients were very high activity. [Conclusions] We experienced the long follow-up time that was 10 years over, but then follow-up time about cases of implant failure that was 2 years. There are few cases, and every cases were not any differences of medical treatment about rheumatoid arthritis. The good alignment of implantation and patient education are important.

P1-168

Clinical outcome of the PROSNAP linked elbow prosthesis for the rheumatoid elbows

Shunji Okita¹, Keiichiro Nishida¹, Minami Matsushashi¹, Masahito Watanabe¹, Yohei Kiso¹, Hideki Ohashi¹, Ryuichi Nakahara², Yoshihisa Nasu³, Toshifumi Ozaki¹

¹Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ²Department of Intelligent Orthopaedic System, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ³Department of Medical Materials for Musculoskeletal Reconstruction, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

Conflict of interest: None

[Object] We investigated the mid-term clinical results of total elbow arthroplasty (TEA) using the linked elbow prosthesis (PROSNAP) for the rheumatoid elbows. [Patients and Methods] We investigated 38 elbows of 36 rheumatoid arthritis (RA) patients. The mean follow-up period was 54.0 (range 12-116) months. The clinical condition was assessed according to range of motion (ROM), Japanese Orthopaedic Association-Japan Elbow Society Elbow Function Score (JOA score), and Mayo Elbow Performance score (MEPS). [Results] The mean preoperative ROM in extension and flexion were -33.9 degrees and 105.7 degrees, respectively. The mean preoperative JOA score and MEPS were 45.4 points and 48.0 points, respectively. The mean postoperative ROM in extension and flexion were -29.6 degrees and 140.4 degrees, respectively. The mean postoperative JOA score and MEPS were 87.3 points and 95.1 points, respectively. Two elbows (5.2%) required revision surgery, due to infection and breakage of polyethylene liner of ulnar component. [Conclusions] Although the clinical results of PROSNAP for the RA elbows were satisfactory, two elbows (5.2%) required revision surgery.

P1-169

Aiueo

Yu Sakuma^{1,2}, Haruki Tobimatsu^{1,2}, Naoko Koenuma^{1,2}, Koichiro Yano^{1,2}, Katsunori Ikari^{1,2}, Ken Okazaki¹

¹Department of Orthopedic Surgery, Tokyo Women's Medical University, Shinjuku, Tokyo, ²Joint Surgery, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

Conflict of interest: None

[Object] Swanson (Sw) and AVANTA (Av) is silicone prosthesis which is widely used in the metacarpophalangeal (MP) joint arthroplasty of the patients of rheumatoid arthritis (RA). Here we report the postoperative fracture rates of the implants. [Method] We examined postoperative X-ray of the RA patients who underwent MP joint arthroplasty with Sw or Av from September 2012 to November 2017. [Results] Of all 105 corresponded cases, we reviewed 78 hands (68 hands of 62 female, 10 hands of 10 male, mean age of 63.9) the images of which were available. Sw were inserted in 158 fingers of 50 hands, and mean post-operated period were 2.05 (0.89-9.67) years. Av were in 132 fingers of 38 hands, and post-operated period were 2.65 (1.05-6.65) years. The cases in which at least one prosthesis was broken were 15 hands (39%) in Av group, 3 hands (7.5%) in Sw group. Only one case represented pain symptom and needed revision surgery. [Conclusion] In our study, the fracture rates were significantly high in Av group. Only one fracture case needed revision owing to symptomatic complaints, therefore implant fracture is likely not to be a problem clinically. When we select the silicon implant, we should consider not only its fracture rate, but also clinical results and characteristic features.

P1-170

Boutonniere deformity of rheumatoid thumb-108 cases of Flexible hinge toe Swanson implant arthroplasty

Tetsuya Nemoto^{1,2}, Hajime Ishikawa², Issaku Toyohara^{2,3}, Asami Abe², Hiroshi Otani², Hyunho Lee², Kiyoshi Nakazono², Akira Murasawa², Satoshi Ito², Daisuke Kobayashi², Chinatsu Takai², Takeshi Kijima¹, Katsunori Inagaki¹

¹Department of Orthopedic Surgery, Showa University, ²Department of Rheumatology, Niigata Rheumatic Center, ³Department of Rheumatology, Northern Area Medical Association Hospital

Conflict of interest: Yes

[Objective] We hypothesized flexible hinge toe implant would improve the clinical outcomes and radiological findings of Boutonniere deformity of rheumatoid thumb. [Patients and Methods] Swanson implant arthroplasty for at the thumb MP joint was performed on the 108 cases (male 11, female 97) with minimum follow up of 6 months. The average age was 61 yrs. old and the average follow-up period was 4 yrs. Radiological findings and complications were assessed. [Results] In the radiological assessment, the pre- and the postoperative flexion angles at the MP joint were 42 and 17 degrees, and extension angles at the IP joint were 37 and 0 degree (s). In one case, postoperative infection occurred and implant was removal of required. 3 cases of implant fracture occurred and revision was performed in 2 cases and removal was performed in 1 case with a synovitis. Swanson implant with a grommets did not cause implant fracture. [Conclusion] By the rheumatoid thumb surgery, deformity was corrected. The ratio of implant failure was lower than that in the previous reports.

P1-171

Reverse total shoulder arthroplasty for seronegative rheumatoid arthritis : A case report diagnosed at late stage

Terufumi Shibata¹, Teruaki Izaki¹, Akira Maeyama¹, Tomonobu Hagio¹, Naoko Himuro², Katsuhisa Miyake², Hitoshi Nakashima², Takuaki Yamamoto¹

¹Department of Orthopaedic Surgery, Fukuoka University Faculty of Medicine, ²Division of Nephrology and Rheumatology, Department of Internal Medicine, Fukuoka University Faculty of Medicine

Conflict of interest: None

Report of the case A 80-year-old female complained of pain in her right shoulder after falling on his right side. Assessment at her local hospital reveals no bony injury. Despite participation in a physiotherapy and intra-articular injection for three months, she continued to complain of pain and the development of glenohumeral joint space narrowing was confirmed on radiographs. She referred to our hospital for diagnostic evaluations. She had the diabetes. The physical examination for the shoulder couldn't reveal the signs of infection. Laboratory tests included an elevated CRP (1.06mg/dl). WBC was normal (4900/ μ l), and RF and a CCP antibodies weren't identified. Imaging revealed the destruction of the humeral head and the glenoid and the large glenohumeral joint effusion. Arthroscopic debridement was performed to rule out the septic shoulder arthritis. Intra-articular cultures were negative, but the radiological progression was confirmed. More detailed clinical assessment found the left wrist pain from the past and the prominent erosive changes in bilateral wrists were seen on the radiographs. She was diagnosed with seronegative RA, and the reverse total shoulder arthroplasty was performed. DMARDs were introduced postoperatively, resulting in improvement of her condition.

P1-172

Total Joint Arthroplasty was Improved Quality of Life greater than Synovectomy in Patients with Rheumatoid Arthritis

Jiro Kato, Shusuke Ota, Takanobu Doi
Department of Orthopaedic Surgery, Shizuoka Medical Center, National Hospital Organization, Shizuoka, Japan

Conflict of interest: None

[Object] The aim of this study is to identify the quality of life (QoL)

changes in patients with rheumatoid arthritis (RA) following total joint arthroplasty (TJA) or joint synovectomy. [Methods] A retrospective chart review was conducted in patients with RA. A total of 18 patients (18 females, mean age, 69.6 \pm 7.7 years; mean disease duration, 13.4 \pm 11.0 years) were identified. To explore the QoL changes, we divided the patients into two groups depend on the type of surgery (group T, TJA; group S, joint synovectomy), and tested the differences for statistical significance using t test or chi square test. [Results] Group T showed significantly lower preoperative index value of EQ-5D (group T, 0.504; group S, 0.700), higher preoperative DAS28-CRP (group T, 4.74; group S, 3.07) and better improvement of visual analogue scale (VAS) at 6&12 months after operation (group T, 26/15; group S, 56/60) than group S. After the surgery of lower leg, group T showed significantly better improvement of mHAQ and EQ-5D domain of mobility than group S. [Conclusions] In RA patients with joint destruction, we should operate TJA to improve their QoL. However, we have to arrange the prospective study to clarify the efficacy of synovectomy at upper joint.

P1-173

The association of fall history with performance-based physical function and postural sway in patients with rheumatoid arthritis

Kensuke Kawabata¹, Takumi Matsumoto², Ryutaro Takeda³, Taro Kasai⁴, Song Ho Chang⁴, Jun Hirose⁴, Sakae Tanaka⁴

¹Department of Orthopaedics, National Center for Global Health and Medicine, Tokyo, Japan, ²Bone and Cartilage Regenerative Medicine, Division of Tissue Engineering, Faculty of Medicine, The University of Tokyo, Tokyo, Japan, ³Department of Orthopaedics, Ibaraki Prefectural Central Hospital, Ibaraki, Japan, ⁴Department of Orthopaedics, The University of Tokyo Hospital, Tokyo, Japan

Conflict of interest: None

[Object] Patients with rheumatoid arthritis (RA) are at increased risk of falls; therefore, its prevision and prevention are one of the critical issues to be addressed. The aim of this study was to evaluate the ability of the short physical performance battery (SPPB) and center of pressure (COP) to discriminate between patients with and without a history of falls. [Methods] Fifty patients with RA were enrolled and divided into two groups according to the presence or absence of history of falls within a year. Physical performance was assessed using SPPB. Postural sway was assessed using a force platform in below positions: (1) standing with feet together side-by-side with eyes opened or closed; (2) semitandem with right or left foot forward; (3) tandem with right or left foot forward. The backgrounds, physical function, and postural sway were compared between the two groups. [Results] Fourteen patients (28%) reported falls. There were no significant differences in baseline characteristics and SPPB between the two groups. The group with a history of fall had significantly lower postural stability only in semitandem. [Conclusions] Numerical evaluation of postural sway in the semitandem position seems to be more appropriate than SPPB for assessing the risk of falls in patients with RA.

P1-174

Pre examine interview for outpatients of rheumatoid arthritis by physiotherapist

Akira Inoue¹, Takuro Okari¹, Keio Ayabe²

¹Department of Rehabilitation, Keiyu Orthopedic Hospital, ²Department of Orthopedic Surgery, Keiyu Orthopedic Hospital

Conflict of interest: None

[Object] Report the usefulness of interview by physiotherapist for outpatient rheumatoid arthritis (RA). [Methods] The RA outpatient at our hospital is a reservation system, and we use interviewing using waiting time. Cold symptoms, complications, presence or absence of side effects due to oral administration, residual medicine, presence / absence of other department visits, blood sampling, tender / swollen joints, HAQ survey. In addition, performed self exercise, ADL guidance, ulcer check and insole creation. [Results] The number of registered patients is 1013. 27.4% who had cold symptoms, side effects due to oral administration 10.3%, other departments visits 20.7% (internal medicine 59.7%, ophthalmology 26.2%, dentistry 21.6%). Side effects / complications were found in 49

cases of herpes zoster, interstitial pneumonia, CKD (eGFR 29 or less) and foot ulcer. Insole took effect in 50 cases, foot VAS significantly improved. [Conclusions] As a result of achieving results with insole creation and rehabilitation guidance, there is utility of interview before physical examination by physiotherapist.

P1-175

A pilot evaluation of physical activity by pedometer in a rheumatoid patient (RA) before and after the prescription of rheumatic shoe-type orthosis

Megumi Ato¹, Ikuko Masuda¹, Yukiko Komano¹, Koichiro Ohmura², Toshihiro Mata¹, Aiko Kishida¹

¹Rehabilitation Center, Jujo Takeda Rehabilitation Hospital, Center for Rheumatic Diseases, ²Department of Rheumatology and Clinical Immunology, Kyoto University

Conflict of interest: None

[Object] There are few studies that evaluate a change of the quantity of the walk of RA patients. Using an electric pedometer, we tried to evaluate their physical activity. [Case and Methods] 70 years old patient who has three years history of RA, was admitted to our hospital for evaluation and education of RA. We used a pedometer to evaluate her physical activity. Since her chief complaint was painful feet while walking, she was prescribed rheumatic shoes after the discharge. The change of her physical activity before/after the hospitalization, and after the wearing rheumatic shoes was reported. m-HAQ and functional foot index was also assessed. [Results] The average steps after the discharge improved to 3254, compared to those in the hospital (2311). The average steps after the rheumatic shoe's prescription improved furthermore to 3,535. m-HAQ did not show the major change. The foot function index was improved to 46 points in final assessment from 49 points at the initial evaluation. [Conclusion] This pilot study suggested the importance of continuous physical exercise for RA patient while taking care of the pain when walking. Also, relief of pain by wearing rheumatic shoes, contributed improvement of overall locomotor activity as well as her motivation to keep active.

P1-176

A transitional case of juvenile dermatomyositis (JDM) that has been shown to improve ADL / QOL by rehabilitation

Yusuke Yamada^{1,2}, Yuki Asai^{1,2}, Yoshihiro Ishihara^{1,2}, Naoto Tamura², Masahiko Yasuda^{1,2}

¹Internal Medicine, Nakaizu Spa Hospital, Izu, Japan, ²Internal Medicine and Rheumatology, Juntendo University, Tokyo, Japan

Conflict of interest: None

[Object] In recent years the prognosis of many pediatric chronic illnesses has improved, accompanied by that scenes which are required to seamlessly shift to adulthood are increasing. We report a case in which rehabilitation was useful for such transitional periods. [Methods] We evaluate the ADL / QOL improvement of a 22-year-old female JDM patient using the bio-psycho-social model, who was introduced to our hospital for rehabilitation purposes. She was hospitalized two times for two months with her hope. [Results] In this case, psychotherapy was successful first, from which there was an enhancement of exercise therapy, further correction of cognitive distortion, leading to an improvement not only ADL but also QOL. [Conclusions] In transitional medicine, we realized that a comprehensive approach such as team medical care and family-oriented care in rehabilitation is useful. [Clinical significance] Chronic illnesses such as collagen diseases often have problems including family members as well as their own, depending on the age of the patient and the life stage, not limited to the transition period. We could see the multifaceted expanse of rehabilitation medicine including multi - occupational collaboration system from this experience.

P1-177

The efficacy and safety of mycophenolate mofetil as a maintenance therapy for systemic lupus erythematosus

Shunsuke Sakai¹, Yoko Wada¹, Sayuri Takamura¹, Ayako Wakamatsu¹,

Yukiko Nozawa¹, Hiroe Sato², Daisuke Kobayashi¹, Takeshi Nakatsue¹, Takeshi Kuroda², Masaaki Nakano³, Ichiei Narita¹

¹Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences, 1-757 Asahimachi-dori, Niigata, 951-8510 Japan, ²Health Administration Center, Niigata University, Japan, ³Faculty of Medicine, Niigata University School of Medicine, Niigata, Japan

Conflict of interest: None

[Object] To examine the efficacy and safety of mycophenolate mofetil (MMF) as a maintenance therapy in patients with systemic lupus erythematosus (SLE). [Methods] Thirty-one SLE patients (2 males and 29 females) who visited Niigata University Hospital and treated with MMF between October 2017 to September 2018, were enrolled. We investigated the dosage of prednisolone (PSL), laboratory data, SLE disease activity index (SLEDAI) at the time of MMF initiation, and followed the changes at 12 weeks (n = 31), 24 weeks (n = 28), and 36 weeks (n = 20) after MMF initiation, respectively. Adverse events were also evaluated. [Results] The mean age at MMF initiation was 45 ± 13 years, the mean PSL dosage was 10.9 mg/day, and the mean SLEDAI was 1.52. The mean PSL dosage was decreased to 10.2 mg at 12 weeks, 9.9 mg at 24 weeks, and 9.9 mg at 36 weeks. The mean SLEDAI was 0.87 at 12 weeks, 0.78 at 24 weeks, 0.95 at 36weeks and kept low disease activity. Although adverse events were observed in 3 patients with nausea, 1 patient with loss of appetite, and 2 patients with infections, there was no discontinuation of MMF during study period. [Conclusions] In maintenance phase of SLE patients, MMF was safe and effective to reduce the dosage of PSL and control disease activity.

P1-178

Administration of hydroxychloroquine to treat systemic lupus erythematosus: Is it appropriate for young patients?

Toshiaki Kobayashi, Hiroyuki Yamashita, Shinji Izuka, Sotaro Nakajima, Nanami Mino, Kyoko Motomura, Shunta Kaneko, Yuko Takahashi, Hiroshi Kaneko

Department of Rheumatology, Center Hospital of the National Center for Global Health and Medicine, Tokyo, Japan

Conflict of interest: None

[Object] The effectiveness and safety of administration of hydroxychloroquine (HCQ) to treat systemic lupus erythematosus (SLE) was examined. [Methods] SLE patients who regularly visited our outpatient clinic were examined and compared retrospectively with HCQ-prescribed and non-prescribed cases. [Results] HCQ was prescribed in 41 cases (34 females, 83%). Improvement was found in 19 patients (90.5%) among 21 who had rash or hair loss before commencement. Side effects were observed in 7 cases, 4 at the beginning and 1 at the dose increase, while 3 cases were discontinued. In the case of cessation, there was 1 case of rash at the beginning and 2 of ocular lesions. Thirty cases continued for more than 6 months, with the longest being 72 months. HCQ was selected earlier in cases of first incidence after the approval of HCQ. Among the 226 patients given an immunosuppressive agent, 37 patients (16.4%) continued with HCQ administration. The mean age was 36.2 ± 11.2 years (HCQ), and case 52.6 ± 15.3 years (non - HCQ) (p <0.01); younger patients were prescribed HCQ. [Conclusions] HCQ is effective for the skin eruption and depilation of SLE, and sparing of steroids. It is expected that HCQ-prescribed cases will increase mainly in young people in the future.

P1-179

The real-world tacrolimus use in systemic lupus erythematosus: a cross-sectional study of the LUNA registry

Masaki Mitsunashi¹, Yosuke Kunishita¹, Ryusuke Yoshimi¹, Chiharu Hidekawa¹, Natsuki Sakurai¹, Yumiko Sugiyama², Daiga Kishimoto¹, Yuki Izuka¹, Takaaki Komiya¹, Hideto Nagai¹, Naoki Hamada¹, Naomi Tsuchida¹, Yutaro Soezima¹, Reikou Kamiyama¹, Kouji Kobayashi², Yukiko Asami¹, Yohei Kirino¹, Nobuyuki Yajima³, Ken-ei Sada⁴, Kunihiro Ichinose⁵, Shigeru Ohno², Hideaki Nakajima¹

¹Department of Hematology and Clinical Immunology, Yokohama City University School of Medicine, ²Center for Rheumatic Diseases, Yokohama

ma City University Medical Center, ³Division of Rheumatology, Department of Medicine, Showa University School of Medicine, ⁴Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ⁵Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: None

[Object] To survey the real-world situation of tacrolimus (TAC) use in the clinical practice of systemic lupus erythematosus (SLE) using a multicenter registry. [Methods] SLE patients registered in the LUNA registry were divided into two groups according to whether TAC was administered or not. The patient's demographic, clinical, and laboratory data were compared between the two groups. [Results] Among 591 patients with SLE, 189 (32%) used TAC. The mean age was significantly lower in the TAC user group than in the non-user group (44.7 ± 13.3 vs 48.5 ± 15.5 years old, $p = 0.0021$). Disease activity did not differ between the two groups (SLEDAI 5.6 ± 5.4 vs 4.7 ± 4.6 , $p = 0.057$), but arthritis was significantly more frequent in the TAC user group as compared with the non-user group (16.4 vs 10.5% , $p = 0.045$). Furthermore, the TAC user group tended to have better renal function (eGFR 94.5 ± 31.3 vs 88.9 ± 36.0 mL/min/1.73m², $p = 0.074$) and higher frequency of lupus nephritis class V (34.5 vs 22.8% , $p = 0.067$) as compared to the non-user group. [Conclusions] TAC tended to be used frequently in younger cases and cases with arthritis or lupus nephritis class V in real-world clinical practice.

P1-180

The effectiveness in dose reduction of corticosteroids by combination use of hydroxychloroquine in maintenance phase of systemic lupus erythematosus

Takayoshi Kurabayashi, Yasushi Kondo, Mai Sugiyama, Yuto Izumi, Yoko Nakagome, Kazuki Hirano, Sho Sasaki, Yasushi Koyama, Chiho Yamada, Shinji Sato

Department of Rheumatology, Tokai University, Isehara, Japan

Conflict of interest: None

Purpose: To clarify the effectiveness and predictors of prednisolone (PSL) sparing effect by combination use of hydroxychloroquine (HCQ) in systemic lupus erythematosus (SLE) patients with maintenance therapy. **Methods:** We enrolled 63 of SLE patients who continued to use HCQ over 24 weeks with receiving PSL less than 15mg as maintenance dose at the time of HCQ initiation. We excluded the patients who added immunosuppressant after HCQ initiation. We analyzed the changes of PSL dose and clinical parameters and patients' backgrounds. **Results:** The mean age and disease duration were 41 ± 11 and 13 ± 8.7 years, respectively. Mean PSL dose were significantly reduced from the baseline to 24 and 48 weeks after initiation of HCQ. (PSL dose at HCQ initiation; 9.5 ± 3.0 mg, 24 weeks; 8.5 ± 2.9 mg and 48 week; 8.0 ± 3.1 mg ($p < 0.01$), respectively.) We found the amelioration of serological markers in patient with hypocomplementemia and/or high levels of anti-dsDNA antibody. We also identified that the SLE patients with anti-U1RNP antibody positivity is the predictive factor who was able to reduce the PSL dose within 24 week after HCQ initiation. **Conclusion:** Additional use of HCQ can reduce PSL dose in maintenance phase of SLE and this seemed to be more susceptible in anti U1RNP antibody positive patients.

P1-181

Investigation of the prognosis of lupus nephritis and risk factors for achieving to complete response by EULAR/ERA-EDTA criteria in 1 year

Yasuo Suzuki¹, Yuki Mizutani¹, Kentaro Noda¹, Naohiro Sugitani¹, Eiji Ishikawa², Ayako Nakajima¹

¹Center for Rheumatic Diseases, Tsu, Mie, Japan, Mie University Hospital, ²Department of Nephrology, Japan, Mie University Hospital

Conflict of interest: None

[Objective] To investigate the prognosis of lupus nephritis patients who underwent renal biopsy from 2007 to 2017. [Methods] Patient's

backgrounds, disease activity measured by SLEDAI, renal pathology and treatment were analyzed retrospectively. The prognosis defined by achievement of complete response rates (CR) by EULAR/ERA-EDTA criteria was evaluated in 1 year and additionally according to renal pathology type (II vs III±V vs IV±V vs V) by using Kaplan-Meier method. The factors for achieving CR was analyzed by multivariate analysis. [Results] Forty-four patients underwent renal biopsy, 77.8% were female, median [IQR] age was 35.3 [29.5, 55.2] years. Among 40 patients, 18 patients (45%) treated with steroid alone and the rest were in combination with immunosuppressants (19 with CNi and 2 with IVCY). CR was achieved in 18 cases (51.4%) in 35 patients in 1 year. There was no significant difference in cumulative CR ratio according to renal pathological types. Cr was a significant risk factor for achieving to CR in 1 year with odds ratio 0.059 (95% CI:0.001-0.736, $p < 0.05$) by multivariate analysis. [Conclusion] CR was achieved in 51.4% of patients in the cohort that immunosuppressive drugs were used in 55%.

P1-182

The prevalence and the risk factor of hypertension and dyslipidemia in systemic lupus erythematosus patients: Exploratory research

Nobuyuki Yajima¹, Tomoki Hayashi¹, Kosuke Sakurai¹, Nao Oguro¹, Yoko Miura¹, Mayu Saito¹, Sakiko Isojima¹, Ryo Takahashi¹, Kunihiro Ichinose³, Shigeru Ohno⁵, Ken-ei Sada², Ryusuke Yoshimi⁴, Yusuke Miwa¹

¹Division of Rheumatology, Department of Medicine, Showa University School of Medicine, ²Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ³Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, ⁴Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, ⁵Center for Rheumatic Diseases, Yokohama City University Medical Center, Yokohama, Japan

Conflict of interest: Yes

[Object] There were few reports about the risk factors of hypertension (HT) and dyslipidemia (DL). The purpose of this study is to describe a prevalence of HT and DL and to evaluate the risk factor of HT and DL. [Methods] Participants were patients who satisfied ACR criteria were targeted. They were registered in LUNA databases. The definition of HT and DL was a use of anti-HT drug or $>130/80$. The definition of DL was anti-DL drug or LDL-cho ≥ 100 mg/dl or TG ≥ 175 mg/dl. We performed descriptive statistics and binomial logistic regression analysis to evaluate the risk factors of HT and DL. Missing data were imputed by multiple imputation. [Results] Patients were 618. Mean age was 45.9 ± 15.1 years old. 88% was female. Mean corticosteroids dosage was 6.9 ± 7.0 mg. Mean SLEDAI and SLICC-DI were 4.96 ± 4.8 , 0.86 ± 1.4 . A prevalence of HT and DL was 345/598 (57.4%), 385/600 (64.2%). On binomial logistic regression analysis to evaluate the risk of HT, age, sex, BMI, drinking status, current corticosteroid dose, and lupus nephritis were the independent factors. On binomial logistic regression analysis to evaluate the risk of DL, age was the independent factor. [Conclusion] The prevalence of HT and DL was over 50%. We should take care of HT and DL to prevent atherosclerosis.

P1-183

Efficacy and safety of hydroxychloroquine treatment in patients with systemic lupus erythematosus: a single center study

Naoki Matsuoka, Jumpei Temmoku, Yuya Fujita, Makiko Furuya Yashiro, Tomoyuki Asano, Shuzo Sato, Hiroko Kobayashi, Hiroshi Watanabe, Kiyoshi Migita

Department of Rheumatology, School of Medicine, Fukushima Medical University, Fukushima, Japan

Conflict of interest: None

[Object] Hydroxychloroquine (HCQ) has been used to treat lupus patients since 2015 in Japan. We aimed to show the effects of HCQ treatment in this study. [Methods] A total of 172 lupus patients treated in our hospital were analyzed retrospectively. We examined reasons of HCQ use

and nonuse, effects of treatment with HCQ, and adverse effects. [Results] Treatment with HCQ was planned for 42 patients. The aims of HCQ treatment were decreasing corticosteroid doses (42 cases), treatment of cutaneous manifestations (11 cases), and treatment of headache/arthropathy (7 cases). All patients were examined by ophthalmologists before HCQ prescription, and 33 patients received HCQ. The reasons of HCQ nonuse were lupus retinopathy (5 cases), dyschromatopsia congenita (1 case), age-related maculopathy (1 case), hemorrhage in the eye ground (1 case), and decreased disease activity (1 case). After treatment with HCQ, doses of corticosteroid were reduced in 21 patients. HCQ was discontinued in 5 patients because of adverse drug effects, but no eye toxicity was observed. [Conclusions] This study indicates physicians hesitate prescribing HCQ when patients have any retinopathy. Doses of corticosteroid were reduced in approximately two-thirds of patients after HCQ use with no severe adverse effects.

P1-184

A study on of skin adverse events and its clinical outcome of hydroxychloroquine (HCQ) in SLE patients

Eisuke Takamasu¹, Naoto Yokogawa¹, Naoki Tanomogi¹, Masahiro Iida¹, Shuhei Sano¹, Yusuke Nakamichi¹, Tatsuo Mori¹, Nanase Honda¹, Michiru Kina¹, Kae Onishi¹, Takayasu Kise¹, Satoshi Watanuki², Yuji Miyoshi¹, Masako Utsunomiya¹, Yoshiki Nagai¹, Kota Shimada¹, Shoji Sugii¹

¹Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, ²Division of Emergency and General Medicine, Tokyo Metropolitan Tama Medical Center

Conflict of interest: None

[Object] Skin hypersensitivity is important as a skin adverse events of HCQ in the early stage, and skin pigmentation is also important under long-term HCQ use. We collected the data of skin adverse events of HCQ and examined clinical outcome. [Methods] The subjects were SLE patients who started HCQ between Apr 1, 2009 and May 31, 2018 and developed skin adverse events at our hospital. [Results] Of 302 SLE patients studied, skin adverse events were seen in 9.3%. About skin hypersensitivity, 22 patients were mild to moderate and 2 patients were severe (1 patient was suspected drug-induced hypersensitivity syndrome and hospitalized). A simple dose escalation of HCQ was carried out in 14 patients with mild skin hypersensitivity, and only one patient re-experienced hypersensitivity. In addition, 3 patients developed skin pigmentation. Although, in the previous reports, the onset is usually 5 years or more after HCQ starting, each of the 3 occurred at 7, 9, and 10 months, respectively. Among them, 1 patient stopped HCQ, 1 reduced HCQ and 1 continued the same amount of HCQ. [Conclusions] HCQ should be discontinued at the time when skin hypersensitivity is suspected. In case of mild skin hypersensitivity it may be possible to re-introduce. Skin pigmentation needs individual support.

P1-185

Evaluation of the correlation between renal pathology and clinical course of lupus nephritis: single center study

Taro Horino, Satoshi Inotani, Tatsuki Matsumoto, Yoshiko Shimamura, Kosuke Inoue, Yoshio Terada
Department of Endocrinology, Metabolism and Nephrology, Kochi Medical School, Kochi University

Conflict of interest: None

[Object] Lupus nephritis (LN) is one of important prognostic factors in systemic lupus erythematosus (SLE). The damaged area in LN I/II, LN III/IV, or LN V are considered to be mesangial, subendothelial, or subepithelial site, respectively. Our goal is to assess the correlation between renal pathology and clinical course of LN. [Methods] 68 patients with LN proven by renal biopsy from 2001 to 2018 were enrolled. We assess the correlation among clinical characteristics, laboratory data, and pathological findings. [Results] Female were 56. Mean age was 46±2.2 years old. In all cases, oral PSL was administrated. After 1 year, 62 patients had remission, but 6 had poor prognosis (3 death and 3 ESRD). Patients were divided into three groups; group 1 (LN I or II), group 2 (LN III or IV) and group 3 (LN III/IV+V or V). Proteinuria levels in group 3 were high-

er and ds-DNA antibodies levels in group 1 were lower than other two groups. Decline rates of eGFR in 1 year or 5 years were not significant among these 3 groups. [Conclusions] Our results suggest that podocyte and endothelial cytotoxicities might be reflexed in proteinuria and ds-DNA antibody level, respectively. Nevertheless, we consider that proper treatment could better long-term renal outcome.

P1-186

Case Series Report: 'Multitarget Therapy' in Japanese Patients with Lupus Nephritis

Mari Tochihara, Yasuhiro Katsumata, Hirokazu Nishina, Masanori Hanaoka, Yasushi Kawaguchi, Hisashi Yamanaka
Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] Although the management of lupus nephritis (LN) has progressed significantly in the last decade, evidence in Japanese patients is still lacking. We aimed to investigate the outcome of Multitarget Therapy in Japanese LN patients. [Methods] We retrospectively collected the data of LN patients treated with Multitarget Therapy (glucocorticoids, MMF and TAC) and followed for at least 48 weeks. [Results] Four women with mean age 38 years and mean disease duration 8 years were included. Renal biopsies were performed in 3, and their pathological types were IV-S (A/C)+V, IV-G (A/C), and IV-G (A/C). All cases were treated with pulses methylprednisolone followed by oral PSL 0.6 mg/kg/d and combined with MMF 1 g/d and TAC 3 mg/d. Dosage of PSL were tapered to 10 mg/d by 44 weeks in all cases. Urine protein: creatinine ratio (UPCR) decreased to less than 0.5 g/gCr by 48 weeks in all cases. eGFR was normal at baseline and remained normal in all cases. Thus, all cases achieved complete renal response (UPCR<0.56 g/gCr with normal renal function). Urine sediments normalized by 12 weeks in 2 cases. Serological activity also improved in all cases. There was no renal flare or severe adverse events. [Conclusions] This study suggested that Multitarget Therapy were useful in Japanese LN patients.

P1-187

The association between the dose of glucocorticoids and emotional health in patients with systemic lupus erythematosus: a cross-sectional analysis of a lupus registry of nationwide institutions (LUNA)

Yoshia Miyawaki¹, Ken-ei Sada², Kunihiro Ichinose³, Ryusuke Yoshimi⁴, Shigeru Ohno⁵, Nobuyuki Yajima^{1,6}

¹Department of Healthcare Epidemiology, School of Public Health in the Graduate School of Medicine, Kyoto University, ²Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, ³Department of Immunology and Rheumatology Unit of Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences Nagasaki University Graduate School of Biomedical Sciences, ⁴Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan, ⁵Center for Rheumatic Diseases, Yokohama City University Medical Center, Yokohama, Japan, ⁶Division of Rheumatology, Department of Internal Medicine, Showa University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Objectives] Glucocorticoids (GC) were widely used and were generally known to cause emotional health symptoms. We assessed the association between current GC dose and emotional health among patients with systemic lupus erythematosus (SLE). [Methods] We conducted a cross-sectional study. Participants were patients with SLE aged 20 years or older from 6 institutions in Japan. The exposure was daily GC dose. The main outcome was Emotional Health domain (EH) score of Lupus Patient Reported Outcome (LupusPRO). The secondary outcome was the total score of LupusPRO. We performed a simple linear regression and multiple regression analyses. [Results] Overall, 205 patients were included; 80% were female and the median age was 44 (interquartile range (IQR) 35-55) years. The median SLEDAI was 4 (IQR 2-8) and the median GC dose was 5 (IQR 3-9) mg. The daily dose of GC negatively correlated with EH score ($\beta=-0.60$ [95%CI -1.27 to 0.07]) and the total score ($\beta=-$

0.53 [95%CI -1.01 to -0.06]). In multiple linear regression analysis, the daily dose of GC was associated with the EH score ($\beta=-0.18$ [95%CI -1.67 to -0.19]) and the total score ($\beta=-0.27$ [95%CI -1.46 to -0.46]). [Conclusions] The daily GC dose was negatively associated with emotional health among SLE patients.

P1-188

Comparison of the disease control and the treatment of systemic lupus erythematosus between recent 5 years and 15 years ago

Chihiro Imaizumi, Yuki Inoue, Munetsugu Imamura, Hideki Ito, Sayaka Takenaka, Rie Kujime, Norihide Hayashi, Ayako Hirata, Takehisa Ogura, Hideto Kameda

Division of Rheumatology, Department of Internal Medicine Faculty of Medicine, Toho University (Ohashi Medical Center)

Conflict of interest: None

[Object] The prognosis of SLE has dramatically improved, and it has been pointed out introduction of immunosuppressants and reduction of steroid are involved. However, there were few reports comparing actual treatment. The treatment of the last 5 years and 15 years ago was compared. [Methods] SLE patients with Toho Uni. Ohashi Medical Center visit in each 5 years from 2012 to 2017 (GroupA:79) and 1999 to 2003 (group B:68), compared with PSLuse, immunosuppressant use, and relapse. [Results] The incidence of lupus nephritis (A:31%, B:38%, $p=0.40$) and serositis (A:29%, B:28%, $p=0.87$) was similar, but the incidence of CNS was significantly higher in group B (A:7%, B:19%, $p=0.04$). The average number of relapsed significantly decreased in group A (A:0.26, B:0.40/per year, $p<0.01$). The median PSL dose in initial treatment was 30mg/day ($p=0.64$) in both groups, and the median PSL dose at relapse was no difference ($p=0.11$). The dose of PSL increase for relapse was lower in group A (A:6.5, B: 14mg/day, $p<0.01$). The rate of introduction of immunosuppressants in the initial treatment was higher in group A (A:43%, B:6%, $p<0.01$) There was no difference in the incidence of infection ($p=0.58$). [Conclusions] The active immunosuppressants use in recent years resulted decrease SLE relapse and PSL dose.

P1-189

Use of hydroxychloroquine for the treatment of systemic lupus erythematosus: Experience in National Hospital Organization Himeji Medical Center

Akiko Kitagawa¹, Yasutaka Ohnishi², Rinko Katsuda², Kohei Miyake², Tetsuji Kawamura², Akira Okamoto¹

¹rheumatism Department, National Hospital Organization Himeji Medical Center, ²pneumology Department, National Hospital Organization Himeji Medical Center

Conflict of interest: None

[Objectives] In Japan, reimbursement of hydroxychloroquine (HCQ) was initiated in August 2015. We present our experience with the use of HCQ. [Methods] HCQ was administered to six patients with systemic lupus erythematosus (SLE) from Sep. 2015 to Sep. 2017. [Results] Treatment was cancelled in two cases due to lupus enteritis and meningitis ($n=1$) and cough ($n=1$). In those with continuous treatment ($n=4$), slight improvement of fever and general fatigue was observed and reduction of the glucocorticoid dosage was achieved. However, cytopenia did not improve. In one patient who discontinued treatment due to diarrhea, therapy was reinitiated using lactic acid bacillus. [Clinical Importance] Our results are similar to those reported in double-blinded, randomized, clinical trials investigating the efficacy of HCQ against non-severe SLE. The ACR2015 treatment algorithm recommended the use of HCQ, along with glucocorticoids, as first-line therapy for general fatigue and polyarthritides. HCQ plays an important role in the treatment of SLE. Diarrhea was the most common side effect (5-10%) and was treatable. [Conclusion] HCQ assists the reduction of the glucocorticoid dosage in patients with SLE exhibiting clinical manifestations (i.e., arthralgia, fever, and general fatigue).

P1-190

A Review on the Continuity Rate & Termination Cause of HCQ for SLE

Shoshi Shinagawa¹, Machiko Mizushima¹, Tomohiko Shibata¹, Naooki Katsuyama¹, Toshiko Shibata¹, Tohru Yamada¹, Masaomi Yamasaki¹, Naoko Ohya¹, Gen Ito²

¹Department of Rheumatology, St. Marianna University School of Medicine, Yokohama City Seibu Hospital, ²Department of Rheumatology, St. Joseph Hospital

Conflict of interest: None

[Object] Hydroxychloroquine (HCQ) has been used for long as standard medicine for systemic lupus erythematosus (SLE). It was approved in 2015 in Japan. HCQ is relatively safe, while side effects like digestive illness and rash lead to usage termination. Now, we aimed to survey in our hospital about HCQ's continuity rate and termination cause on SLE patients. [Methods] 40 SLE patients were studied. They have used HCQ since April 2016. The time after the treatment, patients' background, continuity rate, and termination cause were studied. The continuity rate was analyzed by Kaplan Meier method. [Results] There were 36 female patients (90%), and HCQ starting age ranges from 19-83 (average=41.8). Median of the study is 8-month, and the 2-yr continuity rate is 71.6%. Termination include rash (4 cases), digestive illness (3), and there are one case of eye symptom and decrease in platelet respectively. Two cases are terminated with unknown reasons. [Conclusion] The 2-yr continuity rate of HCQ on SLE patients is satisfactorily 71.6%. Majority of termination (91%) occurs within 5 months. Termination for digestive illness all occurs within 2 months. Yet, around half of the rash case occurs within a month while some continue for over 4 months. It needs our attention.

P1-191

Association between alcohol, smoking, and disease activity of systemic lupus erythematosus (the third report): cross sectional study: from LUNA registry

Mika Hatano¹, Nobuyuki Yajima¹, Ken-ei Sada², Kunihiro Ichinose³, Ryusuke Yoshimi⁴, Shigeru Ohno⁵

¹Division of Rheumatology, Department of Internal Medicine, Showa University School of Medicine, ²Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ³Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, ⁴Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, ⁵Center for Rheumatic Diseases, Yokohama City University Medical Center

Conflict of interest: None

[Objectives] We aimed to examine whether alcohol and smoking are associated with the disease activity of SLE. [Methods] The research design was cross-sectional study. 618 SLE patients who satisfied ACR criteria were targeted. They were registered in databases currently being constructed at 7 hospitals. Patients divided into 4 groups; group1:smoking (-)alcohol (-), group2:smoking (+)alcohol (-), group3:smoking (-)alcohol (+), group4:smoking (+)alcohol (+). The main outcome was SLEDAI. The linear regression analysis was performed to analyze the association between smoke, alcohol and the disease activity. Confounding factors were sex, age, present corticosteroid dosage and present immunosuppressant use. [Results] The median age was 44 years old. 89% was female. The median corticosteroids dosage was 5mg. Immunosuppressant use was 69%. The median SLEDAI was 4. Group1 was 446/618. Group 2 was 57/618. Group 3 was 90/618. Group4 was 25/618. No significant difference was observed between the 4 groups in Kruskal Wallis test and no significant difference was observed in multiple regression analysis. [Conclusions] We did not show the association between smoking, alcohol and disease activity of SLE.

P1-192

Fragmented qrs in patients with systemic lupus erythematosus: relation to the disease activity: a cross-sectional study

Masahiro Hosonuma, Nobuyuki Yajima, Ryo Takahashi, Ryo Yanai,

Sakiko Isojima, Nao Oguro, Yoko Miura, Mayu Saito, Tomoki Hayashi
Division of Rheumatology, Department of Medicine, Showa University
School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] Cardiovascular disease is an important contributor to mortality in Systemic Lupus Erythematosus (SLE). Fragmented QRS (fQRS) is a convenient marker of myocardial scar by ECG defined as additional spikes within the QRS complex. There is no report that examined the association of disease activity of SLE and fQRS. [Methods] The study design was a cross-sectional study. The participants were SLE patients who diagnosed at Showa University Hospital from January 2010 to December 2017. The patients with cardiac disease, other rheumatic diseases, and already treatment at the time of an ECG measurement were excluded. The outcome was Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). A multiple regression analysis was conducted to assess the association between fQRS and SLE activity adjusted for age, sex and period from the estimated date of onset to the date of diagnosis. [Results] In total, 44 participants were enrolled. The mean age was 39.5 years, and 84.1% were female. The median SLEDAI-2K was 13.5 [IQR, 10 to 20]. 24 patients (55%) had fQRS. The regression coefficients of fQRS for SLEDAI-2K were 2.69 ($p=0.008$) with reference to non-fQRS. [Conclusions] Our results demonstrated that fQRS positive SLE patients have high disease activity.

P1-193

The efficacy of hydroxychloroquine (HCQ) reducing dose of steroid in patients with systemic lupus erythematosus (SLE) for 12 months (Second report)

Kenshi Inoue, Moemi Miyazaki, Naofumi Dobashi, Kenta Misaki
Department of Rheumatology, Kita-Harima Medical Center

Conflict of interest: None

[Object] We had reported in the JCR2018 that dose of steroid was significantly reduced 6 months after administration of HCQ. In this report, we evaluated the efficacy and the safety of HCQ for 12 months as co-treatment in the standard therapy of SLE. [Methods] Thirty-three patients under the maintenance therapy of SLE were enrolled in this study. Dose of prednisolone (PSL), SLE disease activity index (SLEDAI) and titer of anti-DNA antibody were examined retrospectively at 0, 3, 6 and 12 months after administration of HCQ. [Results] Dose of PSL was significantly reduced (mean \pm S.E) (pre-administration of HCQ:10.0 \pm 1.9 mg/day, 12 months after administration of HCQ:5.0 \pm 0.7 mg/day, $p=0.001$). SLEDAI was also significantly reduced. (3.0 \pm 0.6, 2.0 \pm 0.4, $p=0.03$). In the subgroup whose dose of PSL was less than 7.5 mg/day at the baseline, dose of PSL was remarkably reduced (3.8 \pm 0.6 mg/day, 1.9 \pm 0.3 mg/day, $p<0.00001$). HCQ has been continued in 91 percent of all patients for 12 months and stopped in 3 cases. The infection was clarified in 2 cases. The recurrence of SLE was revealed in only one case. [Conclusions] In the patients receiving the maintenance therapy of SLE, it is suggested that administration of HCQ on standard therapy is enable to reduce dose of PSL and might be possible to withdraw PSL.

P1-194

The relevance of P-glycoprotein+CXCR4+CD27-IgD+B cells to clinical manifestation of serositis in systemic lupus erythematosus

Shizuyo Tsujimura, Yoshiya Tanaka

The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan

Conflict of interest: None

[Object] We indicated previously that P-gp⁺CD27-IgD⁺B cells were involved in refractory SLE with serositis and were increased in highly active RA patients with extra-articular involvement, whose P-gp⁺CXCR4⁺B cells expanded and infiltrated to inflammatory sites. We have investigated the relevance of P-gp⁺CXCR4⁺B cells and P-gp⁺CD27-IgD⁺B cells to clinical features in SLE. [Methods] Flow cytometry analyzed molecules on CD19⁺ cells were performed. [Results] The expression level of P-gp on peripheral B cells was high, and that of CXCR4 on

peripheral B cells was varied in patients with SLE ($n=39$). P-gp⁺CXCR4⁺B cells ratio has no relevance to SLEDAI in whole SLE patients, NPSLE, and lupus nephritis. However, P-gp⁺CXCR4⁺B cells ratio strongly correlated with SLEDAI in serositis. P-gp⁺CXCR4⁺B cells ratio correlated with P-gp⁺CD27-IgD⁺B cell ratio but not P-gp⁺CD27⁻IgD⁺B cells ratio. Immunosuppressive therapy resulted in reduction of P-gp⁺CD27-IgD⁺B cells ratio and P-gp⁺CXCR4⁺B cells ratio associated with improvement in clinical manifestation in highly active serositis. [Conclusion] P-gp⁺CD27-IgD⁺B cells, which is involved in disease activity and treatment resistance in serositis, seem to be co-expressed CXCR4 and infiltrate in inflammatory tissue.

P1-195

Clinical differences between macrophage activation syndrome associated with systemic lupus erythematosus and adult still disease

Daisuke Waki, Keisuke Nishimura, Kaoru Mizukawa, Keiichiro Kadoba, Hiroki Mukoyama, Tomohiro Yoshida, Toshihiko Yokota
Department of Endocrinology and Rheumatology, Kurashiki Central Hospital

Conflict of interest: None

[Object] To investigate clinical differences of macrophage activation syndrome (MAS) associated with systemic lupus erythematosus (SLE-MAS) and adult onset still disease (ASD-MAS) [Methods] We retrospectively analyzed the secondary SLE-MAS and ASD-MAS, hospitalized at KCH between 2006-2018. [Results] fifteen patients included (SLE-MAS; $n=8$, ASD-MAS; $n=7$) in this study. The ASD-MAS patients were significantly older than SLE-MAS patients (68.0 vs 34.5, $p=0.005$). ASD-MAS patients had higher serum Alkaline Phosphatase (ALP) (419 U/L vs 132 U/L, $p=0.003$), neutrophil count (11424 / μ l vs 1135 / μ l, $p=0.001$), platelet count (15.6 $\times 10^4$ / μ l vs 6.9 $\times 10^4$ / μ l, $p=0.021$), CRP (12.79 mg/dl vs 0.28 mg/dl, $p=0.001$), and ferritin (18657 ng/ml vs 1522 ng/ml, $p=0.037$) than SLE-MAS patients. All patients finally achieved remission. Five out of 6 ASD-MAS patients needed other immunosuppressants addition to corticosteroids (CS) and calcineurin inhibitor (CI), conversely only 1 out of 7 SLE-MAS patients needed other immunosuppressants addition to CS and CI. Serum ferritin at 4 weeks after starting treatment was significantly higher in ASD-MAS groups ($p=0.02$). [Conclusions] Clinical profiles of MAS in ASD and SLE are quite different, and ASD-MAS patients tend to need more aggressive treatment.

P1-196

A study of 125 cases of neuro-psychiatric systemic lupus erythematosus (NPSLE) in our hospital

Tomoko Miyashita, Yoshiyuki Abe, Ken Yamaji, Naoto Tamura
Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] We conducted retrospective observational study to investigate the baseline clinical features and prognosis of NPSLE at our hospital [Methods] From April 2008 to September 2018, NPSLE was diagnosed at our hospital and 125 patients with NPSLE who had been treated were analyzed retrospectively. Their Clinical features, treatment contents, prognosis etc. were examined. [Results] Central nervous system disorder was found in 105 cases, mental disorder in 71 cases, peripheral neuropathy in 20 cases. As for neurological symptoms, cases with multiple symptoms were also observed. Seven deaths occurred during the observation period of NPSLE, and the cause of death was 2 cases of cerebral infarction, 1 case of renal failure, 1 case of breast cancer, 1 case of suicide, and 2 cases of septic shock. There were 30 cases in which NPSLE was relapsed, and there were cases in which recurrence was observed up to seven times in some cases. [Conclusions] Because NPSLE shows various neurological symptoms by invading the central nerve, spinal cord, peripheral nerve, it is difficult to diagnose and treat NPSLE. To accumulate treatment according to each symptom of NPSLE, further accumulation of cases is necessary.

P1-197

Clinical features of patients with recurrent lupus nephritis

Eiji Suzuki¹, Takashi Kanno¹, Momoko Hazama², Tomoyuki Asano³, Kiyoshi Migita³

¹Department of Rheumatology, Ohta-Nishinouchi Hospital, ²Ohga Clinic, ³Department of Rheumatology, Fukushima Medical University School of Medicine

Conflict of interest: None

Objective We aimed to determine the clinical features of recurrent lupus nephritis (LN). **Methods** We divided 40 patients with LN who were treated between April 2005 and March 2018 at Ohta-Nishinouchi Hospital into groups with early (within one year; n = 29) and late (after one year; n = 11) remission and according to LN onset < 6 (initial n = 27) and > 6 (delayed onset: n = 13) months after being diagnosed with systemic lupus erythematosus. Renal histology, therapies to induce LN remission and recurrence after the first induction therapy were compared among the groups. **Results** Although immunosuppressants were more frequently prescribed, LN tended to recur more frequently among patients with late, than early remission and patients with delayed onset of LN required more time to achieve remission compared with those who had initial onset. The renal relapse-free rate was significantly higher in the group with initial, compared with delayed onset. **Conclusion** Patients with late remission or delayed onset of LN should be treated aggressively because LN might be difficult to treat.

P1-198

Immunohistochemical staining of lupus nephritis using anti-ribosomal P monoclonal antibody

Ayako Wakamatsu¹, Hiroe Sato², Shunsuke Sakai¹, Sayuri Takamura¹, Daisuke Kobayashi¹, Takeshi Nakatsue¹, Yoko Wada¹, Takeshi Kuroda², Masaaki Nakano³, Ichiei Narita¹

¹Clinical Nephrology and Rheumatology, Niigata University Medical and Dental Hospital, Niigata, Japan, ²Niigata University Health Administration Center, ³School of Health Science Faculty of Medicine, Niigata University

Conflict of interest: None

Objectives: Anti-ribosomal P antibody (Anti-P) is frequently detected in patients with systemic lupus erythematosus (SLE). We have reported that patients with anti-P and anti-dsDNA were associated with endocapillary proliferative glomerular lesions. In this study, we investigated whether the antigens of anti-P are expressed in renal biopsy tissue of lupus nephritis (LN). **Methods:** Thirty-four patients who were histologically diagnosed with LN in our hospital from 2005 to 2018 were evaluated. Anti-P was analyzed by an immunoblot assay using total ribosomal proteins of brine shrimp. Laboratory, histological findings and immunohistochemical (IHC) staining by anti-P monoclonal antibody were analyzed. **Results:** Six patients (17.6%) had anti-P, 25 (73.5%) had anti-dsDNA, 5 (14.7%) had both antibodies. One having anti-P only was ISN/RPS Class V. Five patients having both antibodies were ISN/RPS Class III/IV±V and had active lesions. IHC staining revealed that active lesions of some glomeruli were reacted by anti-P monoclonal antibody in a patient with severe LN, ISN/RPS IV-G (A), having both anti-P and anti-ds DNA (>400IU/ml). **Conclusion:** The antigens of anti-P were found in the glomerular lesion of LN, suggesting that anti-P might cause the aggravation of LN.

P1-199

Study of clinical significance of hydroxychloroquine in patients with systemic lupus erythematosus

Noriyoshi Ogawa, Shogo Furukawa, Kumiko Shimoyama, Daisuke Suzuki

Division of Immunology and Rheumatology, Hamamatsu University School of Medicine

Conflict of interest: None

[Objectives] To clarify the clinical significance of hydroxychloroquine (HCQ) in Japanese patients with systemic lupus erythematosus

(SLE). [Methods] 21 SLE patients were subjected for the study. HCQ was administered in 4 patients (ages 35±19 year-old, 4 female, disease duration 0.1~29 years) as an induction therapy, and in 17 patients (41±12 year-old, male:female=2:15, disease duration 12±9 years) as a maintenance therapy. The effectiveness of HCQ was evaluated by SLEDAI, and adverse events were recorded. [Results] HCQ was administered in 21 out of 54 SLE patients (39%). The dosage was 200mg/day in 14 cases, and 300mg/day in 7 cases. In patients with induction therapy, the SLEDAI score was improved from 11±6 (0M) to 3.0±1.2 (6M), and to 1.3±1.2 (12M), respectively. Similarly, PSL dosage was decreased from 36±7.5mg to 12.8±2.9mg, 10.0±8.7mg. In patients with maintenance therapy, the SLEDAI score was improved from 2.8±3.0 to 1.8±1.8, 2.5±3.3. PSL dosage was decreased from 7.2±3.3mg to 6.9±3.4mg, 6.8±3.6mg. One patient of induction therapy showed mild eruption. [Conclusions] HCQ seems to be a relatively safe drug, and can be used in a maintenance therapy as well as in an induction therapy. Steroid sparing effect of HCQ in the maintenance therapy is valuable.

P1-200

Possible involvement of CD14⁺⁺CD16⁺ monocytes expressing CX3CR1 in immunological features of patients with systemic lupus erythematosus

Keiko Yoshimoto, Katsuya Suzuki, Shuntaro Saito, Jun Kikuchi, Tsutomu Takeuchi

Keio University School of Medicine

Conflict of interest: None

[Object] Fractalkine and its receptor, CX3CR1, play an important role in chemotaxis of immune cells. In this study, we investigated the expression level of CX3CR1 in peripheral monocytes from patients with systemic lupus erythematosus (SLE) and HC to elucidate the possible involvement of CX3CR1⁺ monocytes in immunological features of SLE. [Methods] The expression level of CX3CR1 in peripheral monocytes (CD14⁺⁺CD16⁻, CD14⁺⁺CD16⁺, CD14⁺⁺CD16⁺⁺) was analyzed by FACS with whole blood samples from patients with SLE active (SLEDAI: >10, n = 22), inactive (SLEDAI: <4, n = 22) and HC (n = 34). [Results] FACS analysis revealed that the proportion of CD14⁺⁺CD16⁺ monocytes among CD14⁺ cells was significantly elevated in SLE active (p = 0.0017) and SLE inactive (p = 0.0002) patients as compared to HC. Notably, the proportion of CX3CR1 positive cells in CD14⁺⁺CD16⁺ monocytes was significantly lower in SLE active patients than patients with SLE inactive (p = 0.014) and HC (p = 0.002), whereas that proportion was not significantly different between SLE inactive and HC. [Conclusions] These results give the possibility that FKN binds its receptor, CX3CR1, expressed on CD14⁺⁺CD16⁺ monocytes in SLE, and the cells consequently migrate into the organs through peripheral blood.

P1-201

Analysis of systemic lupus erythematosus maintaining LLDAS using RNA-seq

Yusuke Takeshima^{1,2}, Yukiko Iwasaki², Masahiro Nakano², Mineto Ota^{1,2}, Yasuo Nagafuchi², Shuji Sumitomo², Yuta Kochi³, Tomohisa Okamura^{1,2}, Kazuhiko Yamamoto³, Keishi Fujio²

¹Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, ²Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, ³Laboratory for Autoimmune Diseases, Center for Integrative Medical Sciences, RIKEN

Conflict of interest: None

[Objectives] Systemic lupus erythematosus (SLE) is a systemic autoimmune disease and the association with Type I interferon (IFN) is well-known, although the detailed mechanism remains unknown. In recent years, it has been reported that maintaining the disease state at LLDAS (Lupus Low Disease Activity Score) reduces relapse. We explored the relationship between cases maintaining LLDAS and IFN signature. [Methods] Peripheral blood mononuclear cells were isolated from 49 SLE patients, and 19 subsets were collected with multicolor flow cytometer following RNA-seq. [Results] IFN signature for each immune cell subset showed broad influence beyond the cell type, and SLE patients were

grouped according to IFN signature. Antinuclear antibody, anti-dsDNA antibody, serum complement level, peripheral blood Plasmasabst fraction ratio showed correlation with IFN signature, although correlation between IFN signature and LLDAS was not significant. Gene modules detected by network analysis suggested cell-type specific effect to maintenance of LLDAS. [Conclusion] We identified cases where IFN signature remained strongly even when LLDAS was achieved. The importance of elucidating the mechanism of IFN signal in LLDAS cases was suggested because maintenance of LLDAS alone was unable.

P1-202

Synergistic enhancement of production of proinflammatory cytokines on human peripheral blood monocytes by anti-Sm and anti-RNP antibodies

Yu Matsueda, Yoshiyuki Arinuma, Tatsuo Nagai, Sumiaki Tanaka, Shunsei Hirohata, Kunihiko Yamaoka
Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine, Sagami-hara, Japan

Conflict of interest: None

[Object] To elucidate the roles of serum anti-Sm antibodies in the pathogenesis of systemic lupus erythematosus. [Methods] Highly purified peripheral blood monocytes obtained from healthy donors were cultured in the presence of monoclonal anti-Sm antibody (anti-Sm mAb), monoclonal anti-U1-RNP antibody (anti-RNP mAb) or control murine IgG1 or IgG3. After various periods of incubation, levels of IL-6 and TNF- α in the culture supernatants were measured by ELISA and the expression of mRNA for various molecules in monocytes was determined using RT-PCR. [Results] Both anti-Sm mAb and anti-RNP mAb significantly increased the production of IL-6 and TNF- α of human monocytes in a dose-dependent manner, although the latter was more potent than the former. Of note, anti-Sm mAb synergistically enhanced the production and mRNA expression of IL-6 and TNF- α of human monocytes in the presence of anti-RNP mAb. Notably, anti-RNP mAb, but not anti-Sm mAb, significantly enhanced the mRNA expression of RelA in human monocytes. [Conclusions] These results demonstrate that anti-Sm and anti-RNP antibodies synergistically upregulate the expression of IL-6 and TNF- α in human monocytes. The data also suggest that the effect of anti-Sm in the synergy with anti-RNP might not involve NF κ B activation.

P1-203

Serum soluble CD226 levels in patients with systemic lupus erythematosus

Miki Nakano¹, Masahiro Ayano¹, Kazuo Kushimoto¹, Shotaro Kawano¹, Yasutaka Kimoto², Hiroki Mitoma¹, Mitsuteru Akahoshi¹, Yojiro Arinobu¹, Koichi Akashi¹, Takahiko Horiuchi², Hiroaki Niino³
¹Department of Medicine and Biosystemic Science, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan, ²Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, ³Department of Medical Education, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan

Conflict of interest: None

[Object] CD226 is costimulatory molecule expressed on T cells and NK cells, and act as an activating receptor like CD28. Recent studies have shown serum soluble CD226 (sCD226) level is a useful biomarker in patients with cancer or GVHD. We aimed to study the relation between serum sCD226 levels and the clinical characteristics in patients with systemic lupus erythematosus (SLE). [Methods] We measured serum sCD226 levels in 66 SLE patients who were treated at our hospital and 19 healthy controls (HC) by ELISA (quantitation limit, 0.1 ng/ml). We assessed the relation between sCD226 levels and clinical manifestations, SLEDAI, laboratory data, and medications. [Results] Serum sCD226 levels in SLE patients did not differ from HC (median, 0.25 vs 0.50), but the levels in patients with active nephritis were lower than in those without (0.15 vs 0.62, $p=0.009$). Although sCD226 levels had no correlation with SLEDAI ($p=0.01$), they significantly correlated with non-renal SLEDAI ($p=0.28$) and renal SLEDAI ($p=0.35$), serum creatinine ($p=0.25$) and urine protein/creatinine ratio ($p=0.38$). [Conclusions] Serum sCD226 levels are related with nephritis and reflect disease activity, suggesting

that sCD226 could be a useful biomarker and CD226 may be involved in the pathogenesis of lupus nephritis.

P1-204

Transcription factor Fli-1 impacts renal IL-17 expression, but not CXCL1 expression in MRL/lpr mouse

Shuzo Sato¹, Xian Zhang², Jumpei Temmoku¹, Yuya Fujita¹, Naoki Matsuoka¹, Makiko Furuya Yashiro¹, Tomoyuki Asano¹, Hiroko Kobayashi¹, Hiroshi Watanabe¹, Kiyoshi Migita¹

¹Department of Rheumatology, Fukushima Medical University School of Medicine, ²Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC, USA

Conflict of interest: None

[Object] Transcription factor Fli-1 has been reported to affect cytokine and chemokine expression, such as MCP-1, RANTES, CXCL2, G-CSF and IL-6 in the kidney of lupus model mouse. Inflammatory cytokines, IL-17 as well as CXCL1 are associated with lupus nephritis development and tissue inflammation into the kidney. To investigate whether Fli-1 impacts renal IL-17 and CXCL1 expression in lupus model mouse, we performed following experiments. [Methods] Sera of Wild-type (WT) and Fli-1 heterozygote (Fli-1^{+/-}) MRL/lpr mice were collected, and serum IL-17 and CXCL1 concentration were measured by ELISA. Histological examination (IL-17 and CXCL1 expression) on WT and Fli-1^{+/-} MRL/lpr mice were also performed using pathology scoring system. Real-time PCR in the kidney of these mice were analyzed and compared between the 2 groups. [Results] The expression of IL-17 in the kidney interstitium was significantly decreased in Fli-1^{+/-} mice ($p=0.012$). However, expression of CXCL1 in the kidney was similar in both groups. Whereas IL-1 beta and IL-18 expression, which were associated with Th17 immune response, was significantly decreased in Fli-1^{+/-} MRL/lpr mice compared to WT ($p=0.02$). [Conclusions] Fli-1 impacts renal IL-17 expression but not CXCL1 in MRL/lpr mice.

P1-205

Suppressor of cytokine signaling 3 (SOCS3) expressed in podocytes attenuates glomerulonephritis in an imiquimod-induced lupus model

Masashi Fukuda, Kotaro Suzuki, Shigeru Tanaka, Kazumasa Suzuki, Arifumi Iwata, Shunsuke Furuta, Tomohiro Tamachi, Kei Ikeda, Yuko Maezawa, Akira Suto, Hiroshi Nakajima
Chiba University Hospital

Conflict of interest: None

[Background] Lupus nephritis is major organ damage in systemic lupus erythematosus. Previously, we found that suppressor of cytokine signaling 3 (SOCS3) was highly expressed in glomeruli in an imiquimod-induced lupus model and that SOCS3 expression was induced in podocytes upon IL-6 stimulation. However, the role of SOCS3 in lupus nephritis remains unknown. [Purpose] To clarify the roles of SOCS3 expressed in podocytes in glomerulonephritis in the imiquimod-induced lupus model. [Methods] Podocyte-specific SOCS3-deficient mice (Podocin-Cre x SOCS3-floxed; SOCS3-cKO mice) and control mice (SOCS3-WT) were epicutaneously treated with imiquimod, and 1) survival rate, 2) levels of serum creatinine and urine albumin, and 3) renal histopathologic scores and IgM deposition were compared. [Results] SOCS3-cKO mice exhibited 1) decreased survival rate, 2) high levels of serum creatinine and urine albumin, and 3) severe glomerulonephritis and increased IgM deposition, as compared with SOCS3-WT mice. [Conclusion] SOCS3 expressed in podocytes attenuates glomerulonephritis in the imiquimod-induced lupus model.

P1-206

A Study on the Contribution of Monocytes to the Pathogenesis of Systemic Lupus Erythematosus through the Measurements of Serum MCP-1 and Soluble VCAM-1

Masanori Hanaoka, Yasuhiro Katsumata, Hirokazu Nishina, Mari Tochihiro, Shinya Hirahara, Akira Nishino, Yasushi Kawaguchi, Hisashi Yamanaka

Department of Rheumatology, Tokyo Women's Medical University

Conflict of interest: None

[Object] MCP-1 (monocyte chemotactic and activating factor) is a molecule involved in monocyte migration and activation. VCAM-1 (vascular cell adhesion molecule-1) is involved in monocyte adhesion. We aimed to investigate the involvement of monocytes in systemic lupus erythematosus (SLE). [Methods] 62 SLE patients who admitted to our hospital from July 2015 to May 2018 were included. 222 patients with rheumatoid arthritis, systemic sclerosis, polymyositis/dermatomyositis and systemic vasculitis who admitted at the same time were used as controls. MCP-1 and soluble VCAM-1 in stored serum were measured by ELISA and statistically analyzed the relationship with clinical data. [Results] MCP-1 and soluble VCAM-1 were significantly higher in SLE patients than controls (788 pg/ml vs. 428 pg/ml in average, $p = 0.001$ and 1,639 ng/ml vs. 1,088 ng/ml in average, $p < 0.001$, respectively). In the SLE group, MCP-1 and soluble VCAM-1 correlated with SLEDAI-2K, anti-dsDNA antibody titer and inversely correlated with C3 ($r = 0.25, 0.43, -0.31$, and $r = 0.26, 0.25, -0.42$, respectively). [Conclusions] Serum MCP-1 and soluble VCAM-1 were higher in SLE patients and correlated with disease activity index. It was suggested that monocytes are involved in the pathology of SLE.

P1-207

A case of systemic lupus erythematosus manifested with primary central nervous system lymphoma (PCNSL) in the course of neuropsychiatric-SLE

Masafumi Sugiyama^{1,2}, Akinori Okada², Taeko Yumoto¹, Asuka Inoue², Yasuaki Hirooka^{1,2}, Yuji Nozaki², Koji Kinoshita², Masanori Funouchi², Itaru Matsumura²

¹Department of Rheumatology, Kindai University Nara Hospital, Nara, Japan, ²Division of Hematology and Rheumatology, Kindai University Faculty of Medicine

Conflict of interest: None

We have experienced a case of systemic lupus erythematosus (SLE) female patient, she have been diagnosed as SLE with antiphospholipid antibody syndrome. At the age of 19 years-old, she complained of hallucination which diagnosed as neuropsychiatric-SLE, the dosage of glucocorticoid was increased. At the age of 29 years-old, she complained of right hemiparesis with paralysis, accompanied by T2 weighted high signal magnetic resonance imaging (MRI) lesions in the mesencephalon and nucleus basalis, which was interpreted as angioedema caused by NP-SLE, intravenous cyclophosphamide (IVCY) was added. At the age of 34 years-old, her right hemiparesis deteriorated rapidly, the other multiple high signal brain lesions were confirmed. Her level of consciousness got worsened, the brain lesions surgically removed to treat cerebral herniation. Histopathological diagnosis was diffuse-large B-cell lymphoma with the immunostaining results, thought to be other iatrogenic immunodeficiency-associated lymphoproliferative disorders. She was treated with high-dose methotrexate and cytarabine arabinoside (Ara-C) regimen. Although she had a partial short response, she died after 2-months. Primary central nervous system lymphoma with SLE is quite rare, we will report our case and discuss these relationships.

P1-208

Clinical study of fourteen patients with methotrexate-associated lymphoproliferative disorders

Fusayo Ikeda, Tetsu Itami, Kaori Ishimura, Hiroki Akazawa, Chisato Ashida, Atsuhiko Yamamoto, Kenji Sakai, Shinkai Ri, Asuka Inoue, Toshihiko Shiga, Kazuya Kishimoto, Yuji Nozaki, Koji Kinoshita, Masanori Funouchi, Itaru Matsumura

Department of Hematology and Rheumatology, Kindai University of Faculty of Medicine, Osaka, Japan

Conflict of interest: None

[Object] Methotrexate-associated lymphoproliferative disorders (MTX-LPD) are defined as LPD that have developed in patients who are receiving MTX. [Methods] Because there are many clinically unclear

points, we investigated 14 cases that treated with MTX for RA from 1 April 2012 to 31 March 2018. [Results] 12 women and 2 men, the age at onset was 65.4 ± 7.2 years, and the MTX administration period was 292.7 ± 204.9 weeks. In 2 cases, bDMARDs were used, In 5 cases, steroids were used, and in 3 cases, tacrolimus was used in combination. The histology of lymphoma was the 7 cases DLBCL, followed by FL 3 cases, HL 2 cases, and 2 others. There were 5 cases that resulted in remission with withdrawal of MTX, and recurrence after remission was not observed. There were 7 of 9 cases in remission after treatment, none of which showed recurrence. In RA treatment after onset of MTX-LPD, DMARDs such as SASP and IGU are often selected, in which RA activity is suppressed in prednisolone administered to lymphoma are also seen. There were 2 cases in which bDMARDs were used before the onset of lymphoma, and 3 cases were used after onset. [Conclusions] Although it was difficult to evaluate the relation with RA activity, analysis of the association with RA activity will be necessary in the future.

P1-209

A Crohn's disease patient during infliximab treatments with the diagnosis of bone primary diffuse large B-cell lymphoma in the spine and iliac

Kenji Ikuta, Yuka Mukofujiwara

Department of Orthopedic Surgery, Kainan Hospital

Conflict of interest: None

[Object] The bone primary malignant lymphoma (BPML) onset in patients with rheumatoid arthritis and connective tissue diseases during treatments of immunosuppressive drugs and/or biologics has been rare. We experienced the Crohn's disease patient with low back pain and lower leg pain during infliximab treatments and made the diagnosis of BPML. [Case] 28-years old man's digestive symptom had been stable by infliximab and azathioprine combined treatments in contraction of disease six years of large intestine and small intestine type Crohn's disease. Low back and lower leg pains had developed for three months and showed initial diagnosis, compression of the fourth lumbar vertebrae body. We performed CT guided bone biopsies and obtained the diagnosis of BPML in the spine and iliac. Hematologist started R-CHOP chemotherapies and his pains had been decreased. He had continued in remission for three years after treatments. [Discussion] BPML onset in inflammatory bowel diseases by disease activities, drug side effects or synergistic actions has been currently discussed. When we present patients with low back pain during treatments with immunosuppressive drugs and/or biologics, it should be necessary to search by multiple imaging studies and follow it up.

P1-210

Study of lymphoproliferative disorder (LPD) in patients with rheumatic diseases at our hospital

Akikatsu Nakashima¹, Shigeto Horita¹, Takahiro Matsunaga¹, Mitsuhiro Kawano²

¹Division of Nephrology and Rheumatology, Ishikawa Prefectural Central Hospital, ²Division of Rheumatology, Department of Internal Medicine, Kanazawa University Graduate School of Medicine

Conflict of interest: None

[Object] Immunosuppressants such as methotrexate (MTX) and tacrolimus (Tac) have been used for rheumatic diseases, recently LPD related to its use is reported. In order to clarify the issue, we examined LPD patients at our hospital. [Methods] LPD patients from 2012 to March 2018 were extracted from the electronic medical record and examined. [Results] LPD was found in 9 cases with rheumatoid arthritis (RA) and 1 case with scleroderma. There were 8 females and 2 men. The mean age at onset was 75.4 ± 7.0 years and the mean disease duration was 23.4 ± 21.7 years. The MTX was administered in 9 out of 10, the mean dose was 6.4 ± 6.5 mg / week, and the mean administration period was 8.2 ± 5.9 years. Three cases received biological agents. Tac was administered to 4 caees and 1 case was not administered MTX. Four cases had recovered spontaneously with only MTX discontinuation. Six cases required chemotherapy. Diffuse large large cell type B cell lymphoma were 5 cases, B cell lineage 2 cases, and Hodgkin lymphoma 3 cases. Five of 10 EBV-en-

coded small RNAs (EBER) were positive. [Conclusions] The results were almost the same as previously reported. Tac was administered to 4 patients of whom one patient was not administered MTX. Thus, association between LPD and Tac sole was also suspected.

P1-211

A case of methotrexate associated lymphoproliferative disorder which was required to be differentiated from metastatic lung tumor of adrenal tumor

Yosuke Nagasawa¹, Masashi Oshima¹, Yutaka Tanikawa¹, Marina Hamaguchi¹, Shoei Yoshizawa¹, Hiroshi Tsuzuki¹, Kaita Sugiyama¹, Atsuma Nishiwaki¹, Natsumi Ikumi¹, Takamasa Nozaki¹, Hidetaka Shiraiwa^{1,2}, Mitsuhiro Iwata¹, Hitomi Haraoka¹, Noboru Kitamura¹, Masami Takei¹

¹Division of Hematology and Rheumatology, Department of Medicine, Nihon University School of Medicine, ²Shiraiwa Rheumatology Clinic

Conflict of interest: Yes

A 51-year-old woman was diagnosed with mixed connective tissue disease and with rheumatoid arthritis 20 and seven years ago. She had been on methotrexate (MTX) 10 mg/week, iguratimod 50 mg/day and prednisolone 6 mg/day. She was admitted to our hospital for further examination of two weeks of dry cough. Computed tomography examination revealed existence of multiple nodules in the bilateral lungs, lymphadenopathy in axilla, hilus and mediastinum, and enlarged right adrenal gland. However, although biopsy of transbronchial tumor and bone marrow were conducted, the diagnosis was remained unknown. Peripheral blood and bone marrow fluid examination indicated elevation of Epstein-Barr virus DNA levels. Left axilla lymph node biopsy disclosed that B-cell type MTX lymphoproliferative disorder (LPD), which reached a diagnose with MTX-LPD. Her multiple nodules, lymphadenopathy enlarged adrenal gland were improved by withdrawal of MTX. The case of MTX-LPD, which is found among patients having multiple nodules in the bilateral lungs and enlarged adrenal gland, is rarely reported in literature. We report our case with the relevant literature.

P1-212

Multiple lung nodules associated with MTX-LPD in a patient with rheumatoid arthritis

Kenji Tamagawa, Motoko Ishida, Tomoya Miyamura, Tomoaki Iwanaga, Makiko Higuchi, Soichiro Takahama, Rumi Minami, Masahiro Yamamoto, Eiichi Suematsu

Department of Internal Medicine and Rheumatology, Clinical Research Institute, National Hospital Organization Kyushu Medical Center

Conflict of interest: None

A 66 year old female admitted to our hospital because of multiple nodules of bilateral lung and elevated level of serum CRP. She was diagnosed as rheumatoid arthritis 18 years ago and the treatment with methotrexate (MTX) was started. Her blood test revealed high titer of serum CRP and sIL-2 receptor. The significant accumulation of FDG-PET were observed in both submandibular lymph nodes, both cervical lymph nodes, both supraclavicular lymph nodes, splenic hilum, paraabdominal aortic lymph nodes and both pulmonary nodules. There were no malignant findings in bronchial alveolar lavage cytology and lung biopsy. MTX associated lymphoproliferative disorders (MTX associated EBV-positive lymphadenitis) was diagnosed from the finding of lymph node specimen. JH reconstruction was not detected. Pulmonary nodule and lymphadenopathy showed spontaneous regression after MTX withdrawal. MTX should be stopped when appearance lymphadenopathy or abnormal lung field shadow. There are not so many reports of MTX-LPD with lung lesions, but MTX withdrawal often allows improvement of lung lesions. MTX-LPD should be considered when patient's blood test showed high level of CRP without arthritis.

P1-213

Investigation of methotrexate associated lymphoproliferative disorder (MTX - LPD) in rheumatoid arthritis patients in our hospital

Chinatsu Azuma, Tomo Oyakawa, Fuminori Kanaya

Department of Orthopedic Surgery, University of the Ryukyus

Conflict of interest: None

[Introduction] Maximum dose of MTX was approved up to 16mg/W since 2010, and MTX became an anchor drug in JCR recommendation in 2014. Recently, RA patients treated with MTX and its dose are increasing. In our hospital, 6 patients were suffered from MTX associated lymphoproliferative disorder (MTX-LPD). The purpose of this study is to investigate background of MTX-LPD patients. [Materials and Methods] We treated 170 RA patients with MTX. 6 patients were suffered from LPD, 1 man and 5 women. Age of RA onset, RA duration, BMI, MTX dose, MTX duration, disease activity (DAS28-ESR) before the onset of MTX-LPD, sIL-2R value and lymph nodes pathology were investigated. [Result] The mean age of RA onset was 43.3 y-o (19~62 y-o), RA duration to onset MTX-LPD was 19.5 years (2~47y), BMI was 21.1 (18.4~25.3), MTX dose was 9.3mg/W (6~14mg/W), total MTX dose was 2512.2mg (343~4844mg), MTX duration was 6 years (1y~8y10m), DAS28-ESR before the onset of MTX-LPD was 3.83 (2.75~5.33), sIL-2R value 2550.8 U/ml (730~6752 U/ml). Lymph nodes biopsy was performed in 4 patients. MTX-LPD was spontaneously regressed after withdrawal of MTX in all patients. [Conclusions] MTX-LPD patients showed slightly higher total MTX dose and DAS28-ESR before the onset of MTX-LPD and slightly lower BMI.

P1-214

Five cases of methotrexate-associated lymphoproliferative disorders in our hospital

Shinsuke Mogi, Tomoko Matsuzaki, Mayuko Tsukida, Fumie Ohta, Yoshito Tsukada

Fujioka General Hospital

Conflict of interest: None

We examined five cases of methotrexate-associated lymphoproliferative disorders (MTX-LPD) in our hospital since 2016 until 2018. Mean disease duration was 11.6 years, average MTX dose was 6.8mg/week, The pathological diagnosis was diffuse large B cell lymphoma in three cases, classical Hodgkin lymphoma in one case, and Hodgkin-like lymphoproliferative disease in one case. EBER-ISH test was positive in four out of five patients tested. One case gained complete remission with chemotherapy. Four cases achieved spontaneous regression only with cessation of MTX, recurrence was confirmed in one case. Exacerbation of rheumatoid arthritis was observed in one case with cessation of MTX. <Discussion>EB virus-positive MTX-LPD is reported to have high initial remission rate only with cessation of MTX. In our cases, 3 out of 4 cases soon showed partial remission, however 2 out of 3 cases relapsed within 1 year. Therefore, careful follow-up observation is necessary for MTX-LPD. In using MTX for patients with autoimmune diseases, we should consider the possibility of development of lymphoproliferative diseases. In case of MTX-LPD, EBV related protein test is mandatory, and we should continue careful monitoring under cessation of MTX.

P1-215

Clinical characteristics of lymphoproliferative disorders associated with rheumatoid arthritis: A single center study

Ryosuke Hara, Shun Nomura, Wataru Ishii

Division of Rheumatology, Nagano Red Cross Hospital

Conflict of interest: None

[Object] The aim of this study is to clarify clinical characteristics of lymphoproliferative disorders (LPD) associated with rheumatoid arthritis (RA). [Methods] Patients with RA who developed LPD in our hospital between January 2010 to September 2018 were analyzed retrospectively. [Results] Fourteen patients with RA were diagnosed with LPD. Thirteen patients were treated with MTX at the time of LPD development, and 4 of them were combined with anti-TNF- α inhibitors. The average age at the time of LPD development was 71 years. Histological diagnosis of LPD is as follows; Hodgkin's lymphoma in 3 cases, follicular lymphoma in 3 cases, diffuse large B-cell lymphoma in 2 cases, MALT lymphoma in 2 cases, and other in 3 cases. EBER was positive with 6 patients (46.2%).

The average dose of MTX at the time of LPD development was 6.5 mg per week. LPD regressed spontaneously after discontinuation of MTX in 6 patients and the median duration from the time of MTX withdrawal to LPD regression was 4.9 weeks. LPD recurred in 3 of 6 patients, leading to chemotherapy. There were no fatal cases during the observation period. [Conclusions] LPD often regresses after discontinuation of MTX, but it is necessary to pay sufficient attention to recurrence. LPD in our hospital showed good prognosis.

P1-216

Methotrexate related lymphoproliferative diseases for patients with rheumatoid arthritis

Kei Funamura, Masataka Maeda
Nagano Red Cross Hospital

Conflict of interest: None

[Object] One side effect of MTX is LPD, and we also experienced seven cases in our hospital. [Methods] Of the patients who received MTX administration to RA, 2 males and 5 females developed MTX-LPD. [Results] The soluble IL-2 receptor is high in all cases, with an average of 1354 U / ml. LDH was high in 5 of 7 cases, with an average of 242. No cases of Sjogren's syndrome were combined, and 4 cases of EBV positive. Four patients received chemotherapy, and three became conservative treatments. Four patients who underwent chemotherapy had remission, and the remaining three remained unresolved. [Discussion] Of the 7 cases, 4 patients who had remission had undergone chemotherapy and 3 remaining chemotherapy was not enforced. Among the three patients who did not achieve remission, 2 cases were lungs and 1 cases were bones. Future diagnosis / treatment will be carried out while consulting with each department. Re-administration of MTX or TNF inhibitor has not been performed after onset. However, control of pain is poor only with steroids against poor control of RA, and BUC and SASP are used for 3 cases. Recurrence is not admitted. [Conclusions] Treatment after remission of LPD needs to avoid immunosuppressive drugs, but pain is seen in some patients, causing RA treatment difficulties.

P1-217

A case of methotrexate-associated lymphoproliferative disorders (MTX-LPD) presented acute interstitial pneumonia (AIP)

Kazuo Jouyama, Ayuko Sogabe, Atsushi Kondo, Yosuke Murata, Naoya Sawada, Akihiro Yamada, Kenichiro Matoba, Makoto Onishi, Yasuaki Okuda, Kiyoshi Takasugi
Center for Rheumatic Diseases, Dohgo Spa Hospital, Ehime, Japan

Conflict of interest: None

AIP developed in an 80-year-old female with rheumatoid arthritis (RA) who has been treated with prednisolone (PSL) (5mg/day) and methotrexate (MTX) (8mg/week). Pneumocystis pneumonia (PCP) was diagnosed and MTX discontinued, treated with Trimethoprim-Sulfamethoxazole (S/T) and methyl PSL (mPSL) (500mg on 1st, 125mg/day for next 3 days), PSL 10mg/day subsequently. CT on 7th day showed increasing interstitial shadows. The bolus mPSL (500-1000mg) could be commonly choice, but Steroid was reduced, because MTX-LPD was diagnosed by elevated sIL-2R (3800U/ml) and EB virus reactivation and thought exacerbated with Steroid. PSL was reduced to 7.5mg on 14th and 5mg on 19th day. PCP was denied and S/T was discontinued. The respiratory function and pulmonary shadows were improved. We guess that immunity could be inhibited by Steroid with MTX more, hence LPD and AIP exacerbated. Clinical significance is that extranodal pulmonary disease of MTX-LPD presented AIP is extremely rare and reported. Next we showed that AIP in MTX-LPD was exacerbated by Steroid and ameliorated by discontinuation of MTX, and that the bolus mPSL, standard therapy of AIP complicated with RA, was not effective. Finally elevated sIL-2R and EB virus reactivation were useful clinically enough to diagnose MTX-LPD without histology.

P1-218

A case of primary breast diffuse large B-cell lymphoma associated with rheumatoid arthritis during administration of methotrexate and adalimumab

Nobuhisa Hirase¹, Hideyuki Watanabe¹, Minoru Takasaki²

¹Department of Internal Medicine, Kyushu Rosai Hospital, ²Department of Orthopaedic Surgery, Kyushu Rosai Hospital

Conflict of interest: None

A 73-year-old-woman was diagnosed with RA in August 2012. She was treated with MTX from April 2014. The dosage of MTX was gradually increased to 12 mg/week in July 2014. She was additionally treated with ADA from June 2015. A tumor in her right breast was detected in May 2018, and she was diagnosed with diffuse large B cell lymphoma (DLBCL) based on a biopsy of the right breast in July 2018. Because we suspected she might have MTX or biologic-associated lymphoproliferative disorder (LPD), we stopped the administration of ADA on July 17, 2018, and that of MTX on July 27, 2018. After the withdrawal of both drugs, her LDH and sIL2R levels decreased slightly. However, her lymphoma lesion was not ameliorated. She was started on treatment with rituximab on September 20, 2018, but her lymphoma lesion did not respond. She was therefore treated with pirarubicin, cyclophosphamide, vincristine, prednisolone (THPCOP) from September 25, 2018. After being treated with rituximab and THPCOP for three weeks, her lymphoma lesion showed shrinkage. When we suspected MTX or biologic-associated LPD, we stopped the administration of MTX and biologics. There are few case reports of the breast primary malignant lymphoma that MTX or biologics-LPD is suspicious, and accumulation of plural cases is desirable.

P1-219

A case report of methotrexate-associated lymphoproliferative disorder : MTX-LPD was suspected

Keiji Okamoto

Department of Internal Medicine, Izumiotsu Municipal Hospital

Conflict of interest: None

[Case] A 66-year-old female. She was diagnosed with rheumatoid arthritis at 46. She took MTX 8mg/week from 48. She coincidentally got chronic bronchitis and bronchiectasis at 61. She was pointed out the left axillary lymph node increasing on chest CT at 64. sIL-2R was 2042U/mL. It was not palpable, and we couldn't biopsy. We stop MTX. It didn't mostly change or slightly decrease on one month later CT. sIL-2R was increased to 2723U/mL. The size change by no treatment and stopping MTX wasn't inconsistent with MTX-LPD. She was introduced to hematologist for the treatment plan decision. sIL-2R didn't decrease inspite of stopping of MTX, and so the treatment would start as MTX-LPD by hematologist. It decreased on PET-CT performed for the biopsy lesion decision, and so the treatment plan was observation without biopsy. sIL-2R decreased later. [Clinical Significance] MTX-LPD is the lymphoproliferative disorder for taking MTX. There are patients whose tumor decrease only by stopping MTX. It is needed to treat in accordance with malignant lymphoma, if the tumor doesn't decrease or it increase again after decreasing. The lymph node decreased only by stopping MTX, and so this case got a follow-up examination. It is needed to observe carefully for a possibility to increase again in future.

P1-220

A case of diffuse large B cell lymphoma (DLBCL) in a patient treated for rheumatoid arthritis (RA) and mixed connective tissue disease (MCTD)

Junichiro Hagita, Keisuke Kamiya, Kiyomi Koike, Katsushi Koyama
Kariya Toyota General Hospital

Conflict of interest: None

A 35-year-old woman with a 10-year history of rheumatoid arthritis (RA) and mixed connective tissue disease (MCTD) had been treated with infliximab (IFX), tacrolimus (Tac) and prednisolone (PSL). She presented with high-grade fever, cervical and intra-abdominal lymphadenopathy,

and diarrhea. One week later, she was admitted to the hospital because of a sustained fever, high inflammatory reaction, and liver dysfunction. Laboratory findings showed increased liver enzyme and atypical lymphocyte. The soluble interleukin-2 receptor level was 9,940 U/mL. EBV-VCA IgG titer level was high. The symptoms were improved with an increased dose of PSL and discontinuation of IFX and Tac. In contrast, CT revealed that cervical and intra-abdominal lymphadenopathy remained. So, Lymph node biopsy was done, she was diagnosed with diffuse large B cell lymphoma with positive EBV-DNA. Fortunately, disease activity was controlled by increasing dose of PSL, she was transferred to hospitals in order to receive chemotherapy. In this case, the patient with no history of MTX was diagnosed with DLBCL. Several connective tissue diseases and using the long history of immunosuppressive drugs causes reactivation of EBV.

P1-221

Incidence of malignant tumors in the treatment of rheumatoid arthritis using biologics

Masao Sato¹, Masao Takemura², Tomohisa Tani¹, Toshiro Ohashi¹
¹Ohashi-Tani Orthopedics, Gifu, Japan, ²Advanced Diagnostic System Laboratory, Fujita Health University

Conflict of interest: Yes

[Objective] To analyze malignant neoplasia development in rheumatoid arthritis (RA) cases with biologics (BIO) introduced. [Methods] We examined the type of malignant neoplasms for 522 RA patients who can grasp the progress. [Results] The breakdown of cases was 110 males, 412 females, age at introduction of biological products was 11 to 86 years, average 58.2 years, disease duration was 1 to 50 years, average 8.8 years. The incidence of malignant tumors was 40 out of 521 (7.66%). Histopathological diagnosis was performed: malignant lymphoma: 11 cases, breast cancer: 6 cases, colon cancer: 5 cases, prostate cancer, stomach cancer, skin cancer: 3 cases each, lung cancer, renal cancer: 2 cases each, uterine cancer, pancreatic cancer, chondrosarcoma, malignant mesothelioma, choledochal carcinoma: one each. The period from introduction of BIO to establishment of diagnosis of tumor was 3 months to 136 months, average 35 months. In 18 cases where BIO was discontinued at the time the diagnosis was confirmed, in other cases BIO continued or resumed after interruption. Outcome was 22 patients alive, 18 cases were dead. [Discussion] When a malignant neoplasm is confirmed, sufficient explanation and agreement such as how to treat RA after that are necessary.

P1-222

A case of multiple myeloma in an 80 year-old male patient with rheumatoid arthritis

Yuko Fujiwara¹, Hitoshi Tada², Hisaaki Miyahara³
¹Department of Orthopedic Surgery, Haradai Hospital, ²Department of Internal Medicine, Haradai Hospital, ³Department of Orthopedic Surgery, Kyushu International Medical Center

Conflict of interest: None

(Case) An 80-year-old male patient with 10-year history of rheumatoid arthritis had been treated with MTX, SASP and ENT. He did not have any complication these days. This patient presented with low back pain and visited a clinic and had an X-ray test, but there was no evidence of fracture. His low back pain did not improve so he visited our hospital. On MRI test L3 had a compression fracture and hospitalization for treatment was started. One day after admission He had a fever and poor dietary intake, CT showed bronchial pneumonia. An treatment with an antibiotic was started. Three days later, the results of blood test showed a renal failure and marked increase of gamma-globulin (31%). Additional tests showed increase of M-protein also. This patient changed hospital for treatment. (Conclusion) These days the number of lymphoproliferative disorders (LPD) during treatment of rheumatoid arthritis is increasing. The medicine with RA is thought as a reason for these LPD and many clinical research has done for this relationship. The other hands, in our hospital we have three cases like this case, plasma cells proliferative disorders with old patients during RA treatment. We want to report the importance for screening for plasma cells proliferative disorders with old RA patients.

P1-223

Clinical features of connective tissue disease (CTD) patients who evaluated serum protein electrophoresis (SPE)

Takayuki Nakamura^{1,2}, Yosuke Toda¹, Yoko Yabe¹, Kensuke Suga¹, Daisuke Kashiwakuma¹, Shin-ichiro Kagami¹
¹Research Center for Allergy and Clinical Immunology, Asahi General Hospital, ²Internal Medicine, Tohno Hospital

Conflict of interest: None

Objectives: The aim of this study to investigate the clinical features of CTD who evaluated SPE. Methods: We retrospectively analyzed 555 patients with CTD who evaluated SPE in our department from May 2012 to April 2017. M-band was detected in 73 patients, and clinical features were compared. Results: Among 73 patients, 45 patients (61.6%) were female. Mean age was 71.2 years, which was significantly older than the patients without M-band ($p < 0.0001$). Compared to patients without M-band, the albumin-globulin ratio ($p < 0.0001$) and hemoglobin ($p < 0.0001$) were significantly lower in patients with M-band. The most common primary disease was Rheumatoid Arthritis ($n=33$, 45.2%), followed by Sjogren syndrome ($n=16$, 21.9%), SLE ($n=7$, 9.6%). Immunoelectrophoreses were performed in 45 of 73 patients; 18 patients had MG. Bone marrow examinations were performed in 15 of 18 patients, of whom 7 patients were diagnosed with monoclonal gammopathy of undetermined significance (MGUS), 6 patients with multiple myeloma (MM) (MM:4, smoldering MM:2) and 2 patients with malignant lymphoma (ML). Within the follow-up period, 6 of 18 patients died, 3 of them died of hematological diseases (MM:2, ML:1). Conclusion: Since MG is frequent in CTD and death cases exist, screening test by SPE is important.

P1-224

A sporadic case of ATTR amyloidosis involving multiple organs in non-endemic area

Manaka Goto, Eisuke Takamasu, Masahiro Iida, Nanase Honda, Yoshiki Nagai, Naoto Yokogawa, Kota Shimada, Shoji Sugii
Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center

Conflict of interest: None

Hereditary ATTR amyloidosis is caused by an autosomal-dominant mutation in transthyretin (TTR) gene, among which V30M substitution is the most common in Japan. It affects a variety of organs, including peripheral nerves and the heart. In non-endemic area it tends to develop in elderly people. Here we describe a 78-year-old female without family history who presented with 4-year history of progressively worsening weakness and became bedridden. She also reported impaired eyesight and symptoms associated with autonomic dysfunction. Echocardiography on her recent acute heart failure showed left ventricular hypertrophy and pericardial effusion. She was referred for the assessment of possible systemic amyloidosis. Nerve conduction study revealed axonal peripheral neuropathy. Further examinations were notable for vitreous opacities, proteinuria and albuminocytologic dissociation in the spinal fluid. There were no signs of malignancy or inflammatory disorders which would cause AL amyloidosis or AA amyloidosis, respectively. Abdominal wall adipose tissue biopsy demonstrated ATTR amyloid deposits and genomic DNA sequence of TTR gene revealed V30M mutation. ATTR amyloidosis was finally diagnosed. Involvement of such multiple organs is considered to be rare in non-endemic area.

P1-225

Optimal treatments for RA patients complicated by tuberculosis

Koichiro Takahi, Hiroyuki Nakaya, Kazuhiko Imoto
Orthopaedic Surgery and Rheumatology, NHO Toneyama Hospital

Conflict of interest: None

[Background/objective] According to the package insert of Japan, patients with active tuberculosis (TB) are contraindication for using PSL, MTX and biologic agents, though these medicines were often used for RA patients complicated by TB in the real world. The objective of this study is to clarify the influence of RA drugs on the TB treatment, [Pa-

tients/results] 25 patients with RA were selected who had been diagnosed as TB microbiologically and hospitalized from 2012 to 2018. M:F=14:11, average age 80.3 y.o. Number of patients treated each drugs were MTX=8, GC=19, biologics=3 and other csDMARDs at TB developed. After diagnosed as TB, MTX were continued in 4, GC were 18 patients, but biologics were all stopped. While TB treatment MTX was restarted for 1 and increased in the dosage for 2 patients according to RA condition. Standard treatment with HREZ had been conducted for 6 - 9 months. 21 patients including those were prescribed with MTX had been treated successfully in microbiologically, but 6 patients had been dead during hospitalization. [Conclusions] Many patients with TB had been treated successfully together with RA medicine, while not a few patients were dead after TB developed. It is very important to establish the standard medication for RA during TB treatment.

P1-226

A Case of Pericostal Tuberculosis in a Patient with Systemic Sclerosis
Yoshiro Fujita^{1,2}, Naoh Takizawa¹, Hiroyuki Yoshida², Tatsuya Arai¹, Yoshihiro Nakamura¹, Fumiya Kitamura², Hiroki Ikai¹, Yukari Murai², Mari Yamamoto¹, Tsuyoshi Watanabe¹, Waka Kokuryo¹, Koji Takasugi²
¹Department of Rheumatology, Chubu Rosai Hospital, ²Department of Nephrology, Chubu Rosai Hospital

Conflict of interest: None

[Introduction] Autoimmune diseases including systemic sclerosis (SSc) are reported to increase risk of developing tuberculosis (Tb). We report a case of pericostal Tb in a patient with SSc without immunosuppressive agents. [Case] An 83-year old woman with a history of breast cancer and thyroid cancer was diagnosed with SSc by skin thickening of the fingers and anti-centromere antibody at age 75. She developed left pericostal mass at age 82, and received needle biopsy that showed negative result of Ziehl-Neelsen stain and malignancy. A year after, we performed needle biopsy again because of the pain flare and T-SPOT positivity. Although Ziehl-Neelsen stain was negative and granuloma was absent, both PCR and culture of Tb from the drain were positive. She was diagnosed with pericostal Tb, and treatment with antituberculous drugs was started. Pain resolved and culture of repeat biopsy returned to be negative. [Conclusion] The increased risk of developing Tb in patients with autoimmune diseases may be due to immune abnormality itself or immunosuppressive therapies. It has been reported that the risk of Tb in SSc patients is 2.8-6.1 times higher than those in general population. Physicians should be aware of Tb if SSc patient follows unconventional disease course.

P1-227

A case of tuberculous hand arthritis requiring differentiation from rheumatoid arthritis
Masayuki Watanabe, Hideki Takagi
orthopedic Surgery, Nagoya Central Hospital

Conflict of interest: None

We experienced a case of tuberculous hand-arthritis requiring differentiation from rheumatoid arthritis. This case is a 73-year-old man. Patient history is epilepsy and dementia. He noticed right-hand joint swelling so he visited the hospital. He was diagnosed with rheumatoid arthritis and started taking prednisolone. However, the symptoms did not improve, he had started treatment for methotrexate. He consulted our hospital because he had continued symptoms. His right hand joint formed swelling and fistulas. Magnetic resonance imaging confirmed bone erosion and joint fluid accumulation in the right hand joint. RF, MMP-3, ACPA were all negative. Inflammatory reaction was also almost negative. We performed a joint puncture and synovectomy. TB-PCR was positive in synovial fluid. Synovial histopathology was diagnosis of mycobacteriosis. From these results, we diagnosed tuberculous hand-arthritis. This case suggested the importance of TB examination when diagnosing arthritis.

P1-228

Disseminated cutaneous and subcutaneous deep infection caused by Mycobacterium chelonae in a patient with rheumatoid arthritis
Miho Ohshima, Makoto Sugihara, Yuji Miyoshi, Tomohiro Kozuki
Department of Rheumatic Diseases, Tama-Hokubu Medical Center, Tokyo Metropolitan Health and Medical Treatment Corporation, Tokyo, Japan

Conflict of interest: None

An 82-year-old woman with a history of methotrexate associated lymphoproliferative disorder and thyroid cancer surgery received salazosulfapyridine for rheumatoid arthritis (RA) and prednisolone (5mg) for nephrotic syndrome. She developed multiple cutaneous nodules on her left hand and lower limbs, and magnetic resonance imaging revealed deep subcutaneous abscesses near the Achilles tendon. Although several cultures were performed on specimens obtained from the nodules, only 1 new lesion showed *M. chelonae* on day 19. She was clinically diagnosed with disseminated cutaneous and subcutaneous deep infection caused by *M. chelonae*. The nodules gradually resolved. Clarithromycin and tobramycin (TOB) were initiated with further resolution of the nodules; however, TOB was changed to moxifloxacin owing to adverse effects. The deep abscesses were drained; three months later, one of them reappeared and new lesions appeared near her right Achilles tendon, tibial tuberosity and left knee, and drainage was repeated. Her anti-interferon- γ antibody test was negative. *M. chelonae* infection with concomitant RA is rare. Diagnosing and treating nontuberculous mycobacterial infection is difficult. Repeated acid-fast bacterial cultures are needed in patients with skin nodules of unknown origin.

P1-229

A case of exacerbation of severe leg ulcers concomitant with Mycobacterium avium infection after discontinuation of adalimumab in rheumatoid arthritis
Yohei Isomura, Shinji Watanabe, Yuichiro Shirai, Seiji Kobayashi, Takahisa Gono, Mitsuhiro Takeno, Masataka Kuwana
Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo Japan

Conflict of interest: None

A 67-year-old female with a history of rheumatoid arthritis (RA) for 30 years visited her regular doctor because of high fever and swollen right ankle. She had received methotrexate, bucillamine, and adalimumab (ADA) in remission for RA. She was hospitalized under the diagnosis of bacterial cellulitis, antibiotics were administered, ADA was ceased. However, the skin lesions exacerbated. Thus she was transferred to our facility. Cutaneous histopathological findings at the small nodules on her lower legs revealed lobular panniculitis, consistent with erythema induratum of Bazin; however, no evidence of tuberculosis infection or vasculitis was found. We initiated oral prednisolone (PSL) at 30 mg/day because we speculated that the skin lesions were attributed to RA-itself-associated inflammation or excessive immune response against microorganism. Thereafter Mycobacterium avium was isolated from the cultivation. We also initiated anti-mycobacterial agents along with PSL. Her leg ulcers gradually improved, followed by her hospital discharge. This is the first case demonstrating Basin-like skin manifestation as a reaction against Mycobacterium avium. We suspect discontinuation of ADA or immunological abnormality associated with RA may have contributed to the pathophysiology in this case.

P1-230

A case of M. avium complex (MAC) lung disease associated with rheumatoid arthritis (RA) which developed after tofacitinib switched to baricitinib and improved only by discontinuation
Takashi Yamane, Ayaka Inoue, Hiroaki Nakagawa, Midori Kitayama, Takuro Maeda, Noriaki Yo, Chihiro Tanaka
Rheumatic Division, Kakogawa Central City Hospital

Conflict of interest: None

[Case] A 46-year-old female rheumatoid patient treated with MTX

was admitted with the pulmonary abnormal shadow. Though we suspected of NTM, there were no sputum and couldn't prove the fungus. In spite of the treatment of csDMARDs, joint destruction progressed. Then we performed the bronchoscopy before administration of bDMARDs and confirmed no fungus. Abatacept, etanercept were ineffective but the pulmonary lesions were improved and started tofacitinib. But it was ineffective for arthritis. Because deterioration of pulmonary lesions was not observed, we switched to baricitinib and achieved low disease activity. 5 months after batricitinib started, CRP elevation and the deterioration of lung lesion were observed. The bronchoscopy was carried out again, we found positive for *M. avium* in culture. Only by the discontinuation of baricitinib, lung lesion improved and arthritis was controlled with MTX 16 mg + SASP1g. [Clinical Significance] Elevated risk of developing tuberculosis has been reported for JAK inhibitors as well as bDMARDs. Although there is no report on the frequency of NTM episodes caused by JAK inhibitors, in particular the difference in risk between tofacitinib and baricitinib. In this case NTM was developed after the switch of them and we report with literature review.

P1-231

Current treatment of RA patients suspected of nontuberculous mycobacterium (NTM) -the second report-

Hideki Amuro¹, Yonsu Son¹, Akira Onishi², Kengo Akashi², Motomu Hashimoto³, Takashi Matsuo⁴, Wataru Yamamoto^{3,5}, Koji Nagai⁶, Tohru Takeuchi⁶, Masaki Katayama⁷, Toru Hirano⁸, Kosuke Ebina⁹, Ryota Hara¹⁰, Yoshio Ozaki¹, Shosaku Nomura¹

¹First Department of Internal Medicine, Kansai Medical University, Osaka, Japan, ²Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, ³Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, ⁴Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, ⁵Department of Health Information Management, Kurashiki Sweet Hospital, ⁶Department of Internal Medicine IV, Osaka Medical College, ⁷Department of Rheumatology, Osaka Red Cross Hospital, ⁸Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University, ⁹Department of Orthopaedic Surgery, Graduate School of Medicine Osaka University, ¹⁰The Center for Rheumatic Diseases, Nara Medical University

Conflict of interest: None

[Object] To investigate current treatments of RA patients with confirmed/suspected NTM infection who have long term after onset of NTM. [Methods] We extracted NTM culture positive RA patients in ANSWER cohort, and surveyed patient profiles, current RA disease activities, and treatments in case of follow up for 3 years or more. [Results] Thirty-eight RA patients (median age 69; disease duration 113 months) were extracted. Isolated species of NTM were as follows; MAC 34 cases, abscessus 1 case, others 3 cases. At the last visit, 17 patients were treated with biologics or JAK inhibitor (ABT 8, TCZ 6, ETN 1, ADA 1, TOF 1) and 18 patients with MTX, 20 patients with GCs. RA disease activities were as follows; mean DAS28/CRP 2.25±0.96, mean CDAI 7.26±6.52. Nine cases did not achieve LDA at CDAI assessment. Only two cases of these were used with biologics. Seventeen patients received treatment for NTM, and NTM exacerbation was only one case. However, besides our 38 cases, there were 6 cases in which death occurred in malignancy and RA disease activity could not be tracked. [Conclusions] In this study, RA disease activity of most patients were controlled except for several cases. But our report is an analysis for a small number of cases, and accumulation of further cases is necessary.

P1-232

Extrapulmonary infections caused by nontuberculous mycobacteria complicated in patients with rheumatic diseases - report of the three cases

Ritsuko Yokochi¹, Ken Nagahata¹, Keina Yomono¹, Shuhei Hattori¹, Kei Shimogori², Lisa Hirahara¹, Shotaro Suzuki¹, Seiji Takenouchi¹, Noboru Hagino¹

¹Division of Hematology and Rheumatology, Teikyo University Chiba Medical Center, Japan, ²Division of Rheumatology, Joban Hospital, Japan

Conflict of interest: None

[Background] These days, nontuberculous mycobacteria (NTM) infections are increasing worldwide. Many NTM infections are chronic lung infections, but they also cause extrapulmonary infections such as disseminated infections, indolent lymphadenitis, skin, soft tissues, bones, and joints. [Methods] Retrospective chart review of extrapulmonary infections caused by nontuberculous mycobacteria complicated in patients with rheumatic diseases. [Results] The age of the onset was 66, 68 and 73 years old respectively. Two infection bacteria were *Mycobacterium chelonae*, and one case was *Mycobacterium intracellulare*. The site of infection was bursa, skin, and joints respectively. The underlying rheumatic disease is rheumatoid arthritis, dermatomyositis, and SLE respectively. The immunosuppressants used at the onset of NTM infection were prednisolone (PSL) 6 mg / day, mizoribine 100 mg / day, tacrolimus 0.5 mg / day, tocilizumab 162 mg / 2 weeks combined, PSL 7.5 mg / day only, and PSL 10 mg / day respectively. [Conclusions] We treated three extrapulmonary infections caused by nontuberculous mycobacteria complicated in patients with rheumatic disease. Patients were all more than 65 years old, used 6mg/day and more PSL when they are diagnosed.

P1-233

Three cases of soft tissue NTM infection complicated with rheumatic disease

Takuya Nakazawa, Hidekazu Futami, Yoshihiro Oya, Kazuyuki Ishijima, Keiko Umemiya, Ryutarō Matsumura

Center of Rheumatology, Allergy & Clinical Immunology, National Hospital Organization Chiba-East Hospital, Chiba, Japan

Conflict of interest: None

No1. A 77-year-old man with microscopic polyangiitis. He was admitted to our hospital with nodules under skin. He was suspected of the exacerbation of polyangiitis. Steroid semi-pulses were done. Nodules were not improved. An open biopsy revealed *M. chelonae* infection. Despite of our treatment, subcutaneous nodules are repeatedly deteriorated. No2. A 72-year-old woman with dermatomyositis. She was hospitalized with left lower thigh cellulitis. Subcutaneous nodules also appeared in the lower limbs. An open biopsy revealed *M. abscesses* infection. She was treated by LZD, changed to CAM + IPM / CS. Then, CAM alone therapy was done. Exacerbation of nodule and inflammatory reaction worsen again with CAM administration alone. AMK had been administered in addition to CAM, nodules were impaired. During the course, the IVIG was performed to improve dermatomyositis, but nodules also improved. No3. A 74-year-old man with malignant RA. He had artificial joint on his right elbow. Joint edema appeared on the right elbow. *M. avium* isolated culture. Treatment started by CAM, RFP, EB. It is gradually becoming impaired with this treatment for several months. Currently, no diagnostic treatment for soft tissue infection by NTM has been established. We reported 3 cases of valuable cases this time.

P1-234

Clinical features of collagen vascular disease patients with Cytomegalovirus reactivation during immunosuppressive therapy

Risa Yoshihara, Hirofumi Shoda, Haruka Tsuchiya, Toshihiko Komai, Yumi Tsuchida, Yasuo Nagafuchi, Kanae Kubo, Keishi Fujio
The University of Tokyo Hospital

Conflict of interest: None

[Object] To clarify the clinical characteristics of cytomegalovirus (CMV) reactivation in patients with collagen vascular diseases during immunosuppressive therapy. [Methods] We reviewed charts of patients who had reactivation of CMV antigenemia (CMV ag, C10, C11) during immunosuppressive therapy, including PSL ≥0.6 mg/kg/day from October 2017 to September 2018, and investigated the time from initiation of immunosuppressive therapy to CMV reactivation, the count of positive CMV Ag cells and organ involvements. [Results] Twenty seven cases (AAV6, DM5, SLE4, others 12) were included. The mean age was 65 years old. The mean starting dose of steroid was PSL 1.01 mg/kg/day, and 14 patients had mPSL pulses, 17 had immunosuppressive agents and 8 had biologics. The mean time from starting immunosuppressive therapy

to CMV reactivation was 31.6 days. All the 6 cases whose total number of 2 slides of CMV Ag positive cells exceeds 10 experienced severe bacterial (fungal) infection and 3 of them died. In 21 cases with less than 10 positive cells, severe bacterial (fungal) infection were caused in 2 cases, and one of them was dead. [Conclusions] The total number of 2 slides of CMV Ag positive cells exceeds 10 was a risk of severe infection and poor prognosis.

P1-235

The experiences of clinic for human T-cell leukemia virus type 1 (HTLV-1)-positive patients with rheumatic diseases

Kunihiko Umekita, Shunichi Miyauchi, Yumi Kariya, Ayako Aizawa, Takeshi Kawaguchi, Motohiro Matsuda, Ichiro Takajo, Akihiko Okayama
Department of Rheumatology, Infectious Diseases and Laboratory Medicine, Internal Medicine, University of Miyazaki

Conflict of interest: None

[Object] To investigate the significance of clinic for human T-cell leukemia virus type 1 (HTLV-1)-positive patients with rheumatoid arthritis (RA). [Methods] Six patients had visited the specialty outpatient department for HTLV-1-positive patients with rheumatic diseases (RDs) from April 2017 to September 2018. We reviewed clinical information, the first opportunity for HTLV-1 testing and reasons for visiting our department. [Result] Four of six patients were female. Median age was 69 years old. Five and one patients live in South-part of Kyushu and Shikoku region, respectively. Three, two and one patients had RA, RA with Sjogren syndrome and polymyositis, respectively. The first opportunity of HTLV-1 testing was as follows: screening test for HTLV-1 infection during pregnancy, at the onset of RDs, at the onset of HAM before developing RDs, and at the onset of ATL in their family. The most common concern of patient was whether immunosuppressive treatment affects HTLV-1 infection and development of HTLV-1-associated disorders such as ATL. Some patients could not obtain advices until their visits and they felt better only by talk in our clinic. [Conclusion] The clinical guideline or recommendation is necessary to reduce the anxieties of HTLV-1-positive patients with RDs.

P1-236

Risk Stratification of Hepatitis B virus Reactivation in Patients with Rheumatoid Arthritis during Methotrexate Monotherapy

Wataru Fukuda¹, Tadamasu Hanyu², Masaki Katayama⁵, Akitomo Okada³, Shinichi Mizuki⁴, Masatoshi Hayashi⁶, Masayuki Miyata⁷, Yuichi Handa⁸, Yoshinobu Koyama⁹, Hiroyuki Hagiyama¹⁰, Kaoru Arii¹¹, Toshiyuki Kitaori¹², Yoshinori Urushitani¹³, Daigo Taniguchi¹⁴, Yoshihiko Ikeno¹⁵, Takeshi Suzuki¹⁶, Masatoshi Kadoya¹, Atsushi Omoto¹, Shigeko Inokuma¹⁷

¹Center for Rheumatic Disease, Japanese Red Cross Kyoto Daiichi Hospital, ²Department of Rheumatology, Nagaoka Red Cross Hospital, ³Department of Rheumatology, Japanese Red Cross Nagasaki Genbaku Hospital, ⁴Department of Rheumatology, Matsuyama Red Cross Hospital, ⁵Department of Rheumatology, Osaka Red Cross Hospital, ⁶Department of Orthopedics, Nagano Red Cross Hospital, ⁷Department of Internal Medicine, Fukushima Red Cross Hospital, ⁸Department of Rheumatology, Saitama Red Cross Hospital, ⁹Department of Rheumatology, Okayama Red Cross Hospital, ¹⁰Department of Rheumatology, Yokohama-City Bay Red Cross Hospital, ¹¹Department of Internal Medicine, Japanese Red Cross Kochi Hospital, ¹²Department of Orthopedics, Fukui Red Cross Hospital, ¹³Department of Rheumatology, Matsue Red Cross Hospital, ¹⁴Department of Rehabilitation, Japanese Red Cross Kyoto Daini Hospital, ¹⁵Department of Rheumatology, Nasu Red Cross Hospital, ¹⁶Department of Allergy and Rheumatic Diseases, Japanese Red Cross Medical Center, ¹⁷Department of Allergy and Rheumatology, Chiba Central Medical Center

Conflict of interest: None

[Object] Reactivation of hepatitis B virus (HBV) in patients with RA receiving immunosuppressant is a serious complication, and the risk stratification may reduce patients' burden on monitoring and prophylactic treatment. We examined risk stratification that can be clinically applicable. [Methods] RA subjects receiving methotrexate monotherapy and

who were negative for HBs antigen and HBs or HBc antibody positive, were included. [Results] In 553 cases, HBV reactivation was seen in 18 cases (3.25%) for 3.55 years observation. We performed ROC analysis and set the age cutoff value at 65 year. When we calculate the score in which HBc antibody alone positivity was 1 point and the age over 65 years was 1 point, HBV reactivation at the score 0 point was 2/200 (1.0%), and the odds ratio was 3.96 (95% CI: 1.04-25.8) at one point and 7.98 (95% CI: 1.68-56.7) at two points. [Conclusions] In patient whose score with HBc antibody alone positive and old age (> 65 years old) was 0, the reactivation rate in 3.55 years was 1.0%, which was significantly lower than in patient with one or more score points. Considering that the course after reactivation is not rapidly progressive, the monitoring interval for HBV can be extended to 6 to 12 months.

P1-237

The value of CMV-IgM antibody for diagnosis of Cytomegalovirus (CMV) reactivation under immunosuppression

Ayaka Inoue, Hiroaki Nakagawa, Midori Kitayama, Takuro Maeda, Noriaki Yo, Chihiro Tanaka, Takashi Yamane
Department of Rheumatology, Kakogawa Central City Hospital

Conflict of interest: None

[Object] Early diagnosis is important because reactivation of CMV under immunosuppression by treatment of autoimmune diseases may follow fatal outcome, so we are screening with CMV pp65 antigen (C7-HRP) and CMV-IgM antibody. We have examined the value of CMV-IgM antibody for diagnosis of CMV reactivation under immunosuppression. [Methods] We examined retrospectively 56 patients that measured CMV-IgM antibody suspected of CMV reactivation between April 2017 and September 2018 in our department. We diagnosed as CMV reactivation clinically. We defined that CMV-IgM antibody titer was positive with 1.21 or higher. [Results] CMV reactivation occurred in 9 of 56 patients. CMV-IgM negative group were 43, positive group were 13. There was no difference in age, serum IgG / IgM and lymphocytes on both groups. The PSL dose tended to be higher in the positive group (15.2 mg/day) than in the negative group (8.2 mg/day) but there were no significant differences statistically. The sensitivity of CMV-IgM antibody in CMV reactivation was 55.6%, the specificity was 84.0%. And C7-HRP was 55.6%/97.9%. [Conclusions] Even under immunosuppression, the sensitivity of CMV-IgM antibody titer was equivalent to that of C7-HRP and it seemed to be useful as a screening test for reactivation of CMV.

P1-238

SLE complicated by Varicella Zoster virus myelitis from which NP-SLE should be differentiated: A case report

Kohei Nagaya¹, Akimasa Asai², Hironobu Nobata², Shogo Banno², Yasuhiko Ito²

¹Department of Nephrology, Kizawa Memorial Hospital, ²Department of Nephrology, Rheumatology and Collagen Diseases, Aichi Medical University

Conflict of interest: None

[Case] 71-year-old man [chief complaint] constipation, fever [Present illness] A 71-year-old male referred to our department with nephrotic syndrome 3 years ago. He was diagnosed with lupus nephritis. He had been treated with PSL and MMF. Then he referred to dermatology department of out hospital with Herpes zoster 3 weeks ago. On the day of his admission, he was found in toilet and he wasn't able to stand up. He was transported to our hospital and entered for observation. A few days later, he complained right leg paralysis and urinary retention. Because head MRI and nerve conduction velocity were almost normal, disorder of spinal cord was suspected. But lumbar cord MRI was normal. Cerebrospinal fluid test showed high level of cell count and total protein. We made additional checking of cervical and thoracic spinal cord MRI which showed high intensity area in T2 emphasized image. He was treated with aciclovir, steroid pulse therapy and plasma exchange. Then herpes zoster virus DNA was detected in cerebrospinal fluid. Cell count of fluid was decreasing and bladder rectal disorder was improved although right leg paralysis wasn't. [Concideration] Though Herpes zoster is a major complication of MMF, myelitis is rare. Prompt discontinuation of MMF and antiviral

drugs were important.

P1-239

A case of rheumatoid arthritis (RA) patients with schizophrenia following rheumatic care nurse outpatient clinic

Akihiko Hamada¹, Mitsuko Takiguchi¹, Mika Ishibashi¹, Megumi Inoue¹, Erina Shimaoka¹, Yuki Ueno^{2,3}, Minako Wakama³, Katsuhiko Oda^{2,3}, Hideyuki Shiba^{2,3}, Koji Nagai³, Masakazu Sugino²

¹Department of Nurse, Koshokai Aino Hospital, Osaka, Japan, ²Department of Internal Medicine, Koshokai Aino Hospital, Ibaraki, Osaka, Japan, ³Department of Internal Medicine IV, Osaka Medical College, Takatsuki, Osaka, Japan

Conflict of interest: None

<Introduction> In our hospital, we established an outpatient by rheumatic care nurse, and in addition to teaching self injection and medication guidance, we conduct examination and joint echo examination by 'Registered Sonographer' of Rheumatology Association of Japan. **<Case>** 40-year old female. On July 2014, she recognized the joint pains of both hands, both knees and the left elbow. She was diagnosed with RA. Although remission was achieved with MTX, ABT and IGU combination, she self-discontinued internal medicine and since December 2016. The disease activity of RA and has worsened. Psychiatric symptoms also worsened and it was introduced to our hospital. Therefore, not only medication but also future planning such as environmental improvement including family are considered important. First, we promised his father to come with her and encourage him to understand and cooperate with his daughter's illness, we spent a lot of time talking about the importance of drug management and future our goals. And she was gradually in a state of mental stability. For arthritis, echo examination was performed every her visit. Gradually, her motivation for treatment was improved. Outpatient and joint echo by RA-expert nurses was useful. And team treatment is necessary for RA patients.

P1-240

The association of Pain Catastrophizing with residual pain in patients with rheumatoid arthritis with non-inflammatory status

Tamami Yoshida¹, Motomu Hashimoto², Masao Tanaka², Hiromu Ito³, Koichi Murata², Kohei Nishitani², Kosaku Murakami⁴, Tsuneyo Mimori⁴

¹Kyoto Prefectural University of Medicine School of Nursing, Kyoto, Japan, ²Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ³Department of Orthopedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ⁴Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Conflict of interest: None

[Object] Pain catastrophizing is defined as an important component contributing to a distortion in pain perception. In this study, we examined the association between residual pain and pain catastrophizing in RA patients with non-inflammatory status. [Methods] The non-inflammatory condition was defined as CRP \leq 0.3mg/dL, "PCS+" was defined as 33 points or more in the Pain Catastrophizing Scale. 150 RA patients visiting Kyoto University Hospital were examined. Multivariate analysis was performed to assess pain VAS \geq 20 mm as dependent variable, with age, sex, RA related variables, and PCS+ as independent variables. Furthermore, similar analysis was performed in the patient group (123 patients) with CRP \leq 0.3 mg/dL. [Results] Average Age: 66 \pm 11 years, DAS28-ESR: 2.52 \pm 0.98, and CRP: 0.3 \pm 0.55 mg/dL, median pain VAS: 10.5 (range 1-82). 20 patients (13.3%) were PCS+. On multivariate analysis in all patients, HAQ (Odds ratio 5.6, p<0.01), stage4 (OR 4.8, p=0.03), CRP (OR 2.9, p=0.01) were positively associated with pain VAS \geq 20 mm. In patients with CRP \leq 0.3 mg/dL, HAQ (OR 6.1, p<0.01), PCS+ (OR 3.9, p=0.04) were positively associated with pain VAS \geq 20 mm. [Conclusions] Pain catastrophizing is an important target to be treated in RA patients with residual pain even in non-inflammatory status.

P1-241

Usefulness of foot arthralgia of patients with rheumatoid arthritis in RA-nurse outpatient practice

Mika Ishibashi¹, Erina Shimaoka¹, Akihiko Hamada¹, Megumi Inoue¹, Mitsuko Takiguchi¹, Yuki Ueno², Minako Wakama³, Katsuhiko Oda², Hideyuki Shiba², Koji Nagai³, Masakazu Sugino²

¹Department of Nurse, Koshokai Aino Hospital, Osaka, Japan, ²Department of Internal Medicine, Koshokai Aino Hospital, Osaka, Japan, ³Department of Internal Medicine IV, Osaka Medical College, Osaka, Japan

Conflict of interest: None

[Object] To examine that we can select the RA patients who need actual evaluation of foot lesions with ultrasound, we compared patient's joint pains of foot and ankle with ultrasound findings. [Methods] In this study 41 RA patients who are treated in our hospital and Osaka Medical College were included. After dividing the foot part into forefoot, the middle foot and the back foot. We compared and examined the patient's complaints of foot and ankle pains with ultrasound findings. (PD \geq 1 was taken as a positive.) [Results] The average age was 62.7 y.o (8 male, 33 females). The average BMI was 21.6, DAS28-CRP was 3.44 and HAQ was 0.60. The number of "complaints of foot and ankle pain / joint ultrasound findings positive" in the forefoot, middle and back foot were 20/12, 9/7, 15/6 respectively. The overall coincidence rate was 46.3%. Sensitivity, specificity, positive predictive value and negative predictive value for pain complaints and positive ultrasonography findings were 93.8%, 48.0%, 53.6%, 92.3% respectively. [Conclusions] There is some possibility of making more efficient daily practice, we may mainly perform ultrasound for RA patients with complaints of joint pain.

P1-242

The usefulness of rheumatism classes for patients involving many jobs coordinated by nurses

Narumi Sato¹, Hitoha Nomura², Takao Katsuragawa², Takumi Matsumoto², Hiroaki Tamura²

¹Nursing Department, Sapporo City Hokkaido Japan Kinikyo Central Hospital, ²Internal Medicine and Rheumatology, Sapporo City Hokkaido Japan Kinikyo Central Hospital

Conflict of interest: None

Objectives: Our hospital has been conducting rheumatism classes for early stage patients since 2003. In the "Survey of consciousness to treatment of patients using biologics" in 2014, there was a request to want to know about the latest information of treatment, side effect, ingenuity to facilitate housework, T2T and others. Thinking so far was inadequate, led by a nurse, we held new rheumatism classroom for patients with long term of disease with multiple occupations. We conduct and verify "Rheumatic Care Team Staff Questionnaire", so we report usefulness of this coordination. Methods: The target was 15 staffs consisting of 7 occupations. We conducted a questionnaire on the role of nurse as a coordinator, and summarized and verified it. Results: Good point of convening this classroom with the idea of a nurse was "we could tell the information one wishes to know" and "we could confirm of patient's response". Everyone answered "nurse coordination was good" and reasons are "the nearest to the patient", "understanding the needs of the patient", "able to bridge doctors and other occupations". 70% said the team leader should be nurse. Conclusion: In the education to RA patients by multiple occupations, it was effective to coordinate by nurse who understood patient's needs.

P1-243

The issues on the questionnaire to nurses about our monthly rheumatic care professional education workshops

Yoshiko Takamura

Juho Takeda Rehabilitation Hospital, Kyoto Japan

Conflict of interest: None

[Purpose] Current RA treatment requires complicated and sophisticated care. Our "center for rheumatic diseases" was established in 2013. Currently we have >400 RA patients (>150 are using biologics). Starting

in 2014, the center held monthly “RA care professional workshop” for staff to study subjects for disease and treatment. We studied to see whether nurses were comprehending knowledge and showing interest in RA nursing by participating in workshops. [Method] Descriptive survey on RA nursing was conducted with 75 nurses in outpatient clinic and hospitalization unit. [Results] Questionnaire were collected from 63 nurses. 36% had attended workshops. 5% were to earn credits for RA care nursing. Understanding of underlying diseases was sound. Self-injection guidance, foot care and other aspects of RA care were of interest. However, 20% misunderstood that patients should skip MTX when they are in sickness. [Conclusion] 45% participated in workshops with sense of purpose. Through workshops, seemingly their understanding of RA nursing was deepened. We recommend participation so that nurses can provide safe and secure care for patients. Also, certified RA care nurses would be able to play a key role in patients’ education and could function with expertise with both in and outpatients.

P1-244

“Necessity of regional collaboration to come up in rheumatism and collagen disease specialized clinic” 2nd report

Yumiko Arai, Tomoko Takehisa, Ryo Sato, Takanori Azuma
Azuma Rheumatology Clinic

Conflict of interest: None

[Object] Our clinic is specialized in RA, we often ask other medical institutions for consultation, the necessity of collaboration was examined. [Methods] From 2017 / Sep to 2018 / Aug, RA patients requested consultation to other institutions were extracted and examined what kind of clinical department is referring to. [Results] There were 1154 RA patients, and the number of introduced patients was 301 (26%), the number of introductions was 335.30 kinds of field requested consultation, the top ten are dermatology: 36, pulmonology: 35, orthopedic surgery: 33, otolaryngology: 20, dental oral surgery: 19, gastroenterology: 18, urology: 16, ophthalmology: 16, rheumatology 16, cardiovascular department: 15. We consulted to 140 medical institutions, of which only 40% of them are neighborhood collaborative institutions. [Conclusions] The reasons for consulting RA patients to other departments are mostly complications caused by RA itself or induced from RA treatment. Thus, it is difficult to support RA patients comprehensively only with RA clinic alone. Since other collagen diseases are also mixed in RA clinic, the cooperation with other departments is indispensable in the discrimination and treatment.

P1-245

Possible active roles with medical and administrative clerks to improve the quality of rheumatic practice

Keiko Kuroki¹, Mina Kojima¹, Tatsunari Fuwa¹, Yuka Yamashita¹, Koichiro Ohmura², Yukiko Komano¹, Ikuko Masuda¹

¹Center for Rheumatic Diseases, Jujo Takeda Rehabilitation Hospital, Japan, ²Department of Rheumatology and Clinical Immunology, Kyoto University

Conflict of interest: None

[Background] As drug therapy for rheumatic diseases is making great strides, improvement of the quality of team medicine approach is required. We established the center for rheumatic diseases since 2013, medical and administrative clerks have been actively involved with patient-friendly medical care and total team care. [Object] To grasp to what extent efforts to improve patient satisfaction are recognized and evaluated by outpatient with rheumatic diseases. [Methods] To grasp to what extent efforts to improve patient satisfaction are recognized and evaluated by outpatient with rheumatic diseases. [Results] The average satisfaction to the “Waku waku” binder was 8.5/10. The recognition rate of newsletter, opinion box, educational hospitalization was 3%, 5%, 6% respectively. There were various requests, including cutting of waiting time and implementation of outpatient rehabilitation. [Conclusions] Although the patients’ evaluation of “Waku waku” binder was high, it was thought that introduction of utilization method was necessary. We have noticed that there are many problems to be addressed to improve the quality of care. Total team care approach would be essential to improve the rheumatic practice.

P1-246

Investigation of nursing intervention at the time of execution of leukapheresis therapy (LCAP) in rheumatoid arthritis patients

Miyuki Takemoto¹, Masamitsu Natsumeda²

¹Department of Nursery, Rheumatic Disease Center, Mabi Memorial Hospital, Kurashiki, Japan, ²Department of Internal Medicine, Rheumatic Disease Center, Mabi Memorial Hospital, Kurashiki, Japan

Conflict of interest: None

[Objectives] Leukapheresis Remedy Therapy (LCAP) is one of treatment options for such patients, but patients are concerned about pain and effectiveness associated with puncture. As a rheumatic care nurse involved in LCAP, we examined the significance of nursing intervention based on patient questionnaire as Patient Reported Outcome (PRO). [Method] A questionnaire survey was conducted on eleven subjects who underwent LCAP from August 2017 to August 2018, at the time between LCAP enforcement decision and 3 months later. [Result] Patients were with high disease activity, average DAS 28 CRP 6.2, and most of were resistant to multiple BIO and JAK inhibitors. When LCAP therapy was decided, all patients had some anxiety, but expectation for symptom improvement was also high. Regarding the attendance of nurses, 92% of patients felt a sense of security regardless of the effect of LCAP. [Conclusion] All patients has underwent LCAP safely and smoothly and accomplish with one course treatment regardless of patient background including disease activity and LCAP effectiveness. LCAP treatment requires not only precise techniques and knowledge but also nursing intervention to alleviate patient anxiety.

P1-247

A study on teaching intervention of clinical pharmacology on rheumatoid arthritis for nurses

Akiko Matsuda¹, Takashi Fujimoto², Ryota Hara², Takanori Fujimura³, Hiroshi Aoi⁴, Satoko Nishiura⁵, Hiroshi Hagino⁶, Yasuhito Tanaka^{2,7}

¹School of Medicine, Faculty of Nursing, Nara Medical University, ²The Center for Rheumatic Diseases, Nara Medical University, ³Department of Internal Medicine, Takanohara Center Hospital, ⁴Department of Pharmacy, Nara Medical University Hospital, ⁵Department of Nursing, Nara Medical University Hospital, ⁶Faculty of Medicine School of Health Sciences, Tottori University, ⁷Department of Orthopedics, Nara Medical University

Conflict of interest: None

[Object] Biologics have led to successful therapy of RA, while adverse events have increased. Nurses are required risk-management skills based on clinical pharmacology. We investigated the effect of teaching intervention for nurses about comprehensions of clinical pharmacology on RA. We compared the effect between two groups of nurses experienced in RA therapy (group E) and those who have not (group NE). [Methods] Fifty-two nurses (39 in group E, 13 in NE) were involved. An educational program included 4 items of #1 pathophysiology, #2 therapeutic drugs, #3 risk-management and #4 use of package inserts. The program was made of 2-hours lecture. The comprehension of nurses was assessed by completing questions for each item (23 questions in total, 3 for #1, 8 for #2, 8 for #3, 4 for #4). [Results] There were no differences between two groups on the base line in the assessments. After the lecture, the assessments in E group were better (16 correct answers of 23 questions in all items were increased, 1/3, 5/8, 6/8, 4/4 in each item) than before. The assessments in NE group were better only in 2 items (2 correct answers were increased) than before. [Conclusions] We need to educate nurses more about clinical pharmacology to provide a comprehensive care for RA.

P1-248

Actual condition survey of the living guidance to a patient of the biological preparation treatment by our hospital nurse

Aya Oshimura¹, Shiori Tsubouchi¹, Kokoro Takata¹, Takeko Koyama¹, Yuka Horii¹, Ken Takebe², Koji Tateishi², Yasuhiro Terashima²

¹Nursing Unit, Kohnan Kakogawa Hospital, ²Orthopedic Surgery, Kohnan Kakogawa Hospital

Conflict of interest: None

[Object] Rheumatoid arthritis (RA) became the disease remission by progress of methotrexate and biological agents (Bio). However, Bio treatment is at risk of the infectious disease. Thus, we examined the present conditions of the patient education of the nurse. [Method] I examined the object after 44 nurses concerned with the patient who received Bio treatment in our Hospital. We examined recognition for the instruction and the enforcement situation of the nurse using the question of 17 items that made a brochure for patient instruction of our hospital for the cause. [Result] The number of the effective answers is 36 people. The recognition for the instruction were 97% that “important” and “a comparative important” and the enforcement were 75% that “sometimes did it” or “always did it”. As for the comparison in the contents, “common cold symptom” “influenza” “mask at the time of going out” “hand-washing, recognition and enforcement of gargling” did not have the significant difference. There was the answer that “because the long disease duration, there was knowledge” as the reason that I could not carry out. [Conclusion] The instruction of the nurse with many opportunities to share time with a patient occupies the important to improve the self-discipline of the patient.

P1-249

How can the rheumatic clinic prevent patients with deep remission interrupting treatment? Consideration from consciousness survey on RA patients in remission 2nd report

Takaki Ura, Ryoko Okada, Yuka Seida, Yumiko Arai, Takanori Azuma
Azuma Rheumatology Clinic

Conflict of interest: None

Object) In 2017, we reported that “The remission lasts more than 1 year, it can cause of discontinuation of hospitalization.” We investigate the consciousness of remission cases and examine the background. Method) Among 645 patients had remission in August 2017 - January 2018, maintained remission for over half a year, a questionnaire was conducted for 173 patients. The contents are A) change in ADL B) satisfaction of treatment C) intention to continue treatment D) internal condition E) intention to take medicine. Results) A) “ADL improved” 135 (80.4%) B) “Satisfied” 133 (79.2%) “dissatisfied” none C) Continue treatment “want to” 140 (83.3%) “don’t want to” 2 (1.2%) “wondering” 26 (15.5%) D) 131 (78%) “taking” medicine “2 not taking” (1.2%) E) “want to quit medicine” 20 (11.9%) “don’t want to quit” 61 (36.3%). Conclusion) Even though patients satisfied with the treatment and wished to continue treatment are more than 80%, 11.9% who wanted to quit. We compared patients who wanted to “stop taking medication” and “who don’t want to”. Although there was no statistically significant difference, the tendency to stop taking medicines was recognized in patients who are using or used the b DMARDs in the past, and in patients with economic burden between the ages of 40 and 60 years.

P1-250

The association with disease activity and function and sites of hand washing residual parts in patients with rheumatoid arthritis

Yukari Suzuki¹, Shuzo Yoshida², Yuko Kimura², Akitoshi Machida³, Nobuhisa Shibahara⁴

¹Division of Nursing, Arisawa General Hospital, Hirakata, Osaka, Japan, ²Department of Immuno-Rheumatology Center, Arisawa General Hospital, Hirakata, Osaka, Japan, ³Department of Orthopedic Surgery, Arisawa General Hospital, Hirakata, Osaka, Japan, ⁴Department of Urology, Arisawa General Hospital, Hirakata, Osaka, Japan

Conflict of interest: None

[Object] We investigated the influence of disease activity and function of rheumatoid arthritis (RA) patients on hand washing residual parts. [Methods] We used hand washing checker lotion. After hand washing, we checked the site of washing residual parts using hand washing checker (Saraya Co., Ltd). [Results] Thirty patients participated in this study. Twenty-one patients were women. The mean age was 70.6±12.3 years, mean disease duration was 9.9±10.0 years. DAS28-CRP was 2.24±0.72, HAQ was 0.71±0.90, Stage I/II was 23, and Class 1/2 was 26. The most washing residual area was interdigital space. The patients who had resid-

ual parts in interdigital space were associated with higher HAQ (1.2±0.94 vs 0.09±0.2, p=0.0002) and older age (75.4±9.8 vs 62.6±11.9 years, p=0.006). There was no difference in DAS28-CRP. [Conclusions] The patients who had higher HAQ and older age had washing residual parts in interdigital space.

P1-251

The effects of surgical intervention on patient-reported outcomes in with rheumatoid arthritis patients with clinical remission

Yasuko Kobashi¹, Keiichiro Nishida², Masahiro Horita³, Yoshihisa Nasu⁴, Kenta Saiga², Ryuichi Nakahara⁵, Hideki Ohashi², Toshifumi Ozaki²

¹Department of Nursing, Okayama University Hospital, ²Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ³Department of Orthopaedic Surgery, Sayo Central Hospital, ⁴Department of Medical Materials for Musculoskeletal Reconstruction, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ⁵Department of Musculoskeletal Traumatology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

Conflict of interest: None

[Objectives] We investigated the effects surgical treatments on patient-reported outcomes (PROs) in rheumatoid arthritis (RA) patients with clinical remission. [Patients and Methods] 132 RA patients who underwent the surgical intervention of the upper and lower limbs were divided into two groups; patients with clinical remission (R group; DAS28-CRP<2.3) and non-R group (DAS28-CRP≥2.3). Body image, depression, and function were evaluated by body image assessment tool (BIAT), Beck Depression Inventory-II (BDI-II), and HAQ-DI, respectively, at before surgery, 6 months and one year after the surgery. [Results] In R-group, “Body-Depersonalization” and “Low Body-control” in BIAT, and BDI-II were significantly better than those of non-R group at one year. HAQ-DI was significantly better in R-group than in non-R group at baseline, 6 months, and one year after surgery. One year after the surgery, BIAT, BDI-II, HAQ-DI significantly improved in R group. In non-R group, “Body-esteem” in BIAT was significantly improved. However, the improvement of HAQ-DI achieved at 6 months could not be maintained at one year after the surgery. [Conclusion] Pre-operative disease control influenced the improvement of PROs such as body image, depression, as well as patients’ function after the surgery.

P2-001

Effects of SPACIA1/Saal1-deficiency on mice collagen-induced arthritis in severe or mild disease condition

Rie Komatsu¹, Iwao Seki², Tomoo Sato¹, Hiroyuki Aono², Kazuo Yudoh¹, Hisateru Niki³, Kusuki Nishioka⁴, Toshihiro Nakajima^{1,5,6}, Ryoji Fujii¹

¹Institute of Medical Science, St. Marianna University School of Medicine, Kanagawa, Japan, ²AYUMI Pharmaceutical Corporation, Kyoto, Japan, ³Department of Orthopaedic Surgery, St. Marianna University School of Medicine, Kanagawa, Japan, ⁴Global Health Innovation Policy Program, National Graduate Institute for Policy Studies, Tokyo, Japan, ⁵Institute of Medical Science, Tokyo Medical University, Tokyo, Japan, ⁶Misato Marine Hospital, Kohchi, Japan

Conflict of interest: None

[Object] SPACIA1/Saal1 is a gene associated with the aberrant proliferation of RA synovial fibroblasts. We previously reported that collagen-induced arthritis (CIA) in SPACIA1/Saal1 transgenic mice exhibited early onset and rapid progression compared with wild-type mice; however, the mechanism of this effect remains unclear. In this study, we examined the effects of endogenous SPACIA1/Saal1 on CIA using two different production lots of bovine type II collagen which causes severe or mild arthritis. [Methods] We generated SPACIA1/Saal1-deficient mice. To assess the involvement of SPACIA1/Saal1, CIA was performed with two kinds of bovine type II collagen. Arthritis scoring, histopathological examination and the serum levels of anti-type II collagen antibody were compared between these mice and wild-type littermates. [Results] SPACIA1/Saal1-deficient mice developed CIA with delayed onset and reduced severity compared with wild-type mice in severe conditions, but not in mild conditions. [Conclusion] Consistent with our previous study,

this study also indicated that SPACIA1/Saal1 expression associates with the exacerbation of CIA, although CIA progresses slowly in the absence of SPACIA1.

P2-002

The effect of peficitinib on RA FLS

Yuzo Ikari, Masahiro Hosonuma, Airi Nishimi, Shinichiro Nishimi, Sho Ishii, Takahiro Tokunaga, Hidekazu Furuya, Kuninobu Wakabayashi, Takeo Isozaki, Tsuyoshi Kasama
Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] Peficitinib (ASP015K) is a novel JAK inhibitor in development for the treatment of RA. We clarified the effect of peficitinib on RA FLS. [Methods] To determine whether JAK1, JAK2 and JAK3 were expressed in RA ST and FLS, immunohistochemistry was performed. Peficitinib was added to RA FLS and stimulated with IL-6 and IL-6R. The concentration of cytokines in RA FLS cell supernatants was measured by ELISA. In addition, to determine whether peficitinib regulate JAK-STAT pathway in FLS, Western blotting analysis was performed. Next, we performed a proliferation assay of FLS and chemotaxis assay using THP-1 and PBMC to perform functional analysis by peficitinib. [Results] We found JAK1, JAK2 and JAK3 were expressed in RA ST and FLS. Expression of pSTAT1, pSTAT3 and pSTAT5 in RA FLS was suppressed by concentration dependence of peficitinib. In addition, we proved peficitinib suppress the proliferation of FLS. Suppression of chemotaxis of THP-1 and PBMC was also observed through suppression of MCP-1/CCL2 in RA FLS supernatant. [Conclusions] Peficitinib suppressed the JAK-STAT pathway of RA FLS and was involved in the suppression of RA FLS proliferation and mononuclear cell chemotaxis. It was suggested that peficitinib act on RA FLS and suppress inflammatory pathology.

P2-003

The effect of Syk in the IL-1 β production

Daisuke Tsukui, Yoshitaka Kimura, Tamiko Yanagida, Hajime Kono
Department of Internal Medicine, Teikyo University Hospital

Conflict of interest: None

[Object] Atherosclerosis is one of the complications in rheumatic disease and is mediated by chronic inflammatory processes along with altered lipid metabolism. CANTOS trial has reported that anti-IL-1 β monoclonal antibody reduced the cardiovascular events. We previously showed the reduced atherosclerosis in mice with conditional deletion of Syk. Then, we assessed the effect of Syk in the production of IL-1 β with Syk deficient mice. [Methods] First, LPS primed BMDM from Syk^{+/+} or Syk^{del/del} mice were incubated with cholesterol crystals for 24 h. The IL-1 β in the supernatants was measured by ELISA. Next, Syk^{+/+} or Syk^{del/del} mice were injected intraperitoneally with cholesterol crystals which induced IL-1 dependent inflammation. After 6 h, the absolute number of monocytes in peritoneal lavage was measured with FACS. [Results] The IL-1 β production of BMDM from Syk^{del/del} mice was significantly higher than that from Syk^{+/+} mice. The absolute number of monocytes in peritoneal lavage from Syk^{del/del} mice ($1.21 \pm 0.13 \times 10^5$ cells/mouse) [n=14] was significantly higher than that from Syk^{+/+} mice ($6.94 \pm 0.51 \times 10^5$ cells/mouse) [n=17] [p>0.01]. [Conclusions] The possibility has been suggested that the deletion of Syk gene enhanced IL-1 β production rather than suppressed IL-1 β production.

P2-004

Anti-CD11b antibody treatment suppresses the osteoclast generation, inflammatory cell infiltration, and autoantibody production in arthritis-prone Fc γ RIIB-deficient mice

Mareki Ohtsuji¹, Hirofumi Amano², Hideki Okazaki³, Hiroyuki Nishimura¹, Sachiko Hirose¹

¹Faculty of Biomedical Engineering, Toin University of Yokohama, ²Department of Rheumatology and Internal Medicine, Juntendo University School of Medicine, ³Health and Life Science, Musashigaoka Junior College

Conflict of interest: None

[Object] Osteoclasts are derived from osteoclast precursors involved in peripheral monocytes and play an important role for bone destruction in rheumatoid arthritis. Here, we examined the effect of extravascular migration block of monocytes on the severity of arthritis. [Methods] Arthritis-prone Fc γ RIIB deficient B6mice (designated KO1) were treated with rat anti-CD11b mAb (5C6), which blocks the migration of CD11b⁺ cells including monocytes from vessels. [Results] Compared to non-treated and control rat IgG-treated KO1 groups of mice, the development of arthritis was markedly suppressed in the 5C6-treated group associated with the lower expression levels of RANK, RANKL, MCP-1, RANTES, TNF α , and IL-6 in ankle joints. The disease suppression was also associated with the lower serum levels of autoantibodies and the decreased frequencies of activated B cells and plasma cells, along with the decrease in B cell activation/differentiation-related cytokine expressions. [Conclusion] Anti-5C6 antibody treatment KO1 mouse were ameliorated joint inflammation and bone destruction. 5C6 also suppress the activation of B cells with unknown mechanism. Detailed analysis is underway.

P2-005

Peptidyl arginine deiminase inhibition suppresses arthritis via the regulation of citrullinated protein and interleukin-6

Hoshimi Kawaguchi, Isao Matsumoto, Atsumu Osada, Izumi Kurata, Hiroshi Ebe, Naoto Umeda, Yuya Kondo, Hiroto Tsuboi, Takayuki Sumida

Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: None

[Object] To explore the regulation of arthritis and the relevance of citrullinated proteins and anti-citrullinated protein antibodies (ACPA) via protein arginine deiminase (PAD) inhibition in peptide GPI-induced arthritis (pGIA). [Methods] 1) Cl-amidine, a PAD inhibitor, was injected into pGIA, and clinical scores and histopathological findings were assessed. 2) Serum ACPA titers were analyzed. 3) Citrullinated protein expression in joints and sera were examined with immunohistochemistry and Western blot analysis, respectively. 4) Serum levels of IL-6, TNF α , and IL-1 β were measured by CBA. 5) Gene expression levels of IL-6 and TNF α in joints, lymph nodes were analyzed with quantitative PCR. [Results] 1) Cl-amidine treatment significantly reduced the clinical score and ankle joint synovitis score. 2) ACPA titers from Cl-amidine-treated mice tended to be lower than controls, but not significantly different. 3) Citrullinated proteins in joints and sera from treated mice were clearly decreased. 4) With Cl-amidine treatment, serum IL-6 levels were significantly decreased. 5) IL-6 and TNF α gene expressions were significantly reduced in joints from treated mice. [Conclusions] These results suggested that PAD-mediated citrullinated protein was involved in the pathogenesis of arthritis via IL-6.

P2-006

Histone methylation profiling in peripheral white blood cells of Adult-Onset Still's Disease

Yoshimi Aizaki, Yasuto Araki, Kojiro Sato, Toshihide Mimura

Department of Rheumatology and Applied Immunology, Saitama Medical University

Conflict of interest: None

[Object] Although a line of evidence has suggested genetic and environmental contributions to Adult-Onset Still's Disease (AOSD), epigenetic mechanisms may play pivotal roles in the pathogenesis as well. We examined the histone modifications of peripheral white blood cells (WBCs) in AOSD. [Methods] Peripheral WBCs were obtained from 19 patients with AOSD and 16 healthy controls (HC). Peripheral WBCs were classified as below: CD4⁺T cells, CD8⁺T cells, $\gamma\delta$ T cells, neutrophils, regulatory T cells, B cells, and monocytes. All samples were analyzed with a fluorescence-activated cell sorting (FACS). [Results] The mean fluorescence intensity (MFI) levels of H3K27me3 and H3K4me3 of AOSD were different from HC. Particularly, histone methylation in neutrophils, B cells, and monocytes correlated with the disease activity of

AOSD. Histone methylation levels in neutrophils, B cells, or monocytes correlated with the level of CRP, IFN- γ , IL-2, IL-6, IL-10, and IL-18. However, there was no significant correlation between serum ferritin and histone methylation. [Conclusions] Differences in histone modifications were detected by FACS in different subsets of peripheral WBCs in AOSD patients. Our data suggested aberrant histone methylation may be associated with the disease activity of AOSD.

P2-007

The etiological significance of neutrophil extracellular traps in peptide GPI-induced arthritis

Ayako Ohyama, Isao Matsumoto, Hoshimi Kawaguchi, Izumi Kurata, Atsumu Osada, Yuya Kondo, Hiroto Tsuboi, Takayuki Sumida
Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: None

[Object] NETs (neutrophil extracellular traps) has been suggested as source of PAD and citrullinated protein in rheumatoid arthritis. We reported Cl-Amidine (pan-PAD inhibitor) reduced serum and articular citrullinated protein and attenuated arthritis in peptide GPI-induced arthritis (pGIA) (Kawaguchi, in press). This study aimed to clarify the role of NETs in pathogenesis of pGIA. [Methods] 1) Immunohistochemistry (IHC) of citrullinated protein was performed at the immunized skin of pGIA mice. 2) Cl-Amidine was injected into pGIA mice. Citrullinated protein in the skin was assessed by IHC. 3) Anti-Gr1 antibodies (Abs) were injected into pGIA mice. Arthritis and citrullinated protein in skin, serum and joints were explored. 4) NETs in peripheral blood, skin and joints were investigated in pGIA, Cl-amidine group and anti-Gr1 Abs group. [Results] 1) The skins at day 7 (pre-arthritis phase) were composed of inflammatory cells including neutrophils, and citrullinated protein was detected. 2) Citrullinated protein was not detected in the skins of Cl-Amidine injected mice. 3) 4) Currently under investigation. [Conclusions] The neutrophil infiltration and the citrullinated protein were detected in the immunized skin at pre-arthritis phase. NETosis might play an important role in the generation of pGIA.

P2-008

A novel mouse model of connective tissue disease-associated pulmonary arterial hypertension using pristane

Hiroyoshi Mori^{1,2}, Atsushi Kumanogoh², Yoshikazu Nakaoka¹

¹Department of Vascular Physiology, National Cerebral and Cardiovascular Center Research Institute, Osaka, Japan, ²Department of Respiratory Medicine and Clinical Immunology, Osaka University, Graduate School of Medicine

Conflict of interest: None

[Object] Connective tissue disease-associated pulmonary arterial hypertension (CTD-PAH) is difficult to study using hypoxia-induced PH model and SU5416/Hypoxia-induced PH model in mice, since these models do not accompany strong inflammation and fibrosis in the lungs. This study aimed to create a novel mouse model of CTD-PAH. [Methods] Female C57BL/6 mice (8-week-old) were divided into three groups: a group exposed to 4-week-hypoxia after an administration of pristane (PriHx group), the other exposed 4-week-hypoxia (Hx group), and another as control. Hemodynamic analysis, immunohistological analyses, flow cytometry analysis, and gene expression analyses were performed. [Results] Compared to the Hx group, right ventricular systolic pressure, right ventricle/(left ventricle plus septum) weight ratio, and medial wall thickness were significantly elevated in the PriHx group. In addition, excessive infiltration of inflammatory cells was observed in the PriHx group. Moreover, these cells were stained by anti-CD44. Finally, PD-1⁺CD4⁺ cells were increased only in the PriHx group by flow cytometry. [Conclusions] These findings indicate that pristane administration combined with hypoxia could become a novel mouse PAH model of CTD-PAH.

P2-009

Analysis of the regulation mechanism of autoimmune arthritis by T-bet and Ahr

Yuya Kondo, Masahiro Yokosawa, Masaru Shimizu, Kotona Furuyama, Hiroto Tsuboi, Isao Matsumoto, Takayuki Sumida
Department of Internal Medicine, Faculty of Medicine, University of Tsukuba

Conflict of interest: None

[Object] Previous study revealed that T-bet suppresses differentiation of Th17 cells through regulation of Ahr expression. We aimed to clarify the relation between T-bet and Ahr in the development of autoimmune arthritis. [Methods] 1) CD4⁺T cells were isolated from C57BL/6 wild type (WT) mice, T-bet knock out (T-bet KO) mice, and Ahr knock out mice (Ahr KO) mice. These cells were cultured in condition promoting Th17 differentiation. Cytokine production from CD4⁺T cells was examined by FACS. 2) Collagen induced arthritis (CIA) was induced in WT and T-bet KO mice, and severity of CIA were assessed. 3) Sera was collected at 40 days after the immunization of type II collagen (CII), and CII specific IgG antibodies and their subclass was examined by ELISA. [Results] 1) While IL-17 production from CD4⁺T cells tended to be increased in T-bet KO mice, IL-17 was significantly decreased in Ahr KO mice. 2) Severity of CIA was tended to be ameliorated in T-bet KO mice compared with WT mice. 3) CII specific IgG2a antibodies in sera tended to be decreased in T-bet KO mice compared with WT mice. [Conclusions] These results raised the possibility that T-bet and Ahr might affect the pathology of autoimmune arthritis through the modulation of CD4⁺T cell differentiation and autoantibody formation.

P2-010

Negative regulation of TGF-beta1 on RANKL-induced human osteoclast differentiation using peripheral blood monocytes (PBMs) and synovial fluid (SF) monocytes from rheumatoid arthritis (RA) patients

Tadahiro Tokunaga, Hiroki Kohno, Kazutoshi Yukawa, Tatsuomi Kuranobu, Katsuhiko Ohi, Yusuke Yoshida, Sho Mokuda, Shintaro Hirata, Eiji Sugiyama
Department of Clinical Immunology and Rheumatology, Hiroshima University

Conflict of interest: None

[Object] We have reported that TGF β 1 suppressed RANKL-induced human osteoclast differentiation using PBMs from healthy volunteers *in vitro*. We had new insights from the similar experiments using PBMs and SF monocytes in RA patients. [Methods] PBMs from healthy volunteers and PBMs and SF monocytes from RA patients were isolated by the MACS magnetic beads method. Osteoclastogenesis was evaluated by TRAP staining positive multinucleated cell number and the ability to form bone resorption pits on osteo assay surface plates. mRNA expression and protein expression levels of NFATc1 and cathepsin K were examined by realtime RT-PCR and Western Blot, respectively. [Results] TGF β 1 suppressed osteoclastogenesis in a dose-dependent manner. mRNA expressions and protein expressions of NFATc1 and cathepsin K were induced by RANKL and then significantly suppressed by TGF β 1. TGF β 1 also suppressed osteoclastogenesis of activated monocytes taken from peripheral blood and SF in pathological conditions such as RA. [Conclusions] TGF β 1 suppressed RANKL-induced human osteoclast differentiation of activated monocytes taken from peripheral blood and SF in RA patients, as well as PBMs in healthy volunteers *in vitro*. We are under consideration for further experiments such as reporter assay.

P2-011

DRB1 genotype association with younger age onset and elder age onset rheumatoid arthritis

Shomi Oka^{1,2}, Hiroshi Furukawa^{1,2}, Kota Shimada^{1,3}, Atsushi Hashimoto¹, Akiko Komiya¹, Shinichiro Tsunoda^{4,5}, Koichiro Saisho⁶, Naoyuki Tsuchiya², Masao Katayama⁷, Satoshi Shinohara⁸, Toshihiro Matsui¹, Naoshi Fukui¹, Hajime Sano⁴, Kiyoshi Migita^{9,10}, Shigetoh Tohma^{1,11}

¹National Hospital Organization Sagami National Hospital, ²Molecular and Genetic Epidemiology Laboratory, Faculty of Medicine, Univer-

sity of Tsukuba, ³Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, ⁴Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, ⁵Department of Rheumatology, Sumitomo Hospital, ⁶Department of Orthopedics/Rheumatology, Miyakonojo Medical Center, National Hospital Organization, ⁷Department of Internal Medicine, Nagoya Medical Center, National Hospital Organization, ⁸Tochigi Rheumatology Clinic, ⁹Clinical Research Center, Nagasaki Medical Center, National Hospital Organization, ¹⁰Department of Gastroenterology and Rheumatology, Fukushima Medical University School of Medicine, ¹¹Tokyo National Hospital, National Hospital Organization

Conflict of interest: None

[Object] *DRB1* is the most important genetic risk factors for rheumatoid arthritis (RA). The different association pattern of *DRB1* alleles with younger age onset RA (YORA) or elder age onset RA (EORA) was reported, but the sample sizes of these studies were modest. We investigated the genotype association of *DRB1* with YORA or EORA in Japanese populations. [Methods] Associations of *DRB1* were analyzed in YORA or EORA patients and healthy controls. [Results] The frequencies of *DRB1**04:01/*DRB1**04:05 ($P=0.0179$, OR 23.56, 95%CI 2.12-262.47), *DRB1**04:05/*DRB1**09:01 ($P=0.0028$, OR 3.38, 95%CI 1.62-7.06), *DRB1**04:05/*DRB1**12:01 ($P=0.0004$, OR 7.21, 95%CI 2.76-18.82), and *DRB1**04:05/*DRB1**15:01 ($P=1.09 \times 10^{-6}$, OR 11.68, 95%CI 4.81-28.34) were increased in YORA. The frequencies of *DRB1**01:01/*DRB1**04:05 ($P=0.0064$, OR 3.20, 95%CI 1.42-7.19), *DRB1**04:01/*DRB1**04:05 ($P=0.0011$, OR 19.04, 95%CI 2.28-158.74), *DRB1**04:05/*DRB1**04:05 ($P=0.0047$, OR 2.71, 95%CI 1.38-5.33), *DRB1**04:05/*DRB1**09:01 ($P=0.0014$, OR 2.39, 95%CI 1.43-3.99), and *DRB1**04:05/*DRB1**15:01 ($P=0.0049$, OR 3.49, 95%CI 1.53-7.99) were increased in EORA. [Conclusions] This is the first report for the associations of *DRB1* genotype with YORA or EORA in the Japanese population and the differential distribution of the genotypes was noted.

P2-012

Ablation of Shp-1 in CD11c-positive cells induces autoimmune sialadenitis: characterization of a new mouse model for Sjögren's syndrome

Masato Kinoshita¹, Yoriaki Kaneko¹, Mitsuharu Watanabe¹, Shreya Shrestha¹, Yuko Oishi¹, Junya Suwa¹, Masao Nakasatomi¹, Hiroko Hamatani¹, Toru Sakairi¹, Hidekazu Ikeuchi¹, Yoshihisa Nojima², Keiju Hiromura¹

¹Department of Nephrology and Rheumatology, Gunma University Graduate School of Medicine, Maebashi, Japan, ²Department of Rheumatology and Nephrology, Japanese Red Cross Maebashi Hospital

Conflict of interest: None

[Object] Shp-1 is a negative regulator of signaling in hematopoietic cells including dendritic cells (DCs). To analyze the function of Shp-1 in DCs, we generated Shp-1 conditional knockout mice (Shp-1 CKO) in which *Shp-1* gene is deleted in CD11c⁺ cells and found that they developed tubulointerstitial nephritis (TIN). Since TIN is one of the common manifestations in Sjögren's syndrome, we analyzed salivary glands of Shp-1 CKO to confirm the presence of sialadenitis. [Methods] We measured the salivary flow rate and performed histological examination of salivary glands. Single cells prepared from the salivary glands were analyzed by flow cytometry (FCM). [Results] Shp-1 CKO secreted less saliva by pilocarpine stimulation. Histological study showed Shp-1 CKO exhibited the infiltration of CD4⁺, B220⁺ or F4/80⁺ cells with periductal foci in the glands. FCM revealed that B cells increased in the glands of Shp-1 CKO. A distinct B cell subset, B-1 cells, which are an important source of autoantibodies, also increased in the glands of Shp-1 CKO. [Conclusions] CD11c-specific ablation of Shp-1 causes autoimmune sialadenitis characterized by the accumulation of B cells including B-1 cells. Shp-1 CKO have the potential to become a new mouse model for Sjögren's syndrome.

P2-013

Anti-rabbit podoplanin monoclonal antibody useful for evaluating engraftment of osteochondral grafts in a rabbit model

Ryusuke Honma, Tomoto Suzuki, Yuya Takakubo, Michiaki Takagi
Department of Orthopaedic Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan

Conflict of interest: None

[Object] Podoplanin (PDPN) is a type I transmembrane O-glycoprotein. PDPN expression has been reported in chondrocytes and osteocytes. However, there are no reports of PDPN expression in osteochondral grafts. In this study, PDPN expression in osteochondral grafts of a rabbit transplantation model was analyzed using newly established anti-rabbit PDPN monoclonal antibody, PMab-32. [Methods] A full-thickness cylindrical osteochondral defect was created in the left knee of rabbits. An osteochondral plug from the right knee was harvested, and grafted into the distal portion of the osteochondral defect. After 3, 6 and 12-week postoperative periods, the distal part of the femur was resected. PDPN expression in resected tissues was evaluated immunohistochemically using PMab-32. [Results] At 3, 6 and 12 weeks after surgery, PDPN was expressed in osteochondral grafts, but not expressed in the non-grafted defect areas. Nongrafted defect was covered with nonchondrocytic tissue, where there were no chondrocytes stained with PMab-32. [Conclusions] PDPN was expressed in osteochondral grafts of a rabbit transplantation model. PMab-32 was able to evaluate osteochondral grafts. It may also have a potential for assessing the maturity of osteochondral grafts.

P2-014

IL-1 Inhibits the expression of DKK1, an antagonist of the Wnt signaling pathway

Satoshi Yamasaki
Kurume University Medical Center

Conflict of interest: None

[Object] Non-inflammatory articular lesion is a hallmark in neonatal-onset multisystem inflammatory disease (NOMID), also called chronic infantile neurologic cutaneous articular (CINCA), the most severe of the cryopyrin-associated periodic syndrome (CAPS), IL-1 β -related monogenic autoinflammatory diseases. The pathology of joint of the disease are similar to those of fibrous dysplasia, a skeletal disease caused by aberrant activation of Wnt signal. We explored the potential role of IL-1 β on Wnt signaling. [Methods] The expression of *WNT* and *DKK1* mRNA was quantified by qPCR. The concentration of DKK1 was determined by ELISA. TCF reporter were used to evaluate the Wnt signal activity. [Results] The mRNA expression of both *WNT* and *DKK1* was detected in fibroblast-like synoviocytes (FLS). The supernatant of cultured FLS suppressed the Wnt signal, and the effect was reduced by anti-DKK1 antibody. IL-1 β reduced *DKK1*. The supernatant of FLS cultured with IL-1 β showed a reduced inhibitory effect on TCF activity. [Conclusions] FLS suppress Wnt signal via DKK1 production, and that IL-1 β reduce DKK1 production from the cells and, thereby, activates Wnt signal. It is possible that the overproduction of IL-1 β activates the Wnt signal and leads to articular lesion in patients with NOMID/CINCA.

P2-015

The expression of ISG15 induced by zoledronic acid (ZOL) is increased in human gamma-delta T cells

Toru Yago^{1,2}, Manabu Kawamoto¹, Yuki Nanke¹, Hisashi Yamanaka¹, Tsuyoshi Kobashigawa², Hiroki Yabe², Eri Watanabe², Shigeru Kotake²

¹Institute of Rheumatology, Tokyo Women's Medical University, ²Department of Rheumatology, Jichi Medical University Saitama Medical Center

Conflict of interest: None

[Background] $\gamma\delta$ T cells are thought to be involved in various diseases including spondyloarthritis. $\gamma\delta$ T cells are increased by isopentenyl pyrophosphate (IPP) induced by bisphosphonate (BIS) such as ZOL (Morita et al. 2007). In addition, BIS improves clinical manifestations of SAPHO syndrome rapidly; however, the exactly mechanism is unknown. [Objective] To investigate the ISG15 expression induced by ZOL in human $\gamma\delta$ T

cells. [Methods] non-memory Th cells were separated by MACS. After 14 days of culture, the expression of ISG15 or CD36 was evaluated by RT-PCR in 1) unstimulated group, 2) ZOL added group (ZOL+IL-2), 3) non-ZOL added group (PHA+IL-2). [Results] The expression of CD36, an activated $\gamma\delta$ T cell marker, was increased in group 2) compared to group 3). ISG 15 expression was markedly increased in group 2) compared to group 1) and group 3). [Discussion] ISG15 expression was markedly increased in the ZOL added group with enriched human $\gamma\delta$ T cells, indicating that IFN signature was up-regulated. The increased $\gamma\delta$ T cells with up-regulating IFN signature could be involved in clinical remission in BIS-treated SAPHO syndrome. ISG15 could be a useful tool for evaluating clinical response. [Conclusion] ISG 15 expression was elevated in human $\gamma\delta$ T cells increased by ZOL.

P2-016

Podoplanin is a potential biomarker of inflamed fibroblast-like synoviocytes stimulated by lipopolysaccharide

Tomoto Suzuki, Yuya Takakubo, Ryusuke Honma, Hiroharu Oki, Michiaki Takagi

Department of Orthopaedics, Yamagata University Faculty of Medicine

Conflict of interest: None

[Objective] Podoplanin is a transmembrane sialoglycoprotein, which is expressed in several normal tissues and malignant tumors. In this study, we investigated the correlations of PDPN and synovitis using fibroblast-like synoviocytes (FLS) of rheumatoid arthritis (RA) and osteoarthritis (OA). [Methods] FLS were obtained from synovial tissues from five RA and five OA patients undergoing upper and lower limb joint surgery. FLS were stimulated with lipopolysaccharide (LPS: 1 ng/ml) for 24 hours and non-stimulated cells were used as positive and negative controls, respectively. Quantitative real-time PCR was performed to calculate the ratio of all amplified products (PDPN, IL-6, TNF- α) to GAPDH (internal standard). Mann-Whitney U test was performed using EZR. P value of <0.05 was considered as significant difference. [Results] Stimulation with LPS increased mRNA expression levels of PDPN, IL-6, and TNF- α compared to non-stimulated cells in RA and OA (RA: PDPN; 3.4 ± 1.2 , IL-6; 110.8 ± 86.3 , TNF- α ; 4.3 ± 3.6 , OA: PDPN; 5.1 ± 2.8 , IL-6; 124.8 ± 78.8 , TNF- α ; 4.3 ± 2.1). There were no difference of mRNA expression levels of PDPN, IL-6, and TNF- α between LPS stimulated RA-FLS and OA-FLS. [Conclusions] PDPN may have the potential as a new biomarker and therapeutic target for RA and OA.

P2-017

Roles of layilin in human synovial fibroblasts revealed by layilin-silencing and proteomic analysis

Mitsumi Arito¹, Toshiyuki Sato¹, Kazuki Omoteyama¹, Masaaki Sato¹, Manae Kurokawa², Tomohiro Kato¹

¹Clinical Proteomics and Molecular Medicine, St. Marianna University Graduate School of Medicine, ²Disease Biomarker Analysis and Molecular Regulation, St. Marianna University Graduate School of Medicine

Conflict of interest: None

[Object] To understand physiological and pathological roles of layilin in synovial fibroblasts, we investigated protein profile changes caused by layilin-silencing. [Methods] Immortalized human synovial membrane fibroblasts (HSFs) were transfected with siRNA for layilin (siL) in TNF- α -treated and -non-treated conditions. Proteins affected by siL were comprehensively detected by 2-dimensional fluorescence difference gel electrophoresis (2D-DIGE). Proteins of interest were identified by mass spectrometry. [Results] In the 2D-DIGE analysis, 1092 spots were detected. Proteins were identified in 25 out of 87 protein with +1.3-fold or greater intensity changes by siL both in the TNF- α -treated and -non-treated conditions (53 spots and 34 spots, respectively). Sixteen (64%) of the 25 protein spots were assigned to epithelial-mesenchymal transition (EMT)-related proteins. [Conclusions] Our data suggest that layilin is deeply involved in the regulation of EMT-related proteins in synovial fibroblasts. Functions of layilin in synovial fibroblasts should be investigated in the context of EMT, although synovial fibroblasts are not epithelial cells.

P2-018

Significance of auto-antibody titer categorization on disease activity in patients with rheumatoid arthritis

Nobuo Kuramoto, Ryo Matsumiya, Misaki Yasutake, Kayoko Tabata, Katsunori Tanaka, Takao Fujii

Department of Rheumatology and Clinical Immunology, Wakayama Medical University

Conflict of interest: None

[Object] Significance of rheumatoid factor (RF) and anti-CCP antibody (Ab) categorization on diagnosis of rheumatoid arthritis (RA) was established. We examined significance of RF and anti-CCP Ab titer categorization change on the RA activity in this study. [Methods] We categorized RA patients by titers of RF and anti-CCP antibody into negative, positive, high positive in the RA cohort of our hospital. We extracted the patients who were changed to different category 1-year later and examined disease activity. [Results] 194 patients were studied. Patients' age was 61.4, female was 80.4% and RA duration was 8.8 years. In 2017, patients with RF negative, positive, high positive were 19.6, 24.7, 55.7% respectively. Patients with anti-CCP Ab negative, positive, high positive were 19.6, 8.8, 71.6% respectively. DAS28, SDAI and HAQ were significantly improved in patients whose anti-CCP Ab was decreased. On the other hand, DAS28, but not SDAI and HAQ, was significantly improved in patients whose RF was decreased. [Conclusion] In clinical practice, more disease activity indices correlated with anti-CCP Abs than RF whereas anti-CCP Ab titer may be infrequently changed to lower category.

P2-019

Quality of life in rheumatoid arthritis patients who achieved Boolean remission

Tomonori Sakamoto^{1,2}, Hajime Ishikawa¹, Asami Abe¹, Shinji Taniguchi¹, Hiroshi Otani¹, Kiyoshi Nakazono¹, Yoichi Kurosawa¹, Eriko Hasegawa¹, Satoshi Ito¹, Hiroshi Tsumura², Akira Murasawa¹

¹Department of Rheumatology, Niigata Rheumatic Center, Niigata, Japan, ²Rheumatology Orthopedic Surgery, Oita University Hospital, Oita, Japan

Conflict of interest: None

[Object] The purpose of this study was to clarify the level of QOL and the factors that associated with QOL in RA patients who achieved Boolean remission. [Methods] This study included 73 of 180 out-patients with Boolean remission, who visited our hospital in September 2018. For each patient, age, gender, disease duration, EQ-5D, DASH, BDI-II, DAS28-ESR (4), walking speed, body composition, grip strength, Controlling Nutritional status (CONUT) were investigated. Serum MMP-3, CRP and RF were also measured. A multiple regression analysis was performed. [Results] The mean utility index score was 0.89. It was higher than the mean score of 0.76 in RA patients in the daily practice (Hoshi, D. et al. Mod Rheumatol 2016; 26 (1): 40-5). Among the 5 items of EQ-5D, the percentage of "with problems" was 20.6% in mobility, 8.6% in self-control, 17.2% in daily activity, 17.2% in pain/discomfort, and 8.6% in anxiety/uneasiness. There was a positive correlation between EQ-5D score and grip strength ($P < 0.05$), but there was no correlation between the score and other items. [Conclusions] The level of QOL in the patients with Boolean remission was high, but they still had some problems. Grip strength was a factor which associated with QOL in the patients with Boolean remission.

P2-020

Relation between pain catastrophizing and non-inflammatory arthralgia

Takeo Abe

Department of Rheumatology, Kobe Citizen Hospital West

Conflict of interest: None

[Background] Chronic pain exists in patients of Rheumatoid arthritis (RA) without synovitis. Past evidence of psychosocial model in chronic low back pain may support pain catastrophizing (PC) is involved in such

non-inflammatory arthralgia (NIA). [Object] To investigate relation between PC and NIA. [Method] 82 patients with RA who referred to our institution between April to October 2018, fulfilling following requirements were enrolled in this study; disease duration \geq 6 months, maintaining same b DMARDS and MTX treatment at least 3 months, CRP value $<$ 0.5mg/dl, US imaging remission. We excluded patients of stage4. Pain Catastrophizing Scale (PCS) containing 3 subscales, magnification, rumination, and helplessness were used to assess PC. Patients were divided into 2 subgroups, pain VAS \geq 40 as NIA group and pain VAS $<$ 40 as controlled group. We retrospectively analyzed PCS score and other related clinical dates. [Result] The result showed significant positive correlations between PCS and pain VAS. Total, and 3 subscales of PCS score was significantly higher in NIA group than control group. Multivariate logistic regression analysis showed that helplessness (OR 1.21, $p <$ 0.01) was independent predictor of NIA. [Conclusion] We should take psychosocial factor as PC into consideration in NIA.

P2-021

Relationship between rheumatoid arthritis and locomotive syndrome-Longitudinal evaluation of 5 years-

Yasumori Sobue¹, Toshihisa Kojima¹, Koji Funahashi², Nobunori Takahashi¹, Shuji Asai¹, Nobuyuki Asai¹, Takuya Matsumoto¹, Tsuyoshi Nishiume¹, Mochihito Suzuki¹, Naoki Ishiguro¹

¹Department of Orthopedic Surgery, Nagoya University School of Medicine, Nagoya, Japan, ²Department of Orthopedic Surgery, Kariya Toyota General Hospital

Conflict of interest: None

[Object] The aim of this study was to evaluate longitudinally the relationship between Rheumatoid arthritis (RA) and Locomotive Syndrome (LS). [Methods] 16 points or more of the 25-question Geriatric Locomotive Function Scale (GLFS-25) were defined as LS. 58 patients who examined GLFS-25 for 5 consecutive years were non-LS at the initial survey. 15 patients who became LS at the final survey (LSg) and 43 patients who remained non-LS (nLSg) were compared. [Results] The age (median) at the initial survey was 64/61 years (LSg/nLSg). DAS28-CRP was 2.1/2.2 (at the initial survey), 2.0/1.9 (1year), 2.5/1.7 (2years), 2.3/2.0 (3years), 3.1/1.8 (4years), 3.8/1.8 (5years), and that of LSg was significantly higher after 2 years. GLFS-25 was 11/6 points (at the initial survey), 10/4 points (1year), 10/4 points (2years), 11/4 points (3years), 16/3 points (4years), 23/5 points (5years), and that of LSg was significantly higher at any time. The cut-off point of GLFS-25 (at the initial survey) for the prediction of LS at the final survey was 11 points and that of DAS28-CRP (2 years) was 1.9. [Conclusions] It was important to practice tight control of RA disease activity in order to suppress the onset of LS. In addition, we should to focus on not only RA disease activity but also GLFS-25 score.

P2-022

Prediction of therapeutic efficacy of abatacept in rheumatoid arthritis patients

Shigeru Tanaka¹, Kei Ikeda¹, Mieko Yamagata¹, Yoshie Sanayama¹, Shin-ichiro Kagami², Takeshi Umibe³, Ryutaro Matsumura⁴, Takao Sugiyama⁵, Yasushi Nawata⁶, Hiroshi Nakajima¹

¹Allergy and Clinical Immunology, Chiba University Hospital, Chiba, Japan, ²Department of Allergy and Clinical Immunology, Asahi General Hospital, Chiba, Japan, ³Department of Internal Medicine, Matsudo City Hospital, Chiba, Japan, ⁴Allergy and Clinical Immunology, National Hospital Organization Chiba-East Hospital, Chiba, Japan, ⁵Department of Rheumatology, National Hospital Organization Shimoshizu Hospital, Chiba, Japan, ⁶Centre for Rheumatic Diseases, Chibaken Saiseikai Narashino Hospital, Chiba, Japan

Conflict of interest: Yes

[Object] It is difficult to predict the efficacy of DMARDS. In this study, we aimed to develop tools to predict the efficacy of abatacept in rheumatoid arthritis (RA) patients. [Methods] Thirty active RA patients who agreed with abatacept treatment were recruited in this study. Peripheral blood mononuclear cells were collected before treatment and RNAs were subjected to DNA microarray analyses. The treatment efficacy was

evaluated 3 months after initial abatacept injection. Genes whose expression was associated with clinical outcome were determined by using Limma. [Results] Among 30 RA patients, 21 were classified as responders and 9 were non-responders. There were no clinical markers which could predict the efficacy of abatacept. Although we did not find any probes whose expression was significantly different between the responders and the non-responders, there was a trend toward higher *Ccr4* expression in the responders ($P = 0.0000738$, FDR = 0.518). The variation of CDAI correlated with the expression of *Ccr4* ($\rho = 0.552$, $P = 0.00156$) but other clinical parameters did not. [Conclusions] *Ccr4* expression might be a possible marker to predict the efficacy of abatacept.

P2-023

Changes in homocysteine levels when biological products (BIO) are used in patients with rheumatoid arthritis

Syuji Yamada¹, Kentaro Inui², Yuko Sugioka³, Tadashi Okano², Kenji Mamoto², Masahiro Tada¹, Tatsuya Koike^{3,4}

¹Osaka City General Hospital, ²Osaka City University Hospital, ³Center for Senile Degenerative Disorders (CSD), Osaka City University Medical School, ⁴Search Institute for Bone and Arthritis Disease (SINBAD)

Conflict of interest: None

OBJECTIVE: Higher homocysteine (Hcy) is a risk factor for bone degeneration and arteriosclerosis, and it is reported that Hcy value correlates with inflammatory marker in patients with rheumatoid arthritis (RA). We investigated the relationship with markers and also examined the influence of biological products (BIO) over time. METHODS: Data from a cohort study (TOMORROW, UMIN000003876) started in 2010 consisting of 208 RA subjects and 205 volunteers (Vo) were used. To examine the influence of BIO, half of RA patients ($n = 113$, 54.3%) are recruited BIO group. Hcy value was measured and compared between groups with repeated measure ANOVA. RESULTS: The RA group 177 subjects (continuation rate 85.1%) and the Vo group 185 (90.2%) were able to be traced up to 2017. In the BL, the Hcy value was correlated C-reactive protein ($r=0.184$, $p <$ 0.0001) · Matrix metalloproteinase-3 ($r=0.203$, $p <$ 0.0001). In 5 times, the Hcy value was significantly higher in the RA group, ($P <$ 0.0001, repeated measure ANOVA). However, in the RA group, there was no significant difference between the BIO usage group ($n = 65$) and the non-use group ($p = 0.889$, repeated measure ANOVA). DISCUSSION: Hcy value correlated with the degree of inflammation of RA patients. Though using BIO, Hcy value couldn't be controlled.

P2-024

Association between methotrexate dosage and renal impairment in patients with rheumatoid arthritis

Keigo Hayashi, Ken-ei Sada, Yosuke Asano, Yuriko Yamamura, Sumie Asano Hiramatsu, Keiji Ohashi, Michiko Morishita, Haruki Watanabe, Mariko Narazaki, Yoshinori Matsumoto, Tomoko Kawabata, Jun Wada

Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Conflict of interest: None

[Object] Renal impairment is one of the major concerns in treatment with methotrexate (MTX) for malignancy, but it is still unclear whether low dose MTX in treatment for rheumatoid arthritis (RA) affect the renal function or not. [Methods] Of outpatients with RA in our registry between November 2012 and October 2017, 79 patients who had continued administration of MTX for more than 12 months were enrolled. Association between MTX dosage and annual change of estimate glomerular filtration rate (eGFR) were analyzed. [Results] Mean age was 60 years, 72% were female, and mean MTX dosage during the observation period was 8.9 mg/week. Patients treated with \geq 10 mg/week of MTX ($n=33$) exhibited more rapid decrease in eGFR than those treated with $<$ 10 mg/week of MTX ($n=46$) (4.8 ± 1.2 vs. 0.2 ± 1.0 ml/min/year, $p=0.006$). After adjusting confounding factors such as sex, disease activity, NSAIDs use, and biological agents use, \geq 10 mg/week of MTX was still an independent factor for a decrease of eGFR (β -coefficient: 1.97, 95% confidence interval 0.160-3.786, $p=0.033$). [Conclusions] Careful monitoring of renal function should be required in RA patients treated with \geq 10 mg/

week of MTX.

P2-025

Factors associated with the improvement of QOL score (EQ-5D score) after 1 year in patients with early rheumatoid arthritis

Tomoya Miyamura, Motoko Ishida, Makiko Higuchi, Tomoaki Iwanaga, Kenji Tamagawa, Soichiro Takahama, Rumi Minami, Masahiro Yamamoto, Eiichi Suematsu

Department of Internal Medicine and Rheumatology, Clinical Research Institute, National Hospital Organization, Kyushu Medical Center, Fukuoka, Japan

Conflict of interest: None

[Object] The purpose of this study is to clarify the factors that affect the improvement of QOL score in patients with early RA. [Methods] We retrospectively evaluated 112 early RA patients within 2 years of onset from January 2017 to March 2017. To analyze the improvement of QOL after 1 year, we divided into two groups of QOL improvement group (EQ-5D improvement or EQ-5D=1) and non-improvement group (EQ-5D invariable or worsening). [Results] Baseline disease activity was CRP 0.31mg/dl and SDAI 4.74. Corticosteroids, MTX and biologics were used in 29%, 79%, 9% of patients, respectively. The average EQ-5D scores were improved from 0.804 to 0.827 after 1 year, and 69 patients showed improvement in QOL. As for factors contributing to QOL improvement, younger age, male and lower psychological anxiety were extracted. In RA treatment, use of MTX, biologics and corticosteroids were not significant, but MTX dose was significantly higher in QOL improved group. Furthermore, in the QOL improvement group, patient's global assessment, physician's global assessment, SDAI and HAQ-DI were significantly improved after 1 year. [Conclusions] Our data indicated that patient age and administration of sufficient dose of MTX were important factors for improving QOL after 1 year in patients with early RA

P2-026

Influence of gastrointestinal symptoms on patient global assessment in patients with rheumatoid arthritis

Kaoru Nagai¹, Shuji Asai², Toshihisa Kojima², Naoki Ishiguro²

¹Nursing Department, Nagoya University Hospital, ²Department of Orthopedic Surgery, Nagoya University Hospital

Conflict of interest: None

[Object] In spite of good control of joint symptoms and inflammation, Patient's general assessment (PtGA) is poor and Boolean remission is not achieved in the treatment of rheumatoid arthritis (RA). [Objective] Gastrointestinal symptoms To consider PtGA. [Methods] Gastrointestinal Symptom Rating Scale was used for 837 patients with RA to evaluate gastrointestinal symptoms. [Results] Patient background (mean or proportion) is 64 years of age, 80% of females, 13 years of illness, serum albumin 4.0 g / dL, TJC 28 0.8, SJC 28 0.8, CRP 0.5 mg / dL, PtGA 28 mm, PtGA > 10 mm 68%, Boolean remission 28%, MTX use 63%, steroid use 27%, Bio use 28%, symptomatic ratio 28% acid reflux, 24% abdominal pain, 28% indigestion, 28% diarrhea, 45% constipation In each group with gastrointestinal symptoms. PtGA and the ratio of PtGA > 10 mm were significantly higher than that with no symptoms. Multivariate analysis revealed that independent related factors of PtGA > 10 mm were serum albumin, disease duration, indigestion, diarrhea, constipation, TJC, MTX use. [Conclusions] Careful attention should be paid to not only joint symptoms but also gastrointestinal symptoms in order to improve PtGA in RA patients.

P2-027

Ultrasound evaluation after knee joint surgery in patients with rheumatoid arthritis

Rie Kurose^{1,2}, Kazue Ichinohe³, Yasuyuki Ishibashi²

¹Hirosaki Memorial Hospital, ²Hirosaki University Graduate School of Medicine, ³Hirosaki University Hospital

Conflict of interest: None

[Object] Ultrasound assessment is considered useful method for detecting synovitis in RA patients due to its greater sensitivity compared with clinical joint examination. The purpose of this study was to investigate the effectiveness of systemic ultrasound assessment after knee joint surgery in RA patients. [Methods] We evaluated 8 RA patients (7 females and 1 male, average age of 56 years) who underwent total knee arthroplasty or arthroscopic knee synovectomy. Ultrasound assessment was performed at baseline and at 1, 3, and 6 months after knee joint surgery in 42 joints. DAS28-CRP (4) was also evaluated at baseline and at 1, 3, and 6 months after surgery. [Results] In all cases, the DAS28-CRP (4) improved from 3.72±1.16 at baseline to 2.51±0.70 at 3 months after surgery. There were also decreases from baseline to 3 months after surgery in the number of joints with ultrasonographic arthritis (4.9±5.2 to 0.7±0.8), total gray scale score (10.0±14.2 to 4.1±5.6), and power Doppler score (8.4±15.3 to 2.0±3.6); however, these values were slightly increased at 6 months after surgery. [Conclusions] Ultrasound assessment detected systemic arthritis improvement at 3 months and relapse at 6 months after surgery. Thus, ultrasound can accurately evaluate RA disease activity after knee joint surgery.

P2-028

The clinical significance of pain score raise in rheumatoid arthritis patient after attaining clinical remission in accordance with treat to target treatment strategy

Ichiro Yoshii¹, Tatsumi Chijiwa², Naoya Sawada³

¹Rheumatology and Musculoskeletal Medicine, Yoshii Hospital, ²Department of Rheumatology, Kochi Memorial Hospital, ³Department of Rheumatology, Center for Rheumatic Diseases, Dohgo Spa Hospital

Conflict of interest: None

[Object] Pain score is important for rheumatoid arthritis (RA) patient, despite its unclear clinical significance. This study is designed to clarify the significance of pain score in correlating with other indices. [Methods] From August 2010, 473 RA patients have been treated for more than five years under treat to target treatment protocol with monitoring simplified disease activity score and its components, Health Assessment Questionnaire Disability Index, EuroQOL score with 5 dimensions (EQ5D), and pain score with visual analog scale (PS-VAS). Subjects who attained PS-VAS with no more than 10mm, were recruited. They were divided into two groups according to PS-VAS rise, i.e. whether PS-VAS rose to >10mm (G-R) or maintained (G-C). Indices between the two groups were compared statistically with Mann-Whitney U test. [Results] 22 cases in G-R and 49 in G-C were picked up. G-R demonstrated significantly younger and greater increase of tenderness joint count and patient's global assessment, and higher score in pain/discomfort and daily living activity (ADL) in EQ5D than G-C (<0.05). Other indices demonstrated no significant differences. [Conclusions] PS-VAS rise means ADL limitation. These were more sensitive than physician's assessment. We need to care patient's pain more carefully.

P2-029

Correlation between DAS28CRP/DAS28ESR and HAQ/MDHAQ/ treatment goal achievement rate of patients in Rheumatoid Arthritis

Yukie Saio, Miho Tachihara, Kanako Shimura, Setsuko Tajima

Department of Rheumatology, Toho Hospital

Conflict of interest: None

Purpose: HAQ of Rheumatoid Arthritis (RA) patients is one of the index to evaluate activity of RA. Due to incompleteness of HAQ, MDHAQ is invented. In this study, we compared HAQ, MDHAQ, and treatment goal achievement rate (TGAR) of patients with DAS28CRP/DAS28ESR. Patients and Methods: The records of 80 RA patients in Toho hospital were examined. At the first and second visits of the patients, they were examined by HAQ, MDHAQ, and TGAR. They were also assessed by DAS28CRP/DAS28ESR by physician. The data collected above were analyzed for correlation among them. Results: DAS28CRP vs DAS28ESR: r=0.923. DAS28CRP vs HAQ: r=0.551. DAS28ESR vs HAQ: r=0.513. DAS28CRP vs MDHAQ: r=0.518. DAS28ESR vs MDHAQ: r=0.473. DAS28CRP vs TGAR: r=-0.303. DAS28ESR vs TGAR: r=-0.272. The rate of change between the 1st and 2nd visit of DAS28CRP

(RC-DAS28CRP) vs RC-DAS28ESR: $r=0.974$. RC-DAS28CRP vs RC-HAQ: $r=0.472$. RC-DAS28ESR vs RC-HAQ: $r=0.450$. RC-DAS28CRP vs RC-MDHAQ: $r=0.379$. RC-DAS28ESR vs RC-MDHAQ: $r=0.419$. RC-DAS28CRP vs RC-TGAR: $r=-0.141$. RC-DAS28ESR vs RC-TGAR: $r=-0.134$. Conclusions: MDHAQ showed intermediate correlation with activity indexes of RA as well as HAQRA. TGAR showed reverse-correlation with activity indexes of RA.

P2-030

Study of the long-term use of tocilizumab

Shunichi Imai¹, Kikuko Gushiken¹, Ken Hasegawa²

¹Rheumatoid Arthritis Center, Minami Medical Health Cooperation,

²Meinan Hospital, Department of Orthopaedic Surgery

Conflict of interest: None

Objective: To study the long-term use of tocilizumab (TCZ). **Subjects and Methods:** The study followed-up 52 patients at our hospital who could continue treatment for at least 5 years after the introduction of TCZ. The number of patients in each Bio was as follows: first, $n=6$; second, $n=26$; third, $n=13$; fourth and subsequent, $n=7$. For the assessments, DAS28 (ESR), DAS28 (CRP), CDAI, SDAI, RF, MMP-3 were used. **Results:** 40 patients continued treatment and 12 patients had discontinued treatment. Effects similar to those at 5 years after the introduction of TCZ were maintained in 40 patients; however, nine patients experienced recurrence, and five patients discontinued treatment owing to the apparent recurrence. **Discussion and Conclusion:** The effects similar to those at 5 years after the introduction of TCZ were maintained in 40 patients, but nine patients subsequently experienced recurrence. Of these nine patients, seven patients did not take MTX and two patients used MTX (4mg), which suggested the tendency toward recurrence of RA in patients not using MTX and those using lower doses of MTX. Furthermore, as the levels of RF and MMP-3 increased during the course, the importance of monitoring the levels of RF and MMP-3 as predictive factors for the recurrence of RA was suggested.

P2-031

Psychological assessment of the patients with Rheumatoid Arthritis

Yasuo Kunugiza

Department of Orthopedic Surgery, JCHO Hoshigaoka Medical Center, Hirakata, Osaka, Japan

Conflict of interest: None

[Objective] Physiological status was evaluated by Self relating depression scale (SDS scale) for the outpatient of rheumatoid arthritis. [Method] SDS scale questionnaire was performed for the 75 outpatients of rheumatoid arthritis. The median age was 65.8 years and the median disease duration was 13.2 years. The correlation of SDS score and patient age, disease duration, number of operative procedure, CRP, MMP-3, DAS-28, number of tender joint, the score of MHAQ was evaluated. [Results] The score of 39 and below was assessed as without depression state, the score between 40 and 49 was assessed as mild depression state, the score 50 and over was assessed as moderate or severe depression state. 40 patients (53.3%) were assessed as without depression state. 25 patients (33.3%) were assessed as mild depression state. 10 patients (13.3%) were assessed as moderate or severe depression state. The correlation of SDS score and the score of MHAQ was confirmed. [Conclusion] The relationship between clinical activity and depression in rheumatoid arthritis patients was confirmed.

P2-032

Correlation between Extinguish-Th 17 and rheumatoid arthritis disease activity

Shinji Maeda, Shinya Tamechika, Tomoyo Maeda, Taio Naniwa

Department of Respiratory Medicine, Allergy and Clinical Immunology, Nagoya City University Graduate School of Medical Sciences

Conflict of interest: None

[Object] In rheumatoid arthritis pathology, the presence of effector T

cells that inflamate resistantly to immunosuppression of endogenous regulatory T cells is suggested. Recent reports have shown that Extinguish-Th17 (Ex-Th17 (Th17.1)) is resistant to regulatory T cells. Therefore, in this study, we examined correlation between disease activity in active RA patients using csDMARDs and Ex-Th17 in peripheral blood. [Methods] In 40 RA patients using csDMARDs, the correlation between Ex-Th17 Ki67⁺ in CD4⁺ CCR6⁺ CD161⁺ CXCR3⁻ CCR4⁻ Foxp3⁻ Ki67⁺ and disease activity (DAS28-CRP) was analyzed (Spearman's rank correlation coefficient). Moreover, Ki67⁺ in regulatory T cells (Treg; CD4⁺ CD25^{high} Foxp3⁺) were analyzed, and correlation ExTh17-Ki67⁺ / Treg-Ki67⁺ ratios and disease activity (DAS28-CRP) were also analyzed. [Results] Disease activity (DAS28-CRP), and Ki67⁺ rate of peripheral blood Ex-Th17 ($\rho = 0.603$, $p = 0.0000376$), the proportion of Ex-Th17-Ki67⁺ in CD4⁺T cells ($\rho = 0.411$, $p = 0.00847$), and Ex-Th17-Ki67⁺ / Treg-Ki67⁺ ($\rho = 0.455$, $p = 0.00317$) showed a significant positive correlation. [Conclusions] It was suggested that the relative proliferative state of Ex-Th17 may play an important role in csDMARDs treatment resistance of rheumatoid arthritis.

P2-033

Analysis of CARF following abatacept in patients with rheumatoid arthritis in the real world

Masaaki Miya¹, Yutaka Motohashi²

¹Heiseihidaka Clinic, Takasaki, Gunma, Japan, ²Hidaka Hospital, Takasaki, Gunma, Japan

Conflict of interest: None

[Object] To investigate the changes in CARF following Abatacept in patients with rheumatoid arthritis. [Methods] Data of 21 patients were collected retrospectively. Abatacept was injected according to the approved method and the clinical response was evaluated following 6 months of abatacept therapy. [Results] The CARF levels at baseline correlated with ACPA. The % changes from baseline CARF correlated with the % changes from baseline CRP and DAS28-ESR, after 6 months of abatacept treatment. [Conclusions] It is possible that CARF can be used to evaluate the disease activity of rheumatoid arthritis.

P2-034

Influence on the level of ADAM-17 in serum of patients with rheumatoid arthritis by adalimumab or tocilizumab Therapy

Sho Ishii, Masahiro Hosonuma, Airi Nishimi, Shinichiro Nishimi, Takahiro Tokunaga, Yuzo Ikari, Hidekazu Furuya, Kuninobu Wakabayashi, Takeo Isozaki, Tsuyoshi Kasama

Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] A disintegrin and metalloproteinase (ADAM)-10 and ADAM-17 have been reported to be expressed on rheumatoid arthritis (RA) synovial fibroblasts and be involved in inflammatory of RA. Also we have reported that tocilizumab therapy decreased the level of ADAM-10 in RA serum, and might be a predictor of the effectiveness of tocilizumab in treating RA. We examined the expression of ADAM-17 in serum and disease activity in RA patients with adalimumab or tocilizumab therapy. [Method] ADAM-17 expression in serum from normal (NL) subjects and RA patients was measured. We also analyzed the correlation between ADAM-17 and disease activity score 28 (DAS28) in RA. In RA patients who newly started adalimumab ($n=10$) or tocilizumab ($n=12$), we examined the ADAM-17 level in serum and DAS28 before and after treatment. [Results] The expression of ADAM-17 in RA serum was significantly higher compared to NL serum and was correlated with DAS28. The level of ADAM-17 in RA serum after adalimumab therapy were significantly low compared with before. But there is no significant difference at the level of ADAM-17 in RA serum after tocilizumab therapy with before. [Conclusions] Adalimumab decreased the level of ADAM-17 in serum of RA patients, but tocilizumab did not it.

P2-035

The drug retention rate and the suppression rate of large joint destruction by ARASHI change score in patients medicated by Tocilizumab with rheumatoid arthritis

Atsushi Kaneko, Shotaro Mori, Yosuke Hattori

Department of Orthopaedic Surgery and Rheumatism, Nagoya Medical Center

Conflict of interest: None

[Object] The purpose of this current study is to review drug retention rate and joint destruction or remodeling in large joints with early and established rheumatoid arthritis medicated by Tocilizumab [Methods] We investigated the drug retention rate of Tocilizumab in 117 Japanese RA patients, and the change of joint destruction or remodeling in 372 large joints of 44 RA patients. by Cumulative probability plots of ARASHI change score. [Results] The drug retention rate of Tocilizumab is 76.1% at 10 years and the suppression rate of joint destruction is 85.0% y Cumulative probability plots of ARASHI change score. [Conclusions] Tocilizumab is effective and safe in long-term results and suppressed the large joint destruction.

P2-036

Identification of the factors associated with dysfunction in rheumatoid arthritis patients

Yuji Yoshida¹, Shiro Ohshima¹, Eri Oguro¹, Kentaro Kuzuya¹, Yasutaka Okita¹, Hidetoshi Matsuoka¹, Satoru Teshigawara¹, Maiko Yoshimura¹, Kentaro Isoda¹, Yoshinori Harada¹, Shigeyoshi Tsuji¹, Jun Hashimoto², Yukihiko Saeki³

¹Department of Rheumatology and Allergology, National Hospital Organization Osaka Minami Medical Center, ²National Hospital Organization Osaka Minami Medical Center, ³Department of Clinical Research, National Hospital Organization Osaka Minami Medical Center

Conflict of interest: None

[Object] To analyze the association between mHAQ and other factors in rheumatoid arthritis patients in our hospital. [Methods] We use the "MiRAI" system and output the data of our hospital record. We divided them in older group (age ≥ 65) and younger (age < 65). [Results] Disease activity marker such as DAS28, CDAI, DrVAS, PtVAS, CRP were strongly correlated with mHAQ score. eGFR, Hb, LDL-Chol, lymphocyte were correlated with mHAQ only in older group. [Conclusions] For young population, mHAQ clearly reflect the activity and joint destruction of rheumatoid arthritis. However we should be careful for analyzing mHAQ score in older rheumatoid arthritis patients because it also reflect vascular damage, nutrition.

P2-037

Investigation of the scoring system predicting the efficacy of tocilizumab in patients with rheumatoid arthritis

Yukimi Otsuka^{1,2}, Yasutaka Kimoto¹, Daisuke Oryoji¹, Tetsushin Murakami¹, Masahiro Ayano², Hiroki Mitoma², Mitsuteru Akahoshi², Yojiro Arinobu², Jin Nakagawa³, Yoshinobu Koyama⁴, Hiroaki Niiro⁵, Koichi Akashi², Takahiko Horiuchi^{1,5}

¹Department of Internal Medicine and Clinical Immunology, Kyushu University Beppu Hospital, ²Department of Medicine and Biosystemic Science, Kyushu University Graduate School of Medical Sciences, ³Munakata Medical Association Hospital, ⁴Japanese Red Cross Okayama Hospital, ⁵Department of Medical Education, Kyushu University Graduate School of Medical Sciences

Conflict of interest: None

[Object] To investigate the validity of the scoring system predicting the efficacy of tocilizumab (TCZ) in patients with rheumatoid arthritis (RA). [Methods] RA patients in whom treatment with TCZ was initiated from 2008 to 2015 in Kyushu University Beppu Hospital were studied retrospectively. According to the report from Nakagawa and Koyama et al. (Arthritis Res Ther 2017), the scoring system was performed as followed; platelet count $\geq 381000/\text{mm}^3$, Hemoglobin ≤ 11.7 g/dL (female) or ≤ 13.2 g/dL (male), AST ≤ 16 IU/L, ALT ≤ 15 IU/L. Each item gave 1

point. We analyzed patients whose DAS28-ESR were measured both before and 24 weeks after the initiation of TCZ. DAS28-ESR response at 24 weeks was evaluated. [Results] In all 40 patients, there were 6 non-responders (15%), 12 moderate responders (30%), and 22 good responders (55%). In 17 patients predicted as good TCZ responders whose score was ≥ 2 , there were 1 non-responder (6%), 7 moderate responders (41%), and 9 good responders (53%). In contrast, 23 patients whose score was ≤ 1 revealed 5 non-responders (21.7%), 5 moderate responders (21.7%), and 13 good responders (56.5%). [Conclusions] RA patients whose scores predicting the efficacy of TCZ were ≥ 2 tended to turn out to be non-responders less frequently than those whose scores were ≤ 1 .

P2-038

Prospective analysis of Role/Social health QOL in SF-36 in patients with rheumatoid arthritis

Hirahito Endo¹, Yoshie Kusunoki², Aki Shoji², Norihiko Tonozuka²

¹Department of Rheumatology, Jusendo General Hospital, ²Department of Rheumatology, Akishima Hospital

Conflict of interest: None

[Object] We detected the role and social QOL component in patients with RA using patient reported outcome SF36 [Methods] In 348 RA, SF36v2TM assessed at 12Months and 24 Months after therapy. We analyzed the relationship between clinical findings (disease duration, treatment), HAQ-DI, DAS28-ESR, CDAI, SDAI, CRP levels. SF-36 assessed 3 summary component summary (physical component, mental component, role/social component) calculated according to summary standard score50 in 2007 Japanese. [Results] 348 RA patients, mean age was 62 ± 16 , 81% female, mean disease duration 6.5 ± 15 years (early case under 1 year 47%). DAS28 5.12 ± 2.1 , HAQ-DI 0.87 ± 0.85 , SF-36 Physical component summary score (PCS) 32 ± 20 , Mental component summary score (MCS) 49.8 ± 8.5 , Role/Social component summary score (RCS) 34.3 ± 14.6 , 56 weeks after treatment MTX62.8%, bDMARD30%, PSL32%, reached 78% remission or low disease activity. 56 weeks SF-36 PCS 39.9 ± 10 , MCS 49.6 ± 13.9 , RCS 43.3 ± 14.6 . PCS and RCS significantly improved by treatment. RCS in SF-36 is significantly correlated with CRP, HAQ-DI. [Conclusions] Improvement of RCS is one of the important factor in treatment of patients with RA. Measurement of RCS in SF36 is a useful tool in confirm of QOL in patients with RA.

P2-039

Achievement of target with the first 6-months strategy for naive rheumatoid arthritis patients with contraindications to methotrexate - The result of a single-center cohort study -

Hiroshi Oiwa¹, Yohei Hosokawa¹, Kei Araki², Eiji Sugiyama²

¹Department of Rheumatology, Hiroshima City Hiroshima Citizens Hospital, ²Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital

Conflict of interest: None

[Objective] To investigate achievement rate of low disease activity (LDA) and remission at initial six-months treatment in naive rheumatoid arthritis (RA) patients with contraindications to methotrexate (MTX), compared with those treated initially with MTX. [Methods] All the naive RA patients, visiting between April 2015 and April 2018, who started to take conventional synthetic DMARD (csDMARD) were included in the study. The diagnosis of RA was based on physician's diagnosis, meeting at least five scores of the classification criteria 2010. Almost all the cases were evaluated with SDAI, every 2-6 weeks, and the therapy was adjusted according to the T2T strategy. Achievement rate of LDA and remission at Month 6, were compared between those treated initially with none-MTX csDMARD and those with MTX. Non-responder imputation was applied for any missing data (ie, withdrawal). [Result] One hundred and twenty nine patients with naive RA were included; non-MTX (n=27) and MTX group (n=102). Achievement rate of LDA tended to be lower in non-MTX group (52% vs 73%, p=0.061), and that of remission was significantly lower in non-MTX group (11% vs 33%, p=0.030). [Conclusion] Achievement of target in naive RA, with contraindications to MTX was not as satisfactory, as in those treated with MTX.

P2-040

Difference between patient's global health and patient's global assessment of disease activity, and factors influence on these scales in rheumatoid arthritis patients

Naohiro Sugitani, Yuki Mizutani, Kentaro Noda, Yasuo Suzuki, Ayako Nakajima
Center for Rheumatic Diseases, Tsu, Mie, Japan, Mie University Hospital

Conflict of interest: None

[Object] To investigate the importance of patient's global health (PtGH) for DAS28 and patient's global assessment of disease activity (PtGA) for SDAI and CDAI in rheumatoid arthritis (RA) patients. [Methods] We retrospectively investigated the changes in PtGH and PtGA after treatment intensification in 12 weeks through medical records and the improving factors using logistic regression. [Results] Consecutive 37 RA patients (38 events) from October 2017 to September 2018 were enrolled. Women were 76%. The median age was 67 years, disease duration; 2.5 years. DAS28; 2.61. SDAI; 16.8 and CDAI; 15.3. Methotrexate (MTX subset) was used in 63% with median dose of 7 mg/week. Biological DMARDs and JAK inhibitor (BJ subset) were used in 21%. Other DMARDs were used in 16%. The change in PtGH in 12 weeks (Δ PtGH) was -1.68 ($p < 0.01$), and that in PtGA (Δ PtGA) was -2.22 ($p < 0.01$). Δ PtGH and Δ PtGA correlated significantly ($r^2 = 0.61$). Δ PtGH in MTX subsets was not different from that in BJ subsets in ($p = 0.57$) and Δ PtGA was not either ($p = 0.50$). Woman ($p < 0.05$) and usage of steroid ($p < 0.01$) were improving factors in Δ PtGH. There was no significant improving factor in Δ PtGA. [Conclusions] PtGH and PtGA behaved similar, however, the difference should be considered in using there patient oriented reports.

P2-041

Clinical factors associated with therapeutic response in patients with rheumatoid arthritis

Katsunori Tanaka¹, Misaki Yasutake¹, Kayoko Tabata¹, Ryo Matsumiya¹, Nobuo Kuramoto¹, Naoichiro Yukawa², Takao Fujii¹
¹Department of Rheumatology and Clinical Immunology, Wakayama Medical University, ²Yukawa Clinic

Conflict of interest: None

[Objective] To determine clinical factors associated with sufficient response (SR) in rheumatoid arthritis (RA) patients with moderate or high disease activity. [Methods] Among 200 patients (female = 80.0%, age = 61.3 years old, disease duration = 8.9 years) in our RA cohort, 85 patients with moderate or high disease activity (DAS28 ≥ 3.2) were divided into SR (DAS28 < 3.2) and insufficient response (IR) groups (DAS28 ≥ 3.2). We determined clinical factors associated with these therapeutic responses retrospectively. [Results] Compared with IR group, shorter disease duration, higher rate of stage I + II, more elevated Hb level (12.2 vs 11.5 g/dL) and higher HAQ score was recognized in SR group in 2017. Also, SR group had higher level of Hb (12.7 vs 11.4 g/dL) than IR group in 2018. Of note, both KL-6 (272 vs 371 U/mL) and BNP (31.6 vs 52.1 pg/mL) levels in 2018 were lower in patients with SR than in IR group. Whereas KL-6 and BNP levels were increased in both groups during a year, there are no significant differences in 2017. [Conclusions] High Hb level before and after treatment was determined as one of the associated factors with SR in RA patients. Also, after treatment, RA patients with IR group showed higher level of KL-6 and BNP than those with SR group.

P2-042

A study of a replacement for mercury hand dynamometer used for patients with rheumatoid arthritis

Yasushi Miura^{1,2,3}, Koji Fukuda², Nao Shibanuma³, Ryosuke Kuroda²
¹Department of Rehabilitation Science, Kobe University Graduate School of Health Sciences, ²Department of Orthopaedic Surgery, Kobe University Graduate School of Medicine, ³Center for Rheumatic Diseases and Joint Replacement Surgery, Kobe Kaisei Hospital

Conflict of interest: None

[Object] The grip strength of patients with RA reflects disease activity and physical function and is used in clinical practice. Because the decreased grip strength cannot be measured accurately with Smedley hand dynamometer, mercury hand dynamometer has been used. However, the Minamata convention on mercury come into effect and production, import and export of mercury containing products will be prohibited in 2021. The distribution of mercury hand dynamometer was already terminated in 2013. In this study we developed and investigated a possible replacement. [Methods] As a replacement, mercury sphygmomanometer is replaced with mercury-free one, in contrast, the grip cuff is replaced with a clip-on pediatric blood pressure cuff. The patients with RA measured grip strength with both the dynamometers and the results were statistically analyzed. [Results] A total of 130 (110 females, average 61.0 y.o.) patients with RA measured the grip strength once respectively. The average of grip strength with mercury hand dynamometer was 197.89mmHg while that with the replacement was 195.98mmHg. The correlation coefficient between the both dynameters showed a strong correlation ($R = 0.9464$, $p < 0.001$). [Conclusions] The replacement hand dynameter may be used to measure grip strength of patients with RA.

P2-043

The Efficacy of Infliximab Kit (Remi-Check Q) in our clinic RA patients

Akira Sagawa¹, Akira Furusaki¹, Izumi Yasuda²
¹Sagawa Akira Rheumatology Clinic, ²Internal Medicine, Yagi Orthopaedic Hospital

Conflict of interest: None

[Object] We investigate the efficacy of Infliximab Kit (Remi-Check Q; RQ) in our clinic RA patients. [Methods] We determined infliximab (IFX) trough level by RQ from IFX treated thirty-eight patients in our clinic. We compared the clinical manifestations with the result of RQ. [Results] Baseline characteristics of the patients mean age 66.0 \pm 2.1 years, male to female ratio 4:34, disease duration 18.1 \pm 1.3 years, stage classification (1; 3 patients, 2; 16 patients, 3; 19 patients, 4; 0 patients), mean MTX 7.8 \pm 0.4 mg/week, mean IFX use 8.8 \pm 0.6 years, mean IFX dosage 5.38 \pm 0.39 mg/kg, DAS28 2.72 \pm 0.15. 23 patients were RQ-positive, and 15 patients were RQ-negative. RQ-positive patients were more DAS remission than RQ-negative patients (56% vs 34%). 19 patients with RQ-positive were sustained IFX therapy, 4 patients were required intensified therapy. However, 8 patients with RQ-negative were required intensified therapy (Fisher's test; $P = 0.033$). [Conclusions] RQ is the useful device in decision of intensified IFX therapy or change in therapy. However, there are patients that clinical efficacy is poor even in RQ-positive, some patients are low disease activity in RQ-negative, and accumulation of future cases is necessary.

P2-044

Investigation of factors influencing the evaluation of PtGA in rheumatoid arthritis

Sari Takahashi¹, Yoshiko Sasaki², Masataka Komagamine¹
¹Komagamine Rheumatoid Orthopedic Clinic, ²Orthopedics and Rheumatology, Kojin Hospital

Conflict of interest: None

[Object] das 28, sdai / cdai, boolean are used for disease activity evaluation of rheumatoid arthritis but the evaluation content of ptga is not clear. Therefore, factors influencing the evaluation of ptga were examined using a check sheet. [Methods] Using 5 troublesome questions checked in each category of stiffness, pain, and fatigue for 110. (mtx / Bio / jak). Not applicable 0 point duration · das 28 crp · haq · stiffness · Pain-VAS compared for ptga. [Results] Pain-vas (avg 38 mm / 49%) / haq remission not achieved (27 mm / 32.7%) / morning stiffness ≥ 1 minute (21.5 mm / 41.8%) / disease period over 2 years (avg 14.7 mm / 90%) The hand is stiff / painful when turning the lid or door knob / The complaints often heard in daily practice such as feeling fatigue in the evening were high scores. 1, stiffness is an important symptom but not in the evaluation criteria 2, there are cases in which ptga is highly evaluated even in remission 3, ptga is mainly evaluated as fatigue but many factors were involved in this It became clear. [Conclusions] Pain-Vas influences the

evaluation of ptga and is an important item for determining clinical evaluation and thinks that it is necessary to evaluate in detail in the future. The tool used this time is a communication tool for finding the problem.

P2-045

Comparison of the persistent ratio of each biologic agent according to various clinical parameters: double center clinical study

Akitake Suzuki¹, Masanobu Yoshida¹, Takahiro Okai²

¹Department of Rheumatology, Mitsui Memorial Hospital, ²Department of Rheumatology, Kawakita General Hospital

Conflict of interest: None

[Object] We statistically compared the persistent ratio of anti-TNF inhibitors (TNFi), tocilizumab (TCZ), and abatacept (ABT), according to various clinical parameters. [Methods] Our study included patients with rheumatoid arthritis who had been treated with any biologic agents and collected various clinical information of them from medical charts. Subsequently, logrank analysis was conducted to compare the persistent ratio of the three biologic groups. [Results] This study included 214 patients (male 34, female 180, mean age 69.9) and 304 biologic cases were analyzed. TNFi group (mean age 61.0) included 158 cases, while TCZ group and ABT group comprised of 67 cases (mean age 59.8) and 79 cases (mean age 69.2), respectively. Overall, ABT showed significantly the highest persistency compared to TNFi and TCZ ($p < 0.05$). TNFi showed significantly higher persistent ratio when used as first biologic agent ($p < 0.05$). ABT showed significantly the highest persistent ratio for patients with high titer of anti-cyclic citrullinated peptide antibody (ACPA) (≥ 100 U/ml) than with < 100 and negative for ACPA ($p < 0.05$) and in cases of positive rheumatoid factor (RF) ($p < 0.05$). [Conclusions] These results may be useful for efficacious selection of biologics in patients with RA.

P2-046

Inefficient predictors in adalimumab treatment of ADA-naïve rheumatoid arthritis patients

Toshiaki Miyamoto, Kenji Yamazaki, Ryuhei Ishihara

Internal Medicine and Rheumatology, Seirei Hamamatsu General Hospital

Conflict of interest: Yes

Objective: To construct an effective treatment policy in a clinical setting, we investigated remission predictors following ADA treatment. **Methods:** 123 analyzable patients were introduced to ADA at this institution from May 2009 to December 2017. For the DAS28-ESR remission at 256W (n=77) and inefficient discontinuation (n=46) groups, background factors at baseline were extracted and inefficient discontinuation predictors and the cutoff value by ROC analysis were examined. **Results:** Mean age, duration of illness, MTX, and DAS28-ESR were 54.1 yrs, 6.1 yrs, 11.7mg, 4.6, respectively. At baseline, age, PSL concomitant use, Class, DAS28-ESR, SDAI, CDAI, HAQ, MMP-3 etc. were significantly high in the inefficient discontinuation group compared to the remission group. Also, by ROC analysis, DAS 28 - ESR ≥ 4.16 at baseline was extracted as a cut - off value. On the other hand, age, disease duration, MTX dose, RF, ACPA, body surface area etc. were not significantly different between ineffective discontinuation group and remission group. **Conclusion:** The ineffective discontinuation predictors were examined in 123 ADA that can be analyzed in our hospital. Suggesting the possibility that DAS 28-ESR, SDAI, CDAI, HAQ, MMP-3, etc. at baseline may become predictors of ineffective discontinuation.

P2-047

Usefulness of the Infiximab qualitative analysis in the patient receiving Infiximab

Naohide Takigawa, Hisako Eshiro

Department of Orthopedics, Nishinomiya Neurosurgical Hospital

Conflict of interest: None

[Object] The purpose of this study is to clarify the usefulness of the

infiximab qualitative analysis. [Methods] I intended for six cases during the infiximab dosage. At object six cases (one man, woman five, average age 63.8 years old), the MTX dose was an average of 5.7 mg. I investigated MMP-3 and DAS28CRP before the infiximab qualitative evaluation. In addition, I investigated the outcome of a half year after an evaluation. [Results] As for the infiximab qualitative positive, in MMP-3 before the inspection, an average of 106.9, DAS28-CRP were an average of 2.93 in two cases. As for the infiximab qualitative negative, in MMP-3, an average of 100.1, DAS28-CRP were an average of 3.25 in four cases. As a turning point a half year later, two cases became stable in dose escalation of 100 mg and, continued the dosage. However, two cases were dose escalation and interval reduction, but the effect was not provided and switched to a another biotherapy. [Conclusions] There were what could not calculate the trough level and the problems such as inspection being possible only to three times, but The infiximab qualitative analysis was useful at all.

P2-048

Evaluation of the pain in the biological preparation dosage for the rheumatoid arthritis using a stress sensor

Hiroshi Nakamura

Kure Medical Center/Chugoku Cancer Center, Kure, Japan

Conflict of interest: None

[Object] It was intended to examine the clinical usefulness of the objective pain, stress index. [Method] First, we made the apparatus which could measure a heartbeat change and the breathing change using 6 axis gyro sensors by medicine mechanic cooperation at the same time. To measure the change of the pain before and after the intravenous feeding of the biological preparation in five rheumatoid arthritis patients with VAS and weighed it. For five rheumatoid arthritis patients who used biological preparation in hospitalization, we measured a breathing fluctuation index with a body leading note sensor within 30 minutes after intravenous feeding if before intravenous feeding and weighed it against other parameters. [Conclusions] the body sound sensor was able to measure a breathing fluctuation safely. Furthermore, as for the objective stress index, the related thing with the subjective pain evaluation (VAS) was suggested.

P2-049

Efficacy and safety of methotrexate for elderly-onset rheumatoid arthritis patients

Jun Fukui¹, Takashi Hosokawa¹, Takeshi Kaneko¹, Tomomi Tada¹, Kenji Funakoshi¹, Shinichiro Nameki¹, Koji Nomura^{1,2}, Hiroshi Fujiwara¹

¹Department of Rheumatology, Osaka General Medical Center, Osaka, Japan, ²Department of Orthopedic Surgery, Osaka General Medical Center, Osaka, Japan

Conflict of interest: None

[Objectives] We aimed to investigate the efficacy and safety of methotrexate (MTX) to treat patients with elderly-onset rheumatoid arthritis (EORA) within a year after diagnosis. [Methods] This retrospective study analyzed data obtained from 453 patients with RA who visited our hospital between April 2011 and July 2017. [Results] Among the 453 patients enrolled, MTX was administered to 154 patients aged 60 years or ≥ 60 years (EORA group) and to 122 patients aged < 60 years (YORA group). Disease activity (determined by DAS28 and SDAI) of RA at the time of diagnosis in the EORA group was higher than that in the YORA group. A year later, the disease activity was the same in both groups. The dose of MTX administered at the initiation of treatment and a year later to the EORA group was lower than that administered to the YORA group. In terms of adverse reactions, no intergroup difference was observed in the risk of infection. MTX-related toxicity occurred more commonly in the YORA group. [Conclusions] Previous reports have shown that MTX does not increase the risk of infections in patients with RA and that aging increases the risk of infections. In contrast to previous studies, this study showed that aging did not increase the risk of infections in patients using MTX.

P2-050

Change in serum RF titer predicts radiographic progression in RA patients treated with TNF inhibitors

Takayoshi Owada, Kazuhiro Kurasawa, Yuta Takamura, Tomoyuki Miyao, Aya Tanaka, Ryutaro Yamazaki, Satoko Arai, Reika Maezawa, Masafumi Arima
Department of Rheumatology, Dokkyo Medical University

Conflict of interest: None

[Object] To determine whether continuous decrease in serum RF titer predicts radiographic remission in RA patients treated with TNF inhibitors (TNFIs). [Methods] Subjects were 29 RA patients who were treated with TNFIs, had serum RF ≥ 45 IU/ml and were followed up until month 12. Serum RF was measured at month 0, 4 and 12 after starting anti-TNF therapy, and more than 10% decrease in RF titer was considered as significant reduction. Continuous RF decrease was defined as significant reductions during both month 0-4 and 4-12. RA disease activity and radiographic progression were assessed by DAS28-CRP and modified total Sharp score (mTSS). [Results] During anti-TNF therapy, 14 of 29 subjects showed continuous RF decrease (CD group), and 15 cases did not (nonCD). Between these groups, there were no differences in baseline characteristics, and DAS28-CRP and mTSS at month 0 and 12. Median change in mTSS during month 0-12 (Δ mTSS) was 0 in CD and 1 in nonCD, and radiographic progression was smaller in CD. Additionally, Δ mTSS ≤ 0.5 was found in 71.4% of CD and 13.3% of nonCD, and a proportion of radiographic remission was higher in CD. [Conclusions] Continuous RF decrease was associated with radiographic remission in TNFI-treated RA patients, and change in serum RF titer predicts radiographic progression.

P2-051

Examination of 104 weeks of DMARDs (tacrolimus or methotrexate) used in combination with abatacept

Takayoshi Fujibayashi¹, Nobunori Takahashi², Daihei Kida³, Atsushi Kaneko³, Yasuhide Kanayama⁴, Yuji Hirano⁵, Yuichiro Yabe⁶, Takeshi Oguchi⁷, Toki Takemoto⁷, Masashi Kawasaki¹, Toshiaki Ohkura¹, Naoki Ishiguro², Toshihisa Kojima²

¹Department of Orthopedic Surgery, Konan Kosei Hospital, ²Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine, ³Department of Orthopedic Surgery and Rheumatology, Nagoya Medical Center, ⁴Department of Orthopedic Surgery, Toyota Kosei Hospital, ⁵Department of Rheumatology, Toyohashi Municipal Hospital, ⁶Department of Rheumatology, JCHO Tokyo Shinjuku Medical Center, ⁷Department of Orthopedic Surgery, Anjo Kosei Hospital

Conflict of interest: None

[Objective] The efficacy and safety of abatacept (ABT) on rheumatoid arthritis was evaluated by comparing patients receiving ABT plus tacrolimus (TAC group), ABT plus methotrexate (MTX group), and ABT only (non-combination group) in a multicenter study by Tsurumi Biologics Communication Registry: TBCR. [Methods] Of 513 patients who started treatment with ABT after marketing and received ABT for 104 weeks, 342 patients, excluding 15 patients who received TAC and MTX, were assigned to the TAC group (34 patients), the MTX group (166 patients), or the non-combination group (142 patients) to evaluate disease activity, retention rate. [Results] The SDAI scores showed decreases in the TAC group, MTX group, and non-combination group from 30.7, 22.9, and 25.2 at baseline to 9.5, 7.9, and 8.7, respectively, at Week 104. The rates of decrease were 69.1%, 65.5%, and 65.5%, respectively, showing a larger decrease in the TAC group. The retention rate at Week 104 was 73.5%, 71.7%, and 68.3% in the TAC, MTX, and non-combination groups, respectively. No difference was found between the TAC and MTX groups. [Conclusions] A combination of ABT and TAC, which has a mechanism of action that inhibits the activation of T cells, would appear to be as effective and safe as the ABT/MTX combination.

P2-052

Association between functional disability and the elapsed time depending on the dose of glucocorticoids after achieving clinical remission in patients with rheumatoid arthritis

Ryota Hara¹, Motomu Hashimoto², Koichi Murata², Wataru Yamamoto^{2,3}, Tohru Takeuchi⁴, Koji Nagai⁴, Yuichi Maeda⁵, Kosuke Ebina⁶, Yonsu Son⁷, Hideki Amuro⁷, Akira Onishi⁸, Kengo Akashi⁸, Masaki Katayama⁹, Tsutomu Kira¹, Naoki Shimmyo¹, Akira Kido¹, Yasuhiro Akai¹, Takashi Fujimoto¹, Yasuhiro Tanaka¹

¹The Center for Rheumatic Diseases, Nara Medical University, Nara, Japan, ²Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ³Department of Health Information Management, Kurashiki Sweet Hospital, Kurashiki, Japan, ⁴Department of Internal Medicine IV, Osaka Medical College, Osaka, Japan, ⁵Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University, Osaka, Japan, ⁶Department of Orthopaedic Surgery, Osaka University, Graduate School of Medicine, Osaka, Japan, ⁷First Department of Internal Medicine, Kansai Medical University, Osaka, Japan, ⁸Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, ⁹Department of Rheumatology, Osaka Red Cross Hospital, Osaka, Japan

Conflict of interest: None

[Object] To investigate the relationship between the dose of glucocorticoids (GC) and HAQ-DI after achieving clinical remission in patients with rheumatoid arthritis (RA) in a time series. [Methods] A total of 25543 samples from 2649 RA patients who achieved clinical remission was analyzed in the ANSWER cohort. Huber-White robust sandwich estimator of a variance-covariance matrix were used. Interaction between GC dose at each visit and elapsed time was tested and adjusted by covariates at each visit in this model (Significance level 20%). A nonlinear restricted cubic-spline was contained, and missing data were imputed by the LOCF method. [Results] The median age was 59.8 years, female was 77.3%, median disease duration was 5.0 years, median DAS28-ESR was 2.1, HAQ-DI score was 0.125. Of all patients, 705 (26.6%) patients had been treated with oral GC at baseline. The relationship between GC dose and next HAQ-DI changed significantly (p for interaction = 0.056) depending elapsed time, and the impact of GC tended to weaken with Bio use (p for interaction = 0.316). Estimated HAQ-DI score decreased once but had increased more as the time elapsed dose-dependently. [Conclusions] Long-term use of GCs after achieving clinical remission had association with progress of functional disability.

P2-053

Comparison between tenderness joints that declared by the patient and that examined by medical person

Miho Tsujimura^{1,2}, Masato Yamada¹, Eiichiro Watanabe³

¹Center for Rheumatic Diseases, Fuji Orthopedic Hospital, Shizuoka, Japan, ²School of Pharmacy, Nihon University, ³Department of Orthopedic Surgery, Fuji Orthopedic Hospital, Shizuoka, Japan

Conflict of interest: Yes

[Object] We Compare tenderness joints that declared by the patient with that examined by medical person. [Methods] We examined the tenderness joint in 28 joints of 218 RA patients for from September to October, 2018. PtTJ assumed it the report of the patients, and MdTJ was evaluated by a nurse. The group where all MdMJ fitted PtPJ were M, and where one or more differences were N. [Results] Average age was 65.9 \pm 13, CRP in 0.53 \pm 0.87, ESR in 27.5 \pm 19.9, DAS28 (ESR) in 2.79 \pm 1.14, MdTJ fitted PtTJ in 90.5%. M group 112 cases, N group 106 cases, PtTJ=MdTJ=0 were 101 cases, PtTJ=MdTJ>0 were 11 cases. Right fifth finger MP joint fitted it most (57.1%), the left elbow joint fitted it least (7.1%). CRP in 0.35 \pm 0.55 (M), 0.72 \pm 1.08 (N), ESR in 23.1 \pm 16.2 (M), 32.2 \pm 22.3 (N), patient's global assessment (PGA) in 11.6 \pm 14.5 (M), 31.4 \pm 22.5 (N), DAS28 (ESR) were 2.25 \pm 0.74 (M), 3.36 \pm 1.21 (N) when they compared M group and the N group. A significant difference was found all in these (p <0.01), but there were no significant differences in age between groups. [Conclusions] Inflammatory reaction and disease activity significantly showed high level in the patients whom PtTJ was high in. Therefore, the possibility that you should evalu-

ate PtPJ of the patients any place other than MdTJ was suggested.

P2-054

Effects of using deosumab on rheumatoid arthritis patients using biologics

Tetsu Itami, Kazuya Kishimoto, Yuji Nozaki, Koji Kinoshita, Masanori Funauchi, Itaru Matsumura

Department of Rheumatology, Kindai University Hospital

Conflict of interest: None

<Object> Effects of using deosumab on rheumatoid arthritis patients using biologics. <Method> Patients using biologics at our hospital outpatient clinic were divided into two groups, namely, non-combined group with denosumab and combined group with denosumab. In addition, the effects of suppressing bone destruction of both groups were compared. mTSS was used as a criterion for evaluating joint destruction. Bone destruction suppression is evaluated for joints of the hand (16 joints which are the mTSS evaluation joints.) Target patients were 8 patients without denosumab and data for 12 years were used. Denosumab combination group 8 cases, data for 17 years was used. The target joints were 144 joints and 272 joints. <Result> TNF inhibitor is used for nine years of the combined use of denosumab. On the other hand, we used NonTNF inhibitor for 8 years. The disease activity of both groups was 2.68, 3.2 (P=0.247) for DAS 28-CRP. Δ mTSS was 1.65 in the combination group with denosumab and 1.25 in the group without denosumab combination. There was no significant difference between these two groups (P=0.348) <Conclusion> we could not prove the significance of denosumab under the use of biologics. In the future, we need to consider more cases.

P2-055

Body weight and clinical efficacy to intravenous or subcutaneous abatacept in patients with rheumatoid arthritis

Takuji Nishikawa¹, Toshihiro Matsui², Sakae Tanaka³, Jinju Nishino³, Hirota Tsuno², Kenichi Shimane¹, Yoshio Uchida¹, Shigeto Tohma⁴

¹Department of Rheumatology, Tokyo Metropolitan Bokutoh Hospital, Tokyo, Japan, ²Department of Rheumatology, NHO Sagami National Hospital, ³Department of Orthopaedics, The University of Tokyo ⁴Department of Rheumatology, NHO Tokyo National Hospital

Conflict of interest: None

[Object] To evaluate body weight and clinical efficacy to intravenous or subcutaneous of abatacept in patients with rheumatoid arthritis. [Methods] We selected the patients treated with abatacept from the data of Nin-Ja2017. We also selected two patients group, the group with 500mg abatacept intravenously and the group with 125mg abatacept subcutaneously. These groups were divided into two groups, which were the low body weight group (under 50kg) and the normal body weight group (50-60kg), respectively. These groups were evaluated with their backgrounds, the value of CRP, disease activity scores and functional scores, respectively. [Results] The backgrounds were almost similar in these groups. CDAI score in low body weight group of intravenous patients was significantly lower than that in normal body weight one. DAS28-CRP score in normal body weight group of subcutaneous patients was significantly lower than that in low body weight one. HAQ-DI and MDHAQ scores in low body weight group of intravenous patients were significantly lower than that in normal body weight one. [Conclusions] The efficacy of intravenous abatacept might be lower in low body weight patients.

P2-056

A case of latent synovitis that could be evaluated by articular echo with joint destruction progressing without inflammatory reactions, pain and swelling

Shunsuke Sano, Tomonari Horiuchi, Takanori Azuma
Azuma Rheumatology Clinic

Conflict of interest: None

We report a case in which latent synovitis with no pain or swelling and no inflammatory response was detected by joint echo. Case 47-year

old man. Seven months ago, the patient complained of pain on both toes. Observation at first visit: TJC 17 SJC 8 CRP 0.35 MMP - 386.5 DASCRP 4.38 CRP 0.35 Anti - CCP antibody 466.3 RF 44 No bone erosion or stenosis on the X - ray image. Diagnosis and course: Since multiple arthritis was observed and both RF anti-CCP antibodies were positive, we diagnosed rheumatoid arthritis. MTX was prescribed up to 10 mg / week, the findings of the joint quickly disappeared. CRP was also normalized, MMP-3 also maintained normal range, subjective symptoms and other perceptual findings were not found, but one year later X-rays were found in both limb toes, synovium thickening grade 2 Blood flow signal grade 2 was observed. Discussion: Even in the case of rheumatoid arthritis, maintaining remission and no objective findings of symptoms, we experienced progression to potential synovitis and bone destruction. Furthermore, potential active synovitis may be visualized by joint echo. We are currently studying echogenic findings and potential synovitis by performing a joint echo of fingers and toes in a patient maintaining remission.

P2-057

A case of early intensification of treatment and diagnosis of secondary loss of response by using Remicheck Q 3 times

Yuko Kimura¹, Shuzo Yoshida¹, Nobuhisa Shibahara²

¹Department of Immuno-Rheumatology Center, Arisawa General Hospital, Hirakata, Osaka, Japan, ²Department of Urology, Arisawa General Hospital, Hirakata, Osaka, Japan

Conflict of interest: None

[Case] A 57-year-old female was diagnosed rheumatoid arthritis (RA) in X-4 year and was treated with methotrexate (MTX) 10 mg/week in other hospital. In X-2 year, she visited our hospital and increased MTX to 12 mg/week, but due to hepatic injury reduced to 10 mg/week. In June X-1 year, DAS28-ESR was elevated to 4.19, infliximab (IFX) was started. DAS28-ESR improved to 3.63 at 14 weeks after starting IFX, but IFX was increased to 6 mg/kg/6 weeks because Remi Q was negative. However, DAS28-ESR at 20 weeks was not improved, we checked Remi Q again, and it was negative. IFX was increased to 6 mg/kg/4 weeks, clinical and ultrasound remission were achieved. However, CRP was elevated in August X year and DAS 28-ESR became 2.99. We checked Remi Q again in October X year. The result was negative, we diagnosed it was secondary invalid. [Clinical significance] Remi Q at 14 weeks and 22 weeks were negative, we increased IFX dosage and intervals and subsequently maintained clinical and ultrasound remission early. Further, we noticed secondary loss of response by using Remi Q again. The activity also correlated with power doppler findings. We considered that Remi Q was a useful tool that can judge secondary loss of response at the early stage in addition to the introduction of early remission.

P2-058

Experience of using golimumab in rheumatoid arthritis with interstitial lung disease in our hospital

Hideyuki Shiba^{1,2}, Koji Nagai¹, Shogo Matsuda¹, Takao Kiboshi¹, Ayaka Yoshikawa¹, Takaaki Ishida¹, Youhei Fujiki¹, Kenichiro Hata¹, Takeshi Shoda¹, Takuya Kotani¹, Yoko Matsumura¹, Tohru Takeuchi¹, Masakazu Sugino², Shigeki Arawaka¹

¹Department of Internal Medicine IV, Osaka Medical College, Takatsuki, Osaka, Japan, ²Department of Rheumatology, Koshokai Aino Hospital, Ibaraki, Osaka, Japan

Conflict of interest: None

[Object] In the rheumatoid arthritis (RA) treatment algorithm represented by EULAR recommendations in 2016, treatment with bDMARDs is recommended when csDMARDs are not effective. On the other hand, RA is known to be involved with interstitial lung disease (ILD) to about 30% to 50%. Since there is concern that ILD may be exacerbated by anti-TNF α therapy, RA with ILD often has difficulty in treatment. Therefore, we summarize cases using golimumab (GLM) against RA with ILD at our hospital and report on the clinical course. [Methods] We investigated the drug continuation rate for 11 cases in which information could be extracted among 13 RA patients with ILD who had GLM introduced since March 2015, and analyzed disease activity and adverse events. [Results] Among 11 cases, in 1 case GLM was changed to tocilizumab due to pri-

mary invalidity, in 1 case GLM was discontinued due to pneumoniae, in 2 cases GLM was discontinued due to social background, in 7 cases GLM was continued. Disease activity in 7 cases was significantly decreased at 6 months and 12 months after the start of GLM. The mean number of days of administration was 707.4 days, and all patients were still ongoing without exacerbation of ILD. [Conclusions] GLM was suggested to be an option in the treatment of RA with ILD.

P2-059

Relation of combined pulmonary fibrosis and emphysema (CPFE) to anti-CCP antibody (ACPA) in patients with rheumatoid arthritis

Shinji Motojima, Tamao Nakashita, Akira Yoshida, Akira Jibatake
Rheumatology and Allergy, Kameda Medical Center, Kamogawa, Japan

Conflict of interest: None

[Object] We have reported that pulmonary lesions are important not only as a prognostic factor but also as a triggering place of ACPA production. CPFE was first reported by Cottin in 2005 and is a risk factor of lung cancer and pulmonary hypertension. We studied the prevalence of CPFE in RA patients and its relation to ACPA. [Methods] Subjects are 567 RA patients who performed chest CT. Prevalence of interstitial lung diseases (ILD), classification of ILD pattern, and the presence of CPFE were studied using CT findings. [Results] ILD was found in 223 out of 567 RA patients (39.3 %), and UIP, NSIP and OP were found in 41, 167 and 14 patients, respectively. CPFE was found in 36 (6.3 % of total patients and 16.1 % of patients with ILD). Prevalence of CPFE in each ILD pattern were 53.7 %, 8.4 % and 0 % in UIP, NSIP and OP, respectively. All the patients with CPFE were smokers. ACPA titer was significantly higher in ILD group than non-ILD group (median 252 vs. 45.5, $p < 0.005$). In ILD group, ACPA titer was significantly higher in CPFE group than non-CPFE group (median 252 vs. 93, $p < 0.05$). [Conclusions] ACPA titer was higher in ILD group, and in ILD group, CPFE group showed higher ACPA titer.

P2-060

A clinical investigation of the pleurisy combined with rheumatoid arthritis (RA)

Yasuhiko Yoshinaga, Tetsushi Aita, Susumu Nishiyama, Shoji Miyawaki
Rheumatic Disease Center, Kurashiki Medical Center, Kurashiki, Japan

Conflict of interest: None

[Object] To evaluate the clinical characteristics of the pleurisy combined with rheumatoid arthritis (RA). [Methods] We investigated the clinical characteristics of 20 RA patients (10 males, 10 females, mean age 64.9 ± 8.7) admitted to our hospital with pleurisy in 2003-18. [Results] Eight out of 20 cases were RA pleurisy, 8 cases infection (4 general bacteria, 2 non-tuberculous mycobacteria (NTM), a case of tuberculosis and a case of cryptococcosis), 2 malignant pleurisy, a suspicious case of multiple pneumonia caused by MTX-LPD and a case of TNF inhibitor-induced lupus pleurisy). Looking at the causes of pleurisy by year, RA pleurisy has decreased and infectious diseases are increasing. ADA and hyaluronic acid in pleural effusion may show high values even in RA pleurisy and empyema, and to distinguish from tuberculous or malignant mesothelioma, an acid bacteria test of pleural effusion, cytological diagnosis and histologic examination of pleural biopsy are necessary. [Conclusions] Recurrence of pleurisy associated with RA is diverse including RA pleurisy, malignancy, infectiousness, etc. Recently, multiple pneumonia caused by MTX-LPD, TNF inhibitor-induced lupus pleurisy is added, and it is becoming more difficult to differentiate pleurisy combined with RA.

P2-061

Relation of pulmonary function to anti-CCP antibody titer and RF titer

Shinji Motojima, Tamao Nakashita, Akira Yoshida, Akira Jibatake
Rheumatology and Allergy, Kameda Medical Center, Kamogawa, Japan

Conflict of interest: None

[Object] In JCR2018 we reported the relation of the presence of abnormalities in respiratory system evaluated by chest CT to anti-CCP antibody and RF titers in RA patients with short disease duration (less than 1 year). Here we studied the relationship between pulmonary function, and anti-CCP antibody and RF titers. [Methods] Subjects were 164 patients the RA with the disease duration of less than 1 years. [Results] Pulmonary functions tested were VC, FEV1, FEV1/FVC, V50 and V25. When normal values were defined as more than 80%, 80%, 70%, 70%, and 50% in %VC, %FEV1, FEV1/FVC, %V50, and %V25, respectively, percentages of patients in the normal ranges were 79%, 71%, 55%, 19%, and 16%, respectively, suggesting prevalence of small airway obstruction. There was a weak but significant inverse correlation ($r_s = -0.156$) between anti-CCP antibody titer and %FEV1, and correlation to %V25 was tended to be significant ($r_s = -0.143$). RF titer did not show significant correlations to any pulmonary function parameters. [Conclusions] Anti-CCP antibody titer relates to small airway obstruction in pulmonary function tests which suggests the presence of small airway inflammations.

P2-062

Presence of diabetes represented a risk factor for incidence of new carotid plaque in patients with rheumatoid arthritis -TOMORROW study-

Shohei Anno¹, Kentaro Inui², Yuko Sugioka³, Kenji Mamoto², Tadashi Okano², Masahiro Tada⁴, Tatsuya Koike^{3,5}, Hiroaki Nakamura²

¹Department of Orthopedic Surgery, Yodogawa Christian Hospital, ²Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine, ³Center for Senile Degenerative Disorders (CSDD), Osaka City University Graduate School of Medicine, ⁴Department of Orthopedic Surgery, Osaka City General Hospital, ⁵Search Institute for Bone and Arthritis Disease (SINBAD)

Conflict of interest: None

[Object] The objective of this study was to evaluate the morbidity and severity of carotid plaque in patients with RA and in age- and sex-matched controls (Co) who participated in the TOMORROW study. [Methods] This study included 360 participants (RA:175, Co:185) and carotid ultrasound was performed both at 2011 and at 2017. Atherosclerotic plaque was defined as an intima-media thickness > 1.1 mm. Severity of plaque was assessed by plaque score. [Results] Carotid plaque was observed more frequently in RA than Co at 2011 ($n=82$ vs $n=66$, $p = 0.04$). Incidence of new plaque were no differences between RA and Co ($n=33$ vs $n=44$, $p = 0.94$). Comparing RA patients with and without incidence of new plaque, age ($p=0.015$) and presence of diabetes ($p=0.09$) were higher in patients with incidence of new plaque. Plaque score became advanced both RA and Co (RA: $p < 0.001$, Co: $p < 0.001$). However plaque score in RA patients with plaque who had the habit of exercise did not become advanced (RA: $p=0.07$, Co: $p < 0.001$). [Conclusions] There were no significant differences in incidence of new plaque, in progression rate of plaque score between RA and Co. In RA patients, presence of diabetes represented a risk factor for incidence of new plaque, and exercise can decrease the progression of the plaque.

P2-063

Characterization of three rheumatoid arthritis patients with recurrence of lymphoproliferative disorders

Shinya Hirata, Eiko Miyagawa, Rie Furuta, Ayako Yamamura, Mizuho Tsujihashi, Masayuki Murai, Yumiko Mizuhashi, Mikako Iwakura
Departments of Rheumatology and Clinical Immunology, Kumamoto University Hospital

Conflict of interest: None

[Objectives] Lymphoproliferative disorders (LPD) develop in some patients (pts) with rheumatoid arthritis (RA). It is hypothesized that pathogenesis of LPD are immunosuppression and reactivation of Epstein Barr virus (EBV) caused by immunosuppressant including methotrexate (MTX), chronic inflammation of RA and Sjogren's syndrome, and so on. These mechanisms might relate to recurrence of LPD. [Methods] We analyzed 3 pts (a male and 2 females) with recurrent LPD among 21 RA pts with LPD from January 2010 to October 2018. [Results] The age was 53 to 66 years old at onset of LPD. MTX had been administered to all pts,

and the duration of MTX treatment was 15 to 149 months. A patient was treated by etanercept. They were diagnosed to have follicular lymphoma, B cell lymphoma and lymphoproliferative disorder. EBV was not detected in tumor tissues from all pts. 2 pts received chemotherapy, while one patient discontinued MTX. After treatment of LPD, 2 pts experienced relapse of RA at 3 and 13 months. They had been treated by tacrolimus, iguratimod and biological DMARDs. LPD relapsed within 21 to 56 months, and were treated by chemotherapy. [Conclusion] We experienced 3 RA pts with recurrence of LPD. The clinical histories suggested that mechanisms of LPD related to recurrence.

P2-064

The Significance of axillary lymphnode enlargement as a Marker of obesity in Rheumatoid Arthritis

Masanobu Yoshida, Akitake Suzuki

Department of Rheumatology, Mitsui Memorial Hospital, Tokyo, Japan

Conflict of interest: None

<Objective> The present study was conducted to evaluate the association with axillary lymph nodes (ALN) enlargement and Rheumatoid Arthritis (RA) clinical features. <Methods> This was a retrospective observational study performed at our institute on outpatients between 2014 and 2017. All 67 untreated RA patients were performed by chest computed tomography scanning (CT), the maximum long and the maximum short diameter of left and right ALN were measured from the CT image, either the left or right ALN larger values was adopted. Exclusion criteria were malignant tumor and polyvascular disease. <Results> In multivariate analysis, the maximum and minimum short diameter of the ALN was independently associated with Body Mass Index (BMI). Both the maximum long and the maximum short diameter of ALN were significantly longer in subjects strong positive for rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (ACPA) than in seronegative subjects. <Conclusion> ALN diameter seems to reflect RF or ACPA as markers in diagnosing and predicting the prognosis of untreated RA, and ALN diameter is associated with BMI. It suggests that ALN diameter may be an indicator suggesting obesity, not inflammation with untreated RA patients without malignant tumor and polyvascular disease.

P2-065

Is Rheumatoid Arthritis really risk factor of osteoporosis even when T2T is widely permeated?

Ichiro Yoshii¹, Tatsumi Chijiwa², Naoya Sawada³

¹Rheumatology and Musculoskeletal Medicine, Yoshii Hospital, ²Department of Rheumatology, Kochi Memorial Hospital, ³Department of Rheumatology, Center for Rheumatic Diseases, Dohgo Spa Hospital

Conflict of interest: None

[Object] It is a long time since rheumatoid arthritis (RA) is recognized as an independent risk factor of osteoporosis (OP). However, it has already eight years since T2T protocol was advocated. Is RA a real risk factor of OP? We have investigated whether it is still so. [Methods] From September 2017 to August 2018, 687 cases were examined dual energy X-ray absorptiometry, in whom 279 were RA and 408 were non-RA. In the RA cases, subjects who attained clinical remission within 1 year were picked up. From them and non-RA cases, age, sex, Barthel Index Score distribution, Creatinine/CystatinC ratio, number of comorbidities, administered drugs were matched, and then bone mineral density (BMD) of lumbar spine (LS), femoral neck (FN), whole femur (WF), and greater trochanter (GT) were compared between the two groups statistically with Mann-Whitney U test. [Results] 116 cases of RA and 108 of non-RA were recruited. Average DAS28-CRP in RA was 1.73, while average mHAQ score was 0.47. BMD of LS, FN, WF, and GT were 93.5, 77.8, 79.9, and 83.0 (%YAM) in RA, while 77.5, 64.8, 68.3, and 73.1 in non-RA, respectively. [Conclusions] As long as RA treatment is tightly performed and attained clinical remission, RA is no longer OP risk.

P2-066

Patients with rheumatoid arthritis who complicated rapidly progressive glomerulonephritis have high disease activity and are resulted in delayed consultation to nephrologists

Shin Okuyama, Fumito Abe, Masaya Saito, Mizuho Nara, Atsushi Komatsuda

Department of Hematology, Nephrology, and Rheumatology, Akita University Graduate School of Medicine

Conflict of interest: None

[Object] To clarify the characteristics of RPGN that merges with RA and to extract attention points in clinical practice. [Methods] We extracted cases with RPGN concurrently with RA in patients from 1998 to March 2018 at the Akita University Hospital and summarized their characteristics. [Results] Among RA 2264 cases, RPGN was merged in 5 cases (0.22%). Neither treatment history of biological products containing TNF inhibitor was present. The patient age was 53 to 91 years old (average 73.2, median 75), the ratio of male to female was 4: 1, the initial symptom was fever and joint pain, the serum creatinine was 1.9-7.2 mg/dL (average 3.19, median 1.98), CRP was 2.89 - 20.0 mg/dL (mean value 9.32, median 4.48), ANCA was detected in 4 cases. Two patients had end-stage renal failure and three had progressed as chronic kidney disease. [Conclusions] Patients having RPGN with RA tended to have high RA disease activity and delayed consultation to kidney physician. The onset age was older as compared with AAV patients secondary to TNF inhibitors. The cause of delay is that urinalysis was not performed. Based on the above, we would like to encourage regular urinalysis for rheumatoid arthritis patients with high disease activity.

P2-067

The treatment of cutaneous ulcer due to rheumatoid vasculitis in OMMC

Maiko Yoshimura¹, Eri Oguro¹, Kentaro Kuzuya¹, Yasutaka Okita¹, Hidetoshi Matsuoka¹, Satoru Teshigawara¹, Yoshinori Harada¹, Yuji Yoshida¹, Kentaro Isoda¹, Shiro Ohshima^{1,2}, Jun Hashimoto¹, Yukihiko Sasaki²

¹Department of Rheumatology, Osaka Minami Medical Center, ²Department of Research, Osaka Minami Medical Center

Conflict of interest: None

[Object] The skin ulcer due to the rheumatoid vasculitis (RV) is often refractory, but lacks in a well-organized report about the treatment. Steroids and cyclophamide are recommended for the RV. On the other hand, there is the report that anti-TNF agent or Abatacept is effective for a skin ulcer of RV. I would report the treatment of skin ulcer in OMMC. [method] I choose the cases of vasculitis by skin biopsy for the past 3 years in patients of rheumatoid arthritis. I review about the treatment in these cases. [result] We identified 11 cases of skin ulcer due to RV. one case is focal therapy only, 10 cases (almost all) use steroids. 4cases use cyclophosphamide, 4cases use tacrolimus, 1case use anti-TNF agent, 3cases use Abatacept. IVIG, L-CAP therapy is also performed. Infection is most major side-effect (7cases). clinical outcome: 6cases get better or remission, 2cases died, 2cases is no change, 1case is now in the hospital. [Conclusions] Abatacept may be useful for skin ulcer of RV. Steroid monotherapy was failed. Adequate use of immunosuppressive agent or biologics is important for success of the treatment of RV.

P2-068

A case of pulmonary arterial hypertension with rheumatoid arthritis

Daiki Hayashi, Shinji Kitajima, Tadashi Toyama, Akinori Hara, Yasunori Iwata, Norihiko Sakai, Miho Shimizu, Kengo Furuichi, Takashi Wada

Department of Nephrology, Kanazawa University Hospital

Conflict of interest: None

The female patient was a 35-years-old with history of rheumatoid arthritis (RA) since 27 years old. At diagnosis of RA, she presented multiple phalangeal and wrist joint pain with synovitis. However, rheumatoid factor and anti-CCP antibody were negative. She was treated with methotrexate, multiple biological drugs and immunosuppressants. She admitted

to our hospital with a dry cough. Echocardiogram indicated severe elevated right ventricular systolic pressure (RVSP) of 77 mmHg. The left ventricle was D-shape and right ventricle was enlarged in echocardiogram. Left ventricular ejection fraction was preserved. Cardiac catheterization revealed mean pulmonary artery pressure (mPAP) 44 mmHg and pulmonary capillary wedge pressure 13mmHg. Pulmonary embolism and interstitial lung disease were excluded by computed tomography of the chest and pulmonary ventilation-perfusion scintigraphy. Pulmonary arterial hypertension associated with connective tissue diseases was speculated. She was treated three courses of steroid pulse therapy (mPSL 500 mg×3 days), tacrolimus and sildenafil. Her symptoms, abnormal echocardiographic findings and RVSP improved rapidly. We report here a rare case of PH associated with RA.

P2-069

A case of rheumatoid arthritis-associated aortitis

Takahiro Tsuchida, Ko Sudo, Hiroyuki Yano, Mitsuyo Kinjo
Department of Rheumatology, Okinawa Chubu Hospital

Conflict of interest: None

Case: 65 y.o man History of present illness: After being tapered on prednisone for newly diagnosed organizing pneumonia one month earlier, the patient presented with fatigue and bilateral painful red eye. Joint pain and anasarca limited his activity and the patient became wheel-chair bound. Clinical course: Physical examination revealed symmetrical polyarthritis and scleritis, and blood tests showed marked leukocytosis and thrombocytosis, elevated inflammatory markers and high rheumatoid factor and anti-cyclic citrullinated peptide antibody. Computed tomography with contrast revealed arterial wall thickening of the right external carotid artery and aortic arch. The patient was diagnosed with seropositive rheumatoid arthritis with large vessel vasculitis and scleritis. His symptoms significantly improved on high dose prednisone and intravenous tocilizumab. Discussion: Large vessel vasculitis and scleritis in a patient with newly diagnosed active rheumatoid arthritis are uncommon presentations of extra-articular manifestation. We reviewed literature on large vessel vasculitis in rheumatoid arthritis.

P2-070

In the patients with RA, vascular stiffness is related to bone mineral loss, disease activity of RA, and the degree of skeletal muscle atrophy

Yumeko Taniguchi, Ryosuke Hanaoka, Toshiko Haginoya, Sayaka Koizumi

Department of Rheumatology, Kamitsuga General Hospital

Conflict of interest: None

[Object] To clarify the relationship between increased vascular stiffness in rheumatoid arthritis (RA) patients, bone mineral loss, joint destruction and skeletal muscle atrophy. [Methods] Body component analysis was carried out by direct segmental multifrequency bioelectrical impedance analysis (DSM-BIA) for the RA patients. We measured skeletal muscle mass index (SMI), bone mineral content (BMC), body mass index (BMI), brachial circumference, and body fat percentage (BFP). As a simple representative value of joint destruction, the average of the carpal height ratio (CHR) of the two-hand joints was measured. Arterial velocity pulse index (AVI) was measured as a simple representative value of vascular stiffness. We used bone mass density (BMD) of the lumbar vertebrae and femoral neck by double energy X-ray absorption method as an indicator of bone mineral loss. [Results] There was a significant correlation between AVI and indicators of bone mineral loss (BMC, hip joint BMD, lumbar spine BMD), skeletal muscle atrophy (SMI, brachial circumference), and RA disease activity (CDAI, SDAI). [Conclusions] In the patients with RA, vascular stiffness is related to bone mineral loss, disease activity of RA, and the degree of skeletal muscle atrophy rather than BFP or BMI.

P2-071

A Case of Methotrexate-associated Lymphoproliferative Disease with Multiple Masses, Gastrointestinal Ulcers and Perforations

Akira Nishino, Hideto Takada, Mari Tochihiro, Shinya Hirahara,

Hirokazu Nishina, Masanori Hanaoka, Yasuhiro Katsumata, Masayoshi Harigai, Hisashi Yamanaka
Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Case] A woman in her 60s had diagnosed with rheumatoid arthritis (RA) and had been treated with methotrexate (MTX) for 16 years. She visited our hospital with one-month history of cough and dyspnea. At her visit, she presented fever and hypoxia. CT scan showed multiple masses in the lungs and pancreas. Upper endoscopy revealed multiple ulcers in the stomach and duodenum. Pathological examination of the ulcerative lesion revealed large lymphoma cells that were positive for CD20, CD79a, and LMP-1. The patient developed ileal perforation, and emergency ileectomy was performed. CD20-positive lymphoma cells were found at the perforated lesion. Therefore, we concluded that multiple masses as well as gastrointestinal ulcers and perforations were a series of manifestations of diffuse large B-cell lymphoma. Those masses did not reduce one month after withdrawal of MTX so that she was transferred to the Division of Hematology in order to receive chemotherapy. The pulmonary masses partially reduced by 2 cycles of R-CHOP. She is scheduled to receive R-CHOP for 8 cycles in total. [Clinical significance] This case suggests MTX-associated lymphoproliferative disease can cause various extranodal lesions such as multiple masses, gastrointestinal ulcers and perforations.

P2-072

Bloody pleural effusion in a case of rheumatoid arthritis; difficulty in making a differential diagnosis

Tetsushin Murakami¹, Daisuke Oryoji¹, Yasutaka Kimoto¹, Masahiro Ayano², Hiroki Mitoma², Mitsuteru Akahoshi², Yojiro Arinobu², Koichi Akashi², Hiroaki Niuro³, Takahiko Horiuchi¹

¹Department of Internal Medicine, Kyushu University Beppu Hospital, ²Department of Medicine and Biosystemic Science, Kyushu University Graduate School of Medical Sciences, ³Department of Medical Education, Kyushu University Graduate School of Medical Sciences

Conflict of interest: None

[Case] 72-year old male [Chief complaint] Polyarthralgia, Right anterior chest pain, Bloody pleural effusion [Medical history] The patient developed rheumatoid arthritis in February of X-3, and right front chest pain and dyspnea appeared in July, X-3. The infiltrating shadow of the right lower lobe and right pleural effusion were observed, and pleural effusion showed yellow exudative pleural effusion. Pleural effusion gradually improved after starting PSL 30 mg / day, but a small amount of pleural effusion remained. Pleural effusion was re-exacerbated from X-2 in May, and TCZ administration was introduced in December X-2. Continued the infusion, but the right pleural effusion gradually worsened. [Course of treatment] Bloody pleural effusion was found by diagnostic thoracentesis. The result of the pathological examination indicated a granulation increase suspected of cavernous hemangioma. Malignant cells were not observed, and malignant disease was diagnosed as negative from the biopsy results. I diagnosed as malignant rheumatoid arthritis and started ABT administration. [Clinical importance] It is a case of rheumatoid arthritis combined with bloody pleural effusion and it is considered to be a highly suggestive case in distinguishing from malignant tumor.

P2-073

Clinical features of 14 patients with MTX associated lymphoproliferative disorders (MTX-LPD) in our hospital

Chisaki Ajima^{1,2}, Takao Sugiyama¹, Yusuke Yokoyama¹, Mieko Yamagata¹, Ayako Norimoto¹, Yoshie Sanayama¹, Toyohiko Sugimoto¹, Masaaki Furukawa¹, Daiki Nakagomi², Kenichiro Kitamura²

¹Department of Rheumatology, National Hospital Organization, Shimoshizu Hospital, Chiba Japan, ²Third Department of Internal Medicine, University of Yamanashi, Yamanashi, Japan

Conflict of interest: None

[Background] Methotrexate (MTX) is the anchor drug of rheumatoid arthritis, frequently used. On the other hand, many have been reported lymphoma during treatment with MTX. [Purpose] We examined clinical pictures of 14 patients with MTX-LPD in our hospital since 2007-2018. [Result] Three of them were men, 11 were women, average age was 69 y.o. They used 3.5g of MTX for 9 years in average. Five of them used tacrolimus (TAC) together. We followed up for 34 months after MTX-LPD onset. Five patients whose onset was superficial lymphadenopathy and 3 patients discovered by subcutaneous tumor were in stage 1 or 2, and 6 patients who had the onset for an organ infiltration were in stage 4. Some symptoms appeared rapidly in the patients in stage 4, and we discovered tumors in lung or liver or abdominal cavity by image close inspection. Chemotherapy was given 3 patients as soon as discontinuing MTX, and 2 whose lesion had not reduced after MTX cancellation. All patients who used TAC together improved without stopping TAC. [Conclusion] MTX-LPD often happens in elderly patient. MTX-LPD in stage 4 remitted spontaneously only withdrawal of MTX regardless of pathological type, including who used tacrolimus together. We recommend discontinuing MTX and observing at first when you discover MTX-LPD.

P2-074

A case of rheumatoid arthritis (RA) with right forearm soft tissue mass

Norihiro Mayumi, Hiroki Wakabayashi, Masahiro Hasegawa, Akihiro Sudo

Department of Orthopedics, Mie University Hospital, Mie, Japan

Conflict of interest: None

[Object] We report a case of rheumatoid arthritis (RA) who became refractory after excision of right forearm soft tissue mass. [Case] A 38-year-old female with RA sufferers in 19 years. A tumor appeared in the right forearm 9 months before visiting our hospital and was excised by a nearby doctor, but it relapsed and the wound became refractory, so introduced to our hospital. At the first visit, a protruding lesion was observed with leachate. Her disease activity was DAS 28-ESR 5.45. [Results] The IL-2 receptor was normal, but HTLV-1 antibody was positive. Tumor biopsy showed intense inflammatory cell infiltration with intraepithelial and interstitial neutrophils but no malignant findings. In addition, HTLV-1 antibody Western blot and virus analysis were negative and considered rheumatoid nodules. Neoplastic lesions were not observed in whole body examination by trunk CT. RA treatment was changed to iguratimod. The DAS 28 improved from 5.66 to 3.30 in 3 months and the forearm mass cured. Two years after, DAS 28 is 3.83, and recurrence of tumor mass is not admitted. [Conclusions] Although it is less frequently, there are reports of lymphoma onset in RA. However, as a differential disease, it is needed to consider rheumatoid nodules and ulcers associated with disease activity of RA.

P2-075

A Case of Median Neuropathy Caused by Elbow Joint Synovial Cyst with Rheumatoid Arthritis

Ryo Sato, Hiroyuki Matsubara

Hekinan Municipal Hospital

Conflict of interest: None

[Case] A 69-year-old man. Rheumatoid arthritis (RA) develops at age 65 (Stage 3, class 2). I was on follow-up with a near-doctor (MTX 2 mg, PSL 5 mg), but at the age of 67 he underwent regular introduction with degenerative scoliosis and elbow joint pain. From that point on, the mild swelling of both elbow joints and ROM limit (extension -5 / -10°, flex 110/100°) were observed. Drug increase was not improved either only in the left elbow joint, ROM restriction also deteriorated. At the age of 68, numbness of the left fingers and middle finger and difficulty in pinch movement were recognized, and elbow joint MRI imaging was performed. As a result, an elbow joint giant synovial cyst was recognized. As a result of the diagnosis of median neuropathy, dissection drainage was performed as much as possible. However, Symptom sustained from persisted and it was judged that resection of the synovial cyst was appropriate, and cystectomy was performed 4 weeks after the incision drainage. Afterwards, median neuropathy improved. Pathology showed exten-

sive necrosis and inflammatory cell infiltration and fibrin deposition, diagnosis of change by RA and modification by treatment. However, the disease activity as RA was poorly. Currently being followed by biologics.

P2-076

A case of rheumatoid arthritis which aortitis and small vasculitis occurred simultaneously and died due to empyema

Ryo Yamashita, Yusuke Izumi, Takahiro Yamada

Department of General Medicine, The Jikei University Daisan Hospital, Tokyo, Japan

Conflict of interest: None

[Case] A 74-year-old woman visited our hospital with lower leg ulcers and chest back pain. She had been diagnosed as rheumatoid arthritis when she was 30 years old and received tocilizumab and tacrolimus. Skin biopsy from leg ulcers revealed necrotizing vasculitis. Chest MRI suggested the presence of aortitis. She was treated steroid pulse therapy from day 1, prednisolone 50 mg/day from day 4, and cyclophosphamide pulse therapy from day 10. Chest MRI showed the improvement of aortitis, on the other hand lower leg ulcers did not improve. Lower leg ulcers gradually improved after the leukapheresis procedures were used from day 32. Septic shock had occurred on day 43. Antibiotics were initiated but she developed lung abscesses and died due to empyema on day 71. From the result of autopsy, the cause of death was empyema. There were no findings of aortitis. [Discussion] Although it is known that aortitis and small vasculitis are associated with rheumatoid arthritis, it is rare to develop at the same time.

P2-077

A Case of Rheumatic Meningitis with Refractory Progress due to Delayed Initial Treatment

Takuya Yanagida, Atsushi Omoto, Satoshi Omura, Masatoshi Kadoya, Wataru Fukuda

Center for Rheumatic Disease, Japanese Red Cross Society Kyoto Dai-ichi Hospital, Kyoto, Japan

Conflict of interest: None

An 80-year-old woman, who was diagnosed with rheumatoid arthritis 20 years ago, was admitted because of the joint pain. On the 7th day, a rapid decline in cognitive function appeared. Brain MRI revealed high signals in the brain groove and subarachnoid space of the temporal lobe and both side parietal lobes. Cerebrospinal fluid examination revealed increase in IL-6 value, increase in cells and decrease in Glucose. Malignant tumors and infectious diseases were negative, we diagnosed as rheumatic meningitis (RM). She was discharged on the 28th day because symptoms improved without treatment. However, symptoms worsened again and she was re-hospitalized. On the 56th day, Intravenous pulse steroids (methylprednisolone 500mg daily for 3 days) were administered, followed by oral corticosteroids (1.0mg/kg/day). However, symptoms worsened and intravenous cyclophosphamide (IVCY) was added but response was poor, speech became impenetrable at the third IVCY and IVCY was terminated. It is said that RM is often remissionable by steroid therapy in general. This case is an instructive case that showed fluctuation of symptoms at the time of onset and had a refractory course due to delayed treatment, and so we report this case with literature consideration.

P2-078

Two cases of rheumatoid meningitis with different clinical courses

Shoin Mo, Shunsuke Mori, Yasuo Suenaga

Department of Rheumatology, National Hospital Organization, Beppu Medical Center

Conflict of interest: None

Case 1, a 71-year-old male, without history of rheumatoid arthritis (RA), was admitted to our hospital because of fever, headache and gait disturbance. He was diagnosed with rheumatoid meningitis (RM) based on leptomenigeal biopsy specimens and the elevation of anti-cyclic citrullinated peptide antibody (ACPA) in serum and cerebrospinal fluid

(CSF). After treatment with high-dose prednisolone (PSL) and azathioprine, his symptoms improved. Case 2, a 78-year-old female with no prior history of RA presented with cognitive dysfunction and fever. On magnetic resonance imaging, leptomeningeal hyperintensities were observed and the leptomeningeal biopsy specimens revealed cryptococcus fungus body. Cryptococcus meningitis was considered and antifungal agent was started, however she showed consciousness disorder and polyarthritis. Because of the elevation of rheumatoid factor and ACPA in serum and CSF, she was diagnosed with RM. After the treatment with methylprednisolone pulse, she showed dramatic improvement of her consciousness and arthritis, nevertheless cognitive dysfunction was unchanged. Our cases with different clinical courses suggested that RM was not simple reflection of RA disease activity but that their immunological dysregulation could be correlated in their pathogenesis.

P2-079

A Case of RA Patient with Multiple Pulmonary Nodules and Pneumothorax

Akiko Sasaki^{1,2}, Yuya Takakubo^{1,2}, Suran Yang¹, Hiroharu Oki¹, Yasushi Naganuma¹, Yuta Suzuki¹, Hiroshi Orui¹, Michiaki Takagi¹

¹Department of Orthopaedic, Yamagata University Faculty of Medicine,

²Department of Orthopaedic, Yamagata Saisei Hospital

Conflict of interest: None

This case is 74-years old female with a 30-year history of seropositive RA with history of interstitial pneumonia. This patient was treated with tacrolimus and prednisolone, She was admitted due to the appearance of left chest pain in June 2016. Multiple pulmonary nodules accompanied with cavities were increased in CT scan of the chest. *Pseudomonas aeruginosa* was observed slightly in bronchial lavage fluid culture, Levofloxane was administrated. Pulmonary biopsy was performed for definitive diagnosis of nodules. Pathologically it was a diagnosis of rheumatoid nodule without observation of vasculitis. In order to strengthen RA treatment, administration of etanercept was started. Also, the administration was discontinued because of a rapid increase in the nodule shadow and pneumothorax in February 2017. Pneumothorax relieved with rest. We switched to tocilizumab in May, but it was showed a progression of joint symptoms. We switched to abatacept as third biologics in July of the same year. Pulmonary nodules continued to decrease and increase, but joint symptoms tend to reduce and continuing administration.

P2-080

Two cases of rheumatoid meningitis diagnosed with the brain magnetic resonance imaging

Takahito Uema, Keita Uehara, Tadashi Miyara
Naha City Hospital

Conflict of interest: None

The first case is a 68-year-old woman with 3-year history of rheumatoid arthritis (RA), who presented with a 2-month history of headache and occasionally low grade fever. She developed a generalized seizure with no abnormal finding in head CT. Mononuclear cells were mildly increased in the cerebrospinal fluid (CSF). Antibiotics was ineffective, and brain magnetic resonance imaging (MRI) showed abnormal arachnoid leptomeningeal enhancement in her both frontal lobes. The second case is a 60-year-old woman with about 20-year history of RA. Five months ago, she developed subarachnoid hemorrhage, and received coil embolization treatment. She felt the numbness and weakness of her left arms after a discharge. Head CT showed no rebleeding, and brain MRI showed abnormal arachnoid leptomeningeal enhancement in her right frontal lobes. Mononuclear cells were mildly increased in the CSF, but infectious disease was negative. We suspected rheumatoid meningitis (RM) and methylprednisolone pulse therapy was started in both cases. Subsequently, their symptoms and MRI findings rapidly improved. Though RM is rare complication in RA, and its diagnosis is difficult, it must be considered in patients with longstanding RA presenting with neurological symptoms. MRI features may support the diagnosis.

P2-081

Treatment of RA in advanced elderly group

Tamao Nakashita¹, Akira Yoshida¹, Akira Jibatake¹, Shinji Motojima¹, Daisuke Kato², Tamio Takahei³, Yoshiaki Kuga³

¹Rheumatology and Allergy, Kameda Medical Center, Kamogawa, Japan,

²Kato Daisuke Clinic, Futtsu, Japan, ³Tateyama Orthopedic Clinic, Tateyama, Japan

Conflict of interest: None

[Object] Percentage of elderly people is high particularly in Chiba-Boso area. Treatment of RA is done according to the guideline. However, the mean age of the patients in mega-study cited in the guideline was about 50, which is far different from that in our department (late sixties). We compared the treatment of RA in the advanced elderly group (≥ 75 years, group 1) with those in less than 75 years (group 2). [Methods] Subjects were 511 patients with RA, 145 in the group 1 and 366 in the group 2, respectively. [Results] The remarkable difference in the treatment was the use of MTX. The usage of MTX in the group 1 and group 2 were 45 % and 75 %, respectively. The median dose of MTX in the group 1 and 2 were 0 mg and 7.75 mg, respectively. The dosage of MTX inversely correlated the age and positively correlated with eGFR. MTX was not used in patients with eGFR of less than 35. Percentage use of PSL were 50 % (median 3.75 mg) in the group 1 and 12 % (median 0 mg) in the group 2, respectively. There were no differences in the use of SASP, BUC and bDMARDs, however the use of anti-TNF antibody was less in the group 1. The percentage of LDA + remission in group 1 and 2 were 84 % and 76 %, respectively. [Conclusions] Our treatment strategy is so far working well.

P2-082

Medical treatment for rheumatoid arthritis: discontinuation of corticosteroid therapy

Suguru Ohsawa¹, Masao Yukioka¹, Takaaki Shibuya²

¹Department of Rheumatology, Yukioka Hospital, Osaka, Japan, ²Department of Orthopaedic Surgery, Sumitomo Hospital

Conflict of interest: None

[Object] Elucidation of clinical factors for discontinuation of corticosteroid therapy with management of rheumatoid patients. [Methods] According to JCR guideline for the management of rheumatoid arthritis 2014, 161 patients with rheumatoid arthritis were clinically investigated retrospectively. We used 1987 ACR classification and 2010 ACR/EULAR new classification. [Results] Prednisolone (PSL) administration was started in 116 patients, mean age was 63 year-old, consisted 90 women and 26 men. Their mean disease period was 8 years, in which under one year was in 45 cases. All were followed for 79 months in average. At final observation, 66 cases were discontinued steroid therapy, other 50 cases were continued with mean dosage of 3mg. Mean age and disease duration were 59 year-old and 7 years in discontinued group, and 68 year-old, 9 years in continued one. Administration of methotrexate and biological DMARDs (included JAK inhibitors) were 58, and 28 in discontinued group and 30, 15 in continued one, respectively. Comorbidity of chronic renal disease was occurred in 0 case in discontinued group and 12 cases in continued one. [Conclusions] Factors for discontinuation of corticosteroid therapy for the patients with RA were small numbers of comorbidity and younger age.

P2-083

The Boolean remission rate and the annual hospitalization number for serious adverse events for high dose MTX monotherapy in Japanese patients with RA by NinJa 2017 cohort

Atsushi Kaneko¹, Toshihiro Matsui², Shotaro Mori¹, Yosuke Hattori¹, Tomotaro Sato¹, Masao Katayama³, Shigeto Tohma⁴

¹Department of Orthopaedic Surgery and Rheumatism, Nagoya Medical Center, ²Department of Rheumatology, Sagami National Hospital,

³Department of Collagen Disease and Rheumatology, Nagoya Medical Center, ⁴Department of Rheumatology, Tokyo National Hospital

Conflict of interest: None

[Object] The purpose of this current study is to review serious adverse event by MTX dose dependent in Japanese patients with RA. [Methods] In 15185 Japanese RA patients registered with NinJa2016, 4690 patients medicated MTX monotherapy without biological DMARDs and combination synthetic DMARDs were divided 6 groups by MTX dose once a weekly. 1-4mg/week n=565, 6mg/week n=1001, 8mg/week n=1219, 10mg/week n=767, 12mg/week n=548, over 14mg/week n=222, respectively. We defined hospitalization for various infectious disease, interstitial pulmonary disease, pancytopenia, malignant lymphoma as serious adverse event and research annual hospitalization in each group. [Results] The Boolean4 remission rate in each groups were 4mg groups 39.8%, 6mg 34.1%, 8mg 34.6%, 10mg 33.6%, 12mg 29.2%, over 14mg 27.1%, respectively. Incidence of serious adverse event of the all NinJa 2017 cohort was 662 patients (4.4%), and the OR with MTX each groups were 0.65, 0.73, 0.64, 0.51, 0.29, 0.72, respectively.

P2-084

Investigation of reduction and discontinuation of methotrexate in the treatment of rheumatoid arthritis patients

Toshiaki Tsukada¹, Yoichi Miyazaki²

¹Division of Rheumatology, Aino Memorial Hospital, ²Division of Orthopedic Surgery, Aino Memorial Hospital

Conflict of interest: None

[Object] The aim of this study is to evaluate the reason for reduction and discontinuation of methotrexate (MTX) in the treatment of rheumatoid arthritis (RA) patients. [Methods] Out of a group of 126 RA patients who have used MTX, we investigated 55 patients with history of reduction or discontinuation of MTX. We divided 55 patients into 4 groups. Group A: 7 patients with history of MTX reduction (less than 6 months), Group B: 15 patients with history of MTX reduction (more than 6 months), Group X: 13 patients with history of MTX discontinuation (less than 6 months), Group Y: 20 patients with history of MTX discontinuation (more than 6 months). [Results] In group A, MTX reduction was mainly due to liver dysfunction (57%). In group B, MTX reduction was also mainly due to liver dysfunction (40%). In group X, discontinuation of MTX was mainly due to renal dysfunction (54%). In group Y, MTX discontinuation was mainly due to deterioration of renal function (30%) and MTX pneumonitis (20%). [Conclusions] In group A and B, the reason for reduction of MTX was mainly liver dysfunction. In group X, discontinuation of MTX was mainly due to avoid the risk of MTX toxicity. In group Y, MTX was contraindicated for 9 of 20 cases and 70% of patients in this group were treated with biologics.

P2-085

The change of renal function in elderly patients with rheumatoid arthritis receiving MTX therapy

Hiroyuki Matsubara, Ryo Sato

Department of Orthopedic Surgery, Hekinan Municipal Hospital

Conflict of interest: None

[Object] Along with aging of populations, the number of elderly patients with RA is increasing. MTX is anchor drug for RA, but it is needed to use carefully in elderly people with renal dysfunction. Safety was examined in RA elderly patients who were receiving MTX. [Methods] Among RA patients over 75 years as of August 2018, patients receiving MTX for more than 1 year were included. We investigated the change of MTX dosage in 1 year and the change of renal function using eGFR. Changes in chest x-ray and urinalysis were also examined. [Results] There were 23 patients who were receiving MTX. Disease duration was 11.5 years, the RF positive rate was 90.0%. The rate of biologics use was 40%, the rate of PSL use was 50%, and the PSL dosage was 1.0mg. There was no significant change in the dosage of MTX from 6.2mg to 7.0mg per year. Although the eGFR was not significant from 68.5 to 62.3, it showed a decreasing trend. DAS28CRP was 2.59 ± 0.93 . There was no remarkable change in chest X-ray and urinalysis. There were no serious adverse events. [Conclusions] We showed that renal function tends to be lowered also in elderly patients who can receive MTX, and it was suggested that biologics were used in combination with MTX to control disease activity without increasing dosage of MTX.

P2-086

Safety of steroid administration in Japanese rheumatoid arthritis patients

Takao Kodera, Tomoki Takeda, Tomomi Tsutsumi, Yumiko Oka, Yuko Shiota, Miki Takeshita, Junichi Kameoka

Division of Hematology and Rheumatology, Tohoku Medical Pharmaceutical University Hospital

Conflict of interest: None

[Object] The opinions for using steroids for treating RA is changing with the decade. Although 2016 EULAR recommendation was revised that steroid should be used at the beginning of treatment, it contains concerns that it will fall into long-term use. In this study, we investigated the risk of prolonged steroid use in our cases. [Methods] We analyzed 930 RA patients at our hospital using odds ratios for vertebral body fractures, non-vertebral fractures, etc. [Results] Analysis of 364 cases is completed and the results of the intermediate analysis are reported. The number of patients with oral steroid was 110 (30.2%). The average age of the steroid users was 68.2 years, and the non-users 66.9 years ($P=0.37$). In patients with steroid use, 14 cases (12.7%) of vertebral fractures were observed and 14 cases (5.5%) without use. 9 (8.2%) vs 9 cases (3.5%) of non-vertebral fractures, 23 (20.9%) vs 24 cases (9.4%) of diabetes and 7 (6.4%) vs 3 cases (1.2%) of uroline stone were observed. Odds ratio (95% CI) were 2.50 (1.72-3.27), 2.43 (1.47-3.38), 2.53 (1.91-3.16), and 5.69 (4.31-7.05), respectively. Especially, the fracture rate of steroid use over 80 years old was high rate as 41.6% at 85 to 89 years old. [Conclusions] It seems that elderly RA patients should minimize the use of steroids.

P2-087

A retrospective study of the practice use of csDMARDs except MTX for RA

Risa Sagawa¹, Takashi Kida¹, Tomoya Sagawa¹, Akiko Kasahara¹, Kazuki Fujioka^{1,3}, Hidetake Nagahara¹, Shogo Toyama^{2,3}, Ryo Oda^{2,3}, Toshikazu Kubo^{2,3}, Makoto Wada¹, Masataka Kohno¹, Yutaka Kawahito^{1,3}

¹Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan, ²Department of Orthopaedics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan, ³Rheumatic Center, University Hospital, Kyoto Prefectural University of Medicine, Kyoto, Japan

Conflict of interest: None

Objective: Methotrexate (MTX) is known as the anchor drug for rheumatoid arthritis (RA), however, some patients can not be treated with MTX due to poor tolerability or contraindications. So other conventional synthetic disease-modifying antirheumatic drugs (DMARDs) are used for initial treatment, but how to use them is controversial. The aim of this study was to clarify the practice use of csDMARDs and patients' background in our hospital. Methods: RA patients who visited our hospital from January 2016 to July 2018 and initially treated with salazosulfapyridine (SASP), bucillamine (BUC), iguratimod (IGU), or tacrolimus (TAC) were enrolled. The medical records were reviewed retrospectively, and the persistent rate and the effectiveness of these drugs were investigated. Results: We identified 42 patients (SASP:28; BUC:9; IGU:3; TAC:2). The median age was 73 (65-78.5) years, and 30 patients (71%) were female. Persistent rate of initially selected drug at the end of 12 weeks from the start of treatment was 88% (37/42). Without any additional DMARDs, 11 of 42 patients (26%) presented low disease activity state: SDAI (simplified disease activity score) < 11. Conclusion: When MTX could not be used for some reasons, treatment with other csDMARDs may be a useful option.

P2-088

Efficacy of adding iguratimod therapy in rheumatoid arthritis patients who had inadequate response to biologic DMARDs

Toshiaki Miyamoto, Kenji Yamazaki, Ryuhei Ishihara

Internal Medicine and Rheumatology, Seirei Hamamatsu General Hospital

Conflict of interest: Yes

Objective Igaratimod (IGU) was approved in June 2012 and recommended by guideline 2014 in the treatment of rheumatoid arthritis (RA). Although there have been efficacy of monotherapy and concomitant MTX in clinical trials, however, there have been no reports of concomitant biologic DMARDs (Bio). Therefore, we investigated efficacy of concomitant IGU therapy in RA patients who had inadequate response to Bio at the author's institution. **Methods** Subjects were 94 patients adding IGU who had inadequate response to Bio from January 2014 to April 2018. Previous treatment Bio. was ADA. And baseline mean concomitant MTX was 12.4 mg/week. And baseline characteristics were Mean age 53.8 years, mean duration of illness 5.8 years, corticosteroid use 8.5% (mean 2.8mg/day). The course of DAS28, SDAI, CDAI and remission rates were analyzed. **Results** Mean DAS28-ESR, SDAI, CDAI were significantly decreased from the initiation of IGU treatment at 24 weeks (2.25, 2.60, 2.26), at 52 weeks (2.12, 2.49, 2.11). Remission rates of DAS28-ESR, SDAI, CDAI were 71.7%, 71.7%, 72.7% at 24 weeks, 73.4%, 79.8%, 79.8% at 52 weeks. There were almost no side-effect after adding IGU. **Conclusion** IGU might be a new RA treatment option for aiming remission in patients who had inadequate response to Bio.

P2-089

The analysis of retention rate of iguratimod: a multicenter retrospective cohort study

Koji Fukuda^{1,2}, Tsukasa Matsubara^{2,3}, Keiko Funahashi^{2,3}, Marowa Hashimoto³, Shinya Hayashi¹, Tomoyuki Kamenaga¹, Yoshinori Takashima¹, Yoshitada Sakai⁴, Ryosuke Kuroda¹

¹Department of Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan, ²Matsubara Mayflower Hospital, ³Research Institute of Joint Disease, ⁴Division of Rehabilitation Medicine, Kobe University Graduate School of Medicine, Kobe, Japan

Conflict of interest: None

[Object] In Japan, iguratimod (IGU) was applied in 2012 for RA treatment. Since then IGU has been widely administered in treatment for rheumatoid arthritis (RA). In this study, we evaluated the efficacy and the retention rate of IGU. [Methods] Among 336 RA patients who were treated with IGU at Matsubara mayflower hospital and a related facility, 120 patients who started administration of IGU at the facilities and were followed-up for over 6 months were included in this study. Retention rate, background data, and clinical data were evaluated. [Results] The retention rate of IGU at 6 months, 1 year, and 4 years after the start of IGU were 98.3 %, 98.3 %, 92.9 %, respectively. At the final survey in September 2018, 115 of 120 patients continued treatment of IGU. There was no statistically significant difference in age, sex, MTX dosage, PSL dosage, the value of clinical data at the start of IGU, and the IGU administration period between treatment continued group and discontinued group. However, CRP and ESR in continued group were significantly decreased at 6 months after the start of IGU. [Conclusions] In this study, the retention rate of IGU was high for a long time. Our results suggested that IGU treatment could be continued if CRP and ESR decreased 6 months after the start of IGU.

P2-090

Efficacy of iguratimod versus salazosulfapyridine as the first-line csDMARD for rheumatoid arthritis

Yuji Nozaki, Asuka Inoue, Koji Kinoshita, Masanori Funauchi, Itaru Matsumura

Department of Hematology and Rheumatology, Kindai University Faculty of Medicine

Conflict of interest: None

[Object] We retrospectively evaluated the retention rate and clinical responses following treatment for rheumatoid arthritis (RA) with iguratimod (IGU) versus salazosulfapyridine (SASP) as the first-line conventional synthetic disease-modifying antirheumatic drug (csDMARD). [Methods] We analyzed 197 RA patients who were treated with IGU or SASP as the initial treatment in the 3-year study period. The retention rate, clinical response, the dosage and percent user of prednisolone (PSL) and safety profiles were evaluated. [Results] At month 36, the retention rate of the IGU and SASP group was 55.1% vs. 32.1%. The rate of re-

sponders (good or moderate response) at month 36 was 85.8% vs. 65.2% in the IGU and SASP group. At month 36 for the IGU and SASP group, the percentages of PSL users were 16.7% vs. 46.7%, and the PSL dosage was 0.3 mg/day vs. 2.0 mg/day, respectively. The cumulative rates of any adverse event at month 36 were 19.8% vs. 29.2% in the IGU and SASP groups. [Conclusions] IGU is a useful first-line csDMARD treatment for RA patients, showing a high retention rate and good efficacy without an increased risk of serious adverse events, including serious infections. Our findings also indicate a PSL dose-sparing effect of IGU treatment.

P2-091

The incidence and risk factors for renal dysfunction due to iguratimod treatment

Akira Yoshida, Tamao Nakashita, Akira Jibatake, Shinji Motojima
Department of Rheumatology and Allergy, Kameda Medical Center, Chiba, Japan

Conflict of interest: None

[Object] Iguratimod (IGU) is now a commonly used csDMARD in Japan. Peptic ulcer and liver damage are well-known adverse drug reactions of IGU. However, renal dysfunction due to IGU is sometimes overlooked. We investigated the incidence and risk factors for renal dysfunction due to IGU in our institution. [Methods] We retrospectively reviewed all the patients attending to our clinic who received IGU before September 2018. Patients followed until 24 weeks from the initiation of IGU were included in the analysis. Here we defined renal dysfunction as follows: increase of serum creatinine by more than 0.2 mg/dL from the baseline at least twice during the observation period of 24 weeks. [Results] 248 patients were enrolled, and 196 were included in the analysis. The mean age was 62.3 ± 12.2 years. The mean body weight was 56.7 ± 11.3 kg. MTX, bDMARDs, oral glucocorticoids, and NSAIDs were used in 64.2%, 20.9%, 56.6%, 19.9% of the patients, respectively. The incidence of renal dysfunction at week 24 was 5.6%. The multivariate logistic regression analysis identified “baseline eGFR < 60 mL/min/1.73m²” as a risk factor for renal dysfunction (OR 7.1, *p* = 0.0052). [Conclusions] IGU should be administered with caution in patients whose eGFR < 60 mL/min/1.73m².

P2-092

Efficacy and safety of iguratimod in elderly patients with rheumatoid arthritis intolerant to methotrexate

Yuichi Takahashi

Yu Family Clinic

Conflict of interest: None

[Objective] To evaluate the efficacy and safety of iguratimod (IGU) in elderly patients with rheumatoid arthritis (RA) who cannot tolerate methotrexate (MTX) due to toxicity or other reasons. [Patients and methods] This study included 41 RA patients aged ≥65 years who met the 2010 ACR-EULAR classification criteria for RA. Patients were treated with IGU in the standard dose and assessed for VAS, CRP, DAS28, ESR, and HAQ-DI between weeks 0 and 52 of treatment. [Results] Patients' mean age was 73.9 years and mean disease duration was 10.7 years. The mean baseline CRP and DAS28ESR were 2.02 mg/dL and 4.43, respectively. Patient-reported VAS, CRP, and DAS28ESR were reduced after treatment with IGU and stabilized by week 24. Remission based on DAS improvement was observed from week 12, with 50% patients showing remission or low disease activity at and after week 24. A marked decrease in patient-reported VAS was seen by week 8, suggesting high patient satisfaction level. No adverse event requiring IGU discontinuation was seen. [Discussion] The present results suggest that IGU is a viable option for elderly RA patients intolerant to MTX.

P2-093

Interstitial lung disease during iguratimod treatment

Akira Yoshida, Tamao Nakashita, Akira Jibatake, Shinji Motojima
Department of Rheumatology and Allergy, Kameda Medical Center, Chiba, Japan

Conflict of interest: None

[Object] Igaratimod (IGU) is a csDMARD developed in Japan. According to the post-marketing surveillance of IGU, the incidence of interstitial lung disease (ILD) is reported to be 1.16% at week 52. However, these “ILD cases” also include infection such as pneumocystis pneumonia, other drug-induced lung injury, and RA-ILD. Thus, we still do not know the exact incidence and nature of ILD induced by IGU. [Methods] We retrospectively reviewed all the 248 patients attending to our clinic who received IGU before September 2018. [Results] 4 patients developed ILD, and the incidence was 1.6%. One patient was a man, and the other 3 were women. They were 64, 63, 60, and 53 years old, respectively. 3 patients had concomitant or previous history of ILD. MTX and etanercept were used in 2 and 1 patients each. The onset of ILD were 4, 16, 46, and 34 weeks from the initiation of IGU, respectively. No patients experienced respiratory failure, and only 1 needed hospitalization. None of the cases were clearly attributable to IGU itself, since other drug-induced lung injury and exacerbation of RA-ILD were highly possible differential diagnosis. [Conclusions] Further studies are necessary to determine the exact incidence and risk factors for ILD induced by IGU.

P2-094

Effects of acetaminophen on the kidney functions of patients with non-traumatic orthopedic disease treated with long-term nonsteroidal anti-inflammatory drug therapy

Toshiaki Aizawa¹, Tetsuya Kawano¹, Takeshi Kashiwagura², Naohisa Miyakoshi³, Yoichi Shimada³

¹Department of Orthopedics Surgery, Kitaakita Municipal Hospital, ²Department of Orthopedic Surgery, Akita City Hospital, ³Department of Orthopedic Surgery, Akita University Graduate School of Medicine

Conflict of interest: None

[Object] To investigate the kidney functions of patients with non-traumatic orthopedic disease who had been using NSAIDs for a long time and examined the possibility of switching to acetaminophen (AAP). [Methods] The subjects were 105 patients who had been using NSAIDs for at least 3 months. After checking their background characteristics, we measured their kidney functions and VAS scores, and then switched them from NSAIDs to AAP. Six months after the switch, we remeasured their kidney functions and VAS scores, and investigated whether they could continue using AAP and whether they had used NSAIDs. [Results] The patient's mean age was 76 years, and their mean duration of NSAID use was 43 months. The mean VAS was 41 mm and mean eGFR was 67.0 mL/min/1.73 m². After the switch, 69 patients had continuously used AAP. Of these patients, 13 had used NSAIDs for rescue purposes. Overall, the mean VAS declined significantly as compared with before the switch, as did the mean eGFR. Of those who continued to use AAP, 56 patients who did not use any NSAIDs exhibited significantly lower mean VAS scores, but not a significant decline in mean eGFR. [Conclusions] Halting NSAIDs and switching to AAP could help maintain kidney functions, which could continue to decline with NSAID use.

P2-095

Investigation of an influence of body weight on DMARDs selection -a nationwide database study, NinJa2017-

Hideo Ohtsubo¹, Takemasa Matsuda¹, Toshihiro Matsui², Shigeto Tohma³

¹Center for Rheumatic Diseases, Japanese Red Cross Kagoshima Hospital, ²Department of Rheumatology, NHO Sagami National Hospital, ³NHO Tokyo National Hospital

Conflict of interest: None

[Object] Our aim is to investigate if weight influence on DMARDs selection in Japan using a nationwide database (National Database of Rheumatic Diseases by iR-net in Japan, NinJa) [Methods] We examined the impact of weight in DMARDs selection in 13298 patients of NinJa2017. [Results] Age of all patients 65.9±13.2 y.o., body weight 54.1±11.1kg, DAS28-ESR 2.9±1.2, DAS28-CRP 2.3±1.0, salazosulfapyridine 54.8±11.7kg, bucillamine 53.8±11.1kg, iguratimod 53.8±11.2kg, methotrexate 54.6±11.0kg, tacrolimus 53.0±10.5kg, leflunomide 52.8±11.1kg, infliximab 55.0±10.4kg, infliximab BS 55.1±9.2, etanercept

54.2±10.7kg, adalimumab 55.5±10.6kg, certolizumab pegol 54.9±12.4kg, tocilizumab 54.8±11.2kg, abatacept 53.3±11.1kg, tofacitinib 55.7±11.8kg, denosumab 47.9±9.7kg [Conclusions] Mean weight of patients injected denosumab was light (47.9kg). Mean age of these patients was high (74.1±10.3 y.o.), but they weighed less than expected (52.6kg) from (65.2-0.17×age) their age. No patients administered other drugs had any difference in weight. As for tocilizumab, there is no dose set per body weight. So we examined the relationship between body weight and route of tocilizumab administration. There was no difference in weight between percutaneous and intravenous administration of tocilizumab.

P2-096

A case report of tuberculous subcutaneous abscess in a rheumatoid patient's lower leg

Junpei Inoue, Kunio Yamada, Hideki Muro, Keisuke Hoshino, Kaneaki Tawada, Shinji Funahashi

Komaki City Hospital, Komaki, Japan

Conflict of interest: None

[Introduction] Methotrexate (MTX) have a risk of extrapulmonary tuberculous, but it is rare that extrapulmonary tuberculous occur in a lower leg. We report a rheumatoid patient suffered tuberculous subcutaneous abscess in the lower leg. [Case report] The patient was a 74-year-old woman. RA was diagnosed at the age of 50 years. MTX had been prescribed for 8 years. She was aware of gradually increasing mass in her lower leg for 3 months. Abscess was diagnosed by a plastic surgeon and was cutted open. But the mass didn't improve and she came to our hospital. Her lower leg had a pus-like discharge from the incision. RA activity was controlled well with MTX 10 mg / week. The mass 10cm in diameter was resected. Pathological examination revealed caseating granuloma and tuberculous was cultured after 6 weeks. So she started to take anti-tuberculosis drugs. [Conclusion] Rheumatoid patients treated with immunosuppressive drug have risk of extrapulmonary tuberculous.

P2-097

A case of Methotrexate-associated lymphoproliferative disorder (MTX-LPD) developed by short-term MTX therapy, shrunk spontaneously 1 month after MTX cessation

Hiroshi Shimagami, Taro Akira, Michiko Ohashi, Masashi Okamoto, Takehiro Hirayama, Akira Mega, Yoshinobu Matsuura, Akihiro Nakabayashi, Yoshinori Katada

Sakai City Medical Center

Conflict of interest: None

Chief complaint: fever History of Present Illness: A 87-year-old woman with rheumatoid arthritis taking 8mg/week of MTX and 5mg/day of Prednisolon presented pulmonary opacity 2 months before. Fever, sweating while sleeping, and weight loss gradually appeared. Laboratory findings included WBC7190/μL, Lymphocyte 215/μL Hb7.6g/dl Cr1.1mg/dl CRP12.1mg/dl sIL-2R 3132U/ml. CT scan revealed multiple pulmonary nodular shadows in both lung fields. Bronchoscopic biopsy was conducted, showing diffuse large B cell lymphoma. Then MTX was stopped, and PSL was increased to 10mg/day. We observed her without any chemotherapies. For 21 days after MTX cessation, multiple lung nodules did not shrink. But it became smaller on 28th day. Discussion: In average, 1500mg of cumulative dose and 30 months of administration period were required for development of MTX-LPD. In this case, however, it was developed after short term administration. The nodules needed four weeks to start to shrink after MTX cessation, although it usually starts in two weeks. Hyporenal function might be the reason of these phenomenon.

P2-098

A case of Methotrexate-related lymphoproliferative disorder complicated by EB virus meningitis

Hiroaki Nakagawa, Ayaka Inoue, Midori Kitayama, Takuro Maeda, Noriaki Yo, Chihiro Tanaka, Takashi Yamane

Kakogawa City Hospital

Conflict of interest: None

[Case] A 70-year-old man who had diagnosed as RA at the age of 65 and treated with abatacept, MTX, iguratimod, and prednisolone, admitted with complaint of malaise and fever from 1 week ago. CT revealed systemic lymphadenopathy, and blood test revealed high LDH and sIL - 2R. Since the symptoms did not improve by discontinuation of MTX and consciousness disturbance also appeared, we started GC pulse therapy. EB VCA-IgG was 640-fold, EBNA was negative, and EB virus DNA was positive, EBER positive lymphocytes were observed from lymph node biopsy and diagnosed as MTX-LPD. We also diagnosed that meningoencephalitis caused by EB virus, because mononuclear cells were increased and EB virus DNA was positive in CSF. While we tapered the prednisolone, he developed convulsion and had been impaired consciousness even after cessation. We diagnosed as nonconvulsive status epilepticus from the EEG, and his consciousness improved after initiating carbamazepine. Higher order dysfunction gradually improved and EB virus DNA changed to negative in the final examination. The CT showed lymph node reduction, it was thought that he recovered from MTX - LPD. [Clinical Significance] This is a rare case that MTX-LPD causes EB virus meningitis.

P2-099

A case of golimumab-resistant rheumatoid arthritis complicated with psoriasis who was successfully treated by addition of tacrolimus

Junichi Konma, Yumiko Wada, Takeshi Shoda

Department of Rheumatology, Yodogawa Christian Hospital, Osaka, Japan

Conflict of interest: None

A 57-year-old man had gradually complained polyarthralgia and weight loss since the beginning of 2017, he visited our hospital in August. On examination, he had bilateral joint swelling and tenderness in fingers, shoulders, elbows, and knees. He also had red patches covered with scales on scalp and finger nail pitting, so we diagnosed him with psoriasis. Laboratory tests showed elevated levels of CRP, ESR, MMP-3, and RF was positive, ACPA was negative. Joint US demonstrated synovitis in joints of left MCP and both wrists. Joint X-ray did not show bone erosion or new bone formation. He was diagnosed with rheumatoid arthritis (RA) in high disease activity (DAS28-CRP 5.7), but he also could be diagnosed with psoriatic arthritis (PsA). He had interstitial pneumonitis (IP), so we did not use methotrexate and started golimumab (GLM) 100mg/4weeks. But GLM was not fully effective, then we added tacrolimus (TAC) 3mg/day in late November, his symptoms were dramatically improved in 1 month later. He achieved remission (DAS28-CRP 1.1) with negative CRP levels in 3 months later. In addition, his rash and IP were also improved. After we reduced GLM to 50mg/4weeks in late April 2018, he has been in remission. We report the case with review of the literatures.

P2-100

Comparison of cycling and swapping of biological agents in patients with rheumatoid arthritis

Masako Hayashibara¹, Keita Nagira¹, Chikako Takeda¹, Daichi Mukunoki¹, Hiroshi Hagino², Hideki Nagashima¹

¹Department of Orthopedic Surgery, Faculty of Medicine, Tottori University, Tottori, Japan, ²Department of Life Science, Faculty of Medicine, Tottori University, Tottori, Japan

Conflict of interest: None

[Object] It is sometimes difficult to determine the second or third course of biological disease-modifying anti-rheumatic drugs (bDMARDs) when the primary bDMARDs treatment is ineffective or causes adverse events in rheumatoid arthritis (RA) patients. We assessed the reason for switching bDMARDs and subsequent outcomes in our department. [Methods] We studied 49 RA patients who had their primary bDMARDs treatment switched over six months. Five men and 44 women were included, mean age was 69.2 (range: 38-88) years and mean disease duration was 14.6 (range: 2-47) years. Patients were divided in two groups, cycling group (group C), 12 patients who switched to a same class of bi-

ologic agent, and swapping group (S group), 37 patients who switched to a different class (S group). [Results] Methotrexate (MTX) was used in combination in 9 patients (75%) in group C and 15 patients (41%) in group S. The reasons for switching were an insufficient treatment response in group C and adverse events in group S. In both groups, at least 80% had low disease activity or remission following treatment. [Conclusions] Many patients switched bDMARDs due to adverse events in Group S. It is suggested that a swapping strategy is effective for patients who need to switch to bDMARDs with adverse events.

P2-101

Cost-effectiveness of biological DMARDs for rheumatoid arthritis

Masahiko Miya

Department of Rheumatology, Asama Nanroku Komoro Medical Center

Conflict of interest: None

[Object] We examined the effectiveness of biological DMARDs in rheumatoid arthritis treatment from the viewpoint of drug expenses. [Methods] For the 139 treatments of 72 patients who received the biological DMARDs at our hospital, the cost-effectiveness of each preparation was calculated. Improvement in CDAI score (Δ CDAI) per drug cost was calculated at 12 weeks and 52 weeks after dosing. The cost effectiveness was compared with Δ CDAI per 10,000 yen of drug cost for 4 weeks. [Results] Calculating the cost-effectiveness of each formulation with Δ CDAI per 10,000 yen of drug cost for 4 weeks, Tocilizumab was more cost-effective than other drugs, and golimumab and infliximab were inferior in cost-effectiveness. [Conclusions] Tocilizumab is inexpensive, and the drug cost is further reduced by decreasing dosage and prolonging the administration interval. Golimumab and infliximab were allowed to gain dose, resulting in poor cost effectiveness. In terms of drug selection, not only the effectiveness but also cost-effectiveness is necessary.

P2-102

Golimumab Treatment in Patients with Rheumatoid Arthritis -Influences of Baseline Disease Activity-

Yuji Hirano, Daisuke Kihira, Yukiyo Oishi

Department of Rheumatology, Toyohashi Municipal Hospital

Conflict of interest: Yes

[Object] The aim of this study is to evaluate efficacy of golimumab (GLM) in patients with RA, especially influences of baseline disease activity. [Methods] Toyohashi RA database was used. 68 RA patients treated with GLM were used 57 female and 11 male. Disease activity, drug retention rates (Kaplan-Meier) and concomitant drugs were investigated. H group in which baseline disease activity was high (DAS28-CRP 4.1) was compared with M group (2.7-4.1). [Results] Mean age was 61 years old. Mean RA duration was 12.4 years. 91.2% of cases were treated with concomitant MTX. Time-course of mean DAS28-CRP was 3.4-2.3-2.2-2.1-2.2 (0-3-6-12m-last observation). Remission rate at last observation was 65.1%. Drug retention rates were 80.8% at 1 year, 71.3% at 3 years and 62.9% at 5 years. Concomitant rates of PSL were 35% at baseline and 9% at last observation. Concomitant rates of MTX were 89% at baseline and 69% at last observation. Remission rate at last observation were 47.4% in H group and 71.4% in M group. Rates of GLM 100mg treatment at baseline and last observation were 37% and 63% in H group and 29% and 54% in M group. [Conclusions] GLM was effective in RA treatment in real-world clinical setting. In case of high disease activity, GLM 100mg treatment was effectively used.

P2-103

Investigation of rheumatoid arthritis cases using infliximab BS

Masao Sato¹, Masao Takemura², Tomohisa Tani¹, Toshiro Ohashi¹

¹Ohashi-Tani Orthopedics, Gifu, Japan, ²Advanced Diagnostic System Research Laboratory, Fujita Health University

Conflict of interest: Yes

[Objectives] The use of biological drugs (BIO) for rheumatoid arthritis (RA) has significantly improved patient QOL. Biosimilars (BS) with

the same effectiveness and lower drug prices have appeared. We examined cases using infliximab BS (IFX-BS). [Methods] Ten RA cases using IFX-BS so far were examined mainly on the reasons for introduction, efficacy, adverse events, etc. [Results] The breakdown of 10 cases was 2 males and 8 females, ages 43 to 72 years, average 57.1 years. The format of IFX-BS introduction is 6 cases of changes from the original infliximab (IFX), 2 cases of BIO naïve, a switch case from other BIO and a case with history of IFX administration in the past. The total number of times IFX administration was administered at the time of changing the six cases changed from IFX was 2 times, 13 times, 20 times, 63 times, 74 times, and 109 times. The dose (mg / week) of MTX was 4 to 10, and the average was 7.33. Nine out of ten cases have good effectiveness and are under observation for 2 to 9 months, on average 4.7 months. Invalid was a drug-free and re-burned case, we switched to another BIO. There were no adverse events due to use of IFX-BS. [Discussion] The effectiveness of IFX-BS is not inferior compared to IFX and it might become one of the BIOs useful for RA patients.

P2-104

Efficacy and economic performance of infliximab BS in patient with rheumatoid arthritis in a routine care

Yutaka Yoshioka
Handa City Hospital

Conflict of interest: None

[Objectives] Infliximab BS (IFXBS) is a biosimilar of infliximab that has been prescribed as a first line treatment in patient with rheumatoid arthritis (RA) after inadequate response to methotrexate in our hospital. In this study, we investigated the efficacy and economic performance of IFXBS in RA patients. [Methods] RA patients with an inadequate response to methotrexate (MTX) and treated with IFXBS as a first-line biologic agent for longer than 52 weeks were included in this study. We retrospectively reviewed the clinical data. [Results] Sixteen patients were included in this study. Mean age was 63 years old and mean disease duration was 11 years. Mean DAS28-CRP was 4.2 at baseline and 1.4 at 52 weeks. The number of patients who withdrew from IFXBS was six (adverse events: two patients, lack of efficacy: four patients). [Conclusion] IFXBS was effective in RA patients in a routine care. This study provides support for the possible use of IFXBS as a first line treatment in RA patients with an inadequate response to MTX.

P2-105

Assessment of sarilumab for the rheumatoid arthritis patients in real world rheumatology practice

Takeshi Suzuki, Takayasu Ando, Yutaka Goto, Harunobu Iida, Marina Uchida, Kana Ishimori, Hisae Fujimoto, Hiromi Matsushita, Keiichi Sakurai, Tomofumi Kiyokawa, Yukiko Takakuwa, Kumiko Tonooka, Mitsuru Imamura, Yoshioki Yamasaki, Hiroko Nagafuchi, Seido Ooka, Kimito Kawahata

Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine

Conflict of interest: None

[Objective] To assess sarilumab (SAR) for rheumatoid arthritis (RA) in real world rheumatology practice. [methods] Eligible patients had to have a diagnosis of RA and was treated with SAR after its approval. Clinical disease activity was determined using the DAS28-CRP3 (DAS). MRIs of dominant hands at baseline and follow up were obtained in some patients and scored using the RAMRIS system [Result] Fifteen patient was include in this study. The mean (\pm SD) age, disease duration and DAS28-CRP3 at baseline was 72.3 \pm 9.8y, 9.2 \pm 11.5y and 5.00 \pm 1.10. Only 2 patients were bio-naïve and the average number of DMARDs (biologics + JAK inhibitor) before SAR use was 3. DAS was decreased significantly at week 8. The persistence rate at week 16 was 53.3%. The reason for discontinuation was inefficacy (n=3), drug eruption (n=3) and liver enzyme elevations (n=1). RAMRIS synovitis score of a patient who had an inadequate response to tocilizumab was obviously decreased 7 to 3 and bone edema score was 2 to 1. [Conclusion] We conclude that persistence rate of SAR was comparatively acceptable for the RA patients who have long disease duration and had inadequate response to many biologics and

JAK inhibitors and there might be a possibility of effectiveness of switching among different anti-IL-6 receptor antibody.

P2-106

Usefulness of shortening the administration period when the effect of tocilizumab subcutaneous injection is diminished

Masao Sato¹, Masao Takemura², Tomohisa Tani¹, Toshiro Ohashi¹

¹Ohashi-Tani Orthopedics, Gifu, Japan, ²Advanced Diagnostic System Laboratory, Fujita Health University

Conflict of interest: Yes

[Objective] To investigate the utility of shortened period administration in Tocilizumab subcutaneous injection (TCZ) cases. [Methods] Fifteen rheumatoid arthritis (RA) cases in whom TCZ was introduced and observed for more than 24 weeks were included. [Results] The breakdown of cases was 2 men, 13 females, aged 40 to 83 years old, and the average age was 61.3 years. Seven cases were BIO naïve cases, and 6 cases from other BIOs, 2 cases of tocilizumab infusion to TCZ. From the administration interval of TCZ, there were 5 cases each with 14 days or more (no shortening group), shortening 9 to 10 days (9 to 10 days group), shortening 7 days (7 days group). Disease activity at the time of introduction of TCZ in each group tended to be higher in 7 days group. Six patients returned to the administration interval of 14 days or more within 2 months of shortening introduction. Four patients are continuing administration for 6 to 13 months at intervals of 7 to 10 days. Disease activity changes of 10 cases from the time of shortening start to at 24 weeks were 3.28 \rightarrow 1.33 on DAS28-ESR (average) and 2.90 \rightarrow 1.40 on DAS28-CRP. [Discussion] TCZ was thought to be a drug capable of enhancing the drug effect by shortening the administration interval when the effect was weakened.

P2-107

Effect of Abatacept on the level of serum TRACP-5b in Rheumatoid Arthritis

Masayasu Kitano¹, Kazuyuki Tsuboi¹, Mai Nakano¹, Takahiro Yoshikawa¹, Teppei Hashimoto¹, Mai Morimoto¹, Naoto Azuma¹, Hajime Sano², Kiyoshi Matsui¹

¹Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, ²Division of Rheumatology, Kyoto Okamoto Memorial Hospital

Conflict of interest: None

[Object] To clarify the effect of abatacept (ABT) on serum tartrate resistant acid phosphatase (TRACP)-5b in rheumatoid arthritis (RA). [Methods] 28 patients with active RA (all females, mean age:56.7 years, mean disease duration:6.0 years, mean SDAI:21.7, ACPA positive:75%, oral PSL use:61%, mean PSL dose:4.9mg/day, MTX use:75%, mean MTX dose:7.1mg/week, bDMARDs naïve:100%) were started on treatment with ABT for 24 weeks. Serum levels of TRACP-5b were examined by EIA at the baseline and after 12 and 24 weeks. [Results] In the course of ABT treatment, the score of SDAI at 12 and 24 weeks decreased significantly from the baseline (21.7 vs 10.5 vs 9.5: p<0.01). The response for ABT treatment was divided into good responder, moderate responder, and no responder by EULAR criteria. In good responder, TRACP-5b levels at 24 weeks were decreased significantly from the baseline (223 vs 125mU/dl: p<0.05). Moreover, the baseline value of TRACP-5b correlated well with the rate of change value of TRACP-5b after ABT treatment for 24 weeks (R²=0.479, p=0.0267). [Conclusions] Recent study shows ABT improves osteoclastogenesis of RA via the control of inflammation and apoptosis of osteoclast precursor cells. Thus, we conclude that the suppression of TRACP-5b may be specific for ABT treatment.

P2-108

Denosumab ameliorates MRI imaging of synovitis and bone edema in rheumatoid arthritis

Keisuke Hasui, Hirotake Sakuraba, Hiroto Hiraga, Nahoko Tanaka, Rina Watanabe, Yasuhisa Murai

Department of Gastroenterology and Hematology, Hirosaki University Graduate School of Medicine

Conflict of interest: None

[Object] To evaluate the effectiveness of denosumab for rheumatoid arthritis. [Methods] A total of 9 patients treated with denosumab were included in this single center, retrospective study during 2016 and 2018. We compared DAS28-ESR (4) and MRI score according to the Simplified Rheumatoid Arthritis MR Imaging Score (SAMIS) at the beginning of treatment and one year later. [Results] All patients were females. Median age was 75.0 (65-82) years old and disease duration was 10.0 (7.3-22.0) years. 6 patients had malignant diseases. Prednisolone and salazosulfapyridine were used in 5 cases and methotrexate and biologics were used in one case respectively. The mean of DAS28-ESR (4) was 4.6 ± 1.4 at the beginning of treatment and was 3.9 ± 0.8 at one year after treatment. There was no significant improvement. SAMIS, synovitis and bone edema were significantly improved from 22.3 ± 14.5 to 19.6 ± 14.9 ($P=0.0196$), from 6.0 ± 3.5 to 4.8 ± 3.3 ($P=0.0384$) and from 2.5 ± 2.6 to 0.9 ± 1.6 ($P=0.0203$) respectively. There was no significant change in erosion from 13.8 ± 13.4 to 13.9 ± 13.8 . [Conclusions] Denosumab was tended to be used in cases of which could not be treated with MTX or biologics due to malignancy. Our study of MRI findings suggested that denosumab might have inhibitory effects of bone destruction.

P2-109

Study for RA therapeutics after use of IFN-free treatment; Anti-viral therapy (DAA; Direct acting antiviral), for patients with HCV RNA positive in our hospital

Yuichiro Yabe

Department of Rheumatology, JCHO Tokyo Shinjuku Medical Center, Shinjuku, Tokyo, Japan

Conflict of interest: None

[Purpose] Anti-viral therapy (DAA; Direct acting antiviral) can eliminate HCV. RA first selection Drug MTX refrain from use in the hepatitis virus infection sustained cases. There is no definite view for RA treatment after HCV exclusion in DAA therapy. Report on RA treatment after DAA therapy. [Object] From 2008-2018, 14 RA cases were HCV antibody positive. 6 cases of HCV were RNA positive. 3 cases of DAA recipe (Ombitasvir/Paritaprevir/Ritonavir (OBV/PTV/r) 2 cases, sofosbuvir + ribavirin (SOF + RBV) 1 case) were studied. [Methods] Introduction of anti-rheumatoid drugs were shown comparison of HCV RNA positive 6 cases and HCV RNA negative 8 cases, and also clarified about 3 cases of DAA recipe with complications. [Results] About HCV RNA negative, MTX5, SSZ3 cases were introduced. In HCV RNA positive, MXT8mg+ABT+PSL, BUS, SSZ, TAC, GST, DMARDs-free, each one case, were introduced. Three RA cases received ADD kept HCV RNA-negative. One case of ADD was added MTX to GST. One RA case with liver cancer and HCV RNA positive, was received first cancer treatment, and then ADD, moved into HCV RNA negativity. In this case, liver cancer recurrence happened was cared by surgery. [Conclusions] After the HCV RNA-negative achievement of DAA, we can use MTX, bi-DMARDs, recommend checking real liver.

P2-110

Local biologic registry for the patients with rheumatoid arthritis in our hospital -ZAO registry-

Yuta Suzuki, Yuya Takakubo, Yasushi Naganuma, Akiko Sasaki, Suran Yang, Hiroharu Oki, Hiroshi Orui, Michiaki Takagi
Yamagata University Faculty of Medicine Department of

Conflict of interest: None

[Objectives] The aim of this study was to investigate our local biologic (BIO) registry (ZAO registry) for the patients with rheumatoid arthritis (RA) in our hospital. [Methods] 295 patients were registered with ZAO registry from 2004 to April 2018. Switching and changing BIO was decided by the judgment of each doctor. [Results] Of 295 patients, 226 subcutaneous injection, 56 intravenous fluid preparations and 13 oral agents were consisted. Kinds of BIO are TNF inhibitors (TNFi), 218 cases; IL-6i, 45 cases; abatacept (ABT), 19 cases; and Tofacitinib (Tofa), 13 cases. 2nd switching BIO were TNFi, 32 cases; Tocilizumab (TCZ), 13 cases; ABT, 5 cases; and Tofa, 5 cases. 3rd switching BIO were TNFi, 6

cases; IL-6i, 6 cases; ABT, 3 cases; and Tofa, 2 cases. 4th switching BIO were TNFi, 2 cases; TCZ, 1 case; ABT, 1 case; and Tofa, 1 case. 5th switching BIO were TNFi, 3 cases and TCZ, 1 case. 6th switching BIO was ABT, 1 case. We had 38 withdrawn cases consisting with TNFi, 28 cases; TCZ, 6 cases; ABT, 2 cases; and Tofa, 2 cases. The reasons why to withdraw were adverse events in 28 cases. [Discussion] Subcutaneous injection preparations tended to be selected compared to intravenous preparations for the patients with RA in our hospital. The continuation rate of 1st BIO was 64% (213/333).

P2-111

Two cases with rheumatoid arthritis achieving low disease activity immediately after switching from other biologic agents to sarilumab

Masahiro Yokosawa, Hirofumi Toko, Taihei Nishiyama, Shota Okamoto, Masaru Shimizu, Fumika Honda, Ayako Ohyama, Atsumu Osada, Izumi Kurata, Mizuki Yagishita, Saori Abe, Hiroyuki Takahashi, Yuya Kondo, Hiroto Tsuboi, Isao Matsumoto, Takayuki Sumida

Department of Internal Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan

Conflict of interest: None

[Case 1] A 70-year-old woman, who was diagnosed with rheumatoid arthritis (RA) three years ago. Since her symptoms were not improved by prednisolone and methotrexate (MTX), she had been treated with golimumab, however, high disease activity continued. Although DAS28-CRP and CDAI were 4.4 and 19.9 respectively before switching to sarilumab (SAR), low disease activity (LDA) was achieved immediately after the initiation of SAR. After 8 weeks of administration, improvement of synovitis was confirmed by joint ultrasonography (jUS). [Case 2] A 40-year-old woman, who was diagnosed with RA more than 10 years ago. Although she had been treated with the monotherapy of etanercept or adalimumab, or with combination abatacept, tocilizumab or certolizumab pegol and MTX, all of them resulted in primary or secondary failure. Discontinuation of MTX due to adverse effects triggered, and the disease activity rose to high (DAS28-CRP: 4.18, CDAI: 23.5). She was treated with SAR, and LDA was achieved immediately. After 10 weeks of administration, the improvement of synovitis was confirmed by jUS. [Conclusion] Regardless of whether MTX was used, the rapid improvement of RA was achieved with switching to SAR in cases inadequately responded to other biologic agents.

P2-112

A case of rheumatoid arthritis associated with tuberculous pleuritis with a positive conversion of T-SPOT, during anti-TNF-alpha antibody therapy

Yohei Hosokawa, Hiroshi Oiwa

Department of Rheumatology, Hiroshima City Hiroshima Citizens Hospital, Japan

Conflict of interest: None

An 80-year-old woman with rheumatoid arthritis (RA), suffering high fever and right pleuritic pain for three weeks, was admitted to our hospital. Eight months previously, she was diagnosed with RA, and started to take methotrexate. Five months previously, treatment with anti-TNF- α antibody was added to her regimen, when the result of screening test for latent tuberculosis infection, T-SPOT, was negative. CT of the chest showed right pleural effusion and right pulmonary infiltrates. The pleural fluid analysis revealed a white blood cell count of $2094/\mu\text{L}$ with 61% of lymphocytes and an ADA level of 127U/mL. The result of the T-SPOT showed a positive conversion. The diagnosis of tuberculous pleurisy was made, and the patient improved after the antituberculous drugs. Six weeks after the diagnosis, M. tuberculosis was cultured from the bronchoalveolar fluid. Immune system against tuberculosis was achieved through formation and maintenance of the granuloma, which TNF- α and IFN- γ play a major role on. Anti-TNF- α antibody binds to TNF- α -expressing macrophages, leading to apoptosis, and also suppresses production of IFN- γ . Our experience indicates that tuberculosis could be reactivated during anti-TNF- α antibody therapy, even after a negative result of T-SPOT.

P2-113

Analysis of clinical factors related to HAQ in RA patients treated with golimumab

Katsuaki Kanbe

Nippori Rheumatology Clinic

Conflict of interest: None

[Object] In order to analyze clinical factors related to RA patients treated with golimumab [Methods] 57 patients was investigated in HAQ-DI treating in our clinic, mean age with 62.8 years, mean disease duration with 12.7 years, by using Pearson correlation and multiple logistic analysis. [Results] Mean DAS28 (CRP) was 2.78 and mean HAQ-DI was 0.66. Correlation to HAQ-DI were stage ($p=0.007$, $r=0.351$), class ($p<0.001$, $r=0.510$), CRP ($p=0.013$, $r=0.327$), RF ($p=0.004$, $r=0.379$), DAS28 (CRP) ($p<0.001$, $r=0.548$). In multiple logistic analysis showed stage ($p=0.687$), class ($p=0.044$), CRP ($p=0.524$), RF ($p=0.093$), DAS28 (CRP) ($p=0.001$). [Conclusions] HAQ-DI was related to DAS28 (CRP) significantly meaning that regulation of disease activity by tight control was most important among other clinical factors in golimumab treated patients in RA.

P2-114

The efficacy of golimumab for elderly patients with rheumatoid arthritis

Kaneaki Tawada, Kunio Yamada, Keisuke Hoshino, Shinji Funahashi, Junpei Inoue

Department of Orthopaedic Surgery, Komaki City Hospital

Conflict of interest: None

[Object] The purpose of this study was to investigate the efficacy and safety of GLM for the elderly RA patients. [Methods] Eighteen RA patients over 65 years old treated with GLM were included in this study (4 males, 14 females, average age 71.4 years old, average disease duration 14.1 years). MTX was used for 15 patients, the average dose was 5.2 mg / week. There were 15 bio naïve cases and 3 switch cases. CRP, MMP-3, DAS28-CRP, CDAI and SDAI at baseline and 52 weeks were used for the estimation of the efficacy, and complications were investigated. [Results] At baseline the average CRP, MMP-3, DAS28-CRP CDAI and SDAI were 1.6, 165.1, 4.0, 16.6 and 17.8, respectively. These values were improved to 0.2, 50.4, 2.1, 5.5 and 5.6 at 52 weeks. The remission rate of DAS28-CRP was 69.2%. Interstitial pneumonia was developed in one patient as a complication. Including two cases who stopped the treatment due to decreasing of the efficacy, the continuation rate was 72.2%. [Conclusions] The incidence rate of adverse events was approximately 5% in Japanese cohort study. In this study, the incidence rate of infection was 5.5% in elderly RA patients, the rate was similar to Japanese cohort study. From this study, GLM could be a safe and effective treatment choice for elderly RA patients.

P2-115

The evaluation of Akita Orthopedic Group on Rheumatoid Arthritis registry 2018 patients who received adalimumab

Tsutomu Sakuraba¹, Takeshi Kashiwagura², Moto Kobayashi¹, Yusuke Sugimura³, Masaaki Ogino⁴, Yoichi Kataoka⁵, Hiromi Morita⁶, Nobuhiro Ishizawa⁷, Kazuhiro Shoji⁸, Hidetoshi Watanabe⁹, Natsuo Konishi¹⁰, Masakazu Urayama¹¹, Toshiaki Aizawa¹², Hiroshi Aonuma¹¹, Tetsuya Kawano¹², Naohisa Miyakoshi¹³, Yoichi Shimada¹³

¹Orthopedic Surgery, Hiraka General Hospital, ²Department of Orthopedic Surgery, Akita City Hospital, ³Department of Orthopedic Surgery, Nakadori General Hospital, ⁴Department of Orthopedic Surgery, Koto Kousei Hospital, ⁵Joto Orthopedic Clinic, ⁶Morita Orthopedic Clinic, ⁷Department of Orthopedic Surgery, Fujiwara Memorial Hospital, ⁸Shoji Orthopedic Clinic, ⁹Watanabe Orthopedic Clinic, ¹⁰Department of Orthopedic Surgery, Akita Kousei Medical Center, ¹¹Department of Orthopedic Surgery, Ogachi Central Hospital, ¹²Department of Orthopedic Surgery, Kita Akita Municipal Hospital, ¹³Department of Orthopedic Surgery, Akita University Graduate School of Medicine

Conflict of interest: None

[Object] The aim of this study is investigating of the profiles of rheu-

matoid arthritis patients who received adalimumab (ADA). [Methods] We evaluated 92 patients in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry (mean age, 64.2 years) who received ADA. [Results] The mean disease period was 177 months. The cases had Steinbrocker classification stages I/II/III/IV (17/24/22/28 patients), classes 1/2/3/4 (35/40/14/3 patients). Seventy-nine patients (85.9%) received methotrexate (MTX; mean dosage, 7.02 mg/week) and Twenty-nine (31.5%), prednisolone (3.06mg/day). The mean DAS28CRP (4) was 3.98 in the first ADA administration. The mean follow-up period was 103 weeks. Thirty-four patients had failure of ADA administration. Therapy was discontinued because of primary failure in 9 cases and secondary failure in 15. The mean disease activity score was 2.06, and 81 patients (88.0%) had good response in the final examination according to the criteria of the European League against Rheumatism. [Conclusions] The patients who received ADA had a high combination rate with MTX, high continuation rate, and good results, and were therefore appropriately selected and treated.

P2-116

A study on the long-term HAQ improvement effect of Adalimumab (ADA) in RA patients

Koji Nagai^{1,2}, Kenichiro Hata¹, Tomohiko Kuboyama¹, Hidehiko Makino¹, Shogo Matsuda¹, Takao Kiboshi¹, Ayaka Yoshikawa¹, Takayasu Suzuka¹, Yuri Hiramatsu¹, Takaaki Ishida¹, Hideyuki Shiba¹, Youhei Fujiki¹, Takuya Kotani¹, Yoko Matsumura¹, Shigeki Makino³, Tohru Takeuchi¹, Shigeki Arawaka¹

¹Department of Internal Medicine IV, Osaka Medical College, ²Department of Rheumatology, Koshokai Aino Hospital, Ibaraki, Osaka, Japan, ³Department of Rheumatology, Osaka Medical College Mishima Minami Hospital

Conflict of interest: None

<Introduction> Long-term inhibition of structural destruction of ADA has been reported, but they are able to improve and maintain the most important physical function (HAQ) in daily life. We study the long-term improvement of HAQ in patients treated with ADA. <Methods> RA patients treated ADA in our hospital from April 2015 to September 2018 were included. We examined disease activity, therapy and HAQ at the time of administration, 6 months, 1 year and 2 years after. <Results> Average age 59.6 years, disease duration 26 months DAS-ESR 3.67, HAQ 0.875, MTX use 82.6% (8.5mg/week), PSL use 20.7% (2.4mg/day) The ADA continuation rate was 83.5% in 2 years, 1 case was secondary ineffective, 2 were infections, 2 were failed due to lymphadenopathy. DAS-ESR improved significantly after 6 months and the effect was sustained until two years later. HAQ started to improve after the administration and improved significantly after 1 year and improved trend and long term improvement after 2 years. HAQ remission was 65% at baseline, 88% after 6 months, HAQ remission in all cases was achieved after 1 or 2 years. <Conclusion> Continued administration of ADA may maintain long-term sustainable improvement of HAQ. MTX use maintaining, PSL dose reduction, are sufficient merit to continue administering ADA.

P2-117

Treatment with Tocilizumab for elderly patients with rheumatoid arthritis

Katsumitsu Arai¹, Junya Ajiro²

¹Department of Orthopedic Surgery, Niigata Prefectural Central Hospital, ²Department of Internal Medicine, Niigata Prefectural Central Hospital

Conflict of interest: None

[Object] To assess the safety and efficacy of tocilizumab (TCZ) in elderly (≥ 65 years) rheumatoid arthritis (RA) patients. [Methods] We conducted a retrospective study of TCZ use in twelve RA patients over 65 years in our hospitals between 2010 and 2016. TCZ efficacy was evaluated at Dec 2017 by the DAS28ESR score. We also evaluated drug maintenance and safety, relative to adverse events discontinuation. TCZ retention over time was estimated with the Kaplan-Meier method. [Results] Among 12 RA patients treated with TCZ, 7 cases were after 65 years at the initiation of treatment. Mean age at the evaluation was 73 ± 8.2 years old. There were 7 cases that TCZ was the first bDMARD. There were 4

cases that TCZ was second bDMARDs. TCZ retention was 73% at 8 years after the initiation of treatment. Eight cases were treated with TCZ at evaluation point, 5 cases were remission and 3 cases were low disease activity. There was one adverse event discontinuation of TCZ that was suture abscess at total hip arthroplasty (THA), who was second failure of TCZ at THA. [Conclusions] Although there was a bias for the selection of patients treated with TCZ, TCZ seems to be well tolerated in RA patients in elderly patients.

P2-118

Efficacy of Tocilizumab for suppressing radiographic progression of cervical lesions in patients with rheumatoid arthritis comparison with methotrexate therapy ; three years of follow-up ~a Multicenter Registry Study ~

Yasuhide Kanayama¹, Toshihisa Kojima², Yuji Hirano³, Yuichiro Yabe⁴, Nobunori Takahashi², Yukiyo Oishi³, Naoki Ishiguro²

¹Department of Orthopaedic Surgery and Rheumatology, Toyota Kosei Hospital, Toyota, Japan, ²Department of Orthopedic Surgery, Nagoya University, Graduate School of Medicine, Nagoya, Japan, ³Department of Rheumatology, Toyohashi Municipal Hospital, Toyohashi, Japan, ⁴Department of Rheumatology, JCHO Tokyo Shinjuku Medical Center, Tokyo

Conflict of interest: None

[Objectives] To evaluate the efficacy of Tocilizumab (TCZ) for suppressing the radiographic progression of RA cervical lesions comparison with methotrexate (MTX) for 3 years. [Methods] We used TCZ and MTX for treating each 50 and 75 Japanese patients with active RA for at least 3 years. For evaluation of cervical lesions ADI, SAC and the Ranawat value were measured at initiation and Year 1,2,3. [Results] In the patients receiving TCZ (n=50) and MTX (n = 75), the mean age was 58.7 vs 63.6 years old (p=0.046), disease duration was 7.7 vs 8.0 years (p=0.247). The respective changes in cervical lesion parameters after 1 year were as follows: ADI: 0.24 vs 0.27mm (p=0.476), SAC: -0.20 vs -0.17mm (p=0.885) and Ranawat value: -0.16 vs -0.13mm (p=0.679). The respective changes in cervical lesion parameters after 2 years were as follows: ADI: 0.36 vs 0.55mm (p=0.072), SAC: -0.26 vs -0.45mm (p=0.074) and Ranawat value: -0.26 vs -0.33mm (p=0.387). The respective changes in cervical lesion parameters after 3 years were as follows: ADI: 0.46 vs 0.71mm (p=0.044), SAC: -0.34 vs -0.63mm (p=0.027) and Ranawat value: -0.32 vs -0.44mm (p=0.295). [Conclusions] This study suggested that TCZ treatment can be used to suppress the progression of RA cervical lesions.

P2-119

Which DMARDs is better for RA patients who had inadequate response to Tocilizumab?

Tsuneo Kondo, Yusuke Okada, Akiko Shibata, Kentaro Chino, Takahiko Kurasawa, Hirofumi Takei, Koichi Amano
Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University

Conflict of interest: None

[Object] To elucidate next treatments for RA patients who had insufficient efficacy of tocilizumab (TCZ). [Methods] The medical records of 23 RA patients who had received another DMARD due to inadequate response to TCZ and had been followed up for more than 24 weeks were retrospectively evaluated. [Results] Background features at the time of discontinuation of TCZ were as follows; female 91% (21 patients), average age 60.8 years, mean disease duration 14 years, stage 4 ratio 56% (13 cases), MTX usage rate 52% (12 cases), the average TCZ administration duration 2.6 years, and the average DAS 28-ESR 4.3. Next DMARDs after TCZ discontinuation were as follows; tofacitinib (Tofa) 10 (43%), TNF inhibitors 8 (35%), abatacept (ABT) 5 (22%). TNF inhibitors included 4 infliximab, 2 etanercept and 2 golimumab. LOCF analysis revealed that the changes of DAS28-ESR from baseline to week 24 were from 4.2 to 3.3 for Tofa (P=0.058), 4.2 to 3.8 for TNF inhibitors (P=0.494) and 4.8 to 4.2 for ABT (P=0.676), and the changes of CDAI from baseline to week 24 were from 15.9 to 6.6 for Tofa (P=0.003), 17.3 to 9.9 for TNF inhibitors (P=0.040) and 25.7 to 15.4 for ABT (P=0.143). [Conclusions] This study suggested that switching to Tofa and TNF in-

hibitors for TCZ inadequate responders could be effective.

P2-120

Clinical results of tocilizumab (TCZ) in elderly RA patients; more than 5 years follow-up

Hideki Tsuboi, Shoichi Kaneshiro
Osaka Rosai Hospital, Sakai, Japan

Conflict of interest: None

[Object] We investigated the efficacy using TCZ more than five years in elderly patients with rheumatoid arthritis [Methods] 41 RA patients have been continued to treat with tocilizumab in our hospital more than five years. Among them, 26 were less than 65 years old (less 65 group) at the beginning of TCZ, and 15 were more than 65 years old (above 65 group). The average duration of RA were 9.0years/23years (less 65/above 65, respectively). The average DAS28CRP were 4.0/4.1 at the beginning of administration. At the end of this study, we investigated the efficacy of TCZ in both groups, and moreover, we analyzed the reasons of discontinuation in the above 65 group. [Results] At the end point, CRP were 0.05/0.04 (less 65/above 65, respectively), and CDAI were 5.3/6.0. The usage of MTX were 92%/87% at the beginning of TCZ, on the other hand, they were reduced to 31%/47% at the end point. Moreover, the usage of PSL were 65%/80% at the beginning of TCZ, on the other hand, they were reduced to 33.8%/14%. Among 10 patients who have discontinued TCZ, the reason was infectious diseases in 3 patients and malignant diseases in 2 patients. [Conclusions] The treatment with TCZ for elderly patients with RA is safe and it may be useful for elderly RA patients.

P2-121

Efficacy of shortening the dosing interval of subcutaneous tocilizumab to rheumatoid arthritis patients with an inadequate response to subcutaneous tocilizumab every other week

Hirofumi Watanabe, Shuntaro Miyoshi, Jiro Yamana, Mitsuhiro Iwahashi, Rie Sasaki, Seizo Yamana
Department of Rheumatology, Higashi Hiroshima Memorial Hospital, Higashihiroshima, Japan

Conflict of interest: None

[Object] The dosing interval was shortened up to one week for nine cases of rheumatoid arthritis patients who had an inadequate response to subcutaneous tocilizumab every other week. We investigated the effectiveness of these cases. [Methods] Nine patients with rheumatoid arthritis (RA) who had an inadequate response to subcutaneous tocilizumab every other week preparation were included. The dosing interval was shortened, and the continuation rate and efficacy after 6 months were investigated. Efficacy was evaluated using SDAI and CDAI. [Results] The patient background was 5 women and 4 men, with an average age of 59.7 years (17 - 83). The combination medication were 7 prednisone (2 to 5 mg) and 2 methotrexate (4 mg, 8 mg). The CDAI before shortening the dosing interval was 18.78 ± 13.6. CRP <0.05 mg / dL in all cases after 6 months of shortened dosing. In the clinical evaluation, 4 cases achieved remission, 3 cases achieved low disease activity, and 2 cases did not show improvement. Of the 4 patients with CRP <0.05 mg / dL before the start of shortened dosing, 2 patients improved the clinical evaluation. [Conclusions] Many shortened dosing confirmed improvement in disease activity. It was suggested that shortening administration may be effective even in cases with normal CRP.

P2-122

Clinical experience of sarilumab at the author's institution

Yukitaka Ueki, Toshiyuki Aramaki, Shota Kurushima, Kanako Kojima, Natsumi Kawachi, Kaoru Terada, Katsumi Eguchi
Center for Rheumatic Diseases, Sasebo Chuo Hospital, Sasebo, Japan

Conflict of interest: None

[Object] Approved in September 2017, sarilumab, is a novel anti-rheumatoid drug that is classed biologics. Presently, the postmarketing

clinical surveillance is ongoing, and we await the data on the actual clinical safety and efficacy of this drug. We hereby report the safety and efficacy of sarilumab treatment. [Methods] The subjects were 9 patients (1 in bio-naïve, 8 in the other biologics →sarilumab) that were enrolled in RA patients responding poorly to MTX and other biologics. Safety and efficacy of the treatment were assessed in the 14 weeks. [Results] With regard to safety, there were 6 onsets of adverse events in 4 of the 9 patients, however, all were not serious and the outcome was recovery with no dropout cases. Two of the cases were dropout by no-efficacy. With regard to efficacy, changes in CDAI showed remission for 1 patient, effective for 6 patients, and ineffective for 2 patients at 12 weeks. [Conclusions] Safety is comparatively high if attention is paid to infection and so on. Our study suggests that the usefulness of sarilumab is considered high for patients that respond poorly to MTX and other biologics.

P2-123

Experience of sarilumab therapy for RA patients in our hospital

Satoshi Tsutsumi, Daisuke Tomita, Kosuke Okuda, Keiko Funahashi, Tsukasa Matsubara
Matsubara Mayflower Hospital

Conflict of interest: None

[Object] Sarilumab is a fully human anti-IL-6R monoclonal antibody that blocks IL-6-mediated inflammatory signaling cascade. We examined retention rate, efficacy and safety of sarilumab therapy for RA patients. [Methods] For seven RA patients in our hospital (3 males and 4 females) at more than 24 weeks after starting sarilumab, we evaluated retention rate, efficacy and safety. [Results] The mean age 70.5 years, the mean disease duration 8.4 years, bio-naïve cases five and bio-switch cases two (one from ETN and one from TCZ). Four patients initially received MTX at mean dose 8.5 mg/w. Four patients were able to continue sarilumab at 24 weeks after starting it (retention rate 57.1%), and mean DAS28-CRP decreased from 3.85 at the start to 1.87 at 24 weeks. Two of the four experienced neutropenia and required transient withdrawal or dose decrease of sarilumab for continued use. Three patients stopped sarilumab because of ineffectiveness (1 case) and thrombocytopenia (2 cases). Thrombocytopenia was recovered within 4 weeks after stopping sarilumab in one case, but in another case resulted from concomitant idiopathic thrombocytopenic purpura. [Conclusions] More than 24-week treatment of RA with sarilumab resulted in obvious efficacy and safety profile consistent with IL-6 blockade.

P2-124

Short-term efficacy of sarilumab therapy in the patients with rheumatoid arthritis

Yuko Kimura¹, Shuzo Yoshida¹, Akitoshi Machida², Nobuhisa Shibahara³
¹Department of Immuno-Rheumatology Center, Arisawa General Hospital, Hirakata, Osaka, Japan, ²Department of Orthopedic Surgery, Arisawa General Hospital, Hirakata, Osaka, Japan, ³Department of Urology, Arisawa General Hospital, Hirakata, Osaka, Japan

Conflict of interest: None

[Objectives] We examined short-term efficacy of sarilumab therapy in the patients with rheumatoid arthritis (RA). [Methods] Ten patients with RA who underwent sarilumab treatment in our hospital between April and October 2018 were examined. We evaluated the disease activity score (DAS) 28-ESR and ultrasound. [Results] Nine patients were females, the average age was 62.8 years ± 20.3 years, and the mean disease duration was 16.5 ± 14.0 years. Seven patients were anti-CCP antibody positive and six patients were RF positive. The mean CRP was 2.76 ± 2.95 mg/dL, ESR 30.6 ± 22.0/h, HAQ 1.52 ± 1.03 and MMP-3 230.6 ± 220.0 mg/dL. Methotrexate was used as concomitant therapy in 3 patients, tacrolimus in 3 patients and prednisolone in 4 patients. The mean DAS28-ESR at baseline was 5.06 ± 0.98. DAS28-ESR was significantly improved to 2.98 ± 1.02 (p = 0.02) after 4 weeks and to 2.90 ± 0.85 (p = 0.03) after 12 weeks. Evaluation by ultrasound also showed significant improvement in both of gray-scale and power Doppler at 12 weeks compared to baseline. [Conclusions] These results suggested that sarilumab may have therapeutic effect at relatively early stage assessed by DAS28-ESR and ultrasound.

P2-125

Experience of sarilumab therapy for RA patients in our hospital

Yasuhiro Terashima¹, Ken Takebe¹, Koji Tateishi¹, Midori Kitayama², Takashi Yamane², Yo Ueda³

¹Department of Orthopaedic, Kohnan Kakogawa Hospital, ²Department of Rheumatology, Kakogawa City Hospital, ³Department of Immunology, Kobe University Graduate School of Medicine

Conflict of interest: None

[Object] We examined efficacy and safety of sarilumab therapy for RA patients. [Methods] For six RA patients within eleven RA patients that treated by sarilumab at more than 24 weeks after having passed, we examined efficacy and safety. [Results] The mean age 68 years (55-77years), bio-naïve case one and bio-switch cases five. Four patients initially received MTX. Four patients were able to continue sarilumab at 24 weeks after starting it (retention rate 66.7%). The mean DAS28-ESR decreased from 5.8 at the start to 2.37 at 24 weeks. The mean SDAI decreased from 31.9 at the start to 5.88 at 24 weeks. Two patients are stopped sarilumab because of rash. They are recovered within 4 weeks after stopping sarilumab. Four patients that continued sarilumab were no adverse effect. And we confirmed efficacy by patients that sarilumab switch tocilizumab and tocilizumab switch sarilumab. One of the eleven experienced neutropenia. Neutropenia was recovered within 28 days. [Conclusions] More than 24 weeks treatment of RA with sarilumab resulted in obvious efficacy. We experienced side effects that are rashes and the patients continued sarilumab were no adverse effect. And we confirmed efficacy by the case of switching during anti-IL-6R monoclonal antibody.

P2-126

A case of early remission of rheumatoid arthritis with eosinophilia induced by tocilizumab

Taro Akira¹, Michiko Ohashi¹, Masashi Okamoto¹, Hiroshi Shimagami¹, Takehiro Hirayama¹, Akira Mega², Yoshinobu Matsuura¹, Akihiko Nakabayashi¹, Yoshinori Katada¹, Kazushi Konma¹

¹Division of Rheumatology and Clinical Immunology, Sakai City Medical Center, Sakai, Japan, ²Nephrology, Diabetology and Rheumatology, Sakai City Medical Center, Sakai, Japan

Conflict of interest: None

[Case] A 43-year-old woman with polyarthralgia was referred to our hospital 3 years ago. She was diagnosed as RA, 4mg of MTX per week and 3mg of PSL was introduced. After use of tocilizumab, complete remission was achieved and PSL was stopped. 3 months later, since an eosinophilia and leucopenia (WBC 3980/μl, Seg 34.2 %, Eo 14.3 %) developed, presumably due to adverse effect of tocilizumab, both tocilizumab and MTX were stopped. Interestingly, the patient had no symptoms for the next 6 months with no medication. Using sarilumab, she is now in good control. [Discussion] In spite of 3 month use, tocilizumab led a drug-free remission for half a year. As bDMARDs are generally discontinued after several years remission, this is very early remission introduction. After 4 years remission by tocilizumab monotherapy, 10 % of RA patients are described to keep drug-free remission for 1 year (Nishimoto N et al. *Modern Rheumatol* 2014; 24:17-25.). Notably, our patient had an eosinophilia. Frequency of eosinophilia is reported to be 0.35 % in RA patients treated with tocilizumab (Azuma N et al. *Intern Med.* 2017;56:1585-1590.). This case suggests a possibility of early induction of drug-free remission by combination of IL-6 blockade and a certain treatment which cause eosinophilia.

P2-127

Two cases in which ETNBS and intra-articular injection of triamcinolone acetone were co-administered for rheumatoid arthritis with refractory activity

Heiseki Yu

Touei Internal Medicine and Rheumatology Clinic

Conflict of interest: None

[Background] bDMARDs cannot be used for economic reasons even

in the intractable state because of high prices. Two patients who were effective for administration of low cost ETNBS+IAGC with refractory active RA at our clinic will be reported. Case1 67y M visited our clinic with bone destruction at X-ray and joint echo. ACPA629 RF161 CRP2.7 stageIII class2, csDMARDs+IAGC no effective lacks symptoms of pain and rapidly after interruption of treatment for 3M Bone destruction and deformation progression. Even though it was being treated with prostate cancer and stable, so it was effective at simultaneous administration of ETNBS+IAGC. PD on echo disappeared once with administration and is still in remission. Case2 66y F, she refused bio-DMARDs for economic reasons. After 2y of folk remedy, the disease condition suddenly worsened and visited our clinic. StageIV class2 ACPA809 CRP3.5, Bone destruction is highly advanced mainly on the two hand joints and echo was also GS3 PD3. MTX+IAGC no effective, effective for two doses of ETNBS+IAGC. Even now it is remission with PD disappearance [discussion] Low cost and extremely economical IAGC+ETNBS in short-term refractory disease symptoms but also careful administration in tumor-being condition and bone destruction are remarkable in both cases.

P2-128

Safety of Baricitinib (Bari) under Clinical Settings in Patients (pts) with Rheumatoid Arthritis (RA), Using Data from All-case Post-marketing Surveillance and Spontaneous Reports

Hiroaki Matsuno¹, Tatsuya Atsumi², Syuji Takei³, Naoto Tamura⁴, Masayoshi Harigai⁵, Takao Fujii⁶, Shigeki Momohara⁷, Yuko Takahashi⁸, Nobuhiro Narii⁸, Naoto Tsujimoto⁸, Atsushi Nishikawa⁸, Taeko Ishii⁸, Kazuhiko Yamamoto⁹, Masataka Kuwana¹⁰, Michiaki Takagi¹¹

¹Matsuno Clinic for Rheumatic Diseases, ²Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine, Hokkaido University, ³Department of Pediatrics, Graduate School of Medical and Dental Science, Kagoshima University, ⁴Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, ⁵Department of Rheumatology, Tokyo Women's Medical University, ⁶Department of Rheumatology and Clinical Immunology, Wakayama Medical University, ⁷Hakkeikai Incorporated Medical Institution, ⁸Eli Lilly Japan K.K., ⁹RIKEN Center for Integrative Medical Sciences, ¹⁰Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, ¹¹Department of Orthopaedic Surgery, Yamagata University Faculty of Medicine

Conflict of interest: Yes

[Objectives] To evaluate Bari safety under clinical settings in RA pts. [Methods] All-case post-marketing surveillance of Bari (except pts in clinical studies) collects safety and efficacy data for the first 24 weeks starting in Sep 2017; collection of safety data like SAEs continues for 3 years. This interim report summarizes registration data including pretreatment test rates and AEs collected in the surveillance and spontaneous reports. [Results] As of Aug 2018, 1288 pts had been enrolled. Registration data were as follows: women, 81%; mean age, 64 years old; mean RA duration, 12 years; Steinbrocker stage II, 32%; stage III or IV, 52%; Bari 4mg, 68%; Bari 2mg 32%; MTX use, 57%; corticosteroid use, 51%; pretreatment test for TB, 93%; HBV, 95%; HCV, 93%; and eGFR, 96%. Of 299 AEs collected, 53 were SAEs. SAEs reported in 2 or more pts were pneumonia (8), fall (4), osteonecrosis (3), HZ (2) and ILD (2). Pulmonary TB (1), lymph node TB (1) and DVT (1) were also reported as SAEs. [Conclusion] Care is needed to ensure that all pretreatment tests be conducted in all pts; although the most pts underwent all tests, some tests were not conducted in some pts. SAEs including infections were reported, and careful monitoring is continuously needed in pts receiving Bari.

P2-129

Dose reduction of baricitinib for rheumatoid arthritis patients who achieved remission or low disease activity in real world data

Eiji Torikai, Daisuke Suzuki

Department of Rheumatology, Iwata City Hospital

Conflict of interest: None

[Object] To evaluate efficacy and safety of baricitinib (Bari) for rheumatoid arthritis (RA) patients in real world clinic during 24 weeks. [Methods] We included 21 RA patients (Bio naïve (BN): 13 patients and

Bio switch: (BS) 8 patients) who started the treatment with Bari between October 2017 and April 2018. Patients were treated with T2T strategies. We evaluated the disease activity, HAQ-DI and adverse events. [Results] At Baseline, the mean ages, the disease duration, CDAI and HAQ-DI of BN were 63.8 years, 5.03 years, 26.2 and 0.81, respectively, and those of BS were 65.5 years, 5.73 years, 35.0 and 1.16, respectively. At 4 weeks, ACR20/50/70 of BN (%) and BS (%) were 85.6/61.5/38.4 and 50.0/25.0/12.5, respectively. HAQ-DI of BN and BS were 0.39 and 0.67, respectively. At 24 weeks, the percentage of remission/LDA/MDA/HDA in BN and BS were 53.8/30.7/15.4/0 and 25.0/37.5/25.0/12.5, respectively. HAQ-DI of BN and BS were 0.39 and 0.67, respectively. One patient discontinued due to no response. Two patients restarted after withdrawal for a while due to a pneumonia and a herpes zoster. Mild adverse events including laboratory abnormalities occurred in 52.4% of them. [Conclusions] Bari treatment with T2T strategies in real world clinic demonstrated beneficial efficacy and safety.

P2-130

Efficacy of baricitinib (bari) for rheumatoid arthritis in patients with an inadequate response (IR) to tofacitinib (tofa)

Takashi Yamane, Ayaka Inoue, Hiroaki Nakagawa, Midori Kitayama, Takuro Maeda, Noriaki Yo, Chihiro Tanaka
Rheumatology Division, Kakogawa Central City Hospital

Conflict of interest: None

[Object] To investigate the efficacy of bari for tofa IR patients. [Methods] There were 7 tofa IR patients who were switched to bari. Their baseline characteristics, continuation rate, and disease activity were retrospectively assessed up to week 12. [Results] Mean age was 56.4, mean disease duration was 9.2 years, all were ACPA · RF positive. The number of prior biologics use was 2.3 (1-4). 3 had concomitant MTX use (mean 5.3 mg (4-6)) and 4 had PSL (mean 3.3 mg (2-5)). Mean SJC /TJC was 5.0 (1-15)/5.3 (1-15), Physician's /Patient's VAS 71 mm (50-90)/73 mm (50-80), CRP/MMP-3 1.6 mg/dl (0.01-4.3)/ 357.3 mg/dl (27-933). Mean SDI/CDAI 26.3/24.7, DAS 28-CRP was 4.5, 57%with MDA, 43% with HDA at baseline. The mean patient's VAS decreased significantly (P <0.01) at week 2, and at week 4, CDAI/SDAI/DAS28-CRP showed a significant improvement (P <0.05). 2 were discontinued due to lack of efficacy and ILD, the continuation rate at was 71.4%. At week 12, all patients achieved LDA by SDAI/CDAI, 40% achieved MDA, 40% LDA, 20% remission by DAS 28-CRP (mean 2.6). 3 of 4 patients taking PSL were able to withdraw. [Conclusions] Efficacy of bari seemed to be expected from the early stage even in tofa IR patients. Bari was administered for the case of inadequate improvement of patient's VAS with tofa.

P2-131

Study of clinical manifestations by Baricitinib

Shunichi Imai¹, Kikuko Gushiken¹, Ken Hasegawa²

¹Rheumatoid Arthritis Center, Minami Medical Health Cooperation,

²Meinan Hospital, Department of Orthopaedic Surgery

Conflict of interest: None

Objective: To study clinical manifestations by Baricitinib (BARI). **Subjects and Methods:** Data from 23 patients who were treated with BARI in our hospital after the launch of BARI till Sep 2018 were analyzed (17 showed inadequate response to multiple biologic drugs and 6 chose BARI 2 mg due to financial reasons). The assessment items included morning stiffness (MST), VAS, fatigue, grip strength, DAS28 (ESR), DAS28 (CRP), CDAI, SDAI, and HAQ. **Result:** All assessment items rapidly improved 1 week after introduction of BARI treatment. Improvement and maintenance in efficacy were also observed during the subsequent courses. In addition, HAQ tended to improve 6 months after introduction. **Discussion and Conclusion:** BARI was effective in the early phase of introduction and in patients with inadequate response even after the introduction of multiple biologic drugs. BARI was effective in 6 patients who chose BARI 2 mg due to financial reasons, suggesting that BARI 2 mg can be effective in patients in whom the introduction of biologic drugs is difficult due to financial reasons. BARI could also be used for improvement of fatigue in patients with RA that has been difficult to treat conventionally. Furthermore, BARI will be beneficial for treatment

of RA patients without affecting their lifestyle.

P2-132

Baricitinib administration experience of the elderly, including the super elderly

Tamami Kikuchi¹, Takeshi Kuroda², Ichiei Narita²

¹Division of Internal Medicine, Niigata Rosai Hospital, ²Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences

Conflict of interest: None

[Object] Report on the effectiveness of Baricitinib to the elderly and side effects [Methods] Six cases of rheumatoid arthritis patients aged 77 to 90 years. Duration of disease is 2 years to decades or more. I have experienced MTX in all cases, I have never used biologics. Disease activity is moderate to high with SDAI. In all cases, half of Baricitinib (2 mg / day) was administered [Results] Improvement of subjective symptoms was observed from several days to several weeks after administration, and CRP was also lowered. In the evaluation after 1 month, SDAI remission was achieved in 5 out of 6 cases and 1 case was low disease activity. In 1 case of side effects, lower limb vein thrombosis was observed in the same case as serum CK elevation. The continuation rate for 3 months was 100%, for 5 months was 83% [Conclusions] Baricitinib was used for elderly people with MTX resistance. Although 6 cases, small group number and short term observation, Baricitinib was effective in the elderly as well as in adults. In addition, it was possible to obtain necessary and sufficient effect by half dose administration throughout the course. Half dose administration of Baricitinib is expected to become an effective treatment option for the elderly rheumatic patients in the future

P2-133

Treatment with Baricitinib in a Patient with Rheumatoid Arthritis Complicated by Janus Kinase 2 V617F Mutation-positive Essential Thrombocythemia

Makoto Sugihara, Tomohiro Kozuki, Yuji Miyoshi, Miho Ohshima
Department of Rheumatic Diseases, Tama-Hokubu Medical Center, Tokyo Metropolitan Health and Medical Treatment Corporation

Conflict of interest: Yes

[Case] A 75-year-old man, construction company employee, referred to our hospital with arthralgia in his hands and knees. At X-10 years, he was diagnosed with essential thrombocythemia (ET) with JAK2 V617F hetero mutation and followed by hematologist, taking aspirin for thrombocythemia and allopurinol for secondary hyperuricemia. Initial examination revealed the following: TJC 4; SJC 4; WBC 17300/ μ L; Hb 11.6 g/dL; PLT 607000/ μ L; RF 92 IU/mL; ACPA >150 U/mL; CRP 0.65 mg/dL; PGA 5 cm; EGA 4 cm; DAS28-CRP 3.44; SDAI 17.65 and HAQ 0.25. The diagnosis was moderately active RA. MTX treatment was started at 8 mg/wk but was ineffective and interfered with his work. At week X+4, baricitinib (BAR) 4 mg/d was administered. At week X+8, TJC was 0; SJC 0; CRP 0.06 mg/dL; PGA 2 cm; EGA 0.5 cm; DAS28-CRP 1.41; SDAI 2.56; and HAQ 0, he achieved clinical and HAQ remission. His PLT was normalized to 329000/ μ L. [Discussion] JAK2 V617F mutation is common in myeloproliferative disorders, such as ET. Only few RA patients with this mutation have been reported. In our case, JAK2 mutation may be involved in the development of RA by activating lymphocytes through downstream phosphorylated STAT. As BAR has a lower IC₅₀ value against JAK2 than other JAK inhibitors, it was effective in this case.

P2-134

Examination of joint ultrasound findings in JAK inhibitor Baricitinib in our clinical practice

Shigekazu Takahashi, Yasushi Nawata, Kazusa Miyachi, Norihiro Mimura, Taiga Ikezawa, Kazuhiro Hamasato, Norihiko Watanabe
Division of Rheumatology / Clinical Immunology, Chibaken Saiseikai Narashino Hospital, Chiba, Japan

Conflict of interest: None

[Object] We assessed RA patients in our hospital who received JAK inhibitor Baricitinib (Bari), and examined the effectiveness in clinical practice using joint ultrasound (US) findings. [Methods] In 13 cases of administration of Bari, 9 cases continued for 6 months or more were evaluated. Effectiveness was evaluated semi-quantitatively with 26 joints of both hands (wrist, MCP, PIP) with GS and PD by joint US, before, 12 and 24 weeks after administration. We also compared it with disease activity index (DAS28-ESR, SDAI). [Results] Background is age 59.4 years, Bari 2 mg 4 cases / 4mg 5cases, pre-administration DAS 5.28, SDAI 28.1. EULAR good response 67% for week 12, 86% for 24 weeks, remission rate was high at 12 weeks (DAS 43%, SDAI 33%), 24 weeks (DAS 57%, SDAI 57%). In the joint US findings, improvement of average total GS and PD was observed consistent with disease activity index. Maximum number of findings when evaluating joints with the OMERACT-EULAR composite PDUS score, the average GS / PD combined score improved from 2.11 (before), 1.29 (12 weeks), 0.86 (24 weeks). After 24 weeks we achieved grade 1 or less in all cases. [Conclusions] Even in clinical practice, improvement of clinical and joint US findings was recognized from the early stage of administration of Bari.

P2-135

Baricitinib for rheumatoid arthritis (RA) patients with complications in actual clinical practice

Yasushi Nawata, Shigekazu Takahashi
Center for Rheumatic Diseases, Chibaken Saiseikai Narashino Hospital

Conflict of interest: None

[Object] We examined the efficacy and safety of baricitinib (Bari) in actual clinical practice. [Methods] 11 RA patients who received Bari more than 12 weeks were examined. The efficacy of Bari was evaluated by composite measure (DAS28-ESR, CDAI, SDAI), EULAR response, remission/low disease activity achievement rate. [Results] Subjects: 7 Bio-naive (MTX-IR 3, csDMARDs-IR 4) and 4 Bio-switch cases (TNFi 2, IL6Ri 1, tofacitinib 1). Background: age 61 years, disease duration 137 months, Stage I/II/III/IV (3/5/3/0), Class 1/2/3/4 (7/4/0/0), RF/ACPA positive 82%/82%, MTX73%, PSL36%, tacrolimus55%, Bari2mg 4 cases, Bari4mg 7 cases, DAS28-ESR5.16, SDAI26.3, CDAI23.6, HAQ0.56. Complications: collagen disease, interstitial pneumonitis36%, sinusitis18%, bronchiectasis, pulmonary MAC, HBsAb positive, past history (herpes zoster, MTX-pneumonitis). Efficacy: EULAR good response at 12 weeks was 73%, and 78% at 24 weeks. High rate of remission achievement rate at 12 weeks (DAS45%, SDAI36%, CDAI27%), 24 weeks (DAS56%, SDAI56%, CDAI56%). Adverse events: upper respiratory tract infection, diarrhea, high CK, high Chol. There are no serious adverse events, herpes zoster and malignancy. [Conclusions] Baricitinib is useful even in actual clinical practice, where are many complications unlike clinical trials.

P2-136

The annual observational research of tofacitinib in patients with rheumatoid arthritis by NinJa2017 cohort

Atsushi Kaneko¹, Toshihiro Matsui², Shotaro Mori¹, Yosuke Hattori¹, Tomotaro Sato¹, Masao Katayama³, Shigeto Tohma⁴

¹Department of Orthopaedic Surgery and Rheumatism, Nagoya Medical Center, ²Department of Rheumatology, Sagami National Hospital, ³Department of Collagen Disease and Rheumatology, Nagoya Medical Center, ⁴Department of Rheumatology, Tokyo Medical Center

Conflict of interest: None

[Object] The purpose of this current study is to research of tofacitinib in patients with rheumatoid arthritis by NinJa2017 cohort. [Methods] We investigated the drug efficacy and safety of tofacitinib in 277 Japanese RA patients by NinJa2017 cohort. [Results] 58 patients were medicated tofacitinib monotherapy, 139 patients were medicated the combined therapy with MTX, 21 patients the combined therapy csDMARD except MTX, and 25 patients the combined therapy with 2 or 3 cs DMARDs. 58 patients were medicated tofacitinib 5mg/day, 212 patients 10mg/day. The BOOLEAN remission reached 59 patients, and SDAI remission were reached 82 patients. The annual hospitalization and/or serious adverse event were occurred 18 patients involving 10 patients complicated with

herpes zoster. [Conclusions] Tofacitinib is effective and safe era in patients with rheumatoid arthritis.

P2-137

The persistence rate of JAK inhibitor in 50 patients with Rheumatoid Arthritis

Eisuke Ogawa^{1,2}, Yuichiro Amano¹, Tomoki Tanaka², Sadahiro Suzuki²

¹Department of Rheumatology and Infectious Diseases, Kitasato University Medical Center, ²Department of Rheumatology, Shinonoi General Hospital

Conflict of interest: Yes

[Object] To evaluate the persistence rate of JAK inhibitor in Japanese patients with Rheumatoid Arthritis (RA). [Methods] All patients treated with JAK inhibitor for RA at Kitasato University Medical Center or Shinonoi General Hospital were analyzed. The drug retention rates were compared using Log-rank test. [Results] Fifty patients were treated with JAK inhibitor. The mean age of subjects was 64.6 and the mean duration of disease was 8.7 years. Woman accounted for 37 of the 50 cases. 30 patients were treated with MTX and 30 patients were treated with PSL. At the start of JAK inhibitor, DAS28-CRP was 4.5. Age of the subject, concomitant therapy with MTX, remote biological agents use and anti-CCP antibody value did not correlate with the continuation rate of JAK inhibitor. PSL combination group had a significantly lower persistence rate than the noncombined group. In the cases that DAS28-CRP declined by more than 20% within 4 weeks after JAK inhibitor was started, the persistence rate was significantly better than the case that DAS28-CRP did not decline. [Conclusions] There is a possibility that long-term continuation can be expected in the PSL noncombined group or the case that DAS28-CRP is improved by more than 20% within 4 weeks after JAK inhibitor was started.

P2-138

Change of 22 RA patients treated with tofacitinib for three years in Keiyu Orthopedic Hospital

Keio Ayabe, Akira Inoue, Takuro Okari
Keiyu Orthopedic Hospital Gunma Japan

Conflict of interest: None

[Objectives] Most of the function of cytokines that the biological activity is controlled by tofacitinib (following TOF) relates to the function of lymphocyte. It is thought that TOF and abatacept (following ABT) have similar action for the reports about the restraint action for T cell, B cell and dendritic cell by TOF. So we can expect the effectiveness for the autoantibody-positive RA patients about TOF like ABT reported that is effective for the antiCCP antibody-positive RA patients. This study aims to investigate the change of the antiCCP antibody titer which is poor prognosis factor for the treatment of RA patients. [Methods] 34 RA patients passed more than three years after the initiation of the treatment with TOF in Keiyu Orthopedic Hospital, and 22 patients (5males,17females) continued the treatment with TOF. we examined the progress such as changes of the disease activity and laboratory data for them. [Results] Mean DAS28CRP was improved (baseline/3 years after dosage: 3.9/2.1). The patients which antiCCP antibody titer decreased were 14 of 22 patients. [Conclusions] We can expect a drop of the antiCCP antibody titer which was a poor-prognosis factor for the treatment of RA patients by the treatment with TOF.

P2-139

Evaluation of the effectiveness of two JAK inhibitors in rheumatoid arthritis treatment at our hospital

Mai Morimoto, Takahiro Yoshikawa, Chie Ogita, Masao Tamura, Tetsuya Furukawa, Teppei Hashimoto, Naoto Azuma, Masayasu Kitano, Kiyoshi Matsui

Division of Rheumatology Department of Internal Medicine, Hyogo College of Medicine

Conflict of interest: None

[Object] We examined the effectiveness of two JAK inhibitors against RA patients in our hospital. [Methods] 26 patients who were observable continuously for more than 6 months in RA patients who received TOF, and 7 patients who had been able to observe continuously for 12 weeks or more and patient background and efficacy was evaluated. [Results] Patient background was TOF treatment group, mean age 56.5 years, disease term 11.61 years, 19 females, 7 males, 22 cases used MTX at the start, DAS 28-ESR 5.17 at the start of treatment, DAS 28-CRP: 4.49, DAS 28-ESR 3.18, DAS 28-CRP 2.41 after 6 months. Meanwhile, the BAR treatment group had an average age of 60.3 years, 6 women, 1 case of man, 6 cases used MTX at the start, all cases of using biologics, DAS 28-ESR 4.99 at the start of treatment, It was DAS 28-CRP 4.36. The DAS 28 - ESR at the 12th week of the BAR treatment group was 3.62, DAS 28 - CRP 2.80, which was almost the same as the DAS 28 - ESR 3.57 and DAS 28 - CRP 2.75 of the TOF at the same time. [Conclusions] The number of types of molecular targeted drugs has increased and establishment of therapeutic strategies that make use of drug characteristics is required. We will investigate the case including additional administration cases thereafter and report its effectiveness.

P2-140

Efficacy of tofacitinib in elderly patients with rheumatoid arthritis (age >70yrs)

Toyomitsu Tsuchida, Rikiai Tanaka, Yoichi Kamino, Chizuru Shiraiishi
Department of Rheumatology, Tsuchida Clinic, Chiba, Japan

Conflict of interest: None

Introduction Treatment for elderly patients with rheumatoid arthritis (RA) has relied on steroids due to difficulty in introducing biologics or methotrexate. Oral low-molecular-weight JAK inhibitor tofacitinib (TOF) was approved in 2013, but has not been used in elderly patients because of the risk of serious adverse reactions. Objectives In 2013, we treated RA patients aged >70 years with 5 mg dose of TOF. This report summarizes the treatment efficacy as evaluated by MRI. Patients 23 patients (1 male, 22 females) who could continue TOF treatment for >1 year Mean age: 77.4 years Evaluation methods DAS28CRP, MMP-3 The wrist MRI data of 18 patients were retrospectively analyzed for synovitis and osteitis. Results The mean DAS28CRP values before and after 5 years of treatment were 3.23 and 2.00, respectively, and the corresponding MMP-3 values were 140.8 and 38.8. The numbers of patients with and without were 11 and 22 before and 4 and 29 after treatment, respectively; for osteitis, there were 19 and 14 before and 22 and 11 after treatment, respectively. Discussion The 3 patients who worsened after treatment were treated with single-agent TOF, suggesting insufficiency of single-agent treatment at 5 mg. In conclusion, TOF can be used 5 mg in RA patients aged > 70 years.

P2-141

Effect about switching from ABT to TOF having the similar action of ABT for an effect attenuation antiSS-A antibody-positive RA patients of ABT

Keio Ayabe, Akira Inoue, Takuro Okari
Keiyu Orthopedic Hospital Gunma Japan

Conflict of interest: None

[Objectives] Most of the function of cytokines that the biological activity is controlled by tofacitinib (following TOF) relates to the function of lymphocyte. It is thought that TOF and abatacept (following ABT) have similar action for the reports about the restraint action for T cell, B cell and dendritic cell by TOF. We reported the effectiveness of ABT for the antiSS-A antibody-positive RA patients in past conferences. This study aims to evaluate the effect about the switching from ABT to TOF having the similar action of ABT for antiSS-A antibody-positive RA patients attenuated an effect of ABT. [Methods] 34 RA patients passed more than three years after the initiation of the treatment with TOF in Keiyu Orthopedic Hospital, and 6 antiSS-A antibody positive RA patients switched to TOF from ABT. we examined the progress such as changes of the disease activity and laboratory data for them. [Results] Mean DAS28ESR was improved (baseline / 3 years after dosage:4.8/2.8). [Conclusions] Switching from ABT to TOF having the similar action of ABT for antiSS-A an-

tibody-positive RA patients were effective.

P2-142

Clinical experience of JAK inhibitors as a treatment for rheumatoid arthritis with interstitial lung disease

Nobuhito Naito, Hiroshi Kawano, Mayo Kondo, Hirokazu Ogino, Seidai Sato, Yuko Toyoda, Hisatsugu Goto, Yasuhiko Nishioka
Department of Respiratory Medicine & Rheumatology, Graduate School of Biomedical Sciences, Tokushima University

Conflict of interest: None

[Background] Interstitial lung disease (ILD) is a common extra-articular manifestation of rheumatoid arthritis (RA) and is one of the most serious prognostic factors. However, several disease-modifying anti-rheumatic drugs (DMARDs) can be a potential risk for the exacerbation of ILD, and the optimal treatment of RA-ILD has not been established. In the present study, we investigated the effectiveness and safety of JAK inhibitors as a treatment for RA-ILD. [Method] We retrospectively reviewed records of 5 RA-ILD patients treated with JAK inhibitors before October 2018 at our department. [Results] The mean age of the 5 patients was 73.8 years (65-82 years), and 4 patients were female. Of the 5 patients, 3 were administered tofacitinib, and 2 were baricitinib. Median dosing period was 10 months (2-51 months). After the initiation of JAK inhibitors, none of the patients experienced a worsening of ILD. The differences in the mean levels of KL-6 in 5 patients were not statistically significant between baseline and last visit (529.8±263.0 vs. 589.6±371.7 U/mL, $p=0.55$). Additionally, DAS28-CRP values significantly decreased following JAK inhibitors treatment. [Conclusion] JAK inhibitors can be a useful treatment option for RA-ILD.

P2-143

The study of JAK inhibitor monotherapy in treatment of patients with rheumatoid arthritis

Tatsuo Hirose, Yuji Tasaka
Department of Internal Medicine, Saitama City Hospital

Conflict of interest: None

[Object] The aim of this study was to assess the effect of the monotherapy by JAK inhibitors to achieve the therapeutic goal of T2T. [Methods] The patients with RA who visited our hospital since 2015, and who were ineffective with biologic agents were registered. During treatment these patients with JAK inhibitors monotherapy, if the therapeutic goal was not achieved, we tried MTX combination therapy. We set the therapeutic goal by C-DAI as below 3.2. [Results] In total, 23 patients were registered. 3 cases dropped out from this study, two patients stopped visiting our hospital and one stopped JAK inhibitors because of infection. 20 patients remained were analyzed in this study. The patients who did not achieved low disease activity by JAK inhibitor monotherapy, were applied to the treatment with MTX combination therapy. Finally, 10 cases (50%) achieved the therapeutic goal by JAK inhibitor monotherapy, however 10 cases (50%) needed MTX combination therapy. Multivariate analysis showed no significant factors to achieve treatment goal by JAK inhibitor monotherapy. [Conclusions] JAK inhibitor monotherapy was effective in 50% of patients, but failed another 50% of patients with RA. We can not find any factors to achieve therapeutic goal by JAK inhibitor monotherapy.

P2-144

Improvement of periodontal disease condition by tofacitinib administration in two cases with rheumatoid arthritis

Tetsuo Kobayashi¹, Satoshi Ito², Akira Murasawa², Hajime Ishikawa²
¹General Dentistry and Clinical Education Unit, Niigata University Medical and Dental Hospital, ²Department of Rheumatology, Niigata Rheumatic Center

Conflict of interest: None

[Object] Overproduction of proinflammatory cytokines has been implicated as a shared risk factor for rheumatoid arthritis (RA) and peri-

odontal disease (PD). We had previously reported the beneficial effect of inhibitors of tumor necrosis factor (TNF) and interleukin-6 (IL-6) receptor on PD condition in patients with RA. Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA and has been suggested to regulate cytokine signaling. Therefore, we aimed to evaluate the effect of tofacitinib on PD condition in patients with RA. [Methods] We compared RA, PD, and serum parameter values before and after 3 months of tofacitinib administration in 2 patients (43- and 51-year-old women) with RA whose informed consents were obtained. [Results] Both patients showed an improvement in RA condition including simplified disease activity index, tender and swollen joint count, and visual analogue scale, as well as in serum levels of TNF- α and IL-6. Likewise, their PD conditions were ameliorated, as in gingival index, % sites with bleeding on probing, and probing pocket depth, although their oral hygiene levels as determined by plaque control record were relatively unchanged. [Conclusions] Tofacitinib may have a beneficial effect on PD condition in patients with RA.

P2-145

An Operated Case of Lumbar Disc Herniation In Patient with Rheumatoid Arthritis Using JAK Inhibitor without Drug Holiday in safety

Yoshinori Hashimoto
Department of Orthopaedic Surgery, South Miyagi Medical Center

Conflict of interest: None

We report a successful operated case of lumbar disc herniation in patient with rheumatoid arthritis (RA) using JAK inhibitor (Tofacitinib) and MTX without drug holiday. 65 years old male suffered from lumbar disc herniation one month ago, and he had paresis rapidly. In MRI, lumbar disc herniation revealed clearly. We decided resection operation of herniation, but he did not desire drug holiday (withdrawal). So we operated without drug holiday. In result, he cleared paresis and had no post operated complication and no progression of inflammation. In short time and no impanting operation of RA patient using JAK inhibitor, we can complete without drug holiday in safety.

P2-146

Successful treatment with tofacitinib for biologics refractory rheumatoid arthritis, which was aggravated after removal of adrenal tumor

Naofumi Yamauchi¹, Koji Ihara²
¹Department of Rheumatology, Sapporo Kiyota Hospital, ²Department of Internal Medicine, Sapporo Kiyota Hospital

Conflict of interest: None

A 54-year-old male developed rheumatoid arthritis (RA) in February 2013 and was treated with methotrexate (MTX) 6mg /week in our hospital. Lung adenocarcinoma occurred in September 2013 and he was performed a left upper lobectomy. In January 2017, abdominal CT scan revealed a left adrenal tumor and the patient underwent a left adrenalectomy. He was pathologically diagnosed as a metastatic adenocarcinoma. Articular symptoms were aggravated (DAS28-CRP 6.32) after the surgery and the patient was treated with corticosteroid and increasing the dose of MTX. Because the symptoms were continued, abatacept was administered in August. However, it was not effective and switched to golimumab. But the disease activity was not controlled. Therefore, he was administered tofacitinib (TOF) in February 2018 and articular symptoms immediately improved. The low disease activity (DAS28-CRP 3.17) was achieved after 4 weeks of the treatment. Onset or exacerbation of RA after the surgery of Cushing's syndrome has been reported. It was suggested that the adrenalectomy caused progression of articular symptoms and TOF was effective in a RA patient inadequate response to biologics.

P2-147

A case report of successfully treated refractory psoriatic arthritis with tofacitinib

Michinori Ishitoku, Masamoto Funaki
Rheumatology Department, JR Hiroshima Hospital

Conflict of interest: None

(Patient) 66-year-old man (Main complaint) polyarthritis (History of present illness) In 1983 he developed vulgaris psoriasis. In 1995 he developed ulcerative colitis and remission was achieved by mesalazine. Pain in the shoulder joint, elbow joint, wrist joint, fingers joint appeared in May 2017 and he visited our department in June. (Clinical course) CASPAR classification was satisfied and he was diagnosed as psoriatic arthritis. Adalimumab (ADA) was started after introduction of celecoxib. Prednisolone (PSL) was used for a short period. Symptoms were improved, but they worsened after PSL was ended. Methotrexate (MTX) was started in October and it was increased, but the joint symptoms were not improved. Guselkumab was started in June 2018, but the symptoms were not improved. In August Tofacitinib (TOF) was introduced. After the introduction, joint symptoms improved. (Discussion) TOF suppresses the production of inflammatory cytokines by inhibiting JAK pathway. It is effective for rheumatoid arthritis and ulcerative colitis. There are many reports on the efficacy of TOF against psoriatic arthritis that is refractory to TNF inhibitors. In this case TOF was effective. TOF could be an effective treatment option for refractory psoriatic arthritis.

P2-148

A case with bilateral unstable artificial knees treated by constrained total knee arthroplasty

Toshihiro Mata¹, Aiko Kishida¹, Yukiko Komano¹, Ikuko Masuda¹, Koichiro Ohmura²

¹Center for Rheumatic Diseases, Jujoutakeda Rehabilitation Hospital, ²Rheumatology and Clinical Immunology, Kyoto University Hospital

Conflict of interest: None

Instability of artificial knee joint is treated with ligament reconstruction and soft tissue repair followed by long-time cast fixation. Instability of bilateral knees is a great matter for patients. We report one case with instability of bilat. artificial knee joints treated by constrained total knee arthroplasty (TKA). [Case]: The patient is 65ys old female. On February 22, 2017 lt. TKA was done. On December 13, 2017 rt. TKA was done. She fell down and suffered bilat. knee instability on March 16, 2018. Rt. Artificial knee was worse damaged than lt. Knee. The patient could only stand up but could not walk even with knee brace or canes. [Operation & Result]: Rt. constrained total knee arthroplasty was done on march 28, 2018. Lt. constrained total knee arthroplasty was done on April 23, 2018. Just after operation she could start walking without cast and brace. On September 2018, she can walk well with cane. [Discussion]: Instability of artificial knee is treated by reconstruction of ligament and soft tissue followed by casting. But bilateral knee casting is against post operative rehabilitation. It is difficult to revise unstable artificial knee with constrained total knee arthroplasty. But stability, mobility and early rehabilitation are obtained by one operation.

P2-149

A case report: dislocation of PS type TKA with synovial proliferation induced

Hiroaki Hamada

Division of Orthopaedic Surgery, Department of Medicine of Sensory and Mortor Organs, Faculty of Medicine, University of Miyazaki, Miyazaki, Japan

Conflict of interest: None

70 years old female [chief complaint] the left TKA dislocation [Present history] RA on set in 2001, for 2014/11/17, the left TKA operation (PERSONA PS type commented). In January, 2018, like, with the symptoms. First dislocation was carried, but an emergency and rescue crew carries with 3 people, it's said that it fitted in. When twisting the knee inside when standing up from a kotatsu on March 7, 2018, the second dislocation was carried on. [Complication] Interstitial pneumonia Hypothyroidism Hypertension. [RA treatment] TAC 1 mg/day, PSL 6 mg/day [operation view] synovial proliferation was admitted around the bar behind the post, and therefore it seems to have become easy to slip. In scopic view, the post even falls in the level of the bar, and judges a bar as slippery and contrary purpose for a dislocation. We removed the spacer, and the thickness 4 mm, 5 mm higher post were extended. Now, there is no joint instability after an operation, and range of motion is 0-or 140 after

half year operation, and she is walking without support. [Consideration] When I looked back to a record after 2014, DAS-28 had range between LDA and MDA around 3 years after an operation, moreover, a CRP average was 1.7 for RA control between it. New synovial proliferation seems to have affected the dislocation.

P2-150

Two cases that were planned TKA for the knee OA, but elderly onset RA was diagnosed based on a blood test result in preoperation, and canceled their operation

Takeshi Horii

Department of Orthopedic Surgery, Ishikawa Prefectural Central Hospital

Conflict of interest: None

[Case 1] TKA was planned for OA of an 87 y.o. woman, but laboratory data showed elevated CRP (11.7mg/dl). The present illness in detail revealed her symptom to be a polyarthritis. Though the anti-CCP antibody was negative but MMP-3 was high, the diagnosis might be elderly onset RA (EORA). She was started on oral prednisolone (PSL 10mg/day). Then the symptoms were improved immediately, and CRP fell to 0.9 at one week later. PSL was decreased gradually, but her clinical course is good. [Case 2] TKA was planned for OA of a 71 y.o. woman, but laboratory data showed elevated CRP (10.7mg/dl). Though the anti-CCP antibody was negative, there was possibility of EORA because of high MMP-3. She was started on oral PSL (15mg/day). Then the symptoms were improved immediately, and CRP fell to 1.0 at one week later. PSL was decreased gradually, and EORA was controlled by use of MTX and iguratimod. But on ten months later, TKA was performed because the joint destruction had progressed. [Discussion] Even if EORA develops in the case of the OA of an elderly person introduced for the purpose of TKA, only views of the OA of advanced stage on the X-rays may not notice a rheumatic disease. Enough check is needed in preoperation to evade the situation "un-necessary operations had been performed !".

P2-151

Biomechanical analysis of the bone graft for tibial defects in total knee arthroplasty

Koji Toritoribe, Etsuo Chosa, Hiroaki Hamada, Takero Sakamoto, Tomohisa Sekimoto

Department of Orthopaedic Surgery, Faculty of Medicine, University of Miyazaki

Conflict of interest: None

[Object] Achieving stability of the tibial implant is essential following cementless total knee arthroplasty with bone grafting. The present study aimed to investigate the effects of bone grafting on the stability of the tibial implant in the immediate postoperative phase. [Methods] Tibial implant models were developed using a finite element method. Geometric data were obtained from CT scans of the right tibia. Based on a pre-prepared template, ten types of bone graft models of varying sizes and material properties were prepared in the medial and posteromedial portion. A compressive force was applied to the posteromedial portion. Each model was loaded, and the micromotion and stress distribution were analyzed and compared. [Results] The medial side of the tibial tray exhibited subsidence, and the opposite lateral side showed liftoff. Compared with the soft bone graft models, the magnitudes of micromotion in the hard bone graft models were significantly lower. Maximum micromotion and excessive stress in the adjacent bone graft area was observed for the large soft bone graft model. [Conclusions] Our results suggested that grafting defects with hard bone is more likely to yield better fixation especially for larger, posteromedial defects.

P2-152

Aseptic Loosening after Total Knee Arthroplasty in Patients with Rheumatoid Arthritis

Satomi Nagamine, Eriko Ito, Motoki Sonohata, Masaaki Mawatari

Department of Orthopaedic Surgery, Faculty of Medicine Saga University

Conflict of interest: None

[Object] Total knee arthroplasty (TKA) in RA patients are known to have a higher risk of postoperative complications than patients with osteoarthritis. It may cause loosening of component with the bone fragility due RA itself or steroidal osteoporosis. Therefore, it is important to evaluate cautious bone quality before surgery. We investigated aseptic loosening after TKA in RA patients at our hospital. [Methods] It was investigated 293 knees were performed TKA in RA patients. The femoro-tibial angle and component installation angle in migration and aseptic loosening cases were measured using plain radiograph. In addition, as osteoporosis evaluation of preoperative, we were measured bone density and bone turnover markers. [Results] Component migration was observed in 7 knees. Progressive loosening was observed in 4 knees and revision were performed. Preoperative knee alignment in 6 knees of the migration cases were valgus deformity. Tibial components were varus and anteversion in all cases. [Results] If it is revision performed, physical and mental burden of the patient is large, and often it is difficult to treatment. To prevent revision, it is necessary to pay close attention to various points such as bone quality evaluation, osteoporosis treatment, implant selection and so on.

P2-153

Total knee arthroplasty without patellar resurfacing for rheumatoid arthritis

Kazue Hayakawa, Hideki Date, Sho Nojiri, Sota Nagai, Harumoto Yamada

Department of Orthopaedics, Fujita Health University, Toyoake, Japan

Conflict of interest: None

[Object] We investigated the outcome of total knee arthroplasty (TKA) without patellar resurfacing in patients with rheumatoid arthritis (RA). [Methods] The subjects were 74 patients with 97 knees. The mean follow-up period was 8 years and 10 months. The items investigated were clinical and plain X-ray findings. [Results] Knee ROM before surgery/at assessment was $-12.6/-1.1^\circ$ of extension and $120.1/120.6^\circ$ of flexion, while the JOA score was $41.5/90.1$. At assessment, the incidence of anterior knee pain and discomfort was 0% and 8.2%, respectively. There were no significant differences of knee flexion at assessment ($124.4/119.2^\circ$, $p=0.09$), follow-up period, age, use of biological agents, type of TKA, outside dissociation, ROM, JOA score, and FTA between the patients with patellar findings (26.8%) and those without patellar findings. However, the incidence of discomfort was significantly higher in the patients with patellar findings. Patellar resurfacing was not performed in any of the patients. [Conclusion] The clinical outcome of without patellar resurfacing TKA was generally favorable and was similar between the patients with and without patellar findings. We concluded that without patellar resurfacing TKA was an acceptable procedure in patients with RA.

P2-154

Study of the background and the medication of rheumatic patients who received total knee arthroplasty and total hip arthroplasty

Hiroshi Aonuma¹, Takeshi Kashiwagura², Yoichi Kataoka³, Hiromi Morita⁴, Wataru Watanabe⁵, Nobuhiro Ishizawa⁶, Natsuo Konishi⁷, Masakazu Urayama¹, Moto Kobayashi^{8,10}, Yusuke Sugimura⁹, Naohisa Miyakoshi¹⁰, Yoichi Shimada¹⁰

¹Department of Orthopedic Surgery, Ogachi Central Hospital, Akita, Japan, ²Department of Orthopedic Surgery, Akita City Hospital, Akita, Japan, ³Joto Orthopedic Clinic, Akita, Japan, ⁴Morita Orthopedic Clinic, Akita, Japan, ⁵Department of Orthopedic Surgery, Honjo Daiichi Hospital, Akita, Japan, ⁶Department of Orthopedic Surgery, Fujiwara Memorial Hospital, Akita, Japan, ⁷Department of Orthopedic Surgery, Akita Kousei Medical Center, Akita, Japan, ⁸Department of Orthopedic Surgery, Hiraka General Hospital, Akita, Japan, ⁹Department of Orthopedic Surgery, Nakadori General Hospital, Akita, Japan, ¹⁰Department of Orthopedic Surgery, Akita University Graduate School of Medicine, Akita, Japan

Conflict of interest: None

Objective: To investigate the patient background and the current state of medication and disease activity among RA patients with prior surgery of weight bearing joints of the lower extremities. Method: A total of 2172 RA patients were registered with the Akita Orthopedic Group on rheuma-

toid Arthritis in 2017. Of these, patients receiving surgery including 181 total knee arthroplasty (TKA), 70 total hip arthroplasty (THA) were evaluated. Result: Mean age at the time of TKA, THA were 63.8 and 61.8 years. Mean disease duration were 12.1 and 13.3 years. High titer (more than 13.5 U/ml) rate of anticyclic citrullinated peptide antibodies were 73.5 and 65.7. Mean age at the final survey among the four group were 63.8 and 61.8 years. Methotrexate and prednisolone were administered in 56.4 and 55.2 % of patients with TKA, 62.9 and 52.9% patients with THA. The patients with history of one or more biologics use were including 47.0 and 40.0. Mean DAS28-CRP were 2.65 and 2.62. Conclusion: It was old, and a contraction of a disease period was long, and the lower limbs artificial joint substituted postoperative patient was guessed if there were many examples that joint destruction already went.

P2-155

Clinical results of PFCsigmaRP total knee arthroplasty in patients with rheumatoid arthritis

Kiyoshi Nakazono, Akira Murasawa, Hajime Ishikawa, Asami Abe, Hiroshi Otani, Shinji Taniguchi, Satoshi Ito, Eriko Hasegawa, Yoichi Kurosawa

Department of Rheumatology, Department of Rheumatology, Niigata Rheumatic Center, Shibata, Japan

Conflict of interest: None

[Object] To demonstrate the clinical results of PFCsigmaRP total knee arthroplasty (TKA) in patients with rheumatoid arthritis (RA). [Methods] One-hundred seventy-two arthroplasties in 132 patients with RA were performed from January 2004 to December 2017 at Rheumatic Center. There were 15 men and 117 women: the mean patients age at the surgery was 65.0 years (range 33~86 years). The mean followed period was 4.1 years (0.1~15.4 years). We measured RA Japanese Orthopedic association (JOA) knee score, presence of loosening and preoperative and postoperative knee ROM. [Results] A fracture was present in three cases, loosening was absent. 15 patients was died. The mean preoperative RA JOA knee score was 44.1, and the score at the final examination was 81.9. [Conclusions] The clinical results of PFCsigmaRP total knee arthroplasty in RA patients was almost good.

P2-156

Bilateral periprosthetic femur fracture in patient with rheumatoid arthritis

Hiroshi Yonezu, Hiroshi Mikami

Department of Orthopaedic Surgery, Yoshinogawa Medical Center

Conflict of interest: None

[Introduction] The incidence of periprosthetic fracture after total hip arthroplasty (THA) or total knee arthroplasty (TKA) has recently increased with increases in the number of operative cases and the aging of the rheumatoid arthritis patients. We report our experience with one case of bilateral periprosthetic femur fracture. [Case] Patient was 82-year-old, woman who underwent for THA and TKA for rheumatoid arthritis. She consulted our hospital after incurring an injury due to a fall. On radiography, we accepted bilateral periprosthetic femur fracture with transposition. Because the instability was accepted, we chose to perform operative treatment. In addition, we started weekly injections of teriparatide after surgery. We confirmed callus formation on CT performed at 2 months after surgery, at which time she started wheelchair movement. At present, she can walk with T-cane. [Clinical Significance] It is reported that a weekly injection of teriparatide has the ability to stimulate bone formation, but there are few reports on its ability to stimulate bone union. We conclude that operative treatment with teriparatide is effective for periprosthetic fracture accompanying transposition.

P2-157

A case of rheumatoid arthritis who underwent bilateral simultaneous total knee arthroplasties for Windswept deformity

Shiho Nakano, Arata Nakajima, Masato Sonobe, Hiroshi Takahashi, Manabu Yamada, Koichi Nakagawa

Department of Orthopaedic Surgery, Toho University Sakura Medical

Center

Conflict of interest: None

[Case] A 66 years-old female, who had been suffered from rheumatoid arthritis (RA) for 44 years, presented with bilateral knee pain and gait disturbance in December 2010. She could walk with a Lofstrand crutch, but both knees were Larsen grade IV. The preoperative range of motion (ROM) was 20°~90° (right), 10°~70° (left), and the femorotibial axis (FTA) at the standing position was 177° (right) and 159° (left), which is called 'windswept deformity'. Bilateral simultaneous total knee arthroplasties (TKAs) were performed in June 2011. PS type Fine total knees were used with the patella replaced. In September 2018, seven years after surgery, she can walk without auxiliary tools, the range of motion is 0°~105° (right), 0°~105° (left), and Knee Society Score is 95 / 100 points (Knee Score, right / left) and 80/100 points (Functional Score, right / left). [Discussion] According to the previous reports, it is important to perform TKA for the varus knee and gain a normal supportive leg for the 'windswept' deformity accompanied with the severe valgus knee. However, there are problems including valgus instability on the contralateral side, difference in leg length, and gait abnormality due to cross leg. In this case, these problems could be solved by bilateral simultaneous TKAs.

P2-158

Comparative Study of Clinical Outcome after THA in Hemodialysis vs Non-Hemodialysis Patients

Yasumasa Ito

Department of Orthopaedic Surgery, Japanese Red Cross Fukuoka Hospital, Fukuoka, Japan

Conflict of interest: None

[Objectives] We compared the clinical outcomes after total hip arthroplasty (THA) in hemodialysis (HD) patients and non-HD patients. [Methods] We examined 12 patients (male 4 female 8, 13 hips) who underwent THA with PerFix HA system. The average age at THA was 60.7 years. The average duration of HD before THA was 9.0 years. Clinical outcomes were evaluated preoperatively and at 1 year postoperatively by JOA, D'Aubigne & Postel and Oxford scores. [Results] Preoperatively, the average JOA and Oxford scores in HD/non-HD patients are 41.5/43.5 and 15.2/17.8, respectively, with no significant difference statistically. But, there is significant difference in the average D'Aubigne & Postel score (8.9/10.4) between them. At 1 year postoperatively, the JOA, D'Aubigne & Postel and Oxford scores are 81.8/86.1, 15.5/16.5 and 39.4/43.0, respectively, with no significant difference. In terms of the subscales, only in the D'Aubigne & Postel function (walk) score (3.8/5.2) and Oxford walk score (2.7/3.5), non-HD patients achieved more significant improvement. [Conclusion] Despite poorer long-distance walking ability in HD patients, THA in HD patients is expected to bring good short-term outcomes comparable to those in non-HD patients.

P2-159

Occurrence of dislocation and stability were clearly confirmed in recurrent anterior dislocation after total hip arthroplasty when hip arthroscopy was added to open surgery with posterior lateral approach that was used at total hip arthroplasty

Kanzo Amano, Toshikatsu Kanazawa

Orthopedic Department, Hiroshima Clinic, Hiroshima, Japan

Conflict of interest: None

A female, 81 years old in 2018, underwent total hip arthroplasty (THA) with posterior lateral approach due to left hip osteoarthritis in 2012. In 2018, she suffered anterior dislocation of the hip joint three times, therefore, she underwent revision arthroplasty (Modular Dual Mobility and 4 mm lengthen of neck) with posterior lateral approach that was used at THA. Arthroscopy revealed dislocation due to an impingement between an implant neck and an elevated rim liner and acquirement of stability in the hip joint after revision. If revision is performed with anterior approach in patients with recurrent anterior dislocation after THA, dislocation can be easily observed. If anterior approach is performed in

patients who underwent THA with posterior lateral approach, two open surgeries from two directions cause a lot of invasion of the soft tissues around the hip joint. If revision is performed with the same approach in patients who underwent THA with posterior lateral approach, it causes less invasion. However, the mechanism of the anterior dislocation and the stability of the hip joint after revision are not observed under direct vision during surgery. If arthroscopy is added to open surgery with posterior lateral approach that is used at THA, it solves the dilemma.

P2-160

Total hip arthroplasty in patients with juvenile idiopathic arthritis

Suran Yang, Yuya Takakubo, Hiroharu Oki, Akiko Sasaki, Yasushi Naganuma, Yuta Suzuki, Juji Ito, Kan Sasaki, Michiaki Takagi

Department of Orthopaedic, Yamagata University Faculty of Medicine

Conflict of interest: None

[Object] The purpose of this study is to determine the outcomes and surgical complications for total hip arthroplasty (THA) in patients with juvenile idiopathic arthritis (JIA). [Methods] Examine the perioperative clinical condition and course of THA in JIA. [Results] This study included 8 hips in 4 patients. Age at THA averaged 35.8 (30-42) years, disease duration averaged 27.3 (21-36) years, the mean time to follow-up is 15.5 (6-34) years. Height averaged 148.6 cm, weight averaged 57.9kg. Larsen grade IV was observed in 3 hips, grade V was 5 hips. Stelo-Grarze grade I was observed 6 hips, grade II was 2 hips. All operations used cemented implants. We chose an implant of small size with 6 hips for thighbone medullary cavity narrowness. At surgery, difficulty with intubation due to the trismus was found in 2 hips in one patient. The walking ability improved in postoperative all cases. The postoperative dislocation was found in 2 hips in one patient. It were 2 hips in one patient to have needed reoperations (tardive deep part infection in the postoperative 27 years and loosening in postoperative 33 years). [conclusions] It was necessary to consider physique in implant choice. We were thought to need careful follow-up for a long term after surgery.

P2-161

The differences of the activity after total hip arthroplasty between Rheumatoid arthritis and Osteoarthritis

Kenjiro Fujimura, Hisaaki Miyahara, Satoshi Kamura, Hidetoshi Tsushima, Takashi Komatsu, Ryuta Sakurai, Hiroshi Takasu

Orthopaedics and Rheumatology, National Hospital Organization, Kyushu Medical Center

Conflict of interest: None

[Object] The number of patients who received total hip arthroplasty (THA) is increasing year by year because of stable long-term implant survival. We evaluated the activities of the patients after THA. [Methods] Patients who were performed THA more than one year ago were included in this study. They were asked their daily activities including sports, jobs and hobbies by interview. The Japanese Orthopaedic Association (JOA) hip score was also used to evaluate clinical outcome measure for hip function. [Results] We evaluated 33 patients (47 hips) in rheumatoid arthritis (RA) and 156 patients (212 hips) in osteoarthritis (OA). The average JOA hip score was 86 points for RA and 96 points for OA. More than 90 points in JOA hip score was about 53% in RA and about 90% in OA. Exercises and sports activities were done about one third in RA and two thirds in OA. Most of RA patients were satisfied by normal daily lives and only a few cases played low-impact sports. On the other hand, most of OA patients played low-impact sports and moreover a few patients played high- impact sports. [Conclusions] There will be increasing number of RA patients who anticipate to join in sports activities because of no or less joint pain for extensive medications.

P2-162

Experience of bilateral simultaneous ALS-THA for RA patient

Koji Asaumi

Department of Orthopaedic Surgery, Yashima General Hospital, Takamatsu, Japan

Conflict of interest: None

[Object] We report on experiences of bilateral simultaneous ALS-THA for RA patient. [Case] 68 years, woman. Both coxalgia was increased for one year, because a pain aggravated it, it became our department introduction consultation in surgical therapeutic purpose. She had an allergy to metal as a medical history. The diagnosis was both coxarthrosis. It was adaptation of the THA for the pain that was similar to both sides, and the release from an early pain is hoped for even a little and will perform bilateral same time THA. Rheumatoid arthritis was diagnosed in pre-operative examination and started medication by MTX postoperatively. In late years we used Dual Mobility Bearing from the viewpoint of dislocation prevention. However, we used Continuum cup because we had an allergy to metal for the cobalt chromium in the disorder. We performed the THA by the ALS approach so that the dislocation had resistance in the small bone diameter of head. The operative time was left 54 minutes, right 53 minutes. We started a walker walk on the second day after surgery and left the hospital without perioperative complications to the home on day 24 after an operation. [Conclusion] I experienced bilateral simultaneous ALS-THA for RA patient and got a good course.

P2-163

Late infection of total hip joint arthroplasty in 3 rheumatoid arthritis patients treated with biologics

Hiroki Wakabayashi, Masahiro Hasegawa, Akihiro Sudo
Department of Orthopaedic Surgery, Mie University Graduate School of Medicine

Conflict of interest: None

[Object] Three cases of late infection of total hip arthroplasty (THA) following biologics therapy in rheumatoid arthritis (RA) patients are reported. [Case] THA were performed in 3 patients with RA. They were received biologics therapy 3 year after THA (patient 1; tocilizumab), 2 month after THA (patient 2; etanercept) and 1 month before THA (patient 3; etanercept). However, they were age at the time of THA infection was 71 male (patient 1) and 64 females (patient 2, 3) years old. The causative organism were shown to be MSSA (patient 1) and *Listeria* (patient 3), and unknown (patient 2). All patients underwent open debridement and exchange of modular components. Currently, 7 years (patient 1), 11 months (patient 2) and 10 months (patient 3) after the operation, the patient is able to walk without pain, reports no symptoms in the previously infected hips. [Significance] Postoperative infection and delayed healing are a concern during biologics therapy. These cases were late infection from 3 years to 10.5 years after THA operation. Biologics therapy after the total joint arthroplasty also takes possibility of postoperative infection merger into consideration. It seemed necessary to observe carefully.

P2-164

Transition of total hip arthroplasty for RA hip in our department

Junya Mibe¹, Kengo Yamamoto²

¹Tokyo Metropolitan Ohtsuka Hospital, Tokyo, Japan, ²Tokyo Medical University

Conflict of interest: None

[Object] We investigated all cases of THA in our department. [Methods] We performed one hundred nineteen THA from 1994 to 2018 for RA patients. The operative age was 27 to 85 years old (average 62.3 years old), 17 male 101 female, and we clinically examined. [Results] The number of surgeries and age in every 5 years are 1994 ~ 1998: 27 cases, 59.8 years, 1999 ~ 2003: 34 cases, 59.6 years, 2004 ~ 2008: 13 cases, 67.3 years, 2009 ~ 2013: 13 cases, 67.3 years, 2014 - 2018: 15 cases, 65.3 years old. On the acetabular side, we did cement fixation from 1994 to 1999, and cementless fixation from 1999 to 2018. On the femur side, all cases were fixed with cement until 1998, and fixed without cement from 2001. From 2009 we adopted muscle sparing antero-lateral approach, and from 2014 we use X-ray image in supine position, and it is possible to recover promptly without complications due to the progress of drug therapy. [Conclusions] THA is said to be the most successful operation. Prior, high risk of dislocation, fracture, vulnerability, bone loss were pointed out in THA for RA hip, but nowadays, THA can expect a

reliable result.

P2-165

Middle and long-term results of ankle arthrodesis using intramedullary nail with fin for rheumatoid arthritis

Naoto Yamauchi¹, Sadamu Shibata¹, Tadashi Okawa¹, Kiyoshi Yamauchi²

¹Department of Orthopedic Surgery, Kin-ikyo Chuo Hospital, ²Department of Orthopedic Surgery, Kin-ikyo Ichijo Hospital

Conflict of interest: None

[Object] The objective of this study was to evaluate the clinical results and problems associated with ankle arthrodesis using an intramedullary nail with fin for patients with rheumatoid arthritis more than 5 years after surgery. [Methods] Ankle arthrodesis was performed using an intramedullary nail with a fin to treat 16 rheumatoid arthritis patients. The mean age at surgery was 61.0 years and the mean follow-up time was 9 years and 1 months. Clinical evaluation was assessed by the patients' pain and the union of the tibiotalor and talocalcaneal joints, additional surgery and degeneration of middle foot. [Results] Tibiotalor arthrodesis was achieved after surgery in all patients. Talocalcaneal arthrodesis was not done in 4 cases. Pain occasionally occurred in 5 cases. Additional surgery for implant removal was performed on 3 joints. Also, talocalcaneal arthrodesis was performed on 2 joints. Degeneration of middle foot of 10 joints progressed. [Conclusions] Ankle arthrodesis with an intramedullary nail with a fin was useful for patients requiring union of the tibiotalor and talocalcaneal joints. However careful postoperative observation of the talocalcaneal joint is necessary. Degeneration of the middle foot progressed at 63%, but no additional surgery was required.

P2-166

Investigation of osteoporosis in elderly patients with rheumatoid arthritis

Ken Kumagai, Hyonmin Choe, Shunsuke Yamada, Akiko Nagaoka, Yutaka Inaba

Department of Orthopaedic Surgery, Yokohama City University School of Medicine

Conflict of interest: None

[Object] In recent years, elderly population is increasing in patient with rheumatoid arthritis (RA). We investigated the status of osteoporosis in elderly patients with RA. [Methods] RA patients with 65 years of age or older were extracted in this study. [Results] Twenty-eight percent of patients have a history of fracture. Fracture rate in patients with use of corticosteroid is significantly greater than in patients with no use of corticosteroid. [Conclusions] Elderly patients with use of corticosteroid should be careful about osteoporosis treatment.

P2-167

Insufficiency fractures adjacent joints in patients with rheumatoid arthritis

Hidetoshi Tsushima, Takashi Komatsu, Satoshi Kamura, Kenjiro Fujimura, Hisaaki Miyahara

National Hospital Organization Kyushu Medical Center

Conflict of interest: None

[Object] Patients with long-standing rheumatoid arthritis (RA) tend to represent severe bone fragility, which improved with long-term use of corticosteroids. Usually, atraumatic periarticular symptoms with RA patients may be considered arising from arthritis. This study shows the cases that the causes of pain in adjacent a joint are the insufficiency periarticular fractures in RA patients. [Results] The cases were 8 female RA patients. The mean age at onset was 70 (64 -79) years and the mean duration of the disease was 17.2 (5-36) years. Three patients complained of gonalgia with proximal tibia fracture and others complained of ankle pain with distal tibia fracture without obvious injuries over the site of involvement. Corticosteroid was used in 7 patients of 8. According to the Steinbrocker stages, 4 patients belonged to stage III and 2 to stage IV. All case represented stable fracture on X-ray and treated conservatively. [Conclu-

sions] They were the group that have the risk factors of osteoporosis including long disease duration, aged female and use of corticosteroid. If a patient with RA, especially have these risk factors, experiences pain without obvious injuries around their joint, you might need also suspect fracture besides arthritis as a cause of pain.

P2-168

Gain of bone mineral density in rheumatoid arthritis patient

Ichiro Yoshii¹, Tatsumi Chijiwa², Naoya Sawada³

¹Rheumatology and Musculoskeletal Medicine, Yoshii Hospital, ²Department of Rheumatology, Kochi Memorial Hospital, ³Department of Rheumatology, Dohgo Spa Hospital

Conflict of interest: None

[Object] Bone mineral density (BMD) gain in rheumatoid arthritis (RA) patient, and factors that affect BMD were investigated. [Methods] From April 2013 to September 2018, BMD had been measured 2596 times. Patients were divided into RA patient group (G-RA) and non-RA group (G-nRA). Patients' background, drugs administration, BMD of lumbar spine (LS), femoral neck (FN), whole proximal femur (WF), and greater trochanter (GT) after age was corrected, and their changes were statistically compared between the two groups with Mann Whitney U test, and significant factors in G-RA were compared. [Results] In 918 case of G-RA and 1678 of G-nRA, G-RA demonstrated significantly younger age, and significantly more patient who administered glucocorticoid steroid. There is no other background factors or blood test results that demonstrated significantly different. G-RA demonstrated significantly more BMD in all bones, while significantly higher BMD gain only in GT. G-RA demonstrated significantly less patient who gained BMD only in LS. Activities of daily life (ADL) and gait speed (GS) correlated with BMD gain in LS. [Conclusions] RA patient demonstrated more BMD than non-RA even age factor was diminished. There is still unclear, however, it is suggested that ADL and GS affect.

P2-169

Osteoporosis treatment of patients with rheumatoid arthritis in our hospital

Norie Yoshikawa¹, Koichiro Saisho², Hiroaki Hamada³, Etsuo Chosa³

¹Department of Orthopedics, NHO Miyakonojo Medical Center, ²Tanimura Hosiptal, ³Department of Orthopedics, Faculty of Medicine, University of Miyazaki

Conflict of interest: None

[Object] We investigated osteoporosis treatment of patients with rheumatoid arthritis in our hospital. [Methods] The contents of osteoporosis treatment examine in 333 RA patients visited in 2017. There were 70 males patients 263 female patients, with mean age of 68.9 years. [Results] 153 (46%) patients were treated for osteoporosis. There were 107 (70%) patients treated bisphosphonate (alendronate in 48 patients, risendronate in 14 patients, minodronate in 25 patients, ibandronate in 17 patients), 14 (9%) patients treated denosumab, 4 (7.5%) patients treated teriparatide, 5 (3%) patients treated SERM, 23 (15%) patients treated vitamin D. The use of teriparatide and ibandronate has increased since 2014. There were 38 patients treated bisphosphonate in 100 patients with steroid osteoporotic fracture risk factor score of over 3. [Conclusions] RA patients with high risk of fracture should be treated appropriately for osteoporotic fracture.

P2-170

A functional polymorphism on ALDH2 gene and bone mass among community-dwelling persons

Kazuhiko Arima¹, Naoki Iwamoto², Shin-ya Kawashiri², Mami Tamai², Tomoki Origuchi², Atsushi Kawakami², Kiyoshi Aoyagi¹

¹Department of Public Health, Division of Advanced Preventive Medical Sciences, Nagasaki University, ²Department of Immunology and Rheumatology, Nagasaki University

Conflict of interest: None

[Object] To evaluate the relationship between a functional single nucleotide polymorphism (SNP) on ALDH2 gene and bone mass among community-dwelling persons. [Methods] This cross-sectional study was nested in Nagasaki Islands Study, which is a prospective cohort in Goto City, in islands of Japan. Participants (206 men and 336 women) were recruited at medical check-ups for community dwelling population. Alcohol drinking behavior was categorized as "everyday drinker," "periodic drinker," "former drinker" or "non-drinker". Body height and weight were measured and body mass index (BMI) was calculated. Stiffness index of the calcaneus was obtained from quantitative ultrasound measurements. Peripheral blood mononuclear cells were obtained from these subjects. The SNP (rs671) was genotyped using hydrolysis probe. [Results] Logistic regression analysis revealed an association of the SNP on ALDH2 and bone loss (Odds Ratio 1.80, 95% C.I. 1.01-3.23, p=0.047) in men. There was no significant association in women. [Conclusions] The SNP might be associate with bone health.

P2-171

The investigation of bone metabolic markers according to the functional disorders among patients with rheumatoid arthritis

Tetsuya Kawano^{1,2}, Takeshi Kashiwagura², Toshiaki Aizawa^{1,2}, Natsuo Konishi², Masakazu Urayama², Moto Kobayashi², Hiroki Ito², Hiroshi Aonuma², Yusuke Sugimura², Keiji Kamo², Hidekazu Abe², Takayuki Tani², Norio Suzuki², Tsutomu Sakuraba², Naohisa Miyakoshi^{2,3}, Yoichi Shimada^{2,3}

¹Kitaakita Municipal Hospital, ²AORA (Akita Orthopedic Group on RA), ³Department of Orthopedic Surgery, Akita University Graduate School of Medicine

Conflict of interest: None

[Object] RA is one of the causes of secondary osteoporosis. Immobilization progresses with the progress of dysfunction, possibly causing severe osteoporosis. In this study, we examined whether there is a difference in bone metabolism markers in each group according to Steinbrocker classification. [Methods] Of the 2238 cases in AORA registry 2017, 101 cases measuring bone metabolism markers and pentosidine were involved. Patients were divided by Steinbrocker classification into class 1,2 (group A 84 cases) and class 3, 4 (group B 17 cases). [Results] The average age in group B (75.9) was significantly higher than group A (66.9) (p = 0.01). DAS 28 ESR was significantly higher in group B (p < 0.01). The urinary DPD and pentosidine in group B was significantly higher than group A (p < 0.01). No difference was observed between the two groups in other bone metabolism markers. [Conclusions] Based on the results of this study, urinary DPD showed a high value in RA group with high degree of dysfunction, which possibly reflected immobilization due to progress of functional disorder. Moreover, it is known that pentosidine will be higher in cases with high disease activity, severe osteoporosis will be occurred in the group with progressive functional disorder which is difficult to tight control.

P2-172

Bone and cartilage metabolism marker in synovial fluid of hip osteoarthritis

Ryosuke Yamaguchi, Satoshi Ikemura, Junichi Fukushi, Yukio Akasaki, Toshifumi Fujiwara, Yasuharu Nakashima

Department of Orthopaedic Surgery, Kyushu University Graduate School of Medical Sciences

Conflict of interest: Yes

[Object] To compare the levels of bone and cartilage metabolism markers in the synovial fluid of hip osteoarthritis caused by osteonecrosis of the femoral head (ONFH), rapidly destructive arthrosis (RDA) and developmental dysplasia of the hip (DDH). [Methods] We studied 70 synovial fluid samples from 57 patients with ONFH, 21 samples from 21 patients with RDA and 20 samples from 20 patients with DDH. The levels of BAP, TRACP-5b, MMP-3 and keratan sulfate were analyzed. [Results] The levels of BAP, MMP-3 and KS were significantly higher in ONFH group than in RDA and DDH groups. The levels of TRACP-5b were highest in RDA group. The levels of BAP in the ONFH group after the development of osteoarthritic changes were significantly lower than those

observed in earlier stages. In the comparisons between the samples obtained from each group with a terminal condition, ONFH samples exhibited significantly higher MMP-3 and KS levels, while the TRACP-5 levels were highest in RDA group. [Conclusions] ONFH patients showed a relatively bone formative condition before the osteoarthritic stage and maintained a higher rate of cartilage turnover throughout several stages compared to RDA and DDH patients. RDA patients were characterized by a significantly high osteoclast activity.

P2-173

The rate of patients with radiological erosive hand OA (EHOA) findings among patients with rheumatoid arthritis, and the effect of DMARDs on the progression of EHOA

Tsuyoshi Nishiume¹, Takefumi Kato², Nobunori Takahashi¹, Toshihisa Kojima¹, Shuji Asai¹, Takuya Matsumoto¹, Nobuyuki Asai¹, Yasumori Sobue¹, Mochihito Suzuki¹, Yutaka Yokota¹, Naoki Ishiguro¹

¹Nagoya University Orthopedics Department, ²Kato Orthopedics Clinic

Conflict of interest: None

<Objective> To investigate the rate of patients with the image findings of EHOA among patients diagnosed as rheumatoid arthritis and the influence of DMARDs in this patient group on the progression of erosive hand OA. <objects> 1145 patients with rheumatoid arthritis who are visiting Kato orthopedic clinic or Nagoya University hospital. <method> Patients with erosive changes defined by Verbruggen in DIP or PIP joints with the nearest two hands Xp among the subjects were counted. Among them, radiographic changes of the DIP / PIP joints were retrospectively evaluated by the Verbruggen method. <Results> There were 41 patients (40 females, average age 69.4 years) with the findings of EHOA among the 1145 subjects, the complication rate was 3.5% and the seronegative RA was 23 (55%). Among the 35 people (34 females) whose hands Xp were taken over the course of 1 year or more, the Verbruggen score worsened on the Xp image by an average of 3.3 points / year, including 23 people using bDMARDs. <Discussion and Conclusion> Although the incidence of EHOA has been reported to be 2-3%, it was similar in RA patients. From the results of this study, radiographic EHOA changes progressed and it was considered that rheumatoid arthritis treatment including bDMARDs was ineffective.

P2-174

Clinical findings and Pathology of synovitis with combined RA and OA knee

Keita Nagira¹, Hiroshi Hagino², Masako Hayashibara¹, Daichi Mukunoki¹, Chikako Takeda¹, Hideki Nagashima¹

¹Department of Orthopedic Surgery, Faculty of Medicine, Tottori University Hospital, Yonago, Japan, ²School of Health Science, Faculty of Medicine, Tottori University Hospital, Yonago, Japan

Conflict of interest: None

[Object] To compare retrospectively whether there is difference between clinical findings and synovial pathology findings in presence or absence of OA change by X-ray in RA patients who underwent TKA. [Methods] Material was 80 patients with RA who underwent TKA from 2000 to 2017 at our hospital. Twenty one patients who underwent histopathological examination of the synovial membrane during surgery were targeted. Regardless of the change of OA, they were divided into two groups; 1) RA knee; 10 cases, 2) RAOA knee; 11 cases. The variables were age, sex, duration of disease, Steinblocker classification (stage, class), therapeutic agent, disease activity, physical findings, synovial pathology findings. [Results] Age at onset of RA was 44.3 ± 5.6 years for RA knee and 60.4 ± 12.9 years for RAOA knee ($P=0.001$). Age of TKA was 60.0 ± 8.1 years for RA knee, RAOA knee was 68.9 ± 9.3 years ($P=0.029$). There was no significant difference in therapeutic agent, disease activity, physical findings, total synovial pathology score between two groups. However, total score was relatively high both of RA knee 7.4 ± 2.3 and RAOA knee 6.5 ± 1.2 points. [Conclusion] In the RAOA knee, RA seems to have occurred concomitantly with the knee which had originally changed OA.

P2-175

Zoledronic Acid Treatment in Patients with Osteoporosis Who Have Various Kinds of Characteristics -Results in 12 months-

Yuji Hirano, Daisuke Kihira

Department of Rheumatology, Toyohashi Municipal Hospital

Conflict of interest: Yes

[Object] The aim of this retrospective study is to investigate efficacy of zoledronic acid (ZOL) in patients with osteoporosis (OP) who have various kinds of characteristics in daily clinical practice. [Methods] 27 OP patients treated with ZOL over 12 months were used. Time-course of BMD, time-course of bone turnover markers (BTM) and frequency of acute phase reaction (APR) were investigated. Comparison between postmenopausal OP patients (PMOP) and RA patients (RAOP) and comparison between bisphosphonate pretreatment patients (BP-G) and no-pretreatment besides vitamin D patients (ND-G) were also performed. [Results] Mean age was 71 years. 48% had previous fracture history. PMOP: n=8, RAOP: n=16. BP-G: n=12, ND-G: n=9, Pretreatment of denosumab: n=5. LS-BMD was increased in +3.4% at 12m and THBMD was increased in +1.1%. Both were statistically significant. BTMs were significantly decreased. %increase of BMD at 12m was as below. PMOP: LS BMD +1.8% ($p=0.21$), THBMD +1.1% ($P=0.31$). RAOP:LSBMD+4.3% ($p<0.01$), THBMD+1.1% ($p=0.03$). BP-G: LSBMD+4.0% ($p<0.01$), THBMD+1.0% ($p=0.05$), ND-G: LSBMD+4.6% ($p=0.01$), THBMD+2.3% ($p=0.01$). APR occurred in 22.2%. [Conclusions] Although ZOL was comparatively effective in LSBMD and RAOP, pretreatment of BP inhibited efficacy of ZOL. Most APR was mild but frequent.

P2-176

Once-yearly zoledronic acid for osteoporosis patients

Taisei Kawamoto¹, Satoshi Iida¹, Takeshi Umibe²

¹Department of Orthopedics, Matsudo City General Hospital, ²Department of Rheumatology, Matsudo City General Hospital

Conflict of interest: None

[Object] Zoledronic acid is a third-generation bisphosphonate that has recently been approved for the treatment of osteoporosis as an annual intravenous infusion. Objective: To evaluate Zoledronic acid to osteoporosis patients for short-term results. [Methods] From January 2017 eleven cases treated with zoledronic acid were evaluated by bone mineral density (BMD). [Results] the BMD in the lumbar spine and femoral neck increased by 8.2% and 4.4% respectively. Most common side effects are post-dose fever, flu-like symptoms, myalgia, arthralgia, and headache which usually occur in the first 3 days after infusion. [Conclusions] The therapy of Zoledronic acid to osteoporosis was effective for short-term results.

P2-178

The efficacy of anti-RANKL monoclonal antibody (Denosumab) under the treatment of connective tissue disease (CTD)

Naofumi Dobashi, Moemi Miyazaki, Kenshi Inoue, Kenta Misaki

Department of Rheumatology, Kita-Harima Medical Center

Conflict of interest: None

[Object] We evaluated the efficacy of Denosumab (Dmab) by using BMD and serum TRACP-5b and BAP. [Methods] One hundred forty-four CTD patients under the treatment of Dmab were included. Fifty-six among 144 patients were retrospectively analyzed for 12 months by measuring BMD of lumbar vertebra (L), femoral neck (FN) and the serum TRACP-5b and BAP. [Results] Baseline patient characteristics (n=56) was as follows; Mean age:70.5 years old, ratio of male to female (M:21, F:35), RA (n=21), SLE (n=9), IgG4-RD (n=6), MPA (n=5), GCA (n=4), PM/DM (n=3), SSc (n=2), EGPA (n=1), RS3PE (n=1), others (n=4). After the treatment in all patients, BMD of L was $91.7\text{vs }94.9\%$ (pre. vs post., $p=n.s.$), PSL: $13.0 \pm 14.2\text{vs }2.7 \pm 3.4\text{mg/day}$, those of FN was $83.4\text{vs }84.9\%$ ($p=n.s.$), TRACP-5b and BAP were $481.0\text{vs }325.3\text{mU/dL}$ ($p=0.0001$), $12.2\text{vs }9.9\mu\text{g/L}$ ($p=0.022$), respectively. In SLE, BMD of L was $98.3\text{vs }100.6\%$ ($p=n.s.$), those of FN was $90.7\text{vs }90.9\%$ ($p=n.s.$),

TRACP-5b and BAP were 450.3vs271.4mU/dL ($p=0.0023$), 14.1vs9.4 μ g/L ($p=n.s.$), respectively. In MPA, BMD of L was 103.0vs107.8% ($p=n.s.$), those of FN was 92.4vs95.0% ($p=n.s.$), TRACP-5b and BAP were 586.4vs218.0mU/dL ($p=0.036$), 9.6vs7.9 μ g/L ($p=n.s.$), respectively. [conclusions] Patients of SLE and MPA needed the PSL treatment had the improvement of serum TRACP-5b with statistical significant.

P2-179

Glucocorticoid use in patients with rheumatoid arthritis during administration of denosumab increases the risk of developing new vertebral fractures

Eri Narita^{1,2}, Hitoshi Yoshimura^{2,3}, Syuji Yamada^{2,4}, Kazuki Orita^{2,5}, Shuhei Ueno^{1,2}, Tatsuya Koike^{1,2,6}

¹Shirahama Hamayu Hospital, ²Search Institute for Bone and Arthritis Disease (SINBAD), ³Saiseikai Nakatsu Hospital, ⁴Osaka City General Hospital, ⁵Daito Chuou Hospital, ⁶Center for Senile Degenerative Disorders (CSDD), Osaka City University Medical School of Medicine

Conflict of interest: None

[Objective] We examined risk factors of new vertebral fracture in patients using DMAB for 2 years. [Methods] 84 patients who had DMAB for osteoporosis from Aug 2013-2018 and were able to follow spinal X-ray for 2 years. For vertebral body fractures, we evaluated by Genant classification. Genant classification grade 2 or more was defined as vertebral body fracture. Evaluation items were age, lumbar bone mineral density (LBMD), rheumatoid arthritis (RA), glucocorticoid (GC) use. From the fourth thoracic vertebra to the fifth lumbar vertebra were evaluated. [Results] The age was 73.6 ± 9.1 , LBMD at baseline was 0.636 ± 0.121 , 49 cases of RA, 21 cases of GC user. Thirty two cases of new vertebral body fractures (1st year 23 cases, 2nd year 13 cases) were observed. Only age was a significant risk factor in the logistic regression analysis. When we analyzed similarly with focusing on the RA group, only GC use was a significant risk factor. When analysis was made separately for the 1st year and the 2nd year, no significant risk factor was extracted in the 2nd year. [Conclusions] Although RA was not a risk factor for new vertebral body fractures, GC use is a very strong risk factor in the initial stage.

P2-180

Clinical effect of the administration of 1,25-dihydroxyvitamin D3 longer than 2 years on Locomo25 score

Yusuke Ueda¹, Hirokuni Takayama¹, Kei Yamamoto², Norihiro Ichikawa², Ayumu Nishihara³

¹Department of Orthopedic Surgery, Kansai Medical University Kori Hospital, ²Department of Orthopedic Surgery, Kansai Medical University Medical Center, ³Department of Orthopedic Surgery, Yamamoto the Third Hospital

Conflict of interest: None

[Object] Previously, a few reports describe the advantages of 1,25-dihydroxyvitamin D3 in ability of daily life (ADL). In this study, we aimed to evaluate the efficacy of the administration of 1,25-dihydroxyvitamin D3 in ADL. [Methods] 211 female patients, over 65 years old, were included, and classified into two groups, one who administered 1,25-dihydroxyvitamin D3 longer than 2 years (Group A), and the other (Group B). We evaluated Locomo25, bone mineral density (BMD), and lateral roentgenogram of thoracic and lumbar spine. Statistically analyses were performed using Mann-Whitney U test and Fisher's exact test, and we accepted statistical significance at $p<0.05$. [Results] In Group A, 60 cases, average Locomo25 score was 21.3 points, in Group B, 151 cases, 22.7 points ($P=0.65$). Osteoporotic vertebral fractures (OVF) were identified 21 cases in Group A, 26 in Group B, statistically significant differences were detected in existence rate ($P=0.005$). In BMD, there were no significance between two groups ($P=0.64$). [Conclusions] OVF is considered to cause of Locomotive syndrome. However, in this study, Group A demonstrated paradoxically lower score of locomo25 than Group B. In the patients with OVF, administration of 1,25-dihydroxyvitamin D3 suggested to contribute maintaining ADL.

P2-181

The Diagnosis of Atypical Femoral Fracture and Determination of Surgical Intervention by MRI

Koji Nomura^{1,2}, Tomomi Tada², Takeshi Kaneko², Kenji Funakoshi², Shinichiro Nameki², Jun Fukui², Takashi Hosokawa², Hiroshi Fujiwara²

¹Department of Orthopedic Surgery, Osaka General Medical Center, Osaka, Japan, ²Division of Rheumatology, Osaka General Medical Center, Osaka, Japan

Conflict of interest: None

[Background] Many patients with rheumatic disease take bisphosphonate to treat glucocorticoid-induced osteoporosis. Recently atypical femoral fracture (AFF) by long-term use of bisphosphonate has become known. As most of it is diagnosed with X-ray alone, we tend to miss the imminent fracture. [Case] 52-year-old female. SLE occurred at the age of 18 and PSL treatment was started. Bisphosphonate treatment was also done for over 12 years. A few months ago she felt a slight pain in her right hip joint and the pain was exacerbated from one month ago. The X-ray showed the 'beaking' sign, which was specific to AFF, at the lateral cortex of the bilateral femoral subtrochanteric area. Shortly thereafter, she suddenly felt the weakness of right lower limb and fell down to the right AFF. MRI just before the fracture showed the STIR (T2) high signal at the very site of 'beaking' and no signal changes in the bone marrow. Although the similar 'beaking' sign was observed at the left femur, there was no significant finding in either MRI or bone scintigraphy and she had no left thigh pain. [Clinical Significance] MRI is very useful in evaluating the imminent fracture of AFF and the prompt surgical intervention will be needed when the abnormal signal is recognized at the 'beaking' area.

P2-182

A Seven cases report of the atypical femoral fractures treated surgically

Yukio Mikami, Taisei Kawamoto, Satoshi Iida
Matsudo City General Hospital

Conflict of interest: None

[Object] We investigated seven cases report of the atypical femoral fractures treated with internal fixation. [Methods] We targeted AFF cases who underwent operation from March 2016 to July 2018. We examined items such as age, sex, medication, past history, trauma injury, fracture site, thigh bone shape, bone fusion period, YAM, bone metabolism marker. [Results] The subject was ten limbs in seven cases. All cases were female, the average age was 70.8 years (57 to 88 years old). Complete fractures were five cases. Incomplete fractures were two cases. There were three cases on both sides. Bisphosphonate (BP) formulation was used in six of seven cases, and Denosumab was used in one case. Two out of seven patients were taking steroids for more than ten years. Mean bone fusion period with complete fracture was 8.6 months (7 to 10 months). Bone metabolism marker, YAM did not show a remarkable low value. Surgical treatment was done for incomplete fracture cases. A case of incomplete fracture was able to walk with the cane and shopping in three weeks postoperatively. [Conclusions] Bone fusion period was long with complete fractures. Because there is a high possibility of transitioning to complete fracture, preventive nail insertion for incomplete fracture seems to be effective.

P2-183

Osteonecrosis of the jaw in patients with rheumatoid arthritis treated with denosumab: three cases report

Shinichi Mizuki, Tatsuya Kai, Daisuke Hiraoka, Kenji Yoshida, Hiroko Ikeuchi, Kensuke Oryoji

The Center for Rheumatic Diseases, Matsuyama Red Cross Hospital

Conflict of interest: None

BACKGROUND: Denosumab is now widely used for the treatment of osteoporosis and RA. Osteonecrosis of the jaw (ONJ) is a potentially severe adverse event in patients with osteoporosis treated with anti-resorptive drugs. Rheumatoid arthritis (RA) has been hypothesized as a po-

tential risk factor for ONJ. **OBJECTIVE:** To clarify the clinical features of ONJ in patients with RA treated with denosumab. **METHODS:** We present three patients with osteoporosis and RA who treated with denosumab. Demographic, pharmacological, and clinical data were collected. **Case Presentation:** This report describes three patients; a 81-year-old woman, a 77-year-old woman, a 64-year-old man. All patients received treatment with prednisolone, and two were treated with biologic drugs. All patients stopped denosumab, and after the treatment with antibiotics, all patients underwent surgical curettages. Two patients cured. **CONCLUSIONS:** It should be important to monitor oral environment during denosumab treatment.

P2-184

The role of the nurse for rheumatoid arthritis patients complicated with osteoporosis

Kokoro Takata¹, Aya Oshimura¹, Takeko Koyama¹, Ken Takebe², Koji Tateishi², Yasuhiro Terashima²

¹Nursing Unit, Japan Hyougo Kohnan Kakogawa Hospital, ²Orthopedic Surgery, Japan Hyougo Kohnan Kakogawa Hospital

Conflict of interest: None

[Object] We examined the present conditions of the everyday life of RA patients and our purpose is reveal that the role of the nurse for RA patients complicated with osteoporosis. [Method] We research 400 patients who received osteoporotic liaison service in our hospital that is separated by the RA group and non-RA group used by an interview vote. We made the current state clear by comparing a medical record of inspection data and PSL internal. [Result] 139 RA patient group (men:12 women: 127, average ages:70.8 years old, PSL:91 non-PSL:48) a bone fracture career was 47% and twice in the above-mentioned bone fracture career was 32%. An osteoporotic bone fracture was 84% (vertebral fracture:38%, hip fracture:26%, femoral neck fracture:9%, other bone fracture:41%) 261 non-RA patient group (men:10 women: 251, average ages:74.7 years old, non-PSL:247) a bone fracture career was 53% and twice in the above-mentioned bone fracture career was 17%. An osteoporotic bone fracture was 78% [Conclusion] Our result is that a nurse is required to prevent the osteoporotic bone fracture as complications as well as RA treatment, maintain the health of the frame, guide activities of daily living and observe and instruction for treatment continuation.

P2-185

Two cases of tumour-induced osteomalacia treated as RA

Takashi Komatsu, Satoshi Kamura, Hidetoshi Tsushima, Kenjiro Fujimura, Hisaaki Miyahara
Orthopaedic Surgery Rheumatology, National Hospital Organization Kyushu Medical Center

Conflict of interest: None

Tumor-induced osteomalacia (TIO) is overgrown of fibroblast growth factor 23 (FGF23) from tumors. We report that we experienced two cases of tumour-induced osteomalacia treated as RA. Case1 presentation: 37-year-old-male, he recognized front chest pain and lower back pain, and treated as seropositive RA. But he was consulted to our hospital because his pain did not improve. The laboratory data revealed hypophosphatemia, hyperphosphataseemia and decreased bone density was also observed. We suspected TIO from increased FGF23, a mass lesion in the left popliteal region was detected in PET-CT. Case2 presentation:52-year-old-female, she recognized seropositiveRA, polyarthralgia, and treated as RA. She was consulted to our hospital because injured for a calcaneus fracture, a femoral neck fracture. The laboratory data revealed hypophosphatemia, hyperphosphataseemia and increased FGF23, a mass lesion in the left lower leg was detected in PET-CT. A tumor was resected with both cases, as a result, the phosphorus levels increased, and the symptom was improved. there is multiple pain region in TIO, TIO is easy to be mistaken for inflammatory disease such as RA. It is important to put TIO in the differentiation in RA with osteomalacia.

P2-186

The clinical outcome of curved intertrochanteric varus osteotomy for osteonecrosis of the femoral head in Chiba University

Satoshi Yoh

Department of Orthopedic, Chiba University Graduate School of Medicine

Conflict of interest: None

[Object] Osteonecrosis will cause osteoarthritis as it progresses. Our university do curved varus osteotomy for adolescence people. We evaluated long term clinical result of this operation. [Methods] Between April 1997 and January 2018, CVO was performed on 40 hips in 33 patients for the treatment of osteonecrosis. The patients included 12 men and 21 women with a mean age of 32.0 years. The mean follow-up was 8.7 years. [Results] The cause of osteonecrosis was steroid-induced in 26 cases, alcohol associated in 3 cases, idiopathic and posttraumatic in 4 cases. The localisation of the necrotic lesion was type B in 4 cases, C1 in 22 cases, and C2 in 10 cases. In these cases, preoperative osteoarthritis was grade 2 in 1 case, 3A in 29 cases, 3B in 4 cases and 4 in 1 case. Average JOA score was 83.0 point at the latest follow-up. We observed joint-space narrowing in 32.5% cases and 12.5% cases converted to THA. Average term to conversion was 11.9 years. [Conclusions] In this study, there is no conversion case to THA in early phase. Although long term follow-up observation is necessary, good clinical result have been obtained. We conclude that CVO is helpful operation for joint preserving.

P2-187

The risk of irreversible renal failure in patients with systemic lupus erythematosus

Mai Yoshida, Kentaro Minowa, Hirofumi Amano, Ken Yamaji, Naoto Tamura

Juntendo University Hospital, Tokyo, Japan

Conflict of interest: None

Lupus nephritis can cause irreversible renal failure with the systemic lupus erythematosus (SLE) patients. The renal prognosis with SLE has been improved during recent years by development of the immunosuppressants. But some of the cases which lead to renal failure has been still present. We studied clinical characteristics of 21 cases in irreversible renal failure with SLE who comes to our hospital. [Methods] We extracted 21 patients among 1196 patients between 2007 and 2018 whose serum (s)-Cr level was more than 2.0 in over 3 months and the level continues more than 2.0 at last visit. [Methods] Disease duration between onset and reach to s-Cr 2.0 was 14.1±9.4 years. Period from s-Cr 1.0 to s-Cr 2.0 was 31.2±28.3 months. One case was positive for anti-U1-RNP antibody. The anti-Sm antibody-positive patient was not present. Positive rate of anti-DNA antibody at s-Cr 1.0 and s-Cr 2.0 was 75% and 57%. The cases with either low CH50, C3 or C4 was 64% at the time of s-Cr 1.0. [Conclusions] We observed many cases with hypocomplementemia at time of s-Cr1.0 in the ESRD SLE patients. We should consider the risk of the irreversible renal failure in the case with hypocomplementemia, negative anti-U1-RNP/Sm antibodies at the time of s-Cr 1.0.

P2-188

The hydroxychloroquine use in clinical practice for systemic lupus erythematosus: a cross-sectional study of the LUNA registry

Yumiko Sugiyama¹, Ryusuke Yoshimi², Yosuke Kunishita², Chiharu Hidekawa², Natsuki Sakurai², Masaki Mitsuhashi², Daiga Kishimoto², Yuki Iizuka², Takaaki Komiya², Hideto Nagai², Naoki Hamada², Naomi Tsuchida², Yutaro Soejima², Reikou Kamiyama², Kouji Kobayashi¹, Yukiko Asami², Yohei Kirino², Nobuyuki Yajima³, Ken-ei Sada⁴, Kunihiro Ichinose⁵, Shigeru Ohno¹, Hideaki Nakajima²

¹Center for Rheumatic Disease, Yokohama City University Medical Center, ²Department of Hematology and Clinical Immunology, Yokohama City University School of Medicine, ³Division of Rheumatology, Department of Internal Medicine, Showa University School of Medicine, ⁴Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ⁵Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Division of Advanced

Conflict of interest: None

[Object] To investigate the real-world situation of hydroxychloroquine (HCQ) use in the clinical practice of systemic lupus erythematosus (SLE) using a multicenter registry. [Methods] SLE patients registered in the LUNA registry were divided into two groups according to whether HCQ was administered or not. The patient's demographic, clinical, and laboratory data were compared between the two groups. [Results] Of the 591 patients with SLE, 94 (16%) used HCQ. The mean age was significantly lower in the HCQ user group than in the non-user group (42.4 ± 12.7 vs 46.6 ± 15.5 years old, $p = 0.016$). In the HCQ user group, the disease activity was significantly higher (SLEDAI 6.3 ± 4.5 vs 4.7 ± 4.8 , $p = 0.0039$), and arthritis and eruption were more frequent (OR 2.04, 95% CI 1.14-3.62, and OR 2.17, 95% CI 1.16-4.04, respectively) as compared with the non-user group. There was no significant difference in the glucocorticoid dose between the HCQ user group and the non-user group (7.6 ± 5.0 vs 6.8 ± 7.3 mg/day, $p = 0.32$). [Conclusions] HCQ tended to be used in SLE patients with arthritis or rash. HCQ use was not related to the daily glucocorticoid dose. We are planning to assess the relationship between HCQ administration and glucocorticoid dose tapering by a longitudinal observational study.

P2-189

Investigation of hydroxychloroquine (HCQ) therapy for Systemic lupus erythematosus (SLE) in our hospital

Junichi Kondo, Yu Matsueda, Kazuma Ino, Yasuhiro Hasegawa, Takumi Muramatsu, Takayuki Hoshiyama, Toshihiro Tono, Yoshiyuki Arinuma, Tatsuhiko Wada, Tatsuo Nagai, Sumiaki Tanaka, Kunihiro Yamaoka
Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine

Conflict of interest: None

PURPOSE: Last year, we have indicated that HCQ possess the possibility of reducing serum anti-DNA antibody level in SLE patients. We have increased patient number and expanded observation period to clarify the effect of HCQ in Japanese SLE patients. **METHODS:** Retrospective chart review was performed in 74 patients who fulfilled ACR criteria, observed over 12 months and was initiated HCQ therapy in our hospital during October 2016 to October 2017. Sixteen patients treated with PSL over 15 mg/day or increased immunosuppressants at baseline were excluded. **RESULTS:** Average age was 42.1 years old, 68 females and PSL average dose was 11.1 mg/day. Seven patients discontinued HCQ for side effect due to nausea or serum Cr elevation, skin symptoms of drug allergy. Serum anti-DNA antibody significantly decreased compared to baseline at month 6 and month 12, respectively ($p=0.0220$, $p=0.0050$). Platelet count and serum complement had no remarkable change. **CONCLUSION:** Our results demonstrates that HCQ should be administer over 6 months to achieve significant decrease of anti-DNA antibody in SLE patients. In addition, it was suggested that HCQ could show efficacy in patients with high or increasing tendency of anti-DNA antibody during PSL tapering.

P2-190

Consideration of Hydroxychloroquine to patients with systemic lupus erythematosus in our hospital

Motochika Asano, Ayaka Kato, Hideki Tani, Koichiro Taguchi, Yoshihiko Kitada, Takahide Ikeda, Hiroyuki Morita
General Medicine, Gifu University Hospital

Conflict of interest: None

[Object] Hydroxychloroquine (HCQ) has been widely used since it was approved in March 2015 as a treatment for SLE. Side effects of HCQ, PSL weight loss effect retrospectively. [Method] Analyzed sex, age, concomitant medication, complications, PSL weight loss of 36 SLE patients treated with HCQ during the period from September 7, 2017 to April 31, 2018, retrospectively compared did. [Results] The average age at the start of administration was 45.4 years and the ratio of males and fe-

males was 5 males and females in 31 cases. The complications were 3 of NP SLE, 3 of APS, 14 of lupus nephritis and no organ dysfunction was 16. As concomitant medicine, 29 PSL, 1 CyA 1 Tac, 2 MZR, 3 CPA, 4 AZP, 9 MMF. The average dose of PSL at the start of HCQ administration was 16.2 ± 2.3 mg and the average was 8.1 ± 1.6 after 3 months, 5.6 ± 1.4 mg on average after 6 months, PSL weight loss effect was observed, 3 cases were discontinued, all caused by drug eruption. [Conclusions] Although there were cases where HCQ administration was discontinued due to side effects in this survey, there were no cases showing severe side effects and adequate therapeutic effect and PSL weight loss effect were observed.

P2-191

Use results of Belimumab in Hitachinaka General Hospital

Hidetomo Oguni¹, Taichi Hayashi^{1,2}

¹Hitachinaka General Hospital, ²University of Tsukuba Rheumatology

Conflict of interest: None

[Object] Belimumab is the biologic drug used for the treatment of systemic lupus erythematosus (SLE) that launched in december, 2017. We serched the SLE patients treated with Belimumab and studied effect of Belimumab. [Methods] We did retrospective study of 15 patients treated with Belimumab in our hospital. [Results] There was 2 male and 13 female patients. 4 patients was under 30 years old, 5 was 31 to 40, 6 was over 41.6 patients was less than 2 years after diagnosed, 4 was 2 to 10 years, 5 was after 10 years. The average dose of Predonisolone was 32.2mg in the group less than 2 years after diagnosed, 11.8mg in the group 2 to 10 years, 19mg in the group after 10 years. 9 patients was combined with Tacrolimus, 9 with Hydroxychloroquine, 10 with Mycophenolate mofetil, 4 with Cyclosporine. Hypocomplementaemia was ovserved in 9 patients, anti-DNA antibody was positive in 4 patients. No patients were interrupted. Every patients with Hypocomplementaemia or anti-DNA antybody positive was improved. Recurrence was occur in 1 patient in the group 2 to 10 years, and 1 in the group after 10 years. [Conclusions] Belimumab is thought to be effective not only in maintain remission but also in induction of remission.

P2-192

A study on the renal prognosis and the usefulness of antiplatelet therapy in antiphospholipid antibody-positive lupus nephritis patients

Mayumi Ito, Makoto Yamaguchi, Shiho Iwagaitsu, Hironobu Nobata, Takayuki Katsuno, Shogo Banno, Yasuhiko Ito
Aichi Medical University

Conflict of interest: None

[Object] We investigated the renal prognosis and the usefulness of antiplatelet therapy in antiphospholipid antibody (aPL)-positive lupus nephritis patients. [Methods] We analyzed 41 cases who underwent renal biopsy at our hospital between November 2009 and October 2018, diagnosed as initial LN. We investigated the change in the period until reaching CR, the relapse-free rate, and the eGFR according to the presence or absence of antiplatelet therapy in 11 cases of aPL positive patients who did not meet the criteria for a diagnosis of APS. [Results] The eGFR was low at 2 years and 3 years after the initiation of therapy, compared to the negative cases in aPL positive cases. a PL positive patients who did not satisfy the diagnostic criteria showed a significant improvement in eGFR after 2 years in the group receiving antithrombotic therapy ($p = 0.0313$). [Conclusions] In LN patients, aPL positive group may have poor renal prognosis compared with negative group. But in addition to conventional immunosuppressive therapy, antiplatelet therapy may be related to improvement of eGFR in aPL positive LN patients who did not meet the criteria for a diagnosis of APS. Further detailed study in the future is needed.

P2-193

Early induction of Hydroxychloroquine inhibits acute skin lesion in patients with Systemic lupus erythematosus

Nahoko Tanaka, Hirotake Sakuraba, Hiroto Hiraga, Yasuhisa Murai, Rina Watanabe, Shinji Ota, Keisuke Hasui

Conflict of interest: None

[Object] Hydroxychloroquine (HCQ) has been approved as an immunomodulatory drug for treating with SLE. We examined the effect for skin lesions and disease activity and the reduction of prednisolone (PSL). [Methods] Medical records were reviewed until Oct. 2018 in our hospital and 12 SLE cases, who treated with HCQ over 6 months, were enrolled in this study. Labo data, SLEDAI and Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) were assessed before and after treatment of HCQ. [Results] All patients were female, the median age was 41 (26-67) years old and disease duration was 8.0 (1-18) years. As for beginning of therapy and 6 months after treatment of HCQ, the averages of anti ds-DNA antibody were 38 ± 20 and 23 ± 18 ($p=0.06$), SLEDAI were 3.4 ± 2.2 and 1.6 ± 1.6 ($p<0.01$), CLASI activity scores were 10 ± 9.6 and 2.6 ± 4.1 ($p<0.01$), damage scores were 5.5 ± 5.0 and 3.4 ± 4.8 ($p<0.05$), and the doses of PSL were 12 ± 5.7 and 8.4 ± 5.2 ($p=0.05$) respectively. The scores of SLEDAI and CLASI were significantly reduced, and the tendency that the dose of PSL decreased as compared with before treatment was observed. [Conclusions] Treatment with HCQ was useful to control the disease activity and early induction of HCQ inhibits acute skin lesion in patients with SLE.

P2-194

Analysis about the positive transformation of the antiU1-RNP antibody in patients with SLE, the antiSm antibody

Kentaro Minowa, Hirofumi Amano, Yuki Asai, Mai Yoshida, Shinya Kawano, Seiichiro Ando, Ken Yamaji, Naoto Tamura
Internal Medicine and Rheumatology, Juntendo University School of Medicine

Conflict of interest: None

[Objectives] In SLE, various autoantibodies such as anti-ENA antibodies, antiphospholipid antibody, and RF are positive in addition to the anti-DNA antibody. In past reports, anti-U1RNP antibody and mild nephropathy or pulmonary hypertension, anti-Sm antibody and tardive nephropathy or central nerve symptom, anti-SS-A antibody and pulmonary hypertension are related to each other. The titers of anti-ENA antibody are poorly changed due to the treatment, they are considered to be unsuitable for evaluating disease activity. However, anti-U1RNP antibody and anti-Sm antibody have turned positive more closely to SLE onset compared with other autoantibodies, and there is a possibility that they are important for early diagnosis of new pathological conditions. [Methods] We extracted the cases that anti-ENA antibodies became positive to negative and negative to positive, and analyzed the association between anti-DNA antibodies and complement value at that time. [Results] When they became negative to positive, they had decreased C3 level with a significant difference. [Discussion] When C3 values decrease more than 10%, we consider the possibility that antiU1-RNP antibody, anti-Sm antibody change to positive, and it is recommended that we reexamine the autoantibodies.

P2-195

Actual usage of immunosuppressive medications for lupus nephritis in a university hospital

Kurumi Asako, Takafumi Tomizuka, Takahiro Itamiya, Yoshitaka Kimura, Hirotochi Kikuchi, Zenichiro Honda, Akiteru Takeuchi, Hajime Kono
Department of Internal Medicine, Teikyo University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] Immunosuppressive medications are given in addition to steroid therapy to lower the dose of steroids needed and thus spare some of the undesirable side effects of steroid therapy. Actual usage of immunosuppressive medications in our hospital was studied. [Methods] Medical records of 61 patients with lupus nephritis who received immunosuppressive medications in October 2018 were retrospectively reviewed. [Results] 49 patients were female and 12 were male. Mean age was

46 ± 15 year-old. Mean duration of SLE was 10.6 ± 10.2 years. All patients have received corticosteroids. Renal biopsy was performed in 43 patients. IVCY was administered in 10 patients. The number of patients used and the continuation rates were as follows; MMF: 39 patients, 92.3%; AZA: 8 patients, 0%; TAC: 31 patients, 80.6%; HCQ: 17 cases, 88.2%; MZB: 9 cases, 33.3%. PSL was discontinued in 2 patients of class V, one of whom also discontinued immunosuppressives. In remission maintenance phase, 1, 2 or 3 immunosuppressives were given to 21, 23, 6 patients in combination with corticosteroids, respectively. [Conclusions] Continuation of MMF and TAC was higher than others. It seems that MMF will be playing a key role in the induction and maintenance phase of lupus nephritis.

P2-196

Present status of belimumab use in Systemic Lupus Erythematosus at our hospital

Youhei Fujiki¹, Tomohiko Kuboyama¹, Hidehiko Makino¹, Shogo Matsuda¹, Takao Kiboshi¹, Takaaki Ishida¹, Yumiko Wada², Koji Nagai¹, Shuzo Yoshida³, Kenichiro Hata¹, Takuya Kotani¹, Tohru Takeuchi¹, Shigeki Makino⁴, Shigeki Arawaka¹

¹Department of Internal Medicine IV, Osaka Medical College, Takatsuki, Osaka, Japan, ²Department of Rheumatology, Yodogawa Christian Hospital, ³Department of Rheumatology, Arisawa General Hospital, ⁴Department of Internal Medicine, Osaka Medical College Mishima-Minami Hospital

Conflict of interest: None

[Object] We evaluated the efficacy and safety of belimumab for SLE in our department. [Method] We assessed the serological test, SELENA-SLEDAI, prednisolone (PSL) dosage and adverse events of the therapy with add-on belimumab in 7 cases retrospectively. [Result] The following are median values. Age 46 years old, disease duration was 17 years. All cases were female. The reasons for administration were 5 cases of serologic activity remaining and difficulty of steroid dose reduction. While the other 2 cases remained proteinuria of 0.5 g/day or more and remained vasculitis symptoms. C3 level, titer of anti-ds-DNA-antibody and SELENA-SLEDAI before combination were 90 mg/dl, 35.7 IU/ml and 6. PSL dosage was 9 mg/day. Five immunosuppressive agents administered until the addition of belimumab in 3 cases. Five cases were used IVCY and three cases were rituximab before belimumab therapy. Significant differences were not observed in PSL dosage and SELENA-SLEDAI, but C3 levels increased significantly ($P=0.03$) and anti-ds-DNA antibody titer also significantly decreased ($P=0.03$) at 12 weeks. One patient had no improvement in arthritis and was discontinued at 17 weeks, but no adverse events were noted. [Conclusion] Belimumab may contribute to improvement of serologic activity as reported.

P2-197

Efficacy of the add-on treatment of hydroxychloroquine for patients with Systemic Lupus Erythematosus during maintenance phase

Takakazu Hasegawa, Mayu Sugiyama, Kahori Oshima, Syunsuke Yokoi, Kumiko Umemura, Michita Suzuki, Kyoko Takano, Eiji Nagasawa, Nobuyoshi Minemura, Masao Katayama
Division of Rheumatology, Department of Internal Medicine, National Hospital Organization Nagoya Medical Center

Conflict of interest: None

[Object] We evaluated the efficacy of add-on treatment of hydroxychloroquine (HCQ) for patients with Systemic Lupus Erythematosus (SLE) during maintenance phase. [Methods] The subjects were 66 patients with steroid therapy who passed 6 months after remission induction therapy, started HCQ at our hospital between September 2015 and March 2018 and didn't needed additional therapy from 8 weeks before HCQ treatment to initiation of HCQ. The retention rate of HCQ and the changes of prednisolone (PSL) dose, SLE disease activity index (SLEDAI) and titer of anti-DNA antibody were examined retrospectively at 6 months after treatment of HCQ. [Results] The retention rate is 92.4%. The mean dose of PSL was significantly reduced (mean \pm SD) (pre-treatment of HCQ: 6.3 ± 3.1 mg/day, 6 months after treatment of HCQ: 5.4 ± 3.2 mg/day, $p<0.001$) and the mean of SLEDAI was significantly reduced (3.6 ± 2.8 vs

2.7±2.5, $p < 0.001$). In 25 patients with the high titer of anti-DNA antibody (ELISA) before the treatment of HCQ, the mean of titer was significantly reduced (40 ± 41 IU/ml vs 35 ± 51 IU/ml, $p = 0.0347$). [Conclusions] It was suggested that the add-on treatment of HCQ for patients with SLE during maintenance phase might be able to improve the disease activity and reduce the dose of PSL.

P2-198

A Case series of Protein losing enteropathy associated with connective tissue diseases

Takao Nagashima, Ayako Kokuzawa, Yoichiro Akiyama, Akiko Miyayama, Keisuke Saito, Natsuki Shima, Takamasa Murosaki, Yasuyuki Kamata, Katsuya Nagatani, Masahiro Iwamoto, Seiji Minota
Division of Rheumatology and Clinical Immunology, Department of Medicine, Jichi Medical University Hospital

Conflict of interest: None

[Object] To investigate treatment response in patients with protein losing enteropathy (PLE) associated with connective tissue diseases (CTD). [Methods] From January 2006 to March 2018, 7 patients were diagnosed with PLE. PLE was diagnosed by ^{99m}Tc -labeled albumin scintigraphy and/or alpha1-antitrypsin clearance (AT) test. [Results] 6 were women. Median age was 41 (range: 31-72). Underlying diseases were Sjögren syndrome (SS) in 3; SLE in 2; SS plus SLE in 1; and suspected SLE in 1. Median serum albumin (Alb) was 2.0 g/dl (0.9-2.8). Complement levels were low in all the patients. Median AT test was 56 mg/day (27-281) ($n=5$). Treatment options other than high-dose glucocorticoid (GC) were mPSL pulse in 5, GC switch in 2, and use of immunosuppressants in 6 (Tacrolimus, IVCY, MMF). Additional treatment was required in 3. Median days from the start of treatment to the day of serum Alb > 3 g/dl was 50 (9-73) ($n=6$). One patient did not achieve remission. Arterial thrombosis and cerebral infarction occurred in one patient each. In patients who achieved early remission (< 50 days), serum Alb was higher, total cholesterol and AT test was lower than those who did not; but there was no significant difference. [Conclusions] In severe PLE, intensive therapy may be needed from the beginning.

P2-199

Characterization and Comparison of Valvular Disease, Ischemic Heart Disease, and Aortic Aneurysm in SLE Patients who Have Undergone Cardiovascular Surgery

Toshio Kawamoto, Hirofumi Amano, Kentaro Minowa, Mai Yoshida, Yuki Asai, Ken Yamaji, Naoto Tamura
Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] This study determined whether there was a correlation between the SLE activity and the progress and aggravation of heart disease in each category. Identifying these characteristics is expected to be useful in establishing strategies to prevent the occurrence of heart diseases complicated by SLE, and to treat them. [Methods] 29 cardiovascular with SLE patients were operated in 5 years. Indices for SLE activity were anti-DNA antibodies and CH50. Peak and bottom values of these indices before surgery were recorded, and the values obtained during the pre-surgery 180-day period were compared with those that had been determined prior to this period. We also investigated the relationship of anti-phospholipid antibodies to cardiac disease onset and platelet count. [Results] The peak/bottom values for CH50 and anti-DNA antibodies in the pre-surgery 180-day period were no different from those obtained prior to this period. The values of anti-phospholipid antibodies were 0.6 for V, 0.28 for I, and 0.33 for A, and thus, higher in the heart valve disease category. [Conclusions] The integrated value for DNA Ab was lower in the heart valve disease category; therefore, the presence of both anti-phospholipid antibodies and thrombocytopenia may be a risk factor for valvular disease.

P2-200

Retrospective observational study for effect of hydroxychloroquine (HCQ) on glucose and lipid metabolism

Yoshinori Masui, Kenichi Hiraga, Leo Yoshikawa, Naonori Tsuda, Toshikazu Kano
Department of Rheumatology, Kohnodai Hospital, National Center for Global Health and Medicine, Ichikawa, Japan

Conflict of interest: None

[Object] Several overseas studies have reported the effect of HCQ improving glucose and lipid metabolism. However, few reports in Japan. We elucidate the effect of HCQ on glucose and lipid metabolism. [Methods] We picked up adult patients prescribed HCQ for more than a month between Sep. 2015 and Aug. 2018. We included the patients who prescribed low-dose PSL. We retrospectively collected patient's data and metabolic parameters before and after taking HCQ up to 12 months. Comparison between values before and after the start of HCQ was performed by using paired t-test. [Results] Forty adult patients had prescribed HCQ, of which 9 cases had discontinued within a month because of side effect such as fever, diarrhea, drug rash. SLE were 36. Eligible cases were 26. The mean age was 46.5 years and females were 84.6%. Diabetes were 3, and dyslipidemia were 7. HbA1c significantly decreased $0.28 \pm 0.33\%$ from baseline at 6 months after its start. TG significantly decreased 45.2 ± 52.7 mg/dL at 2 months. LDL-C significantly decreased 12.5 ± 13.2 mg/dL at 3 months. No significant change in HDL-C. The eligible cases had taken no additional therapeutic drugs of diabetes and dyslipidemia. [Conclusions] It was suggested that HCQ has an effect improving glucose and lipid metabolism in patients in Japan.

P2-201

The short-term effects of belimumab on 3 Japanese SLE cases with resistance to steroid sparing

Hiroshi Kajiyama, Mayumi Matsuda, Takuma Wada, Yoshihiro Yoshida, Kazuhiro Yokota, Yasuto Araki, Kojiro Sato, Yu Funakubo, Toshihide Mimura
Department of Rheumatology and Applied Immunology, Saitama Medical University

Conflict of interest: None

[Object] There is a paucity of evidence about the optimal condition of Japanese SLE patients for belimumab (BLM) introduction. The purpose of this study is to assess the short-term effects of BLM to SLE patients with resistance to steroid sparing. [Methods] Observational Study. Intravenous BLM 10 mg/kg was introduced to three SLE outpatients on maintenance treatment with resistance to steroid sparing in our department. The changes of serum dsDNA antibody levels, SLEDAI and daily prednisolone doses after BLM introduction were described. [Results] Studied were two female and one male patients. Average age at BLM introduction was 26.7 ± 11.9 (average and standard deviation) years old, and average observational period was 18.7 ± 6.1 weeks. Lupus nephritis was previously diagnosed with renal biopsy in two patients. After BLM introduction, serum anti-dsDNA antibody levels were improved from 90.3 ± 77.5 IU/mL to 37.1 ± 46.2 IU/mL, SLEDAI decreased from 7.3 ± 4.2 to 2.0 ± 0.0 , and daily prednisolone dose was reduced from 23.7 ± 7.1 mg/day to 15.3 ± 1.5 mg/day without any recurrence. No adverse event was seen during the observational period. [Conclusions] BLM might have steroid sparing effects on SLE cases at least during short period after BLM introduction.

P2-202

Bladder carcinoma in situ in a patient with lupus cystitis

Takahiko Akagi, Shunichi Fujita, Mayuko Fukushima, Hiroshi Sawachika, Hiroyasu Hirano, Tomoyuki Mukai, Yoshitaka Morita
Department of Rheumatology, Kawasaki Medical School, Kurashiki, Japan

Conflict of interest: None

Lupus cystitis is a well-known but rare complication of systemic lupus erythematosus. This manifestation is frequently associated with lupus

enteritis. We report here a case of a 34-year-old man with lupus cystitis and enteritis who presented with diarrhea and bladder storage symptoms such as urinary frequency and nocturia. Serological tests showed positivity for anti-dsDNA, anti-SS-A and anti-SS-B antibodies. Enhanced computed tomography showed diffuse thickening and abnormal enhancement of bowel wall as well as right hydronephrosis. Cystoscopy revealed bladder trabeculation, a characteristic ribbed appearance, suggesting the presence of lupus cystitis. However, unexpectedly, a biopsy of randomly selected bladder tissue revealed bladder carcinoma in situ. Treatment with prednisolone (50 mg/day) improved abdominal symptoms, while the bladder irritation symptoms remained unchanged. After tapering the prednisolone dose to 20 mg/day, treatment of the bladder carcinoma in situ was started with intravesical Bacillus Calmette-Guèrin. To our knowledge, no reports of bladder cancer in association with lupus cystitis have been published to date. It is necessary to be aware of this serious complication when caring for patients with lupus cystitis.

P2-203

Consideration of the clinical feature of 3 examples of male late onset systemic lupus erythematosus

Ruriko Kuratani, Rumiko Miyagi, Rina Okita, Satoshi Baba, Shinichiro Tsunoda

Division of Immunology and Rheumatology, Sumitomo Hospital

Conflict of interest: None

[Object] There is a lot of female SLE patients, but there is also late onset SLE. It's learned that late onset SLE has a high percentage of the man in particular. [Methods] 3 examples of male patient of late onset SLE was considered clinically. [Results] 1) A 61 year old man. He had the symptoms by arthritis, renal dysfunction, pericarditis, cytopenia and antinuclear antibody. Renal pathological is type4. We treat it with a mPSL pulse and PSL50mg, and also with Tac and MMF. there was also a colon cancer, and We performed an operation. 2) A 75 year old man. He had the symptoms by the skin, renal dysfunction, pleurisy and anti dsDNA antibody. Renal pathological is type4. We treat it with a mPSL pulse and PSL40mg, and also with Tac. 3) A 62 year old man. He had the symptoms by arthritis, renal dysfunction, pleurisy, cytopenia and antinuclear antibody. Renal pathological is type3. We treat it with a mPSL pulse and PSL40mg, and also with HCQ. [Conclusions] Case1 had a recurrence lupus nephritis but the treatment reaction was good 3examples. There was also a report that I have few mergers of renal dysfunction in late onset SLE, but 3examples admitted lupus nephritis. It's more important to reduce the steroid by multiple drug use than early stage for treatment to reduce a side effect with a steroid.

P2-204

Efficacy and complications of Belimumab in 4 patients with systemic lupus erythematosus

Hideyuki Okada, Yoshihiro Uno, Mami Iida

General Internal Medicine, Gifu Prefectural General Medical Center

Conflict of interest: None

Case1: A 24-yo man, who developed systemic lupus erythematosus (SLE) at the age of 15, has lupus nephritis (LN) and pericarditis (PC). Type of LN is ISN/RPS V+III (A). Although he relapsed SLE as he took prednisolone (PSL) less than 15mg, he was able to reduce the dosage of PSL by using Belimumab (BEL) in combination. Case2: A 21-yo woman was diagnosed with SLE at the age of 10. She has LN (ISN/RPS IV-G), PC and interstitial pneumoniae. She relapsed SLE because of her self-discontinuation of treatment. Due to her resuming treatment with BEL, her disease improved. Case3: A 38-yo woman, who got SLE at the age of 37, has cholecystitis and LN (ISN/RPS IV (A/C)). She complicated pancytopenia during induction therapy. But she treated with BEL, her pancytopenia improved. Case4: A 45-yo man, onset at the age of 33, has LN (ISN/RPS IV+V) with 15.8g/day of proteinuria, alveolar hemorrhage, pulmonary hypertension and antiphospholipid syndrome. He treated with steroid puls therapy, he is currently treating by using antibiotics agents. Although it is necessary to pay attention to the occurrence of adverse events, it was considered that BEL could be effectively used in both induction therapy and maintenance therapy.

P2-205

Belimumab administration on SLE, clinical trial cases and post-marketing neuropsychiatric (NP) cases

Yasushi Nawata, Shigekazu Takahashi, Norihiro Mimura, Kazusa Miyachi, Kaori Masujima, Taiga Ikezawa, Kazuhiro Hamasato, Norihiko Watanabe

Center for Rheumatic Diseases, Chibaken Saiseikai Narashino Hospital

Conflict of interest: None

[Object] Anti-BLyS antibody belimumab (BEL) was effective for SLE in clinical trials, but there is little evidence for NP-SLE. We report the experience of the NP-SLE cases. [Methods] 5 BEL cases, 2 clinical trial (BLISS-NEA) (case1,2) and 3 post-marketing NP-SLE (case3,4,5). SELENA-SLEDAI, anti-dsDNA, complements (C3/C4), IgG are evaluated. [Results] Case1) 48 year-old (PSL12.5mg+MZB), arthritis, alopecia, rash, anti-dsDNA positive, low complement, SLEDAI10. Case2) 35 year-old (PSL10mg+CsA), rash, skin vasculitis, alopecia, anti-dsDNA positive, SLEDAI14. Anti-dsDNA levels decreased by 52 weeks after starting together with increased complement levels. Case3) 46 year-old (PSL16mg+CY), abduction/swallowing disturbance, anti-dsDNA positive, anti-cardiolipin β 2GP1 positive, SLEDAI10. After starting BEL symptoms improved together with anti-dsDNA/anti-cardiolipin decrease. Case4) 43 year-old (PSL12.5mg+CsA), psychosis, arthritis, anti-dsDNA positive, SLEDAI14. Case5) 57 year-old, consciousness disturbance, SLEDAI24. Steroid pulse and IVCY were temporarily effective. Evaluation of BEL was difficult. Although the effect of BEL on NP symptoms was partially recognized, it is still unclear. [Conclusions] Evidence needs to be accumulated in the evaluation of BEL for SLE including NP symptoms.

P2-206

A case of systemic lupus erythematosus with a relapse and refractory infections after living-donor kidney transplantation

Midori Akagi¹, Nozomi Iwanaga¹, Chieko Kawahara¹, Yoshiro Horai¹, Yasumori Izumi¹, Atsushi Kawakami²

¹National Hospital Nagasaki Medical Center, ²Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: None

A 35-year-old Japanese woman was diagnosed with systemic lupus erythematosus (SLE) with lupus nephritis at the age of 11. Her SLE was refractory. After cyclosporine (CyA) was started, her urinary protein was reduced. Her creatinine had been around 4 mg/dl. Because of hope of childbirth, she received a kidney transplantation 11 months ago. Steroid pulse was administered and CyA was changed to tacrolimus (TAC) and mycophenolate mofetil. And mPSL40mg/day was started and decreased to 6mg/day. Her SLE had relapsed with lupus enteritis 7 months ago and she was treated with steroid pulse and intravenous cyclophosphamide. Her urine protein increased 5 months ago. Renal biopsy revealed thrombotic microangiopathy caused by TAC. After TAC was changed to CyA, her urine protein gradually decreased. She was admitted to our hospital 4 months later, because of fever and back pain. MRI revealed suppurative spondylitis of Th10-11. Mycobacterium avium was detected by abscess punctured. She was treated with CAM, EB and RFP, and her symptoms resolved. Because most of patients with SLE performed kidney transplantation required dialysis before transplantation, this case is rare. We report the difficulty of the management after the kidney transplantation in patients with SLE.

P2-207

A case of systemic lupus erythematosus successfully treated with belimumab

Masako Furuyama¹, Sosuke Tsuji², Tomoki Origuchi^{2,3}, Atsushi Kawakami²

¹Department of Rheumatology, Nagasaki Kita Hospital, Nagasaki, Japan, ²Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, ³Department of Rehabilitation Sciences, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: None

(Case) The patient was a 33-years-old woman. She had polyarthralgia and polymyalgia without any treatment for past two years. She had high fever, erythema on her face and forearms, worsening of polyarthralgia and polymyalgia. She had anti-nuclear and anti-double-stranded DNA antibodies and hypocomplementaemia, and was diagnosed as having SLE. She also had type II diabetes mellitus (DM). She started taking 25mg/day of prednisolone (PSL). After then her symptom improved, but her serum glucose concentration and body weight had increased. We added SGLT2 inhibitor, DPP-4 inhibitor and insulin injection therapy. We also tried to reduce the dose of PSL, but failed because of recurrence of SLE activity. Mycophenolate mofetil (MMF) made her symptom better but not enough to taper the PSL dose. Two years later, she started receiving belimumab. SLEDAI was 12 at the initiation of belimumab and 2 at week 24. We could taper the dose of PSL and stopped it. She could reduce her body weight and serum glucose level. (Clinical significance) We herein report a case of a patient with steroid-resistant SLE. Although MMF were not enough to reduce the dose of PSL, belimumab improved her disease activity of SLE. Finally, we could stop PSL, resulted in good control of DM.

P2-208

A case of acquired angioedema associated with SLE
Yohei Takeuchi, Hiromi Hirabayashi, Michiaki Tokuda
Internal Medicine, Saniki Municipal Hospital

Conflict of interest: None

Angioedema (AE) is caused by hypervascular permeability by activating complement system, coagulation fibrinolysis system, kinin-kallikrein system due to deficiency of C1 inhibitor (C1-INH). There are inherited genetic AE, and acquired AE caused by the dysfunction of C1-INH associated with lymphoproliferative diseases and autoimmune diseases. She was 33 year-old, and was diagnosed SLE from X-3 year. In X year, she was urgently hospitalized with sudden eyelids, lips, limbs of edema and abdominal pain. In CT, ascites in abdomen and intestinal wall thickening were observed. All of C3, C4, and CH50 were markedly reduced, C1q was also low, and C1-INH decreased quantitatively. Finally, she was diagnosed as AE, but administration of the C1-INH formulation was ineffective. Because of adult onset, no family history, and ineffectiveness of C1-INH administration, we diagnosed acquired AE associated with SLE. When corticosteroids and cyclophosphamide pulse therapy was performed, the above symptoms and ascites disappeared immediately. Furthermore, serum complement value increased and C1-INH also normalized. Later, no abnormality was observed in the C1-INH gene, suggesting not inherited genetic AE. When accompanied by autoimmune disease, immunosuppressive therapy is thought to be effective.

P2-209

SLE associated with macrophage activation syndrome and cardiac tamponade brought about acute heart failure: A case report
Kohei Nagaya¹, Akimasa Asai², Asako Kachi², Masako Koshino², Nao Asai², Hirokazu Sugiyama², Tomomichi Kasagi², Mayumi Ito², Hironobu Nobata², Takayuki Katsuno², Shogo Banno², Yasuhiko Ito²
¹Department of Nephrology, Kizawa Memorial Hospital, ²Department of Nephrology, Rheumatology and Collagen Diseases, Aichi Medical University

Conflict of interest: None

[Case] 49-year-old female [Chief complaint] fever [Present illness] A 49-year-old female patient noticed face erythema 12 years ago. She enter a hospital one month ago because of fever. CT scan showed lymphadenopathy through out the body, therewith the attending doctor suspect malignant lymphoma and introduced her to hematology department of out hospital. On the admission, the physical examination, blood test and CT scan showed depilation, face erythema, pericarditis, pancytopenia, ANA positive, anti-dsDNA antibody positive, low complement. The result suggested a diagnosis of SLE. She was treated with prednisolone 50mg/day, then fever and blood cell count improved. She got acute respiratory insufficiency on 5th day of the treatment. She was diagnosed with acute heart

failure and cardiac tamponade. She was intubated, got to be on a mechanical ventilator and treated with steroid pulse therapy. At the same time her ferritin level showed surprising increase, that suggest complicated macrophage activation syndrome (MAS). IVIg therapy was added. Pericardial effusion and ferritin level improved quickly, but cardiac function did slowly. [Conclusions] Probably, not only cardiac tamponade, also high level cytokine caused by MAS was the important factor of heart failure.

P2-210

Clinical course of systemic sclerosis patients with digital ulcers treated with bosentan

Takashi Kida, Tomoya Sagawa, Takuya Inoue, Akiko Kasahara, Shunya Kaneshita, Kazuki Fujioka, Hidetake Nagahara, Makoto Wada, Masataka Kohno, Yutaka Kawahito
Inflammation and Immunology, Kyoto Prefectural University of Medicine

Conflict of interest: None

[Objective] Digital ulcers (DUs) in systemic sclerosis (SSc) is a visible manifestation reflecting the extent of systemic vasculopathy. Because its pathogenesis is diverse and complicated, the management is often challenging. Here, we aimed to investigate the clinical course of SSc patients with DUs treated with bosentan (BOS). [Methods] We retrospectively analyzed the consecutive SSc patients with DUs treated with BOS after April 2013. [Results] A total of 21 patients (13 limited; 8 diffuse; median disease duration 7 years) were detected. Six patients had PAH. Of total, 72.9% (35/48) of individual existing DUs were healed within 52 weeks. Also, 42.9% (9/21) patients did not develop new DUs within 52 weeks. Short disease duration, low severity of skin thickness, and concomitant use of alprostadil injection were tend to be associated with healing of existing DUs. PAH was associated with development of new DUs. The most common adverse events were liver damage or adverse hemodynamic effect. Within 52 weeks, 2 patients suffered sudden death and 6 patients discontinued taking BOS. [Discussion] For the optimal management of DUs, multidisciplinary treatment including BOS is required. We will discuss based on our experience and literature review.

P2-211

Analysis of therapeutic target for early systemic sclerosis using of public approval treatments

Hirahito Endo¹, Yoshie Kusunoki², Aki Shoji², Norihiko Tonozuka²
¹Department of Rheumatology, Jusendo General Hospital, ²Department of Rheumatology, Akishima Hospital

Conflict of interest: None

[Object] In real-world clinical state we need the assessment of the efficacy in the standard public approved therapy for early active systemic sclerosis. We analyzed the therapeutic target in these clinical state [Object] 2014~18. 26 patients with SSc, 60.29.1years old, disease duration 3.1±2.1years, dcSSc22 LcSSc, Scl70ab 11, ACA 5, RNA polyab 3 cases We defined the therapeutic goal, mRSS improvement: over 5, %VC improvement over 5%, improve HAQ-DI over 0.5 and SF-36. [Results] Patients with SSc with IP were treated by corticosteroids and intravenous cyclophosphamide therapy. Scleroderma overlapped with rheumatoid arthritis treated by Tocilizumab (TOZ) and MTX. Skin sclerosis mRSS were improved 66.6±12.3 to 68.2±15.6.%VC Δ5over improved cases were 56%. In Patients overlapped RA DAS28 improved from 5.02to 2.6. 78% patients SSc improved HAQ-DI≥0.5. [Conclusions] Improvement of health related QOL is the most important therapeutic target used the combination of approved therapeutic drugs in era there were only treatment with limited effects.

P2-212

Comparison of systemic scleroderma group and non-systemic scleroderma group in pulmonary hypertension associated with connective tissue disease

Kenji Sakai, Kaori Ishimura, Hiroki Akazawa, Chisato Ashida, Fusayo Ikeda, Atsuhiko Yamamoto, Tetsu Itami, Asuka Inoue, Shinkai Ri, Toshihiko Shiga, Kazuya Kishimoto, Yuji Nozaki, Koji Kinoshita,

Masanori Funauuchi, Itaru Matsumura
Department of Hematology and Rheumatology, Kindai University Faculty of Medicine

Conflict of interest: None

[Background] Inflammation is considered to be involved in the pathology of pulmonary hypertension (PH) accompanying connective tissue disease (CTD), and in case of accompanying active findings of CTD, use of immunosuppressive therapy is recommended. However, the effectiveness at PH associated with SSc is low. The pathogenesis of PH with SSc may be different from that of other CTD. [Methods] We analyzed 20 patients with CTD who underwent right heart catheter and were diagnosed as pulmonary hypertension. Patients were divided into 2 groups by SSc group (n=12), non-SSc group (n=8). The average pulmonary artery pressure, pulmonary artery wedge pressure, systolic right ventricular pressure, cardiac output, cardiac index, pulmonary vascular resistance of the right heart catheter were compared. [Results] There was no significant difference between the 2 groups in the right heart catheter findings. One case was duplicated example of SSc and dermatomyositis, and improved PH by administration of prednisolone. [Conclusions] A significant tendency in right heart catheter finding was not recognized. This study is suggested that it may be necessary to add immunosuppressive therapy in duplicate cases of other CTD.

P2-213

Consideration of pulmonary hypertension and borderline pulmonary hypertension associated with systemic sclerosis by YKL-40

Tetsuya Furukawa, Masayasu Kitano, Naoto Azuma, Kiyoshi Matsui
Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine

Conflict of interest: None

[Object] SSc is an intractable connective tissue disease that causes fibrosis of the skin and various organs and affects the prognosis by complication of PH. PH is diagnosed with mPAP \geq 25 mmHg by RHC. In recent years, the intervention for the treatment of the borderline PH (mPAP 20 to 24 mmHg), has been discussed. We reported the possibility that YKL-40 correlated with vascular lesions of SSc and YKL-40. We compared this YKL-40 with the PH of the SSc patient at the borderline PH and examined whether or not the early intervention of PH therapy at SSc was made. [Methods] We conducted a retrospective analysis of 19 patients (11 PH, 8 borderline PH) with SSc who were referred to our institution for treatment between August 2014 and April 2017. We measured serum YKL-40 levels by ELISA. [Results] YKL-40 age percentile significantly increased PH (90.2 \pm 11.2) and borderline PH (94.8 \pm 6.7) from 24.9 \pm 17.4 for healthy controls. There was no difference between PH and borderline PH. [Conclusions] Borderline PH in SSc progresses to disease state, more than 2/3 of pulmonary capillary bed is damaged and PH develops. From the results of YKL-40, which is thought to reflect vascular disorders, it may be possible to improve the prognosis by treatment intervention at the borderline PH.

P2-214

Cobblestone appearance in systemic sclerosis

Ikko Kajihara¹, Masatoshi Jinnin², Katsunari Makino¹, Takamitsu Makino¹, Hironobu Ihn¹

¹Department of Dermatology, Kumamoto University, ²Department of Dermatology, Wakayama Medical University

Conflict of interest: None

Background: A cobblestone appearance (CSA) is a rare skin manifestation of systemic sclerosis (SSc), which is defined as a lesion with characteristic multiple small papules/nodules due to lymphangiectasia caused by an obstruction of the lymphatic channels during the sclerosing process. However, the frequency and the clinical significance of CSA in SSc patients are still unclear. Objective: This study examined the prevalence of CSA on the affected skin of patients with SSc and investigated the clinical features of SSc patients with CSA retrospectively. Methods All 184 patients with SSc in this clinic were evaluated. Diagnosis for CSA

was based on the clinical and histopathological pictures. Results: CSA was found in 3 of 184 patients (1.6%). The CSA patients were all male with diffuse cutaneous SSc, and had significantly higher modified Rodnan's skin score (m-TSS) than those without CSA. Furthermore, these patients were resistant to treatments for skin sclerosis. Conclusions: CSA may be an indicator of severe skin sclerosis and poor prognosis in SSc patients.

P2-215

An Algorithm to Predict Mean Pulmonary Artery Pressure > 20 mmHg in Patients with Systemic Sclerosis

Keita Ninagawa, Masaru Kato, Hiroyuki Nakamura, Kuniyuki Aso, Taiki Sato, Michihito Kono, Yuichiro Fujieda, Kenji Oku, Toshiyuki Bohgaki, Olga Amengual, Shinsuke Yasuda, Tatsuya Atsumi

Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University

Conflict of interest: None

[Object] Early intervention in pulmonary arterial hypertension associated with systemic sclerosis (SSc) may improve its prognosis. We aimed to establish an algorithm to detect mean pulmonary artery pressure (mPAP) > 20 mmHg using non-invasive examinations in patients with SSc. [Methods] This study included 58 SSc patients who underwent right heart catheterization in our hospital during 2010 to 2018. Following variables according to DETECT algorithm were assessed to predict mPAP > 20 mmHg: anti-centromere or U1-RNP antibodies, BNP, serum urate, right axis deviation, FVC/DLco and tricuspid regurgitation velocity. Each cut-off value of these markers was determined by ROC curves, and was compared between mPAP > 20 and \geq 25 mmHg. In addition, cardiac MRI was evaluated. [Results] FVC/DLco and right axis deviation had high specificity (72% and 96%, respectively) to predict mPAP > 20mmHg as well as \geq 25 mmHg. Thus, an algorithm weighted with these two markers showed high AUC of 0.87 (sensitivity: 90% and specificity: 70%). Addition of cardiac MRI increased AUC to 0.89 (sensitivity: 90% and specificity: 70%). [Conclusions] We proposed a pilot algorithm to predict mPAP > 20 mmHg in SSc patients. Weighting FVC/DLco and right axis deviation, and adding cardiac MRI may improve its predictability.

P2-216

Analysis of the relationship between HRCT findings suspecting pulmonary veno-occlusive lesion and clinical factor in pulmonary artery hypertension associated with systemic sclerosis

Kenichiro Hata¹, Takuya Kotani¹, Takao Kiboshi¹, Takayasu Suzuka¹, Youhei Fujiki¹, Reiko Wakura¹, Daisuke Wakura¹, Koji Nagai¹, Takeshi Shoda², Tohru Takeuchi¹, Shigeki Makino³, Shigeki Arawaka¹

¹Division of Rheumatology, Department of Internal Medicine IV, Osaka Medical College, Takatsuki, Osaka, Japan, ²Department of Rheumatology, Yodogawa Christian Hospital, Osaka, Japan, ³Department of Internal Medicine, Osaka Medical College Mishima-Minami Hospital

Conflict of interest: None

[Object] To analyse the relationship between HRCT findings suspecting pulmonary veno-occlusive lesion and clinical factor in pulmonary artery hypertension (PAH) associated with systemic sclerosis (SSc). [Methods] We assessed HRCT findings suspecting pulmonary veno-occlusive lesion in 13 cases of systemic sclerosis complicated with PAH. We suspect pulmonary veno-occlusive lesion basis of thickened septal lines, centrilobular GGO, and mediastinal lymph node enlargement, and divided into 2 groups defined as satisfied over 2 HRCT findings (Group A, n=4) or less than one (Group B, n=9). [Results] Average age was 71.4 \pm 8.0 years old, 7 cases was anti-centromere antibody positive, 7 cases were complicated with ILD. Average %VC, %DLCO, mPAP and PVR were 76.5 \pm 16.2%, 24.9 \pm 10.0%, 31.7 \pm 9.9mmHg, 5.5 \pm 4.1wood, respectively. Thickened septal lines were shown in 6 cases, centrilobular GGO were 3 cases, mediastinal lymph node enlargement were 5 cases. One case had triad HRCT findings, 3 cases had 2 findings, 5 cases had one, 4 cases had none. All cases in Group A were WHO class 3 and needed oxygen therapy. Group A was higher than Group B in the average of mPAP, PVR and AaDO₂. [Conclusions] HRCT findings suspecting pulmonary

veno-occlusive lesion in PAH associated with SSC could reflect clinical severity.

P2-217

Evaluation of the utility of Nailfold videocapillaroscopy (NVC) in anti-centromere antibody (ACA)-positive patients

Tomohiro Sugimoto¹, Kei Araki¹, Hiroki Kohno¹, Kazutoshi Yukawa¹, Tatsuomi Kuranobu¹, Tadahiro Tokunaga¹, Katsuhiro Ohi¹, Yusuke Yoshida¹, Sho Mokuda¹, Keisuke Oda^{1,2}, Takaki Nojima^{1,3}, Shintaro Hirata¹, Eiji Sugiyama¹

¹Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan, ²Department of Internal Medicine, Hiroshima Clinic, Hiroshima, Japan, ³Nojima Internal Medicine Clinic, Hiroshima, Japan

Conflict of interest: None

[Object] The anti-centromere antibody (ACA) is a specific and frequent marker for systemic scleroderma (SSc) or Sjogren's syndrome (SS). We divided the clinical features of ACA-positive patients into three groups (SSc, SS, others) and evaluated them using nailfold videocapillaroscopy (NVC). [Methods] We evaluated the ACA-positive patients which we examined NVC test from April 2018 to October 2018, retrospectively. The 2nd to 5th fingers were observed using NVC and semiquantitatively evaluated the scores of Enlarge, Giant, Hemorrhage, Loss of Capillary, Disorganization, presence of Ramification. Then, subjects were classified into four phases: Normal, Early, Active, Late. [Results] 48 ACA-positive cases fulfilled the entry criteria. All of the cases were women. SSc: 32 cases, SS: 6 cases, others: 10 cases. In patients with SSc, we showed 32 Raynaud phenomena (RP,100%), 31 NVC abnormality (96.8%, Early 5, Active 14, Late 12) and 32 sclerodactyly (100%, puffy finger:4). In patients with SS, 2 RP (33.3%), no sclerodactyly and 3 NVC abnormalities (50%, Early 2, Active 1) were included. And, we detected 6 RP (60%), 1 sclerodactyly (10%) and no NVC abnormality in patients with others. [Conclusions] In ACA-positive patients, NVC abnormality and RP are useful to distinguish SSc from SS.

P2-218

Overlap syndrome of systemic autoimmune rheumatic diseases (SARD)

Yuki Inoue, Yuto Takakura, Chihiro Imaizumi, Kennosuke Mizushina, Munetsugu Imamura, Sayaka Takenaka, Hideki Ito, Rie Kujime, Norihide Hayashi, Ayako Hirata, Takehisa Ogura, Hideto Kameda
Division of Rheumatology, Toho University Ohashi Medical Center

Conflict of interest: None

[Purpose] To analyze the clinical features of patients with SARD. [Method] A total of 952 patients with SARD were included in this study. Applied criteria were: 1997 revised ACR (old) and 2012 SLICC criteria (new) for SLE, 1980 ACR (old) and 2013 ACR/EULAR criteria (new) for SSc, 1987 revised ACR (old) and 2011 ACR/EULAR criteria (new) for RA, and Bohan-Peter (old) and 2017 EULAR/ACR criteria (new) for PM/DM. Overlap syndrome was defined as fulfillment of criteria for ≥ 2 diseases (old-old or new-new). [Results] Twenty-three and 37 patients were identified as overlap syndrome by old and new criteria sets, respectively, and 7 (5 SLE-SSc and 2 SLE-PM) and 9 (7 SLE-SSc, 1 SLE-PM and 1 SLE-DM), respectively, when those with RA-overlap were excluded. All 11 (old-old or new-new) non-RA-overlap patients showed positive ANA with speckled pattern including 5 with anti-RNP antibody. All SSc patients were limited-cutaneous, and all MCTD patients were SLE-SSc overlap. Ten patients received moderate-dose glucocorticoids. Azathioprine and tacrolimus were predominant immunosuppressants. Within the mean observation for 10.7 years, fatal outcome was not observed. [Conclusion] Among patients with overlap syndrome of SARD, RA- and SLE-overlap were predominant and the prognosis was favorable.

P2-219

The Clinical Manifestations In Anti-Ro52 Antibody- Positive Patients With Systemic Sclerosis

Chihiro Iwao, Shunichi Miyauchi, Masatoshi Kimura, Yuki Rikitake,

Kosho Iwao, Mao Rikitake, Ayako Aizawa, Takeshi Kawaguchi, Yumi Kariya, Motohiro Matsuda, Kunihiko Umekita, Katoko Takajo, Ichiro Takajo, Akihiko Okayama

Department of Rheumatology, Infectious Diseases and Laboratory Medicine, Faculty of Medicine, University of Miyazaki, Miyazaki, Japan

Conflict of interest: None

[Objectives] The aim of this study is to clarify the prevalence of anti-Ro52/TRIM21 abs in patients with systemic sclerosis (SSc). [Methods] This study is a retrospective case control study. The medical records of 50 patients who were diagnosed as having SSc admitted to our hospital were reviewed. We evaluated the clinical manifestations at the first-onset of SSc. Co-existing rheumatic diseases were also reviewed. All subjects underwent SSc-associated abs testing using EUROLINE immunoblot assay. The association between clinical features and autoantibody profile was evaluated. [Results] The study group included 6 male and 44 female patients. Twenty-eight patients are limited cutaneous SSc. Twenty-three patients with SSc are positive for anti-Ro52/TRIM21 abs. The prevalence of co-existing rheumatic diseases is tended to be higher in anti-Ro52/TRIM21 abs-positive SSc patients than in negative SSc patients. Unexpectedly, the prevalence of arthralgia was higher in anti-Ro52/TRIM21 abs- negative SSc patients than in positive SSc patients. [Conclusions] The prevalence of anti-Ro52/TRIM21 abs in SSc patients of this study seems to be high compared to other reports. This abs may have potential as a biomarker in SSc patients indicating the existence of other rheumatic diseases.

P2-220

Association study of CD300H gene polymorphisms in systemic sclerosis (SSc)

Akiko Tochimoto, Yasushi Kawaguchi, Manabu Kawamoto, Kae Takagi, Yasuhiro Katsumata, Masanori Hanaoka, Hisashi Yamanaka
Institute of Rheumatology, Tokyo Women's Medical University Hospital

Conflict of interest: None

[Object] SSc is characterized by fibrosis of the skin and internal organs and microvascular injury. Endothelial injury is induced by the actions of free radicals or environmental factors with immune activation. A novel immunoreceptor CD300H is one of CD300 family molecules is identified in 2015. CD300H is expressed on CD16⁺ monocytes and myeloid dendritic cells, and that mediates neutrophil chemoattractant production. In this study, we examined whether *CD300H* polymorphisms are associated with SSc and systemic lupus erythematosus (SLE). [Methods] We investigated 329 SSc patients, 373 SLE patients and 346 healthy controls. Single nucleotide polymorphism (SNP) rs905709 was determined using TaqMan SNP genotyping assay. [Results] The frequency of rs905709 A allele was significant higher in SSc than healthy control and SLE ($P=7.32e-7$, $P=0.01$). [Conclusions] Our results suggest *CD300H* polymorphism may associate occurrence of SSc.

P2-221

Superior efficacy of CD34-selected versus unmanipulated autologous haematopoietic stem cell transplantation for severe systemic sclerosis

Masahiro Ayano^{1,2}, Hiroki Mitoma¹, Hiroshi Tsukamoto³, Yusuke Kashiwado¹, Yasutaka Kimoto⁴, Mitsuteru Akahoshi¹, Yojiro Arinobu¹, Koichi Akashi¹, Takahiko Horiuchi⁴, Hiroaki Niuro⁵

¹Department of Medicine and Biosystemic Science, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan, ²Department of Stem Cell Biology and Medicine, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan, ³Department of Rheumatology, Shin-Kokura Hospital, Kitakyushu, Japan, ⁴Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, ⁵Department of Medical Education, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan

Conflict of interest: None

[Object] This study aimed to compare the efficacy and safety of CD34-selected autologous haematopoietic stem cell transplantation (auto-HSCT) with unmanipulated auto-HSCT to treat severe systemic sclerosis

(SSc). [Methods] The subjects were 19 severe SSc patients who received CD34-selected (n=11) or unmanipulated auto-HSCT (UM, n=8). Changes in skin sclerosis and pulmonary function were assessed over an 9-year follow-up period. Differences in the changes, toxicity and overall survival were compared between the two groups. [Results] Improvement of skin sclerosis was significantly greater in the CD34-selected group than in the unmanipulated group. Forced vital capacity in the CD34-selected group continuously increased over 9 years, whereas in the UM group it returned to baseline 3 years after transplantation. Toxicity and viral infections, such as CMV infection and herpes zoster, were more frequently found in the CD34-selected group than in the UM group. No treatment-related deaths occurred in either treatment group. The 9-year overall survival rates of the CD34-selected and UM group were 81.8% and 43.8% respectively. [Conclusions] CD34-selected auto-HSCT may produce favourable effects on improvement of skin sclerosis and pulmonary function compared with unmanipulated auto-HSCT.

P2-222

Effects of platelet-derived growth factor receptor (PDGFR) inhibitor for the fibrosis of systemic sclerosis

Katsunari Makino, Hironobu Ihn

Department of Dermatology and Plastic Surgery, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan

Conflict of interest: None

[Object] Systemic sclerosis (SSc) is an acquired autoimmune disorder that typically results in fibrosis of the skin and internal organs. We examined the role of crenolanib, an inhibitor of PDGFR signaling, in cultured skin fibroblasts and evaluated its antifibrotic effect in the angiotensin II (Ang II)-induced mice skin and heart fibrosis. [Methods] Healthy control (HC) and SSc dermal fibroblasts were cultured in the presence of crenolanib, TGF- β , PDGF ligands and CTGF. Skin biopsy samples collected from 15 healthy controls and 33 dcSSc were included in the microarray analysis. Ang II was administered by subcutaneous osmotic pumps. [Results] Crenolanib effectively inhibited proliferation of SSc and HC fibroblasts, and attenuated basal and TGF- β -induced expression of CTGF and periostin. In contrast to HC fibroblasts, SSc fibroblasts proliferated in response to PDGFAA, while a combination of PDGFAA and CTGF was required to produce a similar response in HC fibroblasts. PDGFR α mRNA correlated with CTGF and other fibrotic markers in the skin of SSc. Treatment with crenolanib by daily intraperitoneal injections attenuated the skin and heart fibrosis in the Ang II model. [Conclusions] Our data indicate that inhibition of PDGF signaling presents a new attractive therapeutic approach in SSc.

P2-223

Serum KL-6 level and forced vital capacity are prognostic factor of patients with Systemic Sclerosis

Takayuki Kon¹, Yoshiyuki Abe², Masakazu Matsushita², Michihiro Ogasawara², Ken Yamaji², Naoto Tamura²

¹Department of Rheumatology and Internal Medicine, Juntendo University Nerima Hospital, Tokyo, Japan, ²Department of Rheumatology and Internal Medicine, Juntendo University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] We investigated whether serum KL-6 levels and respiratory function in patients with systemic sclerosis (SSc) are prognostic factors. [Methods] Two-hundred ninety-three patients with SSc hospitalized to Juntendo University Hospital were included. Patients with interstitial lung disease (ILD) (185 patients; group A) and without ILD (108 patients; Group B), were investigated for differences in prognosis with normal KL-6 group (< 500 U/mL) and high KL-6 group (\geq 500 U/mL), forced vital capacity (% FVC) and diffusing capacity of the lung for carbon monoxide (% Dlco) in the normal and the declining groups. [Results] One-hundred thirty cases (70.3%) in group A and 35 cases (32.4%) in group B. The high KL-6 group was poor prognosis (p=0.007) compared with the normal group, but in the group B, there was no significant difference. In the low %FVC group (<80%), the prognosis was poor (p=0.009) compared with the normal group, but when compared in each of the Group A and B, there was no significant difference. Only 20 cases has

normal % Dlco levels, there was no significant difference. [Conclusions] Elevated KL-6 levels in SSc patients without ILD was not a prognostic factor. For the characteristics of high serum KL-6 levels, further investigation is considered necessary.

P2-224

Nailfold videocapillaroscopic changes in 2 cases of systemic sclerosis renal crisis

Kae Onishi, Naoto Yokogawa, Naoki Tanomogi, Masahiro Iida, Yusuke Nakamichi, Shuhei Sano, Tatsuo Mori, Nanase Honda, Michiru Kina, Eisuke Takamasu, Takayasu Kise, Yuji Miyoshi, Yoshiki Nagai, Masako Utsunomiya, Kota Shimada, Shoji Sugii

Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center

Conflict of interest: None

[Background] There are few case reports of Nailfold videocapillaroscopy (NVC) findings in scleroderma renal crisis (SRC). [Case1] An 71-year-old female was immediately hospitalized with cardiac failure. She presented the progressive renal dysfunction with erythrocyturia and proteinuria, thrombocytopenia and anemia. The renal biopsy presented moderate glomerular ischemic collapse and vascular thrombosis. Further, she was anti-RNA polymerase 3 antibody positivity, thus we diagnosed her with SRC. ACEI, ARB, and CCB was administered, but she progressed oliguria and fluid retention state, and hemodialysis was initiated. The NVC revealed severe avascular areas and the massive busy capillaries. [Case2] An 81-year-old female with anti-RNA polymerase 3 antibody positivity was admitted for renal dysfunction with proteinuria and thrombocytopenia. The renal biopsy revealed the thrombosis in renal arterioles, which contributed to the diagnosis of SRC for her. She was treated with ACEI and CCB and improved renal function and platelet counts. The NVC finding revealed mostly normal morphological capillaries and only a few giant capillaries and avascular areas. [Clinical implications] We describe the two valuable SRC cases with references in terms of their NVC findings.

P2-225

Scleroderma renal crisis in a patient with diffuse cutaneous systemic sclerosis after persistent elevation of anti-RNA polymerase III antibody levels

Hiroshi Sawachika, Shunichi Fujita, Mayuko Fukushima, Takahiko Akagi, Hiroyasu Hirano, Tomoyuki Mukai, Yoshitaka Morita

Department of Rheumatology, Kawasaki Medical School, Kurashiki, Japan

Conflict of interest: None

A 71-year-old woman was referred to our clinic with Raynaud's phenomenon in September 2014. She had nailfold capillary abnormalities and puffy fingers without skin sclerosis. Serological tests showed positivity for anti-Scl70 antibody. Skin sclerosis progressed gradually, and we diagnosed diffuse cutaneous systemic sclerosis (SSc) during her follow up visit to the clinic. Her serum creatinine level was 0.6 mg/dl in June 2018, while it was elevated to 3.16 mg/dl in September 2018. She also had thrombocytopenia, hemolytic anemia, and hypertension of 238/134 mmHg with hyperreninemia. She was admitted to hospital with a diagnosis of scleroderma renal crisis (SRC). She then started to receive an angiotensin-converting enzyme inhibitor. However, this treatment was not effective, and hemodialysis was needed on the 12th hospital day. Of note, serum anti-RNA polymerase III antibody levels (index <28: negative, 28-50: gray zone, >50: positive) were elevated from 18.4 in September 2014 to 23.1 in August 2015, and were subsequently increased to 32.9 in September 2018. Clinical significance: The follow up measurements of anti-RNAPIII antibody may contribute to early diagnostic assessment of SRC in SSc patients, and improve their outcomes.

P2-226

Nine cases with giant cell arteritis

Daisuke Nakatsubo, Yoshimasa Hamano, Michihito Katayama, Hitoshi Deguchi

Conflict of interest: None

[purpose] Giant cell arteritis (GCA) is a rare disease presenting fever and headache. However, without subjective manifestations, some patients might not be diagnosed or treated properly. We examined the diagnostic process of GCA patients in our hospital. [method] Patients diagnosed having GCA in our department from 2013 to 2018 were analyzed retrospectively. [result] Five male and four female patients were diagnosed. Their mean age at diagnosis was 75.2 ± 8.8 year old. One had ocular manifestation, six complicated with polymyalgia rheumatica and one complicated with lupus. Five patients had dilatation or tenderness of temporary artery (TA). Five had wall thickening in ultrasonography and six had histologically positive findings, among seven patients having both ultrasonography and TA biopsy. Among them, two would not be diagnosed according to 1990 ACR criteria without biopsy. PET-CT was performed to seven patients, and five were classified as having large vessel GCA. One patient complicated with malignancy at diagnosis. We also report instructive cases with details. [conclusion] Positive findings in ultrasonography in more than a half of the patients, suggesting it is recommended as a non-invasive examination. Our report investigated false negative in ultrasonography or TA biopsy.

P2-227

Experience of tocilizumab for Giant Cell Arteritis: A single center cohort

Hiromichi Tamaki, Sho Fukui, Haruki Sawada, Yukihiko Ikeda, Ayako Kitada, Masei Suda, Haruyuki Yanaoka, Ryo Rokutanda, Tokutaro Tsuda, Mitsumasa Kishimoto, Ken-ichi Yamaguchi, Yukio Matsui, Masato Okada

Immuno-Rheumatology Center, St. Luke's International Hospital

Conflict of interest: None

[Object] Giant Cell Arteritis (GCA) is one of the primary systemic vasculitides, which mainly affects elderly. No effective treatment has been described except for glucocorticoids until the recent clinical trial of tocilizumab (TCZ) for GCA. Now TCZ is approved for GCA in Japan since August 2017. Here our experience with TCZ for GCA is described. [Methods] This is a retrospective study of the patients with GCA treated at St. Luke's International Hospital who was on TCZ for at least 3 months. [Results] Nine patients were identified. Three are male. The median age at the initiation of TCZ is 71 years. The median duration of follow up is 9 months. TCZ was used for relapse in 8 patients. One patient received TCZ from the beginning due to a history of recurrent compression fracture. The median dose of prednisone at the initiation of TCZ was 15mg and the median dose of prednisone 3 months after TCZ treatment was 6mg ($p=0.009$, [Wilcoxon signed rank test]). Eight patients used TCZ for more than 6 months. The median dose of prednisone at 6 months was 3.5 mg ($p=0.014$). All of the patients were on prednisone 5mg or less and two discontinued prednisone. Relapse occurred one out of 9 patients. [Conclusions] TCZ appears to have steroid sparing effects in Japanese patients based on our experience.

P2-228

Thinking how to optimize treatment for giant cell arteritis through the experience of three cases

Hideyuki Takahashi, Sayaka Tsuzuki, Fangyi Chin, Keigo Setoguchi
Department of Rheumatology, Tokyo Metropolitan Komagome Hospital

Conflict of interest: None

Background: As for giant cell arteritis (GCA), one of the main purposes of induction therapy is to prevent future relapses and complications, including aneurysm and stenosis. However, it is difficult to evaluate the risk of those events precisely, and to predict the necessity of strong treatment such as tocilizumab. Case: 1:A-64-year-old woman was admitted to our department due to low grade fever, dry cough and backache. She was diagnosed GCA after temporary artery biopsy (TAB), and started to receive mPSL 40mg. During steroid tapering, however, fever and ele-

vation of CRP relapsed when mPSL20mg was prescribed. Concomitant use of AZP 50mg or MTX 14mg was not effective enough. Finally, the inflammation was maintained after tocilizumab was administered. 2:A-67-year-old woman was diagnosed GCA as well and started to receive mPSL 40mg. Administering MTX 6mg concomitantly, dose of steroid had been tapered to PSL 7mg without any relapse. 3:A-66-year-old woman was diagnosed GCA as well and started to receive PSL 40mg alone. Dose of steroid had been tapered to PSL 20mg without any relapse so far, and tapering has gone on. Three cases above seemed similar at first, but showed different reactivity to therapies. Here, we analyze the cause of this difference with some literature review.

P2-229

Efficacy and safety of Tocilizumab therapy for relapsed cases of giant cell arteritis

Yoichiro Haji¹, Takanori Ito¹, Mizuki Kato¹, Naoho Takizawa², Tatsuo Watanabe¹, Hideaki Shimizu¹, Yoshiro Fujita²

¹Daido Hospital, Nagoya, JAPAN, ²Department of Rheumatology, Chubu Rosai Hospital, Nagoya, Japan

Conflict of interest: None

[Object] To investigate its efficacy and safety of Tocilizumab (TCZ) therapy for relapsed cases of giant cell arteritis (GCA) in spite of standard therapy. [Methods] We retrospectively reviewed GCA cases treated with TCZ which is relapsed in spite of standard therapy. Three cranial GCA and one large vessel GCA were included. Their age, gender, disease duration, average steroid dose, number of steroid cessations, number of relapses, and symptoms when relapsing were collected. [Results] All subjects were female, and its average age was 76.3 years old. Disease duration until TCZ started was 4.9 months. There were 2 cases of successful cessation of steroid, zero case of relapse, and zero case of discontinuation of administration due to adverse event. Regarding safety signals, there were one case of nasopharyngitis, one case of bronchitis, and one case of diabetes exacerbation. [Conclusions] It was suggested that the use of TCZ for relapsed case of giant cell arteritis may contribute to discontinuation of steroids, steroid sparing, and prevention of recurrence.

P2-230

Two cases of giant cell arteritis that treatment with steroids could be discontinued by using tocilizumab

Tatsuya Kai, Kensuke Oryoji, Daisuke Hiraoka, Kenji Yoshida, Hiroko Ikeuchi, Shinichi Mizuki

Matsuyama Red Cross Hospital, Matsuyama, Ehime, Japan

Conflict of interest: None

[Case 1] She is a 68-year-old woman. She was diagnosed relapsing polycondritis and treated with prednisolone (PSL). After that, PSL was discontinued. 6 years after, she felt discomfort in the neck and CRP increased. PET-CT revealed FDG uptake in the common carotid artery and aorta, and giant cell arteritis (GCA) was suspected. After steroid pulse treatment, we treated with oral PSL. When PSL was tapered to 5 mg/day, it had a flare. By using tocilizumab (TCZ), symptoms disappeared and PSL was able to be discontinued. [Case 2] She is a 88-year-old woman. She presented with two-months of fever and headache, and four-days of right visual loss. Her temporal arteries were swollen. We diagnosed as GCA, after steroid pulse treatment, treated with oral PSL. When PSL was tapered to 7.5 mg/day, it had a flare. By using TCZ, symptoms disappeared and PSL was able to be discontinued. [Clinical Significance] Although steroids are used to treat GCA, we also experience cases that it is difficult to reduce or stop steroids. In recent years, the effectiveness of TCZ against GCA has been shown, and there is a possibility that steroid can be reduced or stopped by using TCZ. We also experienced cases that steroids could be discontinued by using TCZ and report with literature consideration.

P2-231

A case of giant cell arteritis presented with abducens nerve palsy

Yu Katayama, Nobuyuki Shimizu, Hiroshi Wakabayashi

Department of Rheumatology, Okayama City Hospital, Okayama, Japan

Conflict of interest: None

[Chief complaint] diplopia [Presentation of case] A 77-year-old woman was admitted to our hospital because of diplopia and malaise. 14 days before admission, diplopia, malaise and headache appeared. Her headache was spontaneously improved in several days, but diplopia was continued and laboratory data in the clinic revealed elevation of CRP, and then she was referred to our department. [Course] Physical examination revealed an enlarged left temporal artery and left abducens nerve palsy. Since color doppler ultrasonography showed halo sign, giant cell arteritis (GCA) was strongly suspected. Temporal artery biopsy was done, and the next day after biopsy, prednisolone (PSL) 50mg/day (=1mg/kg/day) was administered. Histopathologic findings revealed destruction of external elastic lamina, thickness of internal lamina with arterial stenosis and infiltration of inflammatory cells including Langhans giant cell in the arterial wall. We diagnosed GCA, and tocilizumab (TCZ) was added. 3 days after TCZ administration, left abducens nerve palsy was improved and diplopia disappeared. [Clinical significance] GCA typically presents fever, headache and polymyalgia rheumatica-like symptoms, but abducens nerve palsy as an initial presentation is rare. So we report a case of GCA presented with abducens nerve palsy.

P2-232

A Case of 'Temporal Arteritis' without Intracranial Ischemic Symptoms Diagnosed by Imaging Tests and Superficial Temporal Artery Biopsy

Risa Yamada, Hirokazu Nishina, Akira Nishino, Shinya Hirahara, Mari Tochihiro, Masanori Hanaoka, Yasuhiro Katsumata, Hisashi Yamanaka
Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Case] A man in his 70s had cough, sputum, anorexia, malaise and slight fever for five months before hospitalization. Antimicrobial agents didn't work. He visited our general department three months ago. CRP was prolonged high. PET-CT showed that FDG accumulated in large vessels and temporal artery. He visited our department for examination of large vessel vasculitis. There were no symptoms of headache, scalp pain, side of the head pain, jaw claudication, diplopia, blurred vision, visual field loss and limb claudication. Laboratory results were ESR 100 mm/h, CRP 4.54 mg/dl, and no swelling or weak beating at palpation. There was halo sign of temporal artery in ultrasonic echo and giant cells founded in vessel wall media at biopsy. There were no eye symptoms but thickened intima and lumen constriction. We treated PSL 30mg/day, tocilizumab 162mg/week and aspirin Day 9. His fever had gone and ESR and CRP decreased Day 22. PSL is now reduced, but there is no reactivation. [Clinical significance] Febrile patients with unknown origin, who had no headache or ischemic cranial symptoms, are sometimes diagnosed as large vessel giant cell arteritis by imaging tests. However, it is very rare that temporal artery involvement is confirmed by imaging test and biopsy in such cases.

P2-233

Azathioprine use in a patient with methotrexate-intolerant giant cell arteritis

Kyoichi Nakajima, Yasufumi Shindo
Department of Rheumatology, National Hospital Organization Higashi-Saitama Hospital

Conflict of interest: None

[Background] It is necessary for some glucocorticoid (GC)-resistant giant cell arteritis (GCA) patients to use therapeutic options. The evidence levels of methotrexate (MTX) and tocilizumab (TCZ) are high, while other immunosuppressants are low, such as azathioprine (AZP), cyclosporine, and tacrolimus. I report a case of MTX-intolerant GCA treated with AZP. [Case] A 68-year-old woman had fever, temporal headache, tenderness of temporal artery, and jaw claudication. Her erythrocyte sedimentation rate (ESR) level was elevated to 122 mm/h. She was diagnosed as GCA and treated with prednisolone (PSL) 55 mg (1 mg/kg) daily. Then her headache disappeared and ESR was reduced, but her head-

ache relapsed after tapering PSL to 45 mg daily. PSL dose was increased to 50 mg daily and 4 mg weekly of MTX was started. PSL dose was decreased to 20 mg daily with 10 mg weekly of MTX, but ESR level was elevated and her hair was lost gradually. MTX was discontinued finally because of her alopecia. After administration of 50 mg daily of AZP, ESR level reduced and PSL was tapered to 11.5 mg daily. AZP has been continued with tapering to 25 mg daily due to liver dysfunction. [Clinical significance] AZP can be used for GC-resistant, MTX-intolerant GCA.

P2-234

A case of temporal arteritis in which echo examination was useful for diagnosis and treatment effect determination

Hiromi Hirabayashi¹, Yohei Takeuchi², Michiaki Tokuda²

¹Examination Department, Sanuki Municipal Hospital, ²Department of Rheumatology, Sanuki Municipal Hospital

Conflict of interest: None

«Case» 77 year old female «Current medical history» Headache, posterior neck pain occurred and a previous doctor was consulted. Using NSAIDs did not improve headaches, but was introduced to our hospital for the purpose of scrutiny. Headache, scalp pain, jaw claudication, shedding disorder, swallowing pain was recognized, and the superficial temporal artery was tactile. In the blood test, marked inflammatory reaction was observed. Temporal arteritis was suspected from the above, but echocardiography was performed because there was no abnormality in MRI. Echocardiography revealed a circumferential low luminance thickening image including the vessel wall and a narrowing of the vascular lumen, suspected of temporal arteritis, and biopsy was performed. The lumen narrowing, the destruction image in intima-media infiltrating numerous inflammatory lymphocyte, a large number of giant cells in elastic fibers, led to the diagnosis of temporal arteritis. Steroids and tocilizumab 162 mg / w subcutaneous injection resulted in remission, and subsequent echocardiography improved wall thickening and restored blood flow. «Conclusion» Echo can be obtained noninvasively and accurate biopsy findings. Moreover, it was considered to be useful not only for diagnosis but also for judgment of therapeutic effect.

P2-235

The effectiveness of tocilizumab to Takayasu arteritis in the real-world

Toshiki Nakajima, Yumiko Nakano, Kohei Tsujimoto, Masaaki Fujita, Yoshitaka Imura

Department of Clinical Immunology and Rheumatology, Tazuke Kofukai Medical Research Institute Kitano Hospital, Osaka, Japan

Conflict of interest: Yes

[Object] Although Japanese Ministry of Health, Labor and Welfare admitted the use of tocilizumab (TCZ) to the patients with Takayasu arteritis (TAK) in August 2017, the effectiveness of TCZ to TAK in the real-world is still unclear. In this survey, we aimed to evaluate the effectiveness of TCZ to TAK. [Methods] We examined the medical records of 19 patients with TAK, who have been treated in our hospital since September 2017, then checked the changes in the treatment of TAK and relapse of TAK between September 2017 and September 2018. [Results] Two of 19 patients with TAK were treated with TCZ. Every patient with TAK except 1 patient was treated with glucocorticoids. The dose of glucocorticoids was reduced in 2 patients treated with TCZ and in 10 patients treated without TCZ. Before the administration of TCZ, patients treated with TCZ used methotrexate, which was discontinued after TCZ administration. No one relapsed in the patients treated with TCZ, whereas 2 patients had relapsed in the patients treated without TCZ. [Conclusions] Patients with TAK, who need immunosuppressant to control their disease, could discontinue immunosuppressant if TCZ is administered. This may suggest that TCZ is effective to the patients with TAK, who are resistant to conventional therapy.

P2-236

A case of severe Takayasu arteritis successfully treated with upfront combination of tocilizumab and conventional immunosuppressive treatment

Natsuko Watanabe, Takako Hashimoto, Masashi Suzuki, Tatsuaki Naganawa, Ai Umeda, Konomi Ashihara, Megumi Kurumizawa, Daisuke Hirano, Jo Nishino, Shusaku Fukaya, Shunji Yoshida, Hidekata Yasuoka
Division of Rheumatology, Department of Internal Medicine, Fujita Health University School of Medicine

Conflict of interest: None

[Case] A 21-years old female firstly suffered from faintness and blurry vision in January, 2018. In March, jaw claudication appeared. In April, she visited a clinic because those symptoms were persisted. Brain MRI showed multiple old cerebral infarction. In June, she visited to the emergency room because she felt the numbness of right upper limb and dysarthria. Cervical MRA revealed an occlusion of the bilateral common carotid artery, and stenosis of the left vertebral artery. An image of carotid US showed swelling of vascular wall and narrow of the lumen. Furthermore, PET-CT found that FDG uptake was detected on the artery wall from the aortic base to descending thoracic aorta. Base on these findings she was diagnosed as Takayasu arteritis (TAK) type2B. We started upfront combination therapy with PSL 50mg/day (1mg/kg/day) and tocilizumab (TCZ) because the symptoms of ischemia are progressing. Follow-up US and MRA showed no progression of hyperplasia of vessel wall. Dose of PSL was successfully decreased to 25mg/day on day 86 at admission and she discharged from hospital. [Discussion] For seriously ill cases, upfront combination of tocilizumab and conventional immunosuppressive treatment may be one of the choice which contribute to improvement of prognosis.

P2-237

Therapeutic effect of biologics for Takayasu arteritis with rapid progressive arterial stenosis

Tomoyuki Asano, Makiko Furuya Yashiro, Jumpei Temmoku, Yuya Fujita, Naoki Matsuoka, Shuzo Sato, Hiroko Kobayashi, Hiroshi Watanabe, Kiyoshi Migita
Department of Rheumatology, Fukushima Medical University

Conflict of interest: None

[Object] We have evaluated effect of biologics for Takayasu arteritis (TA) with progressive arterial stenosis. [Methods] Cases of TA with arterial stenosis were included. Biomarkers, Ankle-Branchial-Index (ABI) and CT images were examined over time. [Results] Case 1: A 20-year-old woman had a diagnosis of TA, because of a history of intermittent claudication, and stenosis of mesenteric and left femoral artery from CT findings. Prednisolone (PSL) and subcutaneous tocilizumab (TCZ) was administered to her. After TCZ therapy, serum IL-6 level was improved from 29.3 to 18.4 pg/mL. ABI was also improved from 0.70/0.60 (right/left) to 0.85/0.81. Stenosis of femoral artery was disappeared significantly. Case 2: A 18-year-old woman had a diagnosis of TA. She had a history of intermittent claudication and gangrenous pyoderma. Stenosis in common carotid artery, descending aorta and femoral artery were shown from CT findings. After PSL therapy, TCZ was added. ABI was remarkably improved from 0.40/0.39 to 0.62/0.79. However, IL-6 level was not reduced. Stenosis of carotid and femoral artery were remarkably improved. [Conclusions] Immunosuppressive treatment in early stage seems to be effective to improve arterial stenosis in patients with TA.

P2-238

A study of Takayasu arteritis treated with the biological preparations

Hiroki Yabe, Eri Watanabe, Chihiro Terai, Tsuyoshi Kobashigawa, Toru Yago, Shigeru Kotake
Division of Rheumatology, Jichi Medical University Saitama Medical Center

Conflict of interest: None

Takayasu arteritis (TA) is LVV which is relatively frequent in young women and Japan. We examined the clinical features of cases using bio-

logical products (Bio) against TA at our hospital. Treatment course before and after introduction of Bio was examined in 5 patients with TA who received Bio in 2009-2018 and were followed more than half a year. All cases were females and the age at onset and diagnosis was 17-43 years (average 30 years old). As initial treatment, all patients were treated with steroids with PSL 30-50 mg/day, and the minimum PSL dose before Bio was 3-10 mg/day (avg. 7.6). The PSL dose at introduction of Bio was 10-15 mg/day (avg. 11.7). The immunosuppressive agents before Bio were MTX in 5 cases, TAC in 3, and CyA in 1. The period from the first treatment to Bio was 17 to 82 months (avg. 53), and the first Bio was TOC in 2 cases, ETN in 2, and ADM in 1. ETN was primarily ineffective in 2 cases and switched to TOC after 3 months. At average 36 months (10-70 mo.) after Bio-introduction, dose of PSL was decreased to 6.4 mg/day (5-7.5 mg/day). Although this survey is performed in a small number of TA cases, a good persistence rate of Bio and the steroid sparing effect was shown in TOC and ADM.

P2-239

RORγt antagonist suppresses Sjogren's syndrome like sialadenitis in RORγt transgenic mouse

Yuko Ono^{1,2}, Hiroto Tsuboi¹, Masafumi Moriyama², Hiromitsu Asashima¹, Hanae Kudo¹, Fumika Honda¹, Saori Abe¹, Hiroyuki Takahashi¹, Yuya Kondo¹, Isao Matsumoto¹, Seiji Nakamura², Takayuki Sumida¹

¹Department of Internal Medicine, Faculty of Medicine, University of Tsukuba, ²Section of Oral and Maxillofacial Oncology, Division of Maxillofacial Diagnostic and Surgical Sciences, Faculty of Dental Science, Kyushu University

Conflict of interest: None

[Object] We previously reported that T cells specific RORγt transgenic (RORγtTg) mice developed spontaneous sialadenitis like Sjögren's syndrome in which reduced regulatory T cells and RORγt-overexpressed CD4⁺T cells contributed to the pathogenesis. The purpose of this study was to clarify suppressive ability and its mechanisms of RORγt antagonist (A213) for sialadenitis of RORγtTg mice. [Methods] 6 weeks (W) aged RORγtTg orally received A213 or PBS every 3 days for 2W. We compared 1) saliva volume, 2) histopathology of salivary glands, 3) expressions of CD25 and Foxp3 in CD4⁺T cells of spleen and cervical lymph nodes (cLN), between treatment groups. [Results] 1) The ratio of saliva volume at 2W to that at baseline was significantly increased in A213 (3.4±1.4) compared with PBS group (1.3±0.3) ($p < 0.05$). 2) The focus score of sialadenitis at 2W was significantly lower in A213 (0.2±0.2) than in PBS group (2.0±0.6) ($p < 0.05$). 3) The percentage of CD25⁺Foxp3⁺/CD4⁺T cells in spleen and cLN was comparable between groups. The percentage of CD25⁺Foxp3⁺/CD4⁺T cells in cLN was significantly lower in A213 (18±6%) than in PBS group (45±11%) ($p < 0.05$), while similar in spleen. [Conclusions] A213 reduced CD4⁺CD25⁺Foxp3⁺ T cells in cLN and suppressed sialadenitis in RORγtTg mice.

P2-240

Regulatory mechanism of rice seeds expressing altered peptide ligands against M3 muscarinic acetylcholine receptor (M3R) induced experimental sialadenitis-like Sjögren's syndrome

Hanae Kudo, Hiroto Tsuboi, Hiromitsu Asashima, Hiroyuki Takahashi, Yuko Ono, Saori Abe, Fumika Honda, Izumi Kurata, Mizuki Yagishita, Masahiro Yokosawa, Yuya Kondo, Isao Matsumoto, Takayuki Sumida
Department of Internal Medicine, Faculty of Medicine, University of Tsukuba, Japan

Conflict of interest: None

[Object] We previously found that Rag1^{-/-} mice inoculated with splenocytes from M3R^{-/-} mice immunized with M3R peptides developed sialadenitis like Sjögren's syndrome (M3R induced sialadenitis; MIS). We also reported that intravenous administration of altered peptide ligands of N1 region (N1-APL7) suppressed MIS. In this study, we aimed to evaluate the suppressive ability and its mechanisms of rice seeds expressing N1-APL7 against MIS. [Methods] 1) Transgenic rice expressing N1 and N1-APL7 were generated. 2) After oral administration of rice seeds to MIS mice, the change of saliva volume and pathological findings of sali-

vary glands were evaluated. 3) M3R specific cytokine production by splenic CD4⁺T cells of MIS was compared between rice seeds treated groups in vitro. [Results] 1) Expression of N1 and N1-APL7 were detected in the rice seeds. 2) Saliva volume of N1-APL7 rice group tended to increase compared to N1 and non-transgenic rice group. Focus score of N1-APL7 rice group was significantly lower than those of other groups. 3) M3R specific IFN γ and IL-17 productions by splenic CD4⁺T cells were detected. M3R specific IFN γ production in N1-APL7 rice group tended to decrease compared with other groups. [Conclusions] Oral administration of N1-APL7-expressing rice suppressed MIS.

P2-241

Analysis of blood Tfh/Tph subsets in primary Sjogren Syndrome

Shotaro Kawano¹, Shoichiro Inokuchi¹, Hiroki Mitoma¹, Kazuhiko Higashioka¹, Kensuke Irino¹, Masahiro Ayano¹, Yasutaka Kimoto³, Mitsuteru Akahoshi¹, Yojiro Arinobu¹, Takahiko Horiuchi³, Hiroaki Niuro²
¹Department of Medicine and Biosystemic Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, ²Department of Medical Education, Graduate School of Medical Science, Kyushu University, Fukuoka, Japan, ³Department of Internal Medicine, Kyushu University Beppu Hospital, Oita, Japan

Conflict of interest: None

[Object] Recent reports showed that PD-1^{hi}CXCR5⁺CD4⁺ T cells in synovium of patients with rheumatoid arthritis poised to promote B-cell responses and antibody production. Interplay between T follicular helper cells and germinal center B cells is essential for the formation and maintenance of germinal centers and for the generation of memory B cells and long-lived plasma cells. Abatacept reduced percentages and numbers of circulating follicular helper T (Tfh) cells, autoantibodies, and serum levels of cytokines. Rituximab reduced circulating Tfh cells. This suggests the importance of T-B interaction in pSS. We study the T cell subsets which may help B cell differentiation in pSS. [Methods] We analyse Tfh/Tph subsets from pSS patients and healthy controls using flowcytometry. [Results] Ratio of Tfh-like cell, especially CXCR3⁺ Tfh-like cell, to CD4 T cell and Tph-like cell/CD4T ratio in patients with primary SS increased. CCR6⁺CXCR3⁺Tph-like/CD4T ratio correlates with serum IgG level in pSS. [Conclusions] Tph-like cells may be increased in pSS and contribute the pathogenesis of pSS.

P2-242

Novel therapeutic strategy using T-induced pluripotent stem cells (T-iPSCs) derived from M3R-reactive Th1 cell clone of a patient with Sjögren's syndrome (SS)

Hiroyuki Takahashi¹, Hiroto Tsuboi¹, Seiji Segawa¹, Hiromitsu Asashima¹, Saori Abe¹, Hanae Kudo¹, Yuko Ono¹, Fumika Honda¹, Yuya Kondo¹, Isao Matsumoto¹, Makoto Otsu², Takayuki Sumida¹

¹Faculty of Medicine, Department of Internal Medicine, University of Tsukuba, ²Division of Stem Cell Processing/Stem Cell Bank, Center for Stem Cell Biology and Regenerative Medicine, The University of Tokyo

Conflict of interest: None

[Purpose] To establish antigen-specific CD4⁺ regulatory T cells for development of a novel treatment via iPSCs generated from antigen-specific T cells in a SS patient. [Methods] 1) We identified peripheral M3R reactive IFN- γ -producing CD4⁺ T cells, which were single cell sorted to establish CD4⁺ T cell clones, in a primary SS patient. 2) T-iPSCs were generated from CD4⁺ T cell clones by transfection of Yamanaka's factors. 3) TCR β gene rearrangement was compared between the original CD4⁺ T cell clone and the T-iPSCs. 4) T-iPSC-Sacs were generated by culture on 10T1/2 cells for 14 days, and analyzed for expressions of CD45, CD34, and CD43 by FCM. 5) We transferred T-iPSC-Sacs cells or CD34⁺ cells in Sacs into irradiated NSG mice, and analyzed generation of peripheral T cells from T-iPSCs. [Results] 1) We established 35 CD4⁺ T cell clones. 2) 7 T-iPSCs were generated from CD4⁺ T cell clones. 3) TCR β gene rearrangement of the generated T-iPSCs was consistent with that of the original CD4⁺ T cell clone (TRBV20.1*01-D2*02-J2.3*01). 4) T-iPSC Sacs cells expressed CD45, CD34 and CD43. 5) We are now analyzing the generation of T cells from T-iPSCs in NSG mice. [Conclusion] We could establish T-iPSCs from M3R-reactive Th1 cell clones of a SS pa-

tient, and could generate CD34⁺ cells from the T-iPSCs.

P2-243

Initial phase of human T-cell leukemia virus type 1 infection toward salivary gland epithelial cells use biofilm-like structure

Hideki Nakamura, Toshimasa Shimizu, Ayuko Takatani, Atsushi Kawakami

Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: Yes

[Object] To examine initial infection manner of human T cell leukemia virus-1 (HTLV-1) toward salivary gland epithelial cells (SGECs). [Methods] Immunofluorescence (IF) was used when SGECs of patients with Sjögren's syndrome (SS) and non-SS subjects were co-cultures with HTLV-1 infected cell line, HCT-5 or MOLT-4. Scanning and Transmission electron microscope (SEM/TEM) were employed to detect virions. [Results] Extracellular matrix and linker proteins, Galectin-3, Agrin, and Thetherin expressed on the surface of HCT-5. HTLV-1 Gag-positive spots were observed on adjacent SGECs after 1h co-culture with HCT-5. Regardless of presence of pSS, Agrin, and Thetherin co-expressed with HTLV-1 Gag on SGECs 1h co-culture with HCT-5. No polarization of HTLV-1 Gag and Talin was observed after co-culture with HCT-5. Virion-like particles between HCT-5 and SGECs were detected by SEM, in which HTLV-1 virions were found on the surface of HCT. Virions existed at an interspace between HCT-5 and SGECs. TEM image showed that HTLV-1 virions with envelope were transmitted to SGECs at the interface of HCT-5 and SGECs while HTLV-1 virions were released from cell surface of HCT-5. [Conclusions] Initial phase of HTLV-1 infection toward SGECs was mediated by not viral synapse, but biofilm-like components.

P2-244

Clinical feature and outcome of juvenile Sjögren's syndrome; a single center experience

Seira Hattori, Ai Ohnishi, Kenichi Nishimura, Ryoki Hara, Shuichi Ito
Department of Pediatrics, Yokohama City University Graduate School of Medicine

Conflict of interest: None

[Object] To investigate the clinical feature and outcome of juvenile Sjögren's syndrome (SS). [Methods] We retrospectively assessed the clinical symptom, laboratory data, radiological findings and treatment in 34 children with SS who were diagnosed in our hospital since April 1987 until April 2018. [Results] Thirty patients (88%) were female, and median age of diagnosis was 10.9 (4.6-15.9) years old. Thirteen patients had primary SS, and 21 had the secondary SS, in which 12, 8 and 1 patients were complicated with systemic lupus erythematosus, mixed connective tissue disease and juvenile dermatomyositis, respectively. Primary SS were discovered by fever or rash or arthralgia. No one showed dry mouth and dry eye. Rheumatoid factor, anti SS-A antibody, anti SS-B antibody was positive in 65%, 94%, 50% of the patients, respectively. Schirmer test, Saxon test, lip biopsy abnormality was positive in 15%, 35%, 100% of the patients, and abnormal magnetic resonance sialography and salivary scintigraphy were observed in 69% and 88% of the patients respectively. [Conclusions] In juvenile SS patients, few patients developed dry mouth or dry eye, and primary SS patients were diagnosed with fever or rash or arthralgia. Sicca symptoms had presented over time regardless of whether they were treated or not.

P2-245

A retrospective analysis of clinical manifestation in primary Sjögren's syndrome-related interstitial lung disease

Eriko Ishioka Takei¹, Katsuya Suzuki¹, Naoshi Nishina¹, Hidekata Yasuoka^{1,2}, Tsutomu Takeuchi¹

¹Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, ²Division of Rheumatology, Fujita Health University School of Medicine, Nagoya, Japan

Conflict of interest: None

[Object] Lung involvement is a systemic manifestation of primary Sjögren's syndrome (pSS). The aim of this study is to investigate patients back ground and clinical course of pSS-interstitial lung disease (ILD). [Methods] Total 300 consecutive patients with pSS diagnosed according to the 1999 revised Japanese criteria for the diagnosis of pSS at our division were enrolled. Clinico-radiological characteristics were retrospectively investigated and statistically analyzed. [Results] Lung involvements were confirmed in 31.4%. This included ILD (n=23, 9.6%). Radiological patterns of 23 pSS-ILD were followings: 17 for NSIP, 5 for UIP and 1 Organizing pneumonia. 9 were progressive and 17 were stable during observation periods. Comparing ILD-progressive group with stable group, serum IgG level was significantly elevated. Notably, In ILD-progressive group, a serum IgG level in the progressive group of UIP and LIP was significantly higher than a progressive group of NSIP. (p=0.027) [Conclusions] This study demonstrated that there is possibility of involvement of ILD in 10% of pSS patients and UIP patterns with high level of serum IgG needed the follow-up that a lot of progress examples in particular were careful in that.

P2-246

Effective glucocorticoid treatment in a case of pulmonary artery hypertension associated with long-term follow up of Sjögren's syndrome

Mayuko Koyama¹, Masakazu Matsushita¹, Taiga Kuga¹, Seiichiro Ando¹, Takayuki Kon², Kurisu Tada¹, Hirofumi Amano¹, Ken Yamaji¹, Naoto Tamura¹

¹Department of Rheumatology and Internal Medicine, Juntendo University School of Medicine, ²Department of Rheumatology and Internal Medicine, Juntendo University Nerima Hospital

Conflict of interest: None

A 47-year-old man with a history of hepatic dysfunction in 11 years ago underwent further evaluation. He was positive for anti-SS-A/B antibody and direct/indirect Coombs tests, and also haptoglobin was decreased. The results of liver biopsy and other tests suggested a diagnosis of Sjögren's syndrome (SS), with autoimmune hemolytic anemia (AIHA) and autoimmune hepatitis (AIH). Two years ago, the patient developed dyspnea on exertion, and the symptom began to worsen, therefore he was hospitalized for evaluation. Right heart catheterization (RHC) revealed a mean pulmonary arterial pressure (mPAP) of 26 mmHg. Pulmonary arterial wedge pressure was 7 mmHg. He had interstitial pneumonia (IP), but lung perfusion scintigraphy showed no abnormality. From these results, the patient was diagnosed with SS complicated by AIHA, AIH, IP and pulmonary arterial hypertension (PAH). Tadalafil was initiated. However, RHC didn't show a decrease in mPAP. He was thought to have systemic lupus erythematosus (SLE), based on positive anti-Sm antibody, decreased complement and AIHA. Therefore, prednisolone and hydroxychloroquine was initiated. RHC showed an improvement in mPAP at 17 mmHg. Here, we report a case of PAH associated with SS, AIHA, AIH, and SLE that was effectively treated with glucocorticoid.

P2-247

Effectiveness of intravenous cyclophosphamide therapy for connective tissue disease-associated pulmonary hypertension with refractory cardiopulmonary complication: a case report

Norihiko Amano, Soshi Takahashi, Saki Mukohara, Yasuhiro Nohda, Katsuhiko Yoneda, Miwa Nishida, Saori Hatachi, Shunichi Kumagai
Shinko Hospital Kobe Japan

Conflict of interest: None

[Case report] A 61-year-old woman with interstitial lung disease (ILD), who was diagnosed with Sjögren's syndrome at the age of 56, had treated with prednisolone, mizoribine and tacrolimus. But, progression of ILD was observed and home oxygen therapy was started. February 2018, she presented with worsening dyspnea and edema in her legs. Echocardiography revealed estimated systolic pulmonary artery pressure (esPAP) of 89mmHg and right heart catheterization (RHC) demonstrated mean pulmonary artery pressure (mPAP) of 56mmHg. Though she was treated

with diuretics and combination therapy of pulmonary vasodilators after diagnosis with pulmonary hypertension (PH), mPAP improved only to 36mmHg, and progression of ILD and pericardial effusion were observed. Therefore, we initiated Intravenous cyclophosphamide (IVCY) therapy for connective tissue disease-associated pulmonary hypertension (CTD-PH). 2 weeks after IVCY therapy, her clinical condition was smoothly improved and mPAP decreased to 25mmHg with mild improvement of ILD and pericardial effusion. So we completed IVCY therapy for total 6 times [Conclusion] This case suggested immunotherapy treatment, such as IVCY, can provide improvement of CTD-PH when conventional treatment, such as pulmonary vasodilators are ineffective.

P2-248

A case of myositis in primary Sjögren syndrome

Rina Okita, Rumiko Miyagi, Satoshi Baba, Ruriko Kuratani, Shinichiro Tsunoda

Division of Immunology and Rheumatology, Sumitomo Hospital

Conflict of interest: None

A 56-year-old female developed right facial numbness and visit our hospital. Her laboratory data showed CK 2370U/L, IgG 2028 mg/dL, antinuclear antibody 40 times and anti SS-A antibody/anti SS-B antibody-positive. She was suspected Sjögren syndrome and myositis and admitted to our hospital. MRI showed high signal STIR in upper and lower limb. Blood test results showed anti-ARS antibody-negative. Muscle biopsy was performed from the right deltoid muscle due to findings in EMG. Biopsy result showed the possibility of immune-mediated necrotic myopathy and we requested measurement of anti-SRP antibody /anti-HMGCR antibody but results were negative. Lip biopsy showed advanced lymphocytic infiltration and we diagnosed myositis in primary Sjögren syndrome. She was treated with mPSL 500 mg pulse therapy and PSL (20mg/day). Her clinical symptoms were not improved and blood test results showed CK 1000U/L, so we increased to PSL 40mg/day and added tacrolimus. Third mPSL 500mg pulse therapy in combination with IVIG and MTX showed effectiveness with decreased CK titer. Frequency of myositis in primary Sjögren syndrome is reported to be 5.6%. In addition, this case is steroid resistant. We discuss about myositis in primary Sjögren syndrome with literature review.

P2-249

Zinc Status and subjective symptoms in Sjögren's syndrome

Kumiko Akiya, Misako Konishi, Mari Ushikubo, Keisuke Izumi
Internal Medicine, National Hospital Organization Tokyo Medical Center.

Conflict of interest: None

[Purpose] Zinc is an essential trace element for living organisms and their biological processes. Zinc plays a key role in many enzymes and it is involved in cell communication, proliferation, differentiation and survival. Zinc plays also a role in regulating the immune system with implications in pathologies where zinc deficiency. [Method] The subjects received a medical examination from the medical center from April to May of 2018 and received a test of serum zinc concentration. (Sjögren's syndrome (SS) 162, RA 144). I examined subjective symptoms by interview questionnaire. [Result] Among the Primary SS low serum zinc concentration (30.6%) was significantly higher than RA (18.8%). The serum concentration of zinc, was not correlated to the serum albumin. In subjective symptoms, taste disorder alone was significantly higher in the latent zinc deficient group than in the normal group. [Conclusion] In Primary SS, the risk of low serum zinc was higher than that of RA. Taste disorder in SS is often caused by Zn deficiency and it seems necessary to be careful.

P2-250

Hydroxychloroquine in Japanese children with systemic lupus erythematosus

Toaki Kohagura, Asami Oohara, Daisuke Nishida, Naoki Abe, Haruna Nakaseko, Shinji Kawabe, Naomi Iwata

Department of Infection and Immunology, Aichi Children's Health and Medical Center

Conflict of interest: None

[Object] To investigate the safety and the efficacy of hydroxychloroquine (HCQ) in Japanese childhood-onset systemic lupus erythematosus (SLE) patients. [Methods] Subjects included 25 children aged over 10 years old (3 male, 22 female) suffering from SLE who received HCQ and were observed for 6-months or more. HCQ efficacy and side effects were retrospectively investigated. [Results] The mean age at introduction of HCQ was 17 years. The mean duration from diagnosis of SLE to start of HCQ was 5.9 years. The mean observation period was 1.4 years. The average HCQ dose was 4.3 mg / ideal body weight kg. The dose of prednisolone (PSL) was reduced in 12 (80%) of 15 patients observed for more than 1 year. The mean PSL dose at the start of HCQ was 0.18 mg / kg / day, and was reduced to 0.11 mg / kg / day after 1 year. Adverse reactions of HCQ were found in 15 of 25 patients; 15 had gastrointestinal symptoms and one had eruptions. Of these 15 patients, five temporarily discontinued HCQ and three reduced HCQ dosage. Four of the five who discontinued HCQ subsequently resumed with a reduced dose. The other received hyposensitization therapy. Finally, all patients were able to continue HCQ. [Conclusions] HCQ was effective and safe in Japanese childhood-onset SLE patients.

P2-251

2 Unique Cases of Thrombotic Microangiopathy (TMA) in Childhood Systemic Lupus Erythematosus (SLE) resistant to Plasma Exchange (PLEX): Thrombotic Thrombocytopenic Purpura (TTP) responsive to Rituximab (RTX) and atypical Hemolytic Uremic Syndrome (aHUS) responsive to Eculizimab (ECU)

Keiji Akamine¹, Riku Hamada¹, Naoto Yokogawa², Kota Shimada², Shoji Sugii², Hiroshi Hataya^{1,3}

¹Department of Nephrology, Tokyo Metropolitan Children's Medical Center, Tokyo, Japan, ²Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan, ³Department of General Pediatrics, Tokyo Metropolitan Children's Medical Center, Tokyo, Japan

Conflict of interest: None

Case 1: 18 year old male with SLE and class V lupus nephritis presented with fever, jaundice, vomiting, and headache. Labs revealed hemolytic anemia with schistocytes and thrombocytopenia. PLEX was initiated for presumed TTP but he did not respond. ADAMTS13 activity was undetectable (<0.5 %) and its inhibitor was positive. RTX was administered with prompt resolution of symptoms and normalization of his labs. Case2 of the U.S.: 18 year old female with SLE and class III lupus nephritis presented with vomiting and headache. Labs revealed hemolytic anemia with schistocytes, thrombocytopenia, and acute kidney injury. She received PLEX and steroids for presumed TTP but she was unresponsive to these treatments. ADAMTS13 activity was normal (97%), thus, we diagnosed her with aHUS. After ECU administration, her labs improved and schistocytes ultimately resolved. We should consider TMA when SLE patients present with microangiopathic hemolytic anemia and thrombocytopenia. ADAMTS13 activity will distinguish between TTP and aHUS. RTX is a chimeric monoclonal antibody to B cells that reduces various autoantibodies. On the other hand, ECU is a monoclonal antibody to C5 that blocks the terminal complement cascade. Consider RTX for TTP and ECU for aHUS if the patient does not respond to PLEX.

P2-252

A case of secondary hemophagocytic lymphohistiocytosis in a 15-year-old boy with systemic lupus erythematosus

Kazuomi Sekine¹, Nami Okamoto², Yuko Sugita², Keisuke Shindo², Kosuke Shabana²

¹General Medicine, Osaka Medical College Hospital, ²Department of Pediatrics, Osaka Medical College Hospital

Conflict of interest: None

[Case] A 15-year-old boy with fever and comedo-like erythema on his cheeks, visited a clinic. He was treated with antibiotics making no improvement, and visited another hospital. Bicytopenia and elevated ferritin level (9,968 ng/mL) was found there, and he was hospitalized for suspected HLH. The bone marrow histology showed hemophagocytic mac-

rophages, and he was diagnosed as HLH. On day 15 of admission, mPSL pulse therapy was started, and his symptom improved the next day. Primary HLH was denied from the family and past history, and the blood test to identify the possible cause of secondary HLH revealed positive anti-ds DNA antibody (400 times) and ANA (160 times). He was diagnosed as SLE and was transferred to our hospital after receiving 3 courses of mPSL pulse therapy. Renal pathology showed ISN/RPS class II lupus nephritis. She was considered as severe SLE associated with HLH, and a therapeutic regimen of prednisolone, hydroxychloroquine and cyclosporine was started. Prednisolone was gradually decreased, and he discharged on day 48 of admission. [Consideration] In case of HLH, screening for autoimmune disease is important. Also, we considered that aggressive multi-target therapy from early stage of disease is useful in childhood SLE with severe organ damage.

P2-253

A 13-year-old boy with newly diagnosed SLE who had developed an abscess of the gluteus maximus muscle

Tadayasu Kawaguchi^{1,2}, Yasuji Inamo^{1,2}, Yukihiko Fujita^{1,2}

¹Department of Pediatrics and Child Health, Nihon University School of Medicine, ²Department of Pediatrics and Child Health, Nihon University Itabashi Hospital

Conflict of interest: None

[Aim] Patients with SLE are easily infected by an immunodeficiency of the disease during clinical courses. We report a newly diagnosed SLE who had developed an abscess of the gluteus maximus muscle. [Case report] A 13-year-old boy, was admitted to our hospital with complaints of fever, nausea and diarrhea. Laboratory test results were shown pancytopenia, hypocomplementemia, proteinuria, and coombs positive. Abdominal CT revealed edema of small intestine. He was made a diagnosis as SLE, lupus enteritis, lupus nephritis, and hemolytic anemia. He was treated two times methylprednisolone pulse therapy. He complained left hip pain caused by an abscess of the gluteus maximus muscle after second pulse therapy. He was performed incisional drainage and antibiotic therapy. *Staphylococcus aureus* was detected in the culture of the abscess. The abscess gradually improved by incisional drainage. [Conclusion] Patients with SLE are easily infected by an immunodeficiency of the disease during clinical courses. However, it is rarely, patients with newly diagnosed SLE developing infections, especially, an abscess of the gluteus maximus muscle.

P2-254

A case of C1q nephritis with autoimmune hemolytic anemia

Noriko Kinjo, Kazuya Hamada, Koichi Nakanishi

Department of Child Health and Welfare (Pediatrics), Graduate School of Medicine, University of the Ryukyus

Conflict of interest: None

[Background] There are few studies of C1q nephropathy with childhood onset. In this case, autoimmune hemolytic anemia (AIHA) was diagnosed subsequently developed nephrotic syndrome (NS). C1q nephropathy was diagnosed by the renal biopsy. [Case] 14 years old, female. [Present Illness] Two years before the visit, thrombocytopenia observed during the treatment of right knee suppurative bursitis (50,000/ μ l). Idiopathic thrombocytopenia, AIHA was suspected. Thereafter, butterfly erythema, hemolytic anemia, lymphocytopenia, thrombocytopenia, hypomyacolonemia were observed. Systemic lupus erythematosus (SLE) was diagnosed, according to the classification criteria. After steroid therapy, the patient visited to our hospital. In our laboratory tests, antinuclear antibodies (ANA) and other autoantibodies were also negative. Anemia and thrombocytopenia improved, subsequently developed NS, diagnosed C1q nephropathy. Urinary protein/urinary creatinin value was improved from 5.0 to 0.6 g/gCr by steroid and cyclosporine combination therapy. [Discussion] We experienced a case of NS during the treatment of AIHA, leading to the diagnosis of C1q nephropathy. The appearance of autoantibodies may change the pathological condition, and it is necessary to carefully observe the course.

P2-255

Clinical features of systemic onset type juvenile idiopathic arthritis presenting chronic articular course in adulthood

Yumi Tani^{1,3}, Takayuki Kishi^{1,3}, Takako Miyamae^{1,3}, Eiichi Tanaka², Satoru Nagata³, Hisashi Yamanaka^{1,2}

¹Pediatric Rheumatology, Institute of Rheumatology, Tokyo Women's Medical University Hospital, ²Department of Rheumatology, Tokyo Women's Medical University, School of Medicine, ³Department of Pediatrics, Tokyo Women's Medical University, School of Medicine

Conflict of interest: None

[Object] Systemic inflammation in patients with systemic juvenile idiopathic arthritis (sJIA) is suppressed in a long-term follow up duration, however some patients developed to progressive arthritis without systemic inflammation. To clarify the difference of treatment effect between systemic onset arthritis and rheumatoid arthritis (RA) is important from the viewpoint of transition from pediatric to adult care. [Methods] A retrospective review of functional disability, complications, and efficacy of medication was performed in patients with systemic onset arthritis. [Results] Six patients (3 females) were identified. The median (range) age at onset of sJIA was 4 (0.6-11.0) years, and at evaluation was 29 (20-48) years. All patients received corticosteroid most of the time of follow-up. Four patients received tocilizumab, and 1 received etanercept without effectiveness. Three complicated with hip arthritis could not walk due to severe functional disability. All patients had short stature, 3 patients complicated bone fracture, and 1 died cause of renal amyloidosis. [Conclusions] The pathology of adulthood systemic onset arthritis is different from that of RA and close to that of sJIA. It is desirable to apply medication after consideration.

P2-256

A case report: improvement of sternoclavicular joint pain by tonsillectomy for tonsillitis-related reactive arthritis

Mao Suzuki, Yuya Takakubo, Suran Yang, Akiko Sasaki, Yuta Suzuki, Hiroharu Oki, Yasushi Naganuma, Hiroshi Orui, Michiaki Takagi
Department of Orthopedic Surgery, Yamagata University Faculty of Medicine

Conflict of interest: None

Tonsillitis related-arthritis has been defined as an acute sterile arthritis developing after or during infection in other parts of body. Tonsillectomy is one of effective treatments for tonsil-related disease. We have reported a case of 13-year old woman suffering from reactive arthritis related to tonsillitis. She have complained her sternoclavicular and knee joint pain at the first visit of our hospital. Although she has received NSAIDs, her joint pain and swelling became worse. C-reactive protein was 0.1mg/dl, anti-cyclic citrullinated peptides antibody <0.6 U/ml, anti-nuclear antibody <40, anti-streptolysin O (ASO) < 20 IU/ml at her first visit for our hospital. Her tonsil was swelling since she was 2-year old. CT scanning revealed the thickening of her right sternoclavicular joint. She was introduced to departments of otolaryngology and pediatrics of our hospital, and diagnosed with chronic tonsillitis. She had received tonsillectomy. One month after the surgery, her joint pain and swelling have improved. However, one year after the surgery, she has still complained both sternoclavicular joint pain, careful management and observation are required.

P2-257

A Case of Localized Lung Amyloidosis Accompanied by Rheumatoid Arthritis that Required Differentiation from Metastatic Lung Cancer

Ayuko Sogabe, Yasuaki Okuda, Atsushi Kondo, Yosuke Murata, Naoya Sawada, Kenichiro Matoba, Akihiro Yamada, Kazuo Jouyama, Makoto Onishi, Kiyoshi Takasugi
Center for Rheumatic Disease, Dohgo Spa Hospital

Conflict of interest: None

<Case>A 81-year-old woman suffering from rheumatoid arthritis and Sjögren's syndrome for 34 years was hospitalized for rehabilitation. Multiple anti rheumatic drugs have not been effective, therefore her joint dis-

tractions proceeded gradually. Now she takes tacrolimus 2mg/day and arthritis is well controlled. The screening CT scan showed ileocecal tumor (4cm in size) with enlarged lymph nodes around, and multiple nodules (2.5cm at maximum) in both lung fields. Colonoscopy and biopsy revealed poorly differentiated caecum adenocarcinoma. As for lung nodules, bronchoscopy was carried out in order to distinguish mycosis from metastatic lung Cancer. Histological examination showed not malignancy cell but amyloidosis, and immunostaining proved it type AL amyloidosis. Since there was no symptom or finding to suspect amyloidosis in other organs, it was supposed to be lung localized amyloidosis. <Conclusion>The great majority of lung amyloidosis is type AL, and type AA is very rare. Patients suffering from chronic inflammatory disease sometimes accompany amyloidosis other than type AA. Immunostaining was effective in this case.

P2-258

Analysis of AA proteins in amyloid from biopsy samples

Kouhei Kawaguchi^{1,2}, Yasuaki Okuda³, Takeshi Kuroda⁴, Toshiyuki Yamada¹

¹Department of Clinical Laboratory Medicine, Jichi Medical University, Tochigi, Japan, ²Biochemical Research Laboratory-1, Eiken Chemical CO., LTD., Tochigi, Japan, ³Department of Internal Medicine, Center for Rheumatic Diseases, Dohgo Spa Hospital, Ehime, Japan, ⁴Health Administration Center, Niigata University, Niigata, Japan

Conflict of interest: None

[Object] In AA amyloidosis, AA proteins truncated and modified from serum amyloid A (SAA) are fibrillized and deposited in tissues. In this study, we investigated the molecular structure information of AA proteins from the biopsy samples. [Methods] One mg of the biopsy sample was treated with 4 M guanidine and the AA proteins were purified by magnetic beads immunoprecipitation using a monoclonal antibody targeting the N-terminal region of SAA. The purified sample was desalted and concentrated, and measurement by MALDI-TOF MS. [Results] As a result of the measurement by MALDI-TOF MS, the peak of 8391.552 *m/z* (average mass) in the spectrum of sample 1 was estimated to be 2-76 residues of SAA 1.3. In sample 2, peaks at 8387.337 *m/z* and 8418.907 *m/z* (average mass) were estimated to be 2-76 residues of SAA 1.3, SAA 1.1 or SAA 1.5. SAA1.1 and SAA1.5 could not be distinguished because of same molecular weights. AA proteins detected in both cases are consistent with SAA allelic polymorphisms of patients, and truncated the N-terminal arginine was dominant. [Conclusions] As with the AA proteins in this study, it has been reported that SAA in the serum contains N-terminal arginine truncated form. We will further analyze other *in vivo* post-translational modifications.

P2-259

A case of Rosai-Dorfman disease in which steroids responded to protein-losing gastrointestinal disease associated with gastrointestinal amyloidosis

Ryota Okazaki, Yuriko Sueda, Yoshihiro Funaki, Tomoya Harada, Miki Takata, Yasuhiro Tamimoto, Akira Yamasaki
Division of Medical Ontology and Molecular Respiriology, Tottori University Faculty of Medicine

Conflict of interest: None

Rosai-Dorfman disease (RDD) is a rare non-neoplastic histiocytic proliferative disorder of unknown origin characterized by lymphadenopathy and extranodal lesion. A 63-year old man. In X-3 year, a chest abnormal shadow was pointed out at medical examination. In X-1 year, he visited our hospital because a right lung nodule shadow was increasing in the chest CT examination. PET-CT showed high accumulation in the paranasal sinuses, pulmonary nodule shadows, prostate glands, cervical lymph nodes, and bones. Biopsy of the cervical lymph node, paranasal sinuses, prostate was performed, and revealed histiocyte infiltration S-100 (+), CD68 (±), CD1 (-) by immunohistochemical staining and empipole-sis. We diagnosed with RDD. In X year, he had fever, abdominal pain, diarrhea, anorexia, and was admitted to our hospital. Both biopsies of small intestine and colon by colonoscopy were positive for Congo red staining and diagnosed as amyloidosis. Protein leakage scintigraphy was diag-

nosed as protein leaky gastroenteropathy. After treatment with prednisolone, abdominal symptoms and hypoproteinemia were improved. This case was suggested for the effectiveness of steroid on protein-losing gastrointestinal disease with RDD-derived amyloidosis.

P2-260

Tocilizumab decreased urinary protein excretion by improving AA amyloidosis secondary to RA and might help to suppress CKD worsening

Daisuke Kanai, Yuji Uzawa, Yuji Yoshioka, Akiko Suda, Shohei Nagaoka
Yokohama Minami Kyousai Hospital

Conflict of interest: None

We report a case of 81 year-old lady whose RA was diagnosed at 49 years old. She was treated with oral steroids, sulfasalazine and methotrexate, but her disease activity remained high. She was given prosthetic joint replacement operations for her both knees and elbows between 51 and 61 years old. At 78 years old, she visited our hospital first time. Her condition of RA was in stage IV and class III, and SDAI was 11.45. She also had CKD, which was in stage G3bA2 (eGFR 40.1, urinary protein/creatinine ratio (U-PCR) 0.25g/gcr). We started to use golimumab 50mg s.c. every 4 weeks. SDAI decreased to 5.58. One year later from her first visit, she got a left femoral neck fracture during traveling and was admitted to get operated for joint replacement in a hospital there. Golimumab was not used during admission. Four months later, she came back to our hospital, and SDAI increased to 13.91 and her renal function got worse (eGFR 28.2, U-PCR 4.11g/gcr). We obtained biopsy samples of her kidney and gastroduodenal mucosa. AA amyloid deposits were detected in both samples. Systemic AA amyloidosis was diagnosed. Tocilizumab 8mg/kg IV every 4 weeks was started. Four weeks later, serum amyloid A level got to within the normal range, and at 3 months SDAI was 0.52, U-PCR 1.88, at 14 months U-PCR 0.77.

P2-261

Assessment of the prevalence of the sarcopenia in rheumatoid arthritis: Influence of disease activity and insulin-like growth factor-1

Tsuneo Watanabe¹, Koichi Shinoda¹, Masao Takemura², Takahide Ikeda³, Hiroyuki Morita³

¹Division of Clinical Laboratory, Gifu University Hospital, ²Advanced Diagnostic System Research Laboratory, Fujita Health University Graduate School of Health Science, ³Department of General Internal Medicine, Gifu University Hospital

Conflict of interest: None

[Object] The aim of this study was to evaluate the relationship between disease activity, insulin-like growth factor-1 (IGF-1), and prevalence of the sarcopenia in patients with rheumatoid arthritis (RA). [Methods] Twenty-two patients, who met the 2010 ACR/EULAR criterias were enrolled in this study from February 2018 to June 2018. The subjects were classified into two groups according to the DAS28-CRP: remission group (n = 10, 61.5±13.1 years) when DAS28-CRP < 2.3, and low disease activity (LDA; n = 12, 63.7±15.1 years) when DAS28-CRP = 2.3-4.1. Joint synovitis was evaluated by ultrasonography (at the bilateral II/III MCP, wrist and knee joints). The power Doppler ultrasonography (PDUS) index is the sum of the scores of all eight joints assessed. [Results] The prevalence of sarcopenia increased in the LDA group as compared with the remission group (40% vs. 73%, not significant). PDUS index was significantly increased in LDA group compared to remission group (p < 0.001). In addition, insulin-like growth factor-1 (IGF-1) levels were significantly higher in the remission group than in the LDA group (p < 0.05). [Conclusion] Our study shows a significant decrease IGF1 levels in the LDA group, suggesting that sustained disease activity is involved in the progression of the sarcopenia.

P2-262

Investigation of steroid-induced osteonecrosis occurrence site by MRI

Kento Nawata, Junichi Nakamura, Shigeo Hagiwara, Yuya Kawarai, Masahiko Sugano, Kensuke Yoshino, Satoshi Yoh

Department of Orthopaedic Surgery, Graduate School of Medicine Chiba University

Conflict of interest: None

[Object] The purpose of this study was to investigate the site of glucocorticoid-induced osteonecrosis in individual cases and to confirm the effectiveness of the MRI screening method in our hospital. [Methods] We investigated 100 patients with 800 joints who received screening of MRI in all of their hip, knee, shoulder and ankle joints after systemic glucocorticoid therapy from 1986 to 2018. The patient's age at the time of initial glucocorticoid therapy, the proportions of female patients, the dosage of glucocorticoids, the incidence rate of osteonecrosis and the site of osteonecrosis were investigated. [Results] The patient's mean age was 36.2 years. The ratio of male, and also the highest daily glucocorticoid dose were significantly higher in osteonecrosis group than in the non-osteonecrosis group. The incidence of osteonecrosis was 67% in the hip, 44% in the knee, 18% in the ankle, and 14% in the shoulder. If osteonecrosis was not observed in neither the hip or knee, osteonecrosis did not occur in neither shoulder or knee. However, when osteonecrosis was observed in the shoulder or foot, osteonecrosis was always observed at least one place in the hip or knee. [Conclusions] MRI imaging of both hip and knee is considered effective as a screening method.

P2-263

Frailty in patients with rheumatoid arthritis

Kazushi Haraguchi

Department of Orthopaedic Surgery, Kenwakai Ootemachi Hospital, Kitakyushu, Japan

Conflict of interest: None

[Object] Recently, frailty came to attract interest widely. Aged patients with RA are increasing and frailty is a important problem in RA. We performed an investigation about frailty in patients with RA. [Methods] 59 patients were performed questionnaire and measurement of physical functions based on Fried's criteria: (weight loss, exhaustion, low physical activity, low grip strength, slow walking speed). Prevalence of frailty (over 3 criteria), pre-frailty (1 or 2 criteria), normal (no criterion) were evaluated and relations of frailty and Steinbroker stage and class, duration, DAS28CRP and HAQ score were examined. [Results] Number of patients with criteria was 6 weight loss, 44 exhaustion, 20 low physical activity, 33 low grip strength, 16 slow walking speed. 26 patients were evaluated as frailty, 29 pre-frailty and 4 normal. Stage, class, duration, DAS28CRP and HAQ score were highest in frailty-group and higher in pre-frailty group than normal group. Prevalence of frailty was 48.7% in patients with DAS28CRP ≥ 2.7. In patients with HAQ ≥ 1, prevalence of frailty was 80% and 95% of frailty cases had exhaustion. [Conclusions] In patients with RA, prevalence of frailty was very high and functional impairment influenced on not only physical frailty but also mental frailty.

P2-264

Three azathioprine hypersensitivity syndrome cases without cutaneous manifestation

Yusuke Nakamichi, Naoto Yokogawa, Naoki Tanomogi, Masahiro Iida, Shuhei Sano, Michiru Kina, Nanase Honda, Tatsuo Mori, Eisuke Takamasu, Kae Onishi, Yuji Miyoshi, Takayasu Kise, Masako Utsunomiya, Yoshiki Nagai, Kota Shimada, Shoji Sugii
Tokyo Metropolitan Medical Center

Conflict of interest: None

[Introduction] Azathioprine (AZA) Hypersensitivity Syndrome (AHS) is dose independent side effect that presents within few weeks. AHS can present with only systemic symptoms and without cutaneous symptoms. [Case 1] A 42-year-old woman with MCTD admitted with fever and shock without skin symptoms. 16 days before this admission, AZA 50 mg/day was initiated for her worsening of MCTD. The completely resolution after 2 days of AZA discontinuation is suggestive of AHS. [Case 2] A 24-year-old woman with MCTD presented with fever and shock without skin symptoms. 7 days ago, AZA 25 mg/day was started for MCTD maintenance therapy. AZA was discontinued at the time of

the shock. Over the 2 days, her symptoms were disappeared. This made a diagnosis of AHS. [Case 3] A 79-year-old man with ANCA associated vasculitis (AAV) presented with fever and shock without skin symptoms. 5 days ago, AZA 50 mg/day was started for AAV maintenance therapy. One day ago, AZA was discontinued due to allopurinol concomitant. He made an improvement over 24h. The other cause of these symptoms was excluded. A clinical diagnosis of AHS was made. [Discussion] AHS should be considered in a patient presenting with only constitutional symptoms without skin manifestation who starts to take AZA within several weeks.

P2-265

Clinical experience of recombinant thrombomodulin and heparin combination therapy for pediatric patients with disseminated intravascular coagulation

Akira Oshima^{1,2}, Kenichi Nishimura¹, Seira Hattori¹, Ai Ohnishi¹, Ryoki Hara¹, Shuichi Ito¹

¹Department of Pediatrics, Yokohama City University Graduate School of Medicine, ²Department of Pediatrics, Yokosuka Kyosai Hospital

Conflict of interest: None

[Object] We investigate the efficacy and safety of recombinant thrombomodulin (rTM) and heparin combination therapy for pediatric patients with disseminated intravascular coagulation (DIC). [Methods] In this single-center, retrospective study, we evaluated 11 patients with DIC, who received rTM and heparin combination therapy between January 2013 and October 2018. DIC was diagnosed according to the acute phase diagnostic criteria established by the Japanese association for acute medicine. We excluded the DIC associated with malignant diseases. [Results] The age at the start of treatment was median (range) 3 (1-10) years and male patients were 4 (50%). There was 7 patients with underlying disease, of which 7 were hemophagocytic lymphohistiocytosis (HLH), 1 was Kawasaki disease. As the cause of HLH, there were 6 infectious diseases, and was 1 paroxysmal cold hemoglobinuria. The rTM administration duration was 4 (1-5) days, and DIC scores before and after treatment were 5 (4-8) and 0 (0-4), respectively. DIC withdrawal rate was 62.5%. One adverse event related to bleeding tendency was mild nasal bleeding. [Conclusions] This study suggested rTM and heparin combination therapy was safe for DIC in pediatric patients. To evaluate efficacy of combination therapy, we need further study.

P2-266

A case report of thoracic hypertrophic pachymeningitis complicated by eosinophilic granulomatosis with polyangiitis

Isao Matsuura¹, Shohei Nakamura^{1,2}, Yohei Seto^{1,2}

¹Department of Rheumatology, Tokyo Women's Medical University Yachiyo Medical Center, ²Department of Rheumatology, Institute of Rheumatology, Tokyo Women's Medical University

Conflict of interest: None

A 76-year-old male with asthma and chronic sinusitis was referred to our institution complaining fever and right foot drop. Laboratory examination showed high CRP, eosinophilia and MPO-ANCA positive. Motor axonal neuropathy of right peroneal nerve was observed in nerve conduction study and he was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA). His MMT of right calf was improved after high dose prednisolone and intravenous immunoglobulin therapy. In 10 months, he visited us with chest and back pain at rest and bilateral leg weakness. He had hypoesthesia below chest and paraparesis. Epidural T2 high signal at the level Th1-2 was observed on MRI. He was diagnosed with epidural abscess. Laminectomy was performed for decompression and thickening of dura mater was observed. Pathology report showed fibrotic hypertrophy of dura mater and he was finally diagnosed with thoracic hypertrophic pachymeningitis (HP). Steroid pulse and cyclophosphamide pulse therapy improved his paralysis gradually. We often experience secondary HP following vasculitis, however spinal lesion is relatively rare. Furthermore, a few cases of thoracic lesion were reported in microscopic polyangiitis and granulomatosis with polyangiitis but EGPA. We discuss this case referring to literature.

P2-267

Rheumatoid vasculitis of coronary arteries found by autopsy -a case report-

Tomo Oyakawa, Chinatsu Azuma, Fuminori Kanaya

Department of Orthopedics, University of Ryukyus Okinawa Japan

Conflict of interest: None

(Objectives) We report a case with rheumatoid arthritis (RA) of coronary arteries found by autopsy. (Case) a 68-year-old man was suffered from ra for 20 years. He had many medical complications. He was suffered from septic arthritis of the right ankle three months ago. He was transferred to our hospital for the treatment of ra arthritis. (Findings on admission) das28-esr:7.81, crp:16.82mg/dl, esr:90mm, mmp-3:71.7ng/ml, (Image findings):chest x-ray: both pleural effusion, electrocardiogram: sinus rhythm, heart supersonic wave: left ventricle wall motion was normal. (On admission ra therapy) Prednisolone 8mg/day, salazosulfapyridine 1000 mg/day he could treated with steroid puls and abatacept. unfortunately, he suddenly died at 70 days after hospitalization. myocardial infarction caused by the rheumatoid vasculitis of coronary arteries was diagnosed by autopsy. There was no evidence of vasculitis in contrast ct at 40 days after hospitalization. (Discussion) The coronary vasculitis is difficult to find out with a blood test and the diagnostic imaging. Rheumatoid vasculitis of the coronary arteries could be considered one of cause of sudden death. It is necessary to cure in consideration of a merger of the vasculitis in the ra patients of the high disease activity.

P2-268

A case report of rheumatic meningitis occurring while RA treatment with Golimumab

Masamitsu Natsumeda¹, Miyuki Takemoto²

¹Department of Internal Medicine, Rheumatic Disease Center, Mabi Memorial Hospital, Kurashiki, Japan, ²Department of Nursery, Rheumatic Disease Center, Mabi Memorial Hospital, Kurashiki, Japan

Conflict of interest: None

A 75-year-old female, she visited our hospital due to exacerbation of polyarticular pain. It was characterized as DAS 28 ESR 4.4 at the first visit, and initiated Golimumab (GLM) 50 mg from February 7. On March 7, the PSL was reduced to 1 mg with the increase in GLM 100 mg. Cognitive dysfunction and right incomplete paralysis appeared on both left and right paralysis on March 15th. Head MRI revealed meningeal FLAIR and DWI high signal on right temporal parietal lobe. Improvement of various symptoms was observed by administration of antibiotics as sterile meningitis. As joint articular swelling and pain worsened in April, tocilizumab (TCZ) 8 mg / kg was administered on April 16 as primary care for rheumatoid arthritis. The slight convulsion of the left half body appears and gradually worsens on May 11. Treatment with steroid pulses was performed twice as treatment of rheumatoid meningitis and very effective. PSL 30mg maintenance therapy was started and returned to our hospital. As a gradual decrease of PSL, multijoint swelling and pain relapsed. TCZ subcutaneous injection was performed, but no sign of neurological aggravation was observed. Rheumatic meningitis during administration of biological products is reported with consideration on report.

P2-269

A case of rheumatoid arthritis in which Tocilizumab was effective against necrotizing scleritis

Keiichi Yoshimoto, Taro Miyagawa

Department of Internal Medicine, Kurobe City Hospital

Conflict of interest: None

A 50-year-old woman began to complain polyarthralgia from 2012 and was diagnosed as rheumatoid arthritis (RA). She was treated with 6mg/week of Methotrexate (MTX) and 2mg/day of prednisolone (PSL). Although her polyarthralgia was controlled well, In the summer of 2017, she consulted a nearby ophthalmologist with both eyes congested. She was diagnosed as scleritis, and then, received Betamethasone instillation but did not improve, so, she was introduced to our department of ophthalmology. In addition to topical treatment, she received oral administration

of prednisolone 20 mg but did not improve, then, intravenous administration of infliximab (IFX) 3 mg / kg was started. Because scleritis progressed in spite of administration of IFX, Tocilizumab (TCZ) subcutaneous injection was started instead of IFX. As a result, scleritis was dramatically improved. Conclusion: Scleritis is a rare but sometimes complicated with rheumatoid arthritis. Although severe scleritis presents of danger of blindness, recently effectiveness of biological agent were reported. In this case, the anti-TNF α inhibitor was ineffective but the anti-IL6 receptor antibody was effective. This phenomenon is interesting for examining the pathogenesis of scleritis related to RA.

P2-270

A case of suspected myelitis during etanercept administration

Daisuke Nakashima, Atsunori Tokushige, Takashi Imagama, Kazushige Seki
Department of Orthopaedic Surgery, Yamaguchi University Graduate School of Medicine Ube, Yamaguchi, Japan

Conflict of interest: None

[Object] Demyelinating diseases and myelitis are reported as side effects of TNF inhibitors. We report the case of bladder and bowel dysfunction during etanercept administration and it suspected myelitis in spinal cord compression site by ossification of posterior longitudinal ligament (OPLL). [Case] A 45 year old woman was treated with etanercept to RA. She got her right back pain, so she pointed out as OPLL on T3/4. She was admitted to our hospital due to CRP:15.19 mg/dl, numbness both legs, bladder and bowel dysfunction. High signal intensity change of the spinal cord of T3/4 with MRI worsened with symptoms worsening. She was discontinued from etanercept administration, bladder and bowel dysfunction improved after the start of oral administration of PSL:15mg, and numbness gradually disappeared. Thereafter the high signal intensity change of the spinal cord was relieved with MRI. [Conclusions] In this case, clinically isolated syndrome (CIS) and myelitis were suspected because the high signal intensity change of the spinal cord was relieved by stopping etanercept, and there was no relapse of the symptoms without abnormalities in MRI of other parts. In the future, careful follow-up observation is necessary, and treatment of RA other than TNF inhibitor is necessary.

P2-271

Autosomal dominant polycystic kidney disease (ADPKD) combined with polyarthritis

Junko Kawata
Kawata-Junko Clinic

Conflict of interest: None

[Case] A 70-year-old woman developed polyarthritis. Her mother and her brother had PKD. On physical exam, she had arthritis in the third MP joint, both wrists, and both hips and left ankle. Blood pressure was 133/88mmHg, CRP 9.01mg/dl, GOT69U/L, GPT 65 U/L, γ -GTP86U/L, Cre1.15mg/dl and anti-CCP antibody 10.2U/ml. Urine and blood culture were normal. CT and MRI showed polycystic liver and PKD. Renal volumes was 1595.74ml. She was diagnosed that active polyarthritis, especially, suspected RA. CKDG4A1-ADPKD, and liver cysts was diagnosed from family history and other exams. She was treated by Adalimumab (ADA), and introduced to Nephrology nearby hospital. She was admitted there and induced Tolvaptan 3.75mg/day, and took 15mg/day when she was discharge. [Discussion] This case showed ADPKD combined with active polyarthritis. Because of her inflammation, it was caused by RA or crystal arthritis. Treated arthritis completely, and induction of Tolvaptan was succeeded. Tolvaptan is vasopressin V2 receptor antagonist and improves the natural decline of renal function in ADPKD. [Clinical meaning] ADPKD combined with polyarthritis, especially suspected RA, is very rare.

P2-272

The effectiveness of DPP-4 inhibitors and SGLT-2 inhibitors for steroid diabetes mellitus

Yoshiyuki Abe¹, Yosuke Shimada^{2,3}, Michihiro Ogasawara¹, Kurisu Tada¹,

Ken Yamaji¹, Naoto Tamura¹

¹Department of Internal Medicine and Rheumatology, Juntendo University, Tokyo, Japan, ²Medical Informatics Department, Juntendo University Graduate School, ³Intelligent Systems Laboratory, SECOM Co., Ltd.

Conflict of interest: Yes

[Objective] To evaluate the effectiveness of DPP-4 inhibitors and SGLT-2 inhibitors for steroid diabetes mellitus in patients with rheumatic diseases. [Methods] We enrolled 253 patients with rheumatic diseases, who were diagnosed steroid diabetes and treated with DPP-4 inhibitors, SGLT-2 inhibitors, or intensive insulin therapy from January 2008 to March 2018. We defined the day starting the treatment as start date, and the 180th to 280th days as the evaluation date. In order to exclude bias due to changes in dose of corticosteroids, cases in which were changed dose of corticosteroid exceeded 5 mg during the period were excluded. [Results] DPP-4 inhibitor group, SGLT-2 inhibitor group, and intensive insulin therapy group were included 18, 6, and 13 patients, respectively. The median (IQR) of changes of HbA1c were -0.55 (0.54), -0.50 (0.60), and -0.95 (1.45), respectively, and there were no statistical difference. [Conclusion] DPP-4 inhibitors and SGLT-2 inhibitors decreased -0.5 to -0.6 % of HbA1c for steroid diabetes mellitus in patients with rheumatic diseases. Too many biases were included in current study, however our results showed the possibilities that the effectiveness of DPP-4 inhibitors and SGLT-2 inhibitors for steroid diabetes mellitus.

P2-273

Minimal change nephrotic syndrome developing in a rheumatoid arthritis patient under iguratimod, and certolizumab pegol treatment

Daisuke Murakami¹, Masafumi Sugiyama^{2,3}, Atsushi Kawaguchi⁴
¹Department of Rheumatology, Hashima Municipal Hospital, ²Department of Nephrology, Hashima Municipal Hospital, ³Department of Rheumatology, Kindai University Nara Hospital, ⁴Department of Orthopaedic Surgery, Hashima Municipal Hospital

Conflict of interest: None

A 74-year-old female patient has been treated rheumatoid arthritis (RA) with iguratimod (IGU) 25mg daily started 2 years prior to presentation, and certolizumab pegol (CZP) 200mg subcutaneously twice a month started 4 years prior to presentation. On the end of August, she had suddenly fatigue and anasarca. On physical examination, she had a newly elevated blood pressure of 164/76 mmHg with new pitting edema of the bilateral lower extremities. Laboratory examinations revealed profound proteinuria (9428 mg/day) of nephrotic syndrome. Histopathological examination of renal biopsy specimens showed minimal change nephropathy (MCNS). Almost complete resolution of the MCNS was achieved by discontinuation of IGU and CZP, and initiation of steroid therapy. Membranous and amyloid nephropathy in RA patients associated with nephritic syndrome are found in high incidence in literature. There have been no reports from Japan of the occurrence of MCNS caused by IGU or CZP administration in RA patients. Therefore, this case was considered to be very uncommon and worthy of reporting.

P2-274

Is it time to rethink the routine prescription of proton pump inhibitors in rheumatic diseases? : A Retrospective Case Series

Yasuhiro Suyama, Kiyofumi Hagiwara
JR Tokyo General Hospital

Conflict of interest: None

[Object] Steroid is generally not considered to increase the risk of gastrointestinal (GI) bleeding except for intensive care unit (ICU) administration and concurrent use of nonsteroidal anti-inflammatory drugs (NSAIDs) or anticoagulants. On the other hand, in clinical practice, proton pump inhibitors (PPIs) may be routinely prescribed with or without risk factors when initiating steroid therapy. [Methods] We retrospectively evaluated patients who were newly diagnosed as having rheumatic diseases and initiated steroid treatment without PPIs from April 2014 to March 2018 in JR Tokyo general hospital. [Results] There were 84 patients. The average of initial steroid dose was 50 mg/day and steroid ta-

per-off was achieved in 53 patients (63.1%). The mean follow-up period was 10.5 months (2-41 months) in total, and 9.6 months (3-27 months) in steroid tapered-off group and 12 months (2-39 months) in steroid continue group. Finally, there was no complication of gastrointestinal bleeding during the period. [Conclusions] Routine PPIs prescription could not be required when initiating steroid therapy in patients with rheumatic diseases who do not have risk factors of GI bleeding except for steroid use.

P2-275

Parvovirus B19 infection: a rare case of splinter hemorrhage and nodular erythema

Masahiro Minoda, Kiyoharu Muranaka

Suwa Central Hospital Chino, Nagano, Japan

Conflict of interest: None

[Case] A 57-year old female presented with 7 days of fever and leg pain. She had a 1-week history of fever and cough and 4 days history of right ankle joint and left knee joint pain. Physical findings showed arthritis in the right and left knee joints, and tenderness on both elbows. Skin eruption was found splinter hemorrhage accompanied by pain on both fingernails and erythemas with tenderness on the front of both legs were observed. We evaluated it as acute arthritis accompanied by splinter hemorrhage and nodular erythema due to a viral infection and infective endocarditis. We conducted blood test, blood culture, synovial fluid culture and echocardiography examinations. She was admitted to our hospital and celecoxib was administered. After 5 days, blood test revealed positive anti-HPVB 19 IgM antibody 5.12 and diagnosed as HPV-B19 infection. Day 7 hospitalization, symptoms disappeared. All cultivation tests and transthoracic echocardiography were negative. [Clinical Significance] In early stage of HPV-B19 infection, it causes a variety of symptoms such as fever and headache due to viremia. In late stage, it causes infectious erythema and arthritis due to impair by immune mechanism. We report HPV-B19 is rare conditions characterized by splinter hemorrhage and nodular erythema.

P2-276

A case report of myalgia by Human Parechoviruses 1

Fumiya Kitamura, Tatsuya Arai, Hiroyuki Yoshida, Yoshihiro Nakamura, Hiroki Ikai, Tsuyoshi Watanabe, Mari Yamamoto, Yukari Murai, Koji Takasugi, Naoho Takizawa, Waka Kokuryo, Yoshiro Fujita
Department of Rheumatology, Chubu Rosai Hospital

Conflict of interest: None

Introduction: HPeVs have been identified worldwide. HPeVs are responsible for multiple clinical syndromes involving epidemic myalgia. Case report: A 29-year-old male admitted to the hospital for muscle pain and weakness. On admission day, he also complained diarrhea. He went to Indonesia 6 weeks prior to admission and works in airport. The laboratory date showed that WBC count (21,600/ μ L), CRP (29.35mg/dL) and LFT (GPT 37IU/L, ALP 343 U/L) were elevated. GI doctor diagnosed acute bacterial enteritis and treated with cefmetazole followed by levofloxacin His symptoms persisted for one week despite treatment. We were consulted 8 days after admission. At that time, he was still febrile and difficult to move because of muscle pain. All lab tests for infection were negative including blood culture, HBV, HCV, HIV, CMV, EBV, Syphilis. We consider that he was myalgia caused by any virus. We started enough dose of acetaminophen and stopped using antibiotics. He was afebrile on the next day and his muscle pain was disappeared 4 days later. After He discharged, we received a result of antibody for HPeVs (256). Conclusion: Patients with acute muscle pain should be aware that HPeVs can cause epidemic myalgia. It is also important that rule out any other infection and auto immune disease.

P2-277

The current situation of Pneumocystis pneumonia prevention in systemic lupus erythematosus: A study of the multicenter registry LUNA

Ryusuke Yoshimi¹, Yosuke Kunishita¹, Chiharu Hidekawa¹, Natsuki Sakurai¹, Masaki Mitsuhashi¹, Yumiko Sugiyama², Daiga Kishimoto¹,

Yuki Iizuka¹, Takaaki Komiya¹, Hideto Nagai¹, Naoki Hamada¹, Naomi Tsuchida¹, Yutaro Soejima¹, Reikou Kamiyama¹, Kouji Kobayashi², Yukiko Asami¹, Yohei Kirino¹, Nobuyuki Yajima³, Ken-ei Sada⁴, Kunihiro Ichinose⁵, Toshiaki Miyamoto⁶, Shigeru Ohno², Hideaki Nakajima¹

¹Department of Hematology and Clinical Immunology, Yokohama City University School of Medicine, ²Center for Rheumatic Disease, Yokohama City University Medical Center, ³Division of Rheumatology, Department of Internal Medicine, Showa University School of Medicine, ⁴Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ⁵Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, ⁶Department of Rheumatology, Seirei Hamamatsu General Hospital

Conflict of interest: None

[Object] To investigate the current situation of the prophylaxis for Pneumocystis pneumonia (PCP) using a multicenter registry of systemic lupus erythematosus (SLE). [Methods] We collected the data as to the method of PCP prophylaxis from the SLE patients registered in the LUNA registry, and analyzed its relationship with the patient's background. [Results] Among 589 patients, PCP prevention was performed in 97 (16%), and ST was used in all cases (ST group). The prednisolone dose was larger in the ST group than in the non-ST group (12.5 ± 10.3 vs 5.8 ± 5.5 mg/day, $p = 4.7 \times 10^{-19}$). Mycophenolate mofetil, azathioprine and cyclosporine were used more commonly in the ST group. Serum IgG level was significantly lower in the ST group than in the other ($1,220 \pm 448$ vs $1,457 \pm 488$ mg/dL, $p = 4.0 \times 10^{-5}$), but there were no differences in the numbers of leukocyte or lymphocyte. One ST tablet was administered daily in 32%, every other day in 6.5%, 3 times per week in 29%, twice a week in 13%, and weekly in 19%. BMI was lower in the patients not administered daily as compared with those administered daily (20.2 ± 2.0 vs 24.2 ± 3.3 kg/m², $p = 6.7 \times 10^{-4}$). [Conclusions] The dose decrease of ST tended to be done in patients with low BMI. We should consider the optimization of PCP prevention.

P2-278

Treatment for Pneumocystis Pneumonia of Patients with Connective Tissue Disease

Kengo Akashi, Sadao Jinno, Motoko Katayama, Mai Yamashita, Yoko Nose, Yoshikazu Fujikawa, Takumi Nagamoto, Yuzuru Yamamoto, Hirotaka Yamada, Yoshihide Ichise, Ikuko Naka, Takaichi Okano, Yo Ueda, Sho Sendo, Akira Onishi, Jun Saegusa, Akio Morinobu
Kobe University Graduate School of Medicine, Kobe, Japan

Conflict of interest: None

[Purpose] To review the treatment for pneumocystis pneumonia (PCP) of patients with connective tissue disease (CTD) in our hospital. [Method] We collected the medical charts of the PCP patients with CTD from April 2014 to March 2018. PCP was diagnosed with clinical courses, CT images, serum β -D-glucan elevation. [Result] Twenty-five patients with PCP were investigated. They had been treated with immunosuppressive agents because of rheumatoid arthritis in 13 cases, ANCA-associated vasculitis in 7 cases, dermatomyositis in 3 cases and others in 2 cases. Sixteen cases had co-existing lung disease. Seven patients had fatal clinical courses because of PCP. Glucocorticoid were administered for all patients as PCP treatment. As anti-fungal agents, sulfamethoxazole/trime-thoprim (ST) was used in 17 cases, pentamidine (PEN) for 8 cases, atovaquone (ATO) for 9 cases through all clinical courses. ST was used as first-line drug in all cases. PEN was chosen for 1st-line and 2nd-line agent in each 4 cases. ATO treatment was as 1st-line for 1 patient, 2nd-line for 7 patients and 3rd-line for 1 patient. [Conclusion] Sometimes the PCP treatment cannot be accomplished due to adverse events of ST. It is necessary that the efficacy and safety of PEN and ATO are verified.

P2-279

Analysis of discontinuation of trimethoprim/sulfamethoxazole (TMP-SMX) as primary prophylaxis in our Rheumatic division

Rimi Iwamoto¹, Ayaka Inoue², Hiroaki Nakagawa², Midori Kitayama², Takuro Maeda², Noriaki Yo², Chihiro Tanaka², Takashi Yamane²

¹Department of Pharmacy, Kakogawa Central City Hospital, ²Division of Rheumatology, Kakogawa Central City Hospital

Conflict of interest: None

Object: There are a lot of cases to be forced to change or cancel TMP-SMX by allergy. In order to investigate the possibility of re-administration by hyposensitization therapy as we reported JCR2018, we now report the continuation rate, the reason for termination and the condition at the time of discontinuation of TMP-SMX. **Method:** In July 2018, we investigated the continuation rate of TMP-SMX which were administered in July 2016 to October 2017, the reasons for termination, age, primary disease, daily prednisolone dosage, presence or absence of immunosuppressive drugs. The condition at the time of discontinuation of TMP-SMX was examined retrospectively from the medical record. **Result:** Study included 230 patients. Median age was 70 years old. Discontinuation were 103 cases (55.2%), the reason of discontinuation was 3 allergic cases and 12 other harmful phenomena. In all of these cases, the prophylactic drugs were changed to the others. Though the prophylaxes were finished in 51 cases, there were no cases of PCP development. **Conclusion:** Since the case of discontinuation due to allergy were not tried to hyposensitization therapy, I intend to introduce the therapy for safe and effective PCP prevention as a pharmacist.

P2-280

Investigation of lethal mycosis cases with collagen disease in our department

Tomoki Hayashi, Ryo Takahashi, Nao Oguro, Mika Hatano
Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Object] Deep seated mycosis is sometimes emergence in hematology and will be lethal. To suppress immunity for the treatment in rheumatology, we rarely experienced emergence before. We investigated lethal cases with deep seated mycosis in our department. **[Method]** Cases suspected with mycosis were collected from fatal cases hospitalized in our department with medical reports from 2007 to 2017. **[Result]** Four patients (Three females and one male, the average age 62 years) were identified. Two patients were with rheumatoid arthritis. One was with systemic lupus erythematosus. One was microscopic polyangiitis. The classes of mycosis were one pulmonary aspergillosis, one candida pneumoniae, one disseminated cryptococcosis, and one candidemia. At diagnosis, glucocorticoid (minimum 15 mg/day prednisolone equivalent) was administered in all for the therapy of underlying disease aggravation. **[Conclusion]** All lethal cases with mycosis were administered minimum 15mg/day prednisolone equivalent glucocorticoid for therapy of underlying disease. Early differentiation of mycosis and early treatment are needed for patients with glucocorticoid.

P2-281

Infectious diseases as a complication of systemic lupus erythematosus: a cross-sectional study of LUNA registry

Chiharu Hidekawa¹, Yosuke Kunishita¹, Ryusuke Yoshimi¹, Natsuki Sakurai¹, Masaki Mitsuhashi¹, Yumiko Sugiyama², Daiga Kishimoto¹, Yuki Iizuka¹, Takaaki Komiya¹, Hideto Nagai¹, Naoki Hamada¹, Naomi Tsuchida¹, Yutaro Soejima¹, Reikou Kamiyama¹, Kouji Kobayashi², Yukiko Asami¹, Yohei Kirino¹, Nobuyuki Yajima³, Ken-ei Sada⁴, Kunihiro Ichinose⁵, Shigeru Ohno², Hideaki Nakajima¹

¹Department of Hematology and Clinical Immunology, Yokohama City University School of Medicine, ²Center for Rheumatic Disease, Yokohama City University Medical Center, ³Division of Rheumatology, Department of Internal Medicine, Showa University School of Medicine, ⁴Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, ⁵Department of Immunology and Rheumatology,

Unit of Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: None

[Object] To examine the relationship between the frequency of infectious disease and patients' background in systemic lupus erythematosus (SLE) using a multicenter registry. **[Methods]** Patients registered in the multicenter SLE registry "LUNA" were divided into two groups by presence (SI group) or absence (NI group) of the history of severe infection requiring hospitalization, and patients' background parameters were compared between the groups. **[Results]** Of the 618 SLE patients, 255 (41%) had histories of infection, among whom 97 (16%) were pneumonia as the largest number. Eighty-two (13%) had histories of serious infection requiring hospitalization (SI group). There were no significant differences between the SI and NI groups in use of hydroxychloroquine or glucocorticoid and disease activity. The use of tacrolimus (TAC) was significantly less frequent in the SI group as compared to the NI group (7.4 vs 18%, $p = 0.029$). The drinking rate was significantly lower (4.9 vs 40%, $p = 1.0 \times 10^{-11}$), and the smoking rate also tended to be lower (6.3 vs 13%, $p = 0.13$) in the SI group. **[Conclusions]** SLE patients with a history of severe infection use TAC less frequently. The drinking and smoking rates were lower in such cases, suggesting that serious infection history may improve lifestyle.

P2-282

Usefulness of neutrophil-to-lymphocyte ratio (NLR) at the onset of infection to NLR at the baseline ratio for predicting bacterial infections in patients with rheumatoid arthritis treated with tocilizumab

Yoshiki Nagai, Naoki Tanomogi, Masahiro Iida, Shuhei Sano, Yusuke Takamichi, Tatsuo Mori, Nanase Honda, Michiru Kina, Eisuke Takamasu, Kae Onishi, Takayasu Kise, Yuji Miyoshi, Masako Utsunomiya, Naoto Yokogawa, Kota Shimada, Shoji Sugii
Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan

Conflict of interest: None

[Objective] The aim of this study is to describe the usefulness of neutrophil to lymphocyte ratio (NLR) for predicting bacterial infection in patients with rheumatoid arthritis (RA) treated with tocilizumab (TCZ). **[Methods]** We extracted RA patients treated with TCZ who developed any infections between April 2008 and March 2018 from our hospital database. We divided into two groups: bacterial infection group and non-bacterial infection group. We compared the patient backgrounds, CRP, WBC, NLR at the onset of infection and NLR at the onset of infection (post-NLR)/NLR at the baseline (pre-NLR) ratio between two groups. **[Results]** Of 198 patients who received TCZ, 21 cases developed bacterial infections and 20 cases developed non-bacterial infections. Median CRP level, WBC count, NLR and post-NLR/pre-NLR ratio in bacterial group were significantly higher than non-bacterial group. In ROC curve analysis for predicting bacterial infection, AUC of CRP, WBC, NLR and post-NLR/pre-NLR ratio were 0.787, 0.857, 0.887 and 0.975 respectively. The cutoff value of 2.25 in post-NLR/pre-NLR showed the greatest sensitivity (90.5%) and specificity (100%). **[Conclusion]** The post-NLR/pre-NLR ratio may be useful for differentiating bacterial and non-bacterial infections in patients with RA treated with TCZ.

P2-283

Clinical evaluation of RA patients who have severe pneumonia during RA medication using biologics

Kayo Hira, Hideki Tsuboi
Osaka Rosai Hospital, Osaka, Japan

Conflict of interest: None

[Object] To elucidate the clinical background of RA patients using biologics (Bio) who have required hospitalization for severe pneumonia. **[Methods]** Ten patients with RA treated with Bio, whom diagnosed as severe pneumonia requiring hospitalization, between 2014 and 2018 were enrolled and they were female; 9 and male; 1. The mean age was 44.9

years. We evaluated their baseline characteristics which included ages of development of infection, gender, duration of RA, stages (Steinbrocker's), comorbidities including chronic lung diseases and diabetes mellitus, moreover, the use of MTX and PSL, serum RF, ACPA, KL-6 (U/mL), and β -D glucan (pg/ml) at the start of Bio treatment. [Results] In four patients, their duration of RA was more than ten years at the onset of severe pneumonia. The age of onset of RA was above 65 years old in 7 patients, on the other hand, one patient was 42 years old. 6 patients showed stages III/IV. Comorbidities of lung disease were IP in six and one was complicated with *Mycobacterium avium*. 6 patients used MTX and two used PSL. [Conclusions] Although the number of this study were so small, we experienced a severe pneumonia patient who was 42 years old. Our results showed that we have to pay attention to RA patients using Bio if they don't have any risk factors.

P2-284

The consideration of two infection cases in the rheumatoid arthritis patients with total knee arthroplasty during biological therapy

Hiroyuki Wada

Department of Orthopaedic Surgery, Japanese Red Cross Kochi Hospital, Kochi, Japan

Conflict of interest: None

[Object] We report two infection cases in rheumatoid arthritis (RA) patients with total knee arthroplasty (TKA) after the introduction of biological therapy. [Case 1] A 68-year-old woman with RA underwent a right revision TKA. After that, she started biological therapy with ETN. She had the pain and swelling in her right knee. In the synovial fluid of her knee, group B streptococcus was detected. After the suspension of MTX and ETN, we performed irrigation and debridement of her right knee. After that, the patient received antibiotic therapy and the infection had been healed. [Case 2] A 47-year-old woman with RA underwent a left TKA. After that, she started biological therapy with ETN. She had the pain and swelling from left knee to lower extremity. In the synovial fluid of her knee, no bacterium was detected. So we think cellulitis led the symptoms. We treated this patient by the suspension of ETN and administration of antibiotics. However, CRP was still high. We thought not only cellulitis but also RA caused a high CRP level and improved RA disease control. Finally, inflammatory reaction disappeared. [Discussion] There were some reports which indicated the biological agents increased the infection risk and so we needed to take care of infection during using biological agents.

P2-285

A purulent arthritis case in which prednisolone introduction is also difficult to treat for polyarthritis mainly of sternal arthritis and skin vasculitis

Masatoshi Kawatake¹, Hiroyuki Hounoki¹, Miho Yamazaki¹, Ryoko Asano¹, Maiko Okumura², Satoshi Yamaguchi¹, Koichiro Shinoda¹, Hirofumi Taki¹, Kazuyuki Tobe¹

¹Department of Immunology and Collagen Disease, Toyama University Hospital, ²Department of Rheumatology, Saiseikai Takaoka Hospital

Conflict of interest: None

[Case] 65 year old male [chief complaint] Polyarticular pain, purpura [medical history] Eruption appears in the limbs, trunk and head from last year, he was treated steroid ointment but the scabbing eruption remained. Since the sternoclavicular pain appeared from January, he was prescribed loxoprofen, but the pain remained. He received skin biopsy. IgG, IgA, IgM, C3c were deposited along the vessel wall and vasculitis was diagnosed. Prednisolone was started with 10mg but increased to 30mg as shoulder joint and back pain appeared, and CRP elevation didn't improve. He was difficult to move, and hospitalized. In bone scintigraphy, abnormal accumulation was found the right sternoclavicular joint, Th8, L4/5, and the limb joints, and polyarthritis was suspected. Methicillin-resistant *Staphylococcus aureus* was detected in blood culture, and from L4/5 puncture culture, so he was diagnosed as purulent discolitis. Linezolid was started and control was obtained. [Discussion] There was treatment intervention before his visit, pain appeared prior to fever, and skin vasculitis, it was difficult to diagnose. Suppurative sternal arthritis is

about 9% of total sternal arthritis, of which healthy people account for 23%, it is always necessary to keep in mind when scrutinizing sternal arthritis.

P2-286

Rice-body formation and tenosynovitis of bilateral hands in patient with anti-ARS antibody: a case report

Atsushi Kitagawa, Tomoko Nakamura, Fumimasa Maruno
Hyogo Prefectural Central Rehabilitation Hospital

Conflict of interest: None

A 67-year-old woman treated for dermatomyositis and interstitial lung disease presented with severe pain and swelling on the dorsal aspect of bilateral hands, wrists, and left forearm which had started 1 year before. Laboratory tests revealed WBC: 10730/ μ L, ESR: 44mm/H, CRP: 1.32mg/dL, MMP-3: 458.3 ng/mL, KL-6: 904 U/mL, T-spot. TB: negative. There was no sign of lung tuberculosis and nontuberculous mycobacteria. Ultrasonography revealed significant echogenic fluid and magnetic resonance imaging showed tenosynovitis of the extensor tendons and inflammatory mass lesions. Surgical exploration of the lesion revealed multiple rice bodies and through synovectomy and debriement were performed. Pathologic examination showed epithelioid cell granulomatous synovitis and fibrinoid necrosis. However, PCR for tuberculosis was negative. Four weeks later, the specimen grew *Mycobacterium intercellulare* and the patient subsequently received ethambutol and Clindamycin. Conclusions: Ricebody formation is a non-specific inflammatory reaction associated with chronic tenosynovitis and atypical mycobacterial infection should be considered in case of the immunosuppressed patient.

P2-287

A case of chronic *Pseudomonas aeruginosa* arthritis diagnosed by synovial biopsy, which can not be diagnosed by repeated arthrocentesis

Shuhei Sano, Masahiro Iida, Yusuke Nakamichi, Tatsuo Mori, Nanase Honda, Michiru Kina, Eisuke Takamasu, Kae Onishi, Takayasu Kise, Yuji Miyoshi, Naoto Yokogawa, Kota Shimada, Shoji Sugii
Department of Rheumatic Disease, Tokyo Metropolitan Tama Medical Center

Conflict of interest: None

[Background] It is experienced that monoarthritis persists and recurs in rheumatoid arthritis (RA) patients. Synovial fluid examination is useful for discrimination of monoarthritis, but we sometimes encounter difficulty in arthrocentesis. [Case] An 86-year-old woman was diagnosed as RA at the age of 60. She had been treated with methotrexate (MTX) 6mg and prednisolone (PSL) 3mg. X-1 year before presentation, right joint ankle pain appeared. She was treated by PSL dose increase and intraarticular steroid injection, but symptoms did not improve. She was referred to our hospital in April X. At the time of initial examination, right foot monoarthritis was observed. Under ultrasonography I attempted arthrocentesis, but could not collect. At a later date, I did again but only a very small amount of synovial fluid could be collected. Fungus and acid-fast bacteria culture test was submitted. It was negative. Synovial biopsy was performed, and *Pseudomonas aeruginosa* became positive in synovium / synovial fluid culture. She was treated with ceftazidime and ciprofloxacin, arthritis improved. [Clinical implication] Synovial biopsy is useful for diagnosis in arthritis where joint puncture is difficult and the treatment response is not suitable.

P2-288

Severe multiple infections after repeating methylprednisolone pulse therapy in collagen-vascular disease; two case reports

Noriko Sakaguchi, Kenichi Ueno, Takanori Ichikawa, Satoru Ushiyama, Dai Kishida, Yasuhiro Shimojima, Yoshiki Sekijima
The Third Department of Internal Medicine, Shinshu University School of Medicine

Conflict of interest: None

Case1: A 44-year-old female with refractory lupus nephritis (LN) had been treated by repeating intravenous methylprednisolone pulse therapy (mPSL); however, high grade fever appeared without LN improvement. Hemophagocytic syndrome (HPS), cytomegalovirus (CMV) pneumonia, pulmonary aspergillosis, and bacterial sepsis were demonstrated in our hospital. HPS and multiple infections were improved by intensive treatments with antimicrobial agents as well as intravenous immunoglobulin after plasmapheresis. Intravenous cyclophosphamide was subsequently administered, and remission of LN was also achieved. **Case2:** A 52-year-old female, who had a 4-year history of interstitial pneumonia (IP) related to dermatomyositis, was administered mPSL because of IP deterioration. However, respiratory failure due to pneumocystis pneumonia appeared, and progressed even after adding mPSL with pentamidine. In our hospital, CMV infection and multidrug-resistant pseudomonas aeruginosa pneumonia was additionally revealed. She was intensively treated under respirator support, and consequently complete remission was achieved. **Conclusion:** The accumulation of high-dose PSL can induce severe infection. PSL-sparing effect may be expected by concomitant use of immunosuppressant since early phase of disease.

P2-289

Comparative study of prognosis of arthritis rheumatology complicated with interstitial pneumonia and chronic respiratory bacterial infection

Hiroyuki Nakaya, Kouichirou Takahi, Kazuhiko Imoto
Orthopedics & Rheumatology, National Hospital Organization of Toneyama Hospital

Conflict of interest: None

[Object] Therapeutic treatment for Rheumatoid arthritis patient with interstitial pneumonia (IP) or chronic respiratory bacterial infection (such as *Pseudomonas aeruginosa* and NTM) does not often go well smoothly. In this study we investigated the influence of respiratory disease on patient condition and prognosis comparing two groups. [Methods] Among RA patients followed in our hospital, Patients complicated with IP (IP group) and chronic respiratory infection (especially *Pseudomonas aeruginosa* and NTM) (CRI group) was compared. investigation was performed from Oct.2015 to Dec.2018. We compared patient background prognosis, medication, ADL (steinblocker classification and m-HAQ), DMARD use (MTX/TAC/b-DMARD) patient condition (ACPA, RF, CRP, MMP-3, DAS28-CRP and modified sharp score) and respiratory function. [Results] IP group 17 patients and CRI 20 patients were included. We found that RA disease duration, ADL, MMP-3/DAS-28/m-sharp score yearly change were dominant in CRI group. We found characteristic use in MTX and TAC and b-DMARD medication in both groups. [Conclusions] In the treatment of RA patient with chronic respiratory infection, RA prognosis was poor because we have to take much care of b-DMARD indication.

P2-290

Autoimmune lymphoproliferative syndrome with somatic mutation of FAS (ALPS-sFAS); A case report

Shunjiro Kurihara¹, Junichi Ishikawa¹, Norihiro Mimura¹, Hirotohi Kawashima¹, Masaki Hiraguri¹, Yuzaburo Inoue²

¹Rheumatology Department, Narita Red-Cross Hospital, Narita, Japan, ²Division of Clinical Genetics, Chiba University Hospital

Conflict of interest: None

Autoimmune lymphoproliferative syndrome (ALPS) is a rare disease characterized by lymphadenopathy, splenomegaly, and usually complicated autoimmune diseases and malignant lymphoma. It is commonly said most all of ALPS develop in childhood because of its germinal mutation. The present study is a case report of ALPS with somatic mutation of FAS (ALPS-sFAS). The case is a 21 years-old man who presented to the hospital with back pain. CT scan showed splenomegaly and systemic lymphadenopathy. However, lymph node biopsy didn't indicate malignant lymphoma. Three years later (when he was 24 years-old), a fever brought him to the hospital again. As he had intestinal follicular lymphoid hyperplasia together with splenomegaly, we suspected that he had an immunodeficiency causing lymphoproliferative disorder. Flow cytometry

analysis revealed that CD3+TCR $\alpha\beta$ +CD4-CD8- lymphocytes increased in CD3+ cell in the peripheral blood (5.2%). We found a frame-shift mutation of the FAS gene (c.585-595del, p. Thr198fs) in 20 % of peripheral blood cells, but did not detect the mutation in buccal mucosa cells. Thus, we diagnosed his illness as ALPS with somatic mutation of FAS (ALPS-sFAS), which is rarely reported in Japan.

P2-291

A case of anti-EJ positive dermatomyositis (DM) and interstitial pneumonitis (IP) complicated by nephrotic syndrome (NS) due to membranous nephritis (MN)

Syoko Tsubouchi, Fumika Iemura, Kayo Ishii, Takahiro Mizuuchi, Yusuke Yamamoto, Hiroaki Mori, Haeru Hayashi, Koichiro Tahara, Tetsuji Sawada

Department of Rheumatology, Tokyo Medical University Hospital

Conflict of interest: None

A 67-year-old woman with a 10-year history of Raynaud's phenomenon developed DM at age of 37, and was treated with methotrexate (MTX). At age of 65, she developed swelling of her fingers and fingertip ulcers. She was found to be anti-RNP positive, and prednisolone (PSL) was started. However, at age of 67, she was admitted to our hospital because of worsening ulcers, although PSL was increased prior to admission. Since her digital ulcers were attributed to scleroderma-like phenotype of MCTD, we discontinued MTX and tapered PSL with sympathetic nerve block and vasodilation therapy. Although amputation was required due to infectious complication, digital ulcers were ameliorated. However, she presented with recurrence of DM 4 months later, as diagnosed by anti-EJ positivity, elevated CK, muscle MRI, worsening interstitial pneumonia, and mechanic hands. Concurrently, she developed NS, and renal biopsy revealed immune-positive MN. Anti-dsDNA IgG was slightly elevated, albeit negative anti-DNA Ab (RIA). Both DM and MN were controlled by high-dose PSL and cyclosporine. Simultaneous development of DM and MN suggests causal relationship, although chance occurrence cannot be precluded. Further accumulation of similar cases would thus be warranted to explore common pathogenetic mechanisms.

P2-292

Three cases of probable viral infection referred as collagen diseases

Shino Fujimoto, Tomoyuki Sakai, Haruka Iwao, Takafumi Kawanami, Shuichi Mizuta, Hiroshi Kawabata, Toshihiro Fukushima, Yasufumi Masaki

Hematology and Immunology, Kanazawa Medical University

Conflict of interest: None

[Case 1] A 54-year-old man manifesting malaise, edema of the hands and feet, polyarthralgia, sausage-like fingers, and erythema with desquamation on the extension side of the finger joints was referred to our Hospital under a diagnosis of dermatomyositis. He was taking 10 mg of prednisolone with little effects. The anti-human Parvovirus (HPV) B19 IgM antibody was positive in his serum, and his symptoms spontaneously improved within 4 months. [Case 2] A 62-year-old woman was referred to our hospital with slight fever and polyarthralgia under a diagnosis of rheumatoid arthritis. The anti-cytomegalovirus IgM antibody was positive in her serum, and her symptoms spontaneously disappeared in 4 months. [Case 3] A 46-year-old man was referred to our hospital with fever and polyarthralgia under a diagnosis of adult Still disease. The HPV B19 IgM antibody was positive in his serum. There was an outbreak of HPV B19 in his hometown. [Discussion] Viral infection-related symptoms, such as malaise, polyarthralgia, and fever, are usually transient, but they may persist for months. Therefore, viral infection should be carefully excluded when diagnosing collagen diseases before starting corticosteroids or immunosuppressive therapies.

P2-293

Actual condition of medical treatment of rheumatoid arthritis patients using medical collaboration

Makoto Onishi, Atsushi Kondo, Ayuko Sogabe, Naoya Sawada, Akihiro Yamada, Yosuke Murata, Kenichiro Matoba, Kazuo Jouyama, Yasuaki

Okuda, Kiyoshi Takasugi
Center for Rheumatic Diseases, Dohgo Spa Hospital

Conflict of interest: None

Introduction: Current medical treatment is based on the concept of regional inclusive care that provides medical care throughout the fulfilling region. Our hospital has general wards for disabled people, regional inclusive care wards (RICW) and recovery rehabilitation ward (RRW). **PURPOSE:** Medical cooperation with acute phase hospital in our hospital and survey on patients using RICW and RRW **Method:** Investigate the hospitalization purpose, hospital stay, etc for RA using patients who transferred from an acute hospital from January to August 2018 and the RICW ward and RRW **RESULTS:** There were 61 and 20 RA patients who used the RICW and RRW. 10 transferred to the direct RRW, and 43 were hospitalized in the RICW directly. 21 from outpatient, 22 from other hospitals. **T** Reasons for which medical treatment was necessary continuously was the most rehabilitation after orthopedic surgical treatment, Treatment continued after complications. **CONCLUSION:** In RA patients, there is a possibility that it will be difficult to continue the treatment in general hospitals that are in the recovery phase (subacute phase), such as drug management and assessment of ADL disorders for each patient due to the specificity of disease it is conceivable that.

P2-294

Using social resources in the treatment of rheumatoid arthritis

Satoshi Kashiwagi, Yoshikiyo Ohsawa, Hitoshi Nakata, Haruki Imura, Atsushi Saito
Department of Rheumatology, Amagasaki Medical COOP Hospital

Conflict of interest: None

[Object] Rheumatoid arthritis (RA) patients need much money for their treatment. They often use social resources to reduce their payment. We researched the situation in our hospital. [Methods] We researched the number and rate who use social resources such as welfare, medical welfare system and free/low-cost medical project from 2012 to 2017. We also compared them with the situation in other patients. [Results] The number of RA patients increased, whom received welfare were almost same, whom received medical welfare system decreased and whom received free/low-cost medical project increased. The numbers who use social resources in other diseases patients were almost same. In compared with them, the late to use social resources in RA patients were more. [Conclusions] The numbers who used welfare and medical welfare system decreased. On the other hand, the numbers who used free/low-cost medical project increased. RA patients were older and the cost which old patients must pay increased. The total numbers who use social resources will increase by changing the form.

P2-295

A case of elderly-onset eosinophilic temporal arteritis complicated by steroid-responsive occlusion of arteries of upper extremities

Kayo Ishii, Takahiro Mizuuchi, Hiroaki Mori, Mayu Tago, Eri Kato, Haeru Hayashi, Koichiro Tahara, Tetsuji Sawada
Department of Rheumatology, Tokyo Medical University Hospital

Conflict of interest: None

[Abstract] Temporal giant cell arteritis is a large-vessel vasculitis of the elderly, while juvenile temporal arteritis is characterized by eosinophilic infiltration of swollen temporal artery. We describe here a 61-year-old woman with itchy and painful subcutaneous nodules on her forehead who developed digital cyanosis with small nodules on both sides of her fingers. Eosinophil count was 556. Ultrasound examination revealed occlusion of inflamed temporal arteries and corkscrew-like changes of her digital arteries. Temporal-artery-biopsy (TAB) revealed highly inflammatory (transmural) and eosinophilic infiltration without giant cell formation. Angiography revealed occlusion of ulnar and proper palmar digital arteries. Digital cyanosis was ameliorated by low-dose prednisolone, which was reduced over 4 years without recurrence. Eosinophilic inflammation was not observed in the 2nd TBA. Although Burger's disease involving temporal arteries could be a differential diagnosis, the angio-

graphic findings and steroid-responsiveness supported the diagnosis of eosinophilic temporal arteritis involving upper extremity arteries. Further accumulation of similar cases would be warranted given that this type of eosinophilic vasculitis could be a new disease entity.

P2-296

A case of ACNES (anterior cutaneous nerve entrapment syndrome) introduced to department of rheumatic diseases as unknown abdominal pain

Naoki Tanomogi¹, Kota Shimada¹, Masahiro Iida¹, Yusuke Nakamichi¹, Tatsuo Mori¹, Nanase Honda¹, Michiru Kina¹, Eisuke Takamasu¹, Kae Onishi¹, Takayasu Kise¹, Naofumi Chinen², Masako Utsunomiya¹, Yoshiaki Nagai¹, Naoto Yokogawa¹, Shoji Sugii¹

¹Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, ²Department of Internal Medicine, Tamananbu Chi-iki Hospital

Conflict of interest: None

Introduction ACNES (anterior cutaneous nerve entrapment syndrome) is not generally recognized as a cause of abdominal pain with a few reported cases in Japan. We experienced a case introduced due to abdominal pain of unknown cause, which improved after the Transversus Abdominis Plane Block. **A case** A 22 year-old woman without past history was hospitalized with infectious enterocolitis. Though, in a few days, diarrhea improved, localized abdominal pain in two points with nausea persisted for 1 month. She could eat nothing. She was transferred to our department because of the abdominal pain. CRP was negative and no abnormal findings were observed in both endoscopy and the enhanced CT. Carnett sign was positive. Considering ACNES, 1% procaine subcutaneous injection was performed, which had little effect. Then we tried TAP block, which resolved pain in one pain points and reduced the other pain to 30%. The nausea disappeared. She got able to take meals and she was discharged on hospital day 15. **Clinical significance** ACNES causes abdominal wall pain and, if it becomes severe, it may disturb eating. In the case with no test abnormality, localized abdominal pain and positive Carnett signs, we should recall this disease and try trigger point injection or TAP block.

P2-297

A Case of Intravascular Lymphoma Presenting with Proteinuria, Hematuria, Diffuse Pulmonary infiltrative Shadows, and Positive PR3-ANCA/Anti-GBM Antibodies

Hiroyuki Yoshida¹, Naoho Takizawa², Tatsuya Arai², Fumiya Kitamura¹, Hiroki Ikai², Tsuyoshi Watanabe², Mari Yamamoto², Yukari Murai¹, Waka Kokuryo², Koji Takasugi¹, Yoshiro Fujita¹

¹Department of Nephrology, Chubu Rosai Hospital, Nagoya, Japan, ²Department of Rheumatology, Chubu Rosai Hospital, Nagoya, Japan

Conflict of interest: None

[Case] An 81-year-old woman was hospitalized with influenza and treated for 2 weeks. Chest CT was normal at that time. The patient developed cough and dyspnea after discharge. Two weeks after discharge, she was referred to our hospital because of diffuse pulmonary infiltrations in her chest CT. Her body temperature was 37.7°C and SpO₂ was 88%. Laboratory test revealed anemia and thrombocytopenia, high CRP level, LDH 1130 IU/L, positive PR3-ANCA/ant-GBM antibodies, and normal renal function. Her urinalysis showed proteinuria and hematuria. Chest CT revealed bilateral diffuse centrilobular patchy shadows. The bronchoscopy showed no abnormal findings. Serum sIL-2 receptors level was elevated, so we suspected intravascular lymphoma along with elevated LDH levels, cytopenia, and diffuse lung injury. Consequently, a random skin biopsy was performed. Which revealed large CD20-positive lymphocytes in the vessels. She was diagnosed with IVL, and treatment was started. [Discussion] IVL can present with multiple organ failure, including lungs and kidneys, and positive results for autoantibodies. Therefore, physicians should consider possibility of IVL if a patient presents with cytopenia or elevated LDH and ferritin levels when suspecting ANCA associated vasculitis or ant-GBM disease.

P2-298

Risk factors of drug-induced kidney injury due to calcineurin inhibitors: a case-control study

Keiichi Iwanami

Department of Rheumatology, Tokyo Bay Urayasu Ichikawa Medical Center

Conflict of interest: None

[Object] To investigate risk factors of drug-induced kidney injury by calcineurin inhibitors. [Methods] We enrolled 45 patients (male 6, female 39) attending our hospitals regularly as of October 2018 and taking calcineurin inhibitors for more than 1 year. Drug-induced kidney injury (DKI) by calcineurin inhibitors was defined as a decrease of eGFR by more than 10 ml/min/1.73m² from baseline and a decrease of eGFR to less than 60 ml/min/1.73m². Age, underlying disease, comorbidity and medication were investigated and risk factors were analyzed. [Results] Of the 45 patients, 15 developed DKI with calcineurin inhibitors. In all cases, the blood concentration of calcineurin inhibitors was in the expected therapeutic ranges. In univariate analysis, hypertension (odds ratio 6.42, 95% CI: 1.61-25.64), combined use of trimethoprim-sulfamethoxazole (ST) (odds ratio 11.0, 95% CI: 2.54-49.39) was extracted as a risk factor. In multivariate analysis, combined use of ST (odds ratio 13.0, 95% CI: 2.04 - 82.2) was extracted as a risk factor. Age, eGFR at the start of administration did not show any significant difference. [Conclusions] Patients with hypertension and combination with ST have a high risk of developing DKI by calcineurin inhibitors.

P2-299

A SLE-like Case of Idiopathic Membranous Nephropathy with AIHA

Motoko Katayama, Sho Sendo, Mai Yamashita, Yoko Nose, Takaichi Okano, Yo Ueda, Kengo Akashi, Akira Onishi, Jun Saegusa, Akio Morinobu

Department of Rheumatology and Clinical Immunology, Kobe University Hospital

Conflict of interest: None

[Case] A 25 year-old male was admitted to our hospital because of proteinuria and hemolytic anemia in October 2018. He had been diagnosed as membranous nephropathy (MN) by renal biopsy, and daily 30 mg of PSL improved his proteinuria in 2010. He came to our division because of Raynaud's phenomenon in February 2017. Although he had some immunological abnormality (RF:1323IU/ml, ANA×80; Ho+Sp), he did not diagnosed as any connective tissue diseases. In addition to deterioration of proteinuria, he developed acute anemia and was diagnosed as autoimmune hemolytic anemia (AIHA) in January 2018, and high dose GC therapy improved both AIHA and MN. As proteinuria was increased to 4-5 g/gCr in April 2018, renal biopsy was re-performed. It showed full-house pattern in Immunofluorescent stain, while immunohistochemistry revealed phospholipase A2 receptor1 (PLA2R1) was positive. He also had AIHA relapse and admitted to our hospital in October 2018. Although we re-considered the possibility of SLE, we diagnosed him as co-existence of idiopathic MN and AIHA because of negative conversion of ANA and PLA2R1 positive in renal biopsy, and treated with high dose GC and tacrolimus. [Conclusion] We experienced a complication of idiopathic MN and AIHA which needed to distinguish from SLE.

P2-300

A case of adult type hypophosphatasia diagnosed as long-term unclassifiable arthritis

Satsuki Aochi¹, Rieko Murakami², Saho Honda²

¹Japan Self Defense Forces Sapporo Hospital, ²JR Sapporo Hospital

Conflict of interest: None

Case A 43-year-old female. At the age of 34, she was admitted to other hospital with joint pain and diagnosed reactive arthritis, then she was administered prednisolone 5mg/day for 1 year but it was ineffective. At the age of 39, she visited our hospital for examination and pain on both elbows. laboratory test showed Low ALP and FDG-PET/CT, there was no special matter and did not satisfy the diagnostic criteria of

any collagen disease, so As symptomatic treatment as unclassifiable arthritis. At the age of 43 years, a heterozygote of the ALPL gene c.1559delT mutation was found. Think of hypophosphatasia in adults, we started treatment. Clinical Significance Low hypophosphatasia is rare disease caused by ALPL gene mutation. As far as other searches were done in japan, there is no similar report, and as a rare example report based on overseas literature, with some consideration added.

P2-301

A case of arthropathy of familial amyloidosis with a clinical suspicion of concomitant with rheumatoid arthritis

Takuya Inoue^{1,2}, Kazuki Fujioka¹, Hidetake Nagahara¹, Makoto Wada¹, Masataka Kohno¹, Yutaka Kawahito¹

¹Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, ²Internal Medicine, Fukuchiyama City Hospital

Conflict of interest: None

A 44-year-old woman presented to our hospital with 6-month history of progressive joint swelling of left 3rd PIP and bilateral wrist joints. She had been diagnosed with familial amyloid polyneuropathy (FAP) due to detection of intravitreal transthyretin amyloid deposition and systemic involvement (peripheral polyneuropathy, chronic kidney disease, bowel and heart). She also had past history of arthropathy in right 3rd PIP joint and had underwent synovectomy. Histological findings had suggested the joint involvement of FAP. Although her arthropathy hadn't exacerbated for a few years, she was referred to our facility for evaluation of progressive joint swelling described above. Laboratory testing showed high levels of CRP (1.18 mg/dL), MMP-3 (169 ng/mL), RF (300 U/mL) and anti-CCP antibody (316 IU/mL). Radiographic images and MRI revealed some bone erosions, and active tenosynovitis and synovitis in left 3rd PIP and bilateral wrist joints. We suspected of coincidence of rheumatoid arthritis (RA). As of now, administration of Golimumab for 3 months improved elevated CRP and MMP-3 but her joints remained swollen. Further treatment is under consideration. To our knowledge, there are no reported cases of coincidence of FAP and RA. Here we report this case with some literature review.

P2-302

Case report: Case of diagnosis of adult onset hypophosphatasia from general pain and pathological fracture

Kenji Yoshida, Tatsuya Kai, Daisuke Hiraoka, Hiroko Ikeuchi, Kensuke Oryoji, Shinichi Mizuki

Matsuyama Red-Cross Hospital, Matsuyama, Japan

Conflict of interest: None

A 69-year-old man. He injured the right femoral neck fracture in a fall in 2007. In 2009, he injured a left shoulder fracture, both tibial fractures. And, systemic pain has appeared since 2014 and gradually became difficult to walk. In August 2018, he visited the rheumatology department of the hospital. As a result, blood test showed ALP: 97 U / L, it is low. Ca, P, int-PTH, 1-25 Vitamin D was in the normal range. We ordered genetic testing for suspected adult onset hypophosphatasia from pathological fracture history, over 4 years of systemic pain. As a result, the 1375th base of exon 12 of the ALPL gene was replaced by G → A, and the amino acid at position 459 was substituted with valine → methionine. (p.V459M mutation was detected heterozygous.) This mutation has been reported in infant type and Odontohypophosphatasia (tooth limiting type) in the past, and confirmed as adult type hypophosphatasia.

P2-303

A case of palmer fasciitis and polyarthritis syndrome associated with ovarian cancer

Shunya Kaneshita, Tomoya Sagawa, Takuya Inoue, Takashi Kida, Kazuki Fujioka, Hidetake Nagahara, Makoto Wada, Masataka Kohno, Yutaka Kawahito

Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

Conflict of interest: None

(Case) 62-year-old Japanese woman (Chief complaint) Bilateral swelling of hands and palmer pain (Present illness) A 62-year-old patient presented with bilateral swelling of the hands and palmer pain four months before. The patient was seen in an orthopedic clinic and she was followed closely without therapy because of no abnormality in hand X ray. She was examined by abdominal ultrasound and MRI showed left ovarian cancer in a primary care doctor. She was referred for evaluation of hand lesion by rheumatologist before surgery. (Clinical course) Physical examination showed pain at left wrist and palmer and swelling at bilateral hands. In the light of clinical findings and existence of ovarian cancer, we diagnosed as palmer fasciitis and polyarthritis syndrome. She was treated with diclofenac but it was not effective for hands lesion. Although she underwent surgery of total hysterectomy, adnexectomy and lymphadenectomy, her hands lesion didn't change after surgery. So we started prednisolone 50mg every other day and pain and swelling of the hands were dramatically getting better. (Summary) We report a case of palmer fasciitis and polyarthritis syndrome associated with ovarian cancer with some literature review.

P2-304

Acquired factor V inhibitor developing in a patient with interstitial pneumonia

Masanori Seki

Department of Hematology, National Hospital Organization Mito Medical Center, Mito, Japan

Conflict of interest: None

Acquired factor V (FV) inhibitor is a rare hemostatic disorder that presents with hemorrhagic manifestations in the vast majority of patients. In this report, we present a case of acquired FV inhibitor in a patient with interstitial pneumonia who presented with bladder tamponade. A 77-year-old woman had had asymptomatic macroscopic hematuria but was placed under observation. However, she was admitted because of bladder tamponade. Laboratory test showed prolonged prothrombin time and activated partial thromboplastin time. The FV levels decreased and the presence of FV inhibitor was confirmed by Bethesda method. She was managed for bleeding with supportive care, followed by corticosteroid therapy. The bleeding completely stopped 1 week after corticosteroid therapy. The FV levels were normalized, and the inhibitor was successfully eradicated using corticosteroids. The inhibitor disappeared twelve months after the onset. Here, we discuss this rare disorder, its unusual manifestation, and provide a review of the current literature regarding FV inhibitors.

P2-305

Mortality and Risk factors of Death in Patients of Rheumatoid Arthritis in our hospital

Yutaka Chifu¹, Yukiko Takeyama¹, Rie Suematsu²

¹Department of Internal Medicine, Saiseikai Karatsu Hospital, Karatsu, Japan, ²Department of Rheumatology, University of Sage, Saga, Japan

Conflict of interest: None

[Object] To evaluate what factors and comorbidities influence mortality of patients of RA. [Methods] To December 31.2017, We studied mortality of 143 patients of RA (29 males, 143 females, 63.5years old) who were outpatients in our hospital and registered from January to March in 2014. We also investigated the relationship between total hospitalizations and death from January 1.2014 to December 31.2017. [Results] There were ten deaths during the observation period. Five deaths were due to pulmonary disease and two were due to malignant disease, also five were due to infectious disease. The standard mortality ratio during this period was 1.17 for males, 1.56 for females, 1.34 for total. In multivariate analysis, age, male and pulmonary disease were significantly associated with death. During the study period, all hospitalizations were 81, orthopedic disease 23, infectious diseases 27 (pneumonia 16), malignant disease 6. Hospitalization of pneumonia and malignant disease was significantly associated with death. A large part of the causes of death in patients of RA were pulmonary disease, malignant disease and infectious diseases. Control of pulmonary diseases and infectious diseases is impor-

tant for improving prognosis of patients of RA.

P2-306

Usage survey of immunoglobulin preparations for connective tissue disease

Yasushi Koyama¹, Yuto Izumi^{1,2}, Kazuki Hirano¹, Yoko Nakagome¹, Mai Sugiyama¹, Sho Sasaki¹, Yasushi Kondo¹, Chiho Yamada¹, Takayoshi Kurabayashi¹, Noriko Sasaki², Takayuki Wakabayashi², Yasuo Suzuki², Shinji Sato¹

¹Division of Rheumatology, Department of Internal Medicine, Tokai University School of Medicine, ²Division of Rheumatology, Department of Internal Medicine, Tokai University Hachioji Hospital

Conflict of interest: None

[Objective] To examine the usage of immunoglobulin preparations for connective tissue disease [Methods] One hundred twenty two patients with connective tissue disease (CTD) treated with intravenous immunoglobulin (IVIg) between January 2016 and September 2018 at Tokai University Hospital were examined retrospectively their backgrounds, diagnosis, application of IVIg and applied dose and others. [Results] Of 122 patients with CTD, 76 patients are treated for hypogammaglobulinemia, 25 patients for refractory idiopathic inflammatory myopathies (IIM), 11 patients for neuropathies with vasculitis syndrome, and 7 patients for idiopathic thrombocytopenic purpura and 3 patients for other conditions. Of 76 patients treated for hypogammaglobulinemia, 52 patients had no active infection and IVIg were used for infection prophylaxis. Remaining 18 patients suffers from active infectious diseases. Interestingly, 15 patients had cytomegalovirus infection among those who were complicated with active infection. A large amount of IVIg (400mg/body for 5 days) was used for refractory IIM in high frequency. [Conclusions] IVIg therapy was frequently used for infection prophylaxis and cytomegalovirus infection in patients with hypogammaglobulinemia under the treatment for underlying CTD.

P2-307

Clinical manifestations of acute hemorrhagic rectal ulcer (AHRU) in patients (pts) with rheumatic diseases (RD)

Yusuke Yamamoto, Haeru Hayashi, Koichiro Tahara, Tetsuji Sawada
Department of Rheumatology, Tokyo Medical University Hospital

Conflict of interest: None

[Aim] AHRU is an ulcerative lesion restricted to lower rectus, characterized by sudden onset and painless massive hematochezia in long-term bedridden pts with severe underlying disease. The rapidly aging of Japan prompted us examine the manifestations of AHRU in RD. [Methods] The pts hospitalized from Jan 2017 to Jul 2018 were retrospectively examined. [Results] Eight developed AHRU during the period; Mean age: 72 + 9 (2 male, 6 female), background: 4 with RA, and 1 with MRA, SSc, DM, MCTD, and MPA, respectively, mean PSL: 12.6±6.4 mg/day. The reason of hospitalization was infectious complications in 7 out of 8. AHRU occurred from day 5 to 15 in pts with poor ADL (PS 3 or 4), and hypoalbuminemia (2.2 + 0.3 g/dl) and anemia (Hb 7.9 + 0.9 g/dL). AHRU lesion was solitary in all the 8 pts. Two pts who developed recurrent AHRU and required multiple blood infusions had iliopsoas abscess and extensive phlegmon which were treatment-resistant (CRP > 10 mg/dL). [Conclusion] AHRU complicated by RD was prevalent in elderly pts with impaired ADL due to infection. Since AHRU could possibly recur especially in RD pts hospitalized due to infection, it would be important to control underlying diseases and to perform preventive measures, such as frequent repositioning, to circumvent AHRU.

P2-308

Gout presenting as a foramen magnum syndrome

Yuji Miyoshi¹, Miho Ohshima¹, Makoto Sugihara¹, Tomohiro Kozuki¹, Takayasu Kise², Naoto Yokogawa², Shoji Sugii²

¹Department of Rheumatic Diseases, Tama-Hokubu Medical Center, Tokyo, Japan, ²Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center

Conflict of interest: None

[Introduction] Gout can manifest not only as arthritis but also a variety of extraarticular symptoms. We herein report a gout case presenting with foramen magnum syndrome. [Case] A patient was 73-year old male. His serum creatinine and uric acid were 1.3 mg/dl and over 9.0 mg/dl respectively at the age of 70. Cervical neck pain appeared at the age of 73. A few months later, left hemiparesis and hemiparesthesia appeared. Retro-odontoid pseudotumor compressing cervical spinal cord was diagnosed. Laminectomy at C1 and posterior fixation surgery at C1 and C2 were performed. After the surgery, he suffered from bilateral arthritis at ankles and tarsal joints. Synovial fluid from right ankle showed needle shape crystal with negative birefringence. His uric acid level improved with allopurinol and colchicine. One year later, the retro-odontoid pseudotumor disappeared. [Clinical significance] Gout should be considered as a treatable retro-odontoid pseudotumor.

P2-309

A case of tophaceous gout with deposition of monosodium urate crystals on the flexor tendon causing flexion contracture of the fingers

Naomi Ichikawa¹, Atsuo Taniguchi¹, Yohei Seto^{1,2}, Hisashi Yamanaka¹

¹Institute of Rheumatology, Tokyo Women's Medical University, ²Tokyo Women's Medical University Yachiyo Medical Center

Conflict of interest: None

A tophus is a characteristic sign of advanced gout and develops after long-standing untreated gout as a consequence of excessive deposition of monosodium urate (MSU) crystals on joints, tendons and subcutaneous tissue. We report a case of MSU deposition on the flexor tendon of the hands. A 77-year old woman with a history of chronic glomerulonephritis had developed polyarthritis and subcutaneous nodules since 1994 and visited our hospital in 2014 because of persistent articular pain. The patient had multiple subcutaneous nodules in her hands and right forearm, with the fingers showing flexion contracture. Laboratory tests demonstrated hemoglobin level was 9.5 g/dL, serum urea nitrogen 71.6 mg/dL, serum creatinine 2.59 mg/dL, serum uric acid 10.2 mg/dL, CRP 0.09 mg/dL, while the rheumatoid factor was negative. A plain x-ray of the hand showed punched out lesions in finger and carpal bone. MSU crystals were confirmed in subcutaneous nodules, leading to a diagnosis of gout. Dual-energy CT also demonstrated deposition of MSU in both the macroscopic gouty nodules and areas of bone destruction. An interesting finding was that diffuse deposits were found in the flexor tendons, and it appeared that some of the deposits were involved in bone destruction of the medial phalangeal bone trunk.

P2-310

Case report; acute CPP crystal arthritis is complicated by septic arthritis of the knee

Atsushi Goshima, Masataka Nishikawa, Hajime Owaki
Japan Community Health Care Organization Osaka Hospital

Conflict of interest: None

[Object] We present the case of a 86-year-old male who was diagnosed with monoarticular arthritis due to acute calcium pyrophosphate (CPP) crystal arthritis and septic arthritis. [Methods] A 86-year-old man presented to the emergency department complaining of the left knee pain. He was found to have swelling and tenderness of the joint. We performed arthrocentesis of the knee and CPP crystal was detected, culture was negative. So, intra-articular injection with corticosteroids was performed. Swell and tenderness were alleviated. But, in a bit, swell and tenderness were flared, we performed arthrocentesis of the knee and identified coagulase-negative staphylococci. We performed arthroscopic synovectomy and treated with antibiotic agents. His knee pain and swelling resolved. [Results] We are face with a problem of distinguishing monoarthritis, it is difficult to distinguish acute CPP crystal arthritis from septic arthritis. In synovial tests, WBC count of >50000 and polymorphonuclear cells greater than 90% are the possibility of septic arthritis got higher. [Conclusions] We consider to treat with septic arthritis when WBC count of >50000 and polymorphonuclear cells greater than 90% are in synovial tests. [clinical significance] Distinguishing monoarthritis is too difficult.

P2-311

A 15-year-old boy with gout

Yoshiki Nagai¹, Naoto Yokogawa¹, Naoki Tanomogi¹, Masahiro Iida¹, Shuhei Sano¹, Yusuke Nakamichi¹, Tatsuo Mori¹, Nanase Honda¹, Michiru Kina¹, Eisuke Takamasu¹, Kae Onishi¹, Takayasu Kise¹, Yuji Miyoshi¹, Masako Utsunomiya¹, Keiji Akamine², Kota Shimada¹, Shoji Sugii¹

¹Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan, ²Department of Nephrology, Tokyo Metropolitan Children's Medical Center, Tokyo, Japan

Conflict of interest: None

[Background] Juvenile-onset gout is rare. [Case] A 15-year-old boy presented with swelling and pain in his left foot. Two days before presentation, he noticed the pain in his left foot. One day before presentation, he was seen in primary care physician and prescribed antibiotics in the diagnosis of cellulitis. Since his symptom did not improve, he was referred to Tokyo Metropolitan Children's Medical Center. He had received four surgeries of double-outlet right ventricle, corrected transposition of great arteries, and pulmonary artery blockage at 1, 4, 13 months and 5 years old. He had difficulty in walking because of the pain in left foot. He was referred to our department because the pain and swelling in his left foot did not improve with antibiotics. Blood tests showed an elevated serum uric acid level of 11.4 mg/dl. Musculoskeletal ultrasonography revealed moderate fluid in the first and second MTP joint. He underwent arthrocentesis and gout was diagnosed by isolation of monosodium urate crystals in synovial fluid by polarization microscope. After prednisolone was started at the dose of 15 mg/day, his symptom improved immediately. [Clinical implication] We should consider gout and perform arthrocentesis when we suspect the arthritis in juvenile patient.

P2-312

A case of chronic tophaceous gout

Shigeki Miyamoto
Ohmihachiman Community Hospital

Conflict of interest: None

A 61-year-old male presented left hemiplegia October 3,2016 and was hospitalized in the neurosurgery department of our hospital the next day. He complained of polyarthralgia and joint swelling on admission. He had repeated same episodes which were gradually prolonged. He was consulted to the department of rheumatology November 21,2016. He had polyarthritis with nodes on his right wrist and right elbow. Uric acid was 11.0mg/dl. We punctured the node on his right elbow and uric acid crystal was detected, and We diagnosed chronic tophaceous gout. We report the case of chronic tophaceous gout which is rare in the present age.

P3-001

Activities of daily living in patients with rheumatoid arthritis depend on disease activity ~Analysis by a wearable device~

Masahiro Tada¹, Yutaro Yamada^{2,3}, Koji Mandai^{2,4}, Noriaki Hidaka¹

¹Department of Orthopaedic Surgery, Osaka City General Hospital, ²Department of Orthopaedic Surgery, Osaka City University Graduate School of Medicine, ³Department of Orthopaedic Surgery, Yodogawa Christian Hospital, ⁴Department of Orthopaedic Surgery, Osaka Social Medical Center Hospital

Conflict of interest: None

[Object] We investigate the related factors about ADL and activity strength and analyzed relationship with disease activity and locomotive syndrome (locomo) in RA patients. [Methods] We used the data from prospective observational study (CHIKARA study). 85 from 100 RA entered and attached with wearable activity meter during 7 consecutive days. We calculated the daily exercise (EX), calorie consumption, and total calorie. The relationship of disease activity, body composition, muscle function, sarcopenia, locomo, and frailty was analyzed. We compared ADL by disease activity and locomo. [Results] Mean age was 65.2 years (women n=67, men n=18), disease duration was 7.7 years, DAS28ESR was 3.12, and HAQ was 0.6. EX was negatively correlated with MMP3,

DAS28ESR, HAQ, locomo, and frailty, and positively correlated with leg muscle score, muscle power, muscle speed, grip strength, and walking speed. Ex of moderate and high disease activity was significantly lower than that of remission (median 2.8 vs 4.6: $p=0.035$). Ex of locomo was significantly lower than that of non-locomo (median 2.2 vs 5.1: $p=0.001$). [Conclusion] DAS28ESR, locomo and muscle power were independently related factors with EX. EX relatively decreased in RA patients with moderate and high disease activity or locomo.

P3-002

Elucidation of chronic inflammation of rheumatoid arthritis using three-dimensional electron microscopy analysis

Rie Kurose^{1,2}, Takahiro Ochi³, Miwa Uzuki⁴, Kenya Murakami⁵, Yasuyuki Ishibashi², Takashi Sawai⁶

¹Hirosaki Memorial Hospital, ²Hirosaki University Graduate School of Medicine, ³Osaka Police Hospital, ⁴Tohoku Bunka Gakuen University, ⁵Iwate Medical University, ⁶Tohoku University

Conflict of interest: None

[Object] We focus on nursing phenomenon formed by a complex of synovial dendritic and plasma cells. The objective of this study is to investigate the mechanism of long duration of immunological inflammation in RA using electron microscope technology. [Methods] Synovial tissue collected from RA patients undergoing elbow or knee synovectomy was prepared for this study. From the wide fields of view of synovial tissue, we could easily select areas containing the nursing phenomenon by multiscale electron microscopy, and image 3D features by focused ion beam-scanning electron microscopy and construct the tomography by transmission electron microscopy with double-axis electron microscopy. [Results] Using multiscale electron microscopy, the numbers of synovial dendritic and plasma cells were observed in various areas of the lymphonodular infiltration. Synovial dendritic cells patronize the plasma cells by the long slender axis, and forming the membranous fusion of the plasma cells. [Conclusions] The meaning of the nursing phenomenon is not yet known, however it may provide a new aspect for analyzing the mechanism of long duration of immunological inflammation in RA.

P3-003

Research of body composition and prevalence of sarcopenia from two regions, in patients with rheumatoid arthritis from the CHIKARA study

Koji Mandai¹, Yutaro Yamada^{2,3}, Tatsuya Koike^{4,5}, Tadashi Okano³, Noriaki Hidaka⁶, Masahiro Tada⁶

¹Department of Orthopaedics, Osaka Social Medical Center, ²Department of Orthopaedic, Yodogawa Christian Hospital, ³Department of Orthopaedics, Osaka City University Graduate School of Medicine, ⁴Center for Senile Degenerative Disorders, Osaka City University Graduate School of Medicine, ⁵Department of Orthopaedic, Search Institute for Bone and Arthritis Disease, ⁶Department of Orthopaedic, Osaka City General Hospital

Conflict of interest: None

[Object] We investigated the differences in the prevalence of sarcopenia in patients with rheumatoid arthritis (RA) according to the size of the city. [Methods] The data from a prospective observational study (CHIKARA study) were used. 190 RA patients were measured by body composition analyzer MC-780A (TANITA). We evaluated the differences in the prevalence of sarcopenia and body composition by region (Metropolis: group M, Provincial city: group P). [Results] A total of 190 patients (group M:100, group P:90) with rheumatoid arthritis was included. Mean age was 66 years old at group M and 67 years old at group P ($p=0.9$). Mean disease duration was 5.5 years at group M and 8.5 years at group P ($p<0.001$). DAS28-ESR was 3.5 at group M and 2.9 years at group P ($p<0.001$). Mean appendicular skeletal muscle mass index (ASMI) was $6.4\text{kg}/\text{m}^2$ at group M and $6.2\text{kg}/\text{m}^2$ at group P ($p=0.057$). Prevalence of presarcopenia was 29% at group M and 43.3% at group P ($p=0.049$). Prevalence of sarcopenia was 20% at group M and 32.2% at group P ($p=0.068$). [Conclusions] RA patients live in provincial city tended to have a higher prevalence of sarcopenia than those who live in metropolis. Further research including living environment and work is necessary.

P3-004

What are the risk factors for developing sarcopenia in patients with rheumatoid arthritis during 2 years? -from the CHIKARA study-

Yutaro Yamada^{1,2}, Masahiro Tada³, Koji Mandai^{1,4}, Noriaki Hidaka³, Kentaro Inui¹, Hiroaki Nakamura¹

¹Department of Orthopedics, Osaka City University Graduate School of Medicine, ²Department of Orthopedics, Yodogawa Christian Hospital, ³Department of Orthopedics, Osaka City General Hospital, ⁴Department of Orthopedics, Osaka Social Care Center

Conflict of interest: None

[Object] Rheumatoid arthritis (RA) often develops into sarcopenia due to joint dysfunction and chronic inflammation. We reported glucocorticoid use and low body fat were independent risk factors for developing sarcopenia during 1 year in patients with RA. We investigated these during 2 years. [Methods] 100 patients (78 female, average age 68 yo) enrolled in the prospective CHIKARA study (UMIN000023744) were examined their body composition, laboratory data, disease activity, HAQ and treatment condition at baseline and 2-year. Among 64 patients without sarcopenia at baseline, those who developed sarcopenia at 2-year were detected and risk factors were investigated. [Results] 6 patients (9.4%) developed sarcopenia during 2 years. Among them, GC use $>5\text{mg}$ was significantly high ($p=0.009$); MMP3 ($p=0.018$) and HAQ ($p=0.045$) elevated during 2 years significantly. Sarcopenia development significantly associated with male sex ($r=0.28$, $p=0.03$), age ($r=0.27$, $p=0.03$), GC use $>5\text{mg}$ ($r=0.33$, $p<0.01$), CRP ($r=0.33$, $p<0.01$) at baseline, ΔMMP3 ($r=0.30$, $p=0.02$) and ΔHAQ ($r=0.25$, $p=0.04$) by univariate analysis. Multivariate analysis identified no independent factor. [Conclusions] RA patients with male, old-age, GC use $>5\text{mg}$, high elevation of MMP3 and HAQ associated with developing sarcopenia during 2 years.

P3-005

The sarcopenia and obesity are predictable by measuring thigh muscle and fat thickness using ultrasound in patients with rheumatoid arthritis - from the CHIKARA study -

Yutaro Yamada^{1,2}, Masahiro Tada³, Koji Mandai^{1,4}, Noriaki Hidaka³, Kentaro Inui¹, Hiroaki Nakamura¹

¹Department of Orthopedics, Osaka City University Graduate School of Medicine, ²Department of Orthopedics, Yodogawa Christian Hospital, ³Department of Orthopedics, Osaka City General Hospital, ⁴Department of Orthopedics, Osaka Social Care Center

Conflict of interest: Yes

[Object] Rheumatoid arthritis (RA) often accompanies sarcopenia. The thickness of quadriceps muscle is known to be related with skeletal muscle mass. We investigated the utility of ultrasound (US) for predicting sarcopenia by examining anterior thigh in patients with RA. [Methods] 94 patients (66 female) enrolled in the prospective CHIKARA study (UMIN000023744) were examined muscle (MT) and fat thickness (FT) at anterior thigh by US. They were also examined muscle and body fat mass by body composition analyzer. We investigated whether MT and FT can predict sarcopenia and obesity. They were diagnosed by Asian Working Group on Sarcopenia and % body fat (%BF). [Results] MT was related with sarcopenia (male $r=0.56$, $p=0.02$; female $r=0.32$, $p=0.01$). The MT cut-off value for sarcopenia was 24.7 in male, 19.7 in female by ROC analysis. FT showed correlation with %BF (male $r=0.66$, $p<0.01$; female $r=0.62$, $p<0.001$). %BF was estimated by $2.21\text{FT}+7.28$ in male, $1.45\text{FT}+14.46$ in female by single linear regression model. This means $\text{FT}>8.0$ in male, $\text{FT}>10.7$ in female deserves obesity. When assessing the accuracy of these cut-off value, kappa value was 0.541 and 0.469 respectively. [Conclusions] The sarcopenia and obesity are predictable by US at anterior thigh in patients with RA.

P3-006

Investigation of bone mass and bone mineral density in patients with rheumatoid arthritis from the CHIKARA study

Koji Mandai¹, Yutaro Yamada^{2,3}, Tatsuya Koike^{4,5}, Tadashi Okano³, Noriaki Hidaka⁶, Masahiro Tada⁶

¹Department of Orthopaedics, Osaka Social Medical Center, ²Department of Orthopaedic, Yodogawa Christian Hospital, ³Department of Orthope-

dics, Osaka City University Graduate School of Medicine, ⁴Center for Senile Degenerative Disorders, Osaka City University Graduate School of Medicine, ⁵Department of Orthopaedic, Search Institute for Bone and Arthritis Disease, ⁶Department of Orthopaedic, Osaka City General Hospital

Conflict of interest: None

[Object] We investigated the correlation between bone mineral density with bone mass in patients with rheumatoid arthritis [Methods] The data from a prospective observational study (CHIKARA study) were used. We measured bone mineral density (BMD) by Dual Energy X-ray Absorptiometry (DEXA) and bone mass by Bioelectrical Impedance Analysis (BIA) on the same day. [Results] A total of 90 patients (women, 83%; mean age, 67.2 years old) with rheumatoid arthritis was included. Median disease duration was 8.5 years, DAS28-ESR was 2.92. Median MTX dose were 10 mg/w. 19 patients use Biologic agent. We evaluated BMD by DEXA and bone mass by BIA. There was significantly correlation in BMD at total hip and bone mass ($r=0.64$, $p<0.001$). BMD at femoral neck and bone mass had significantly correlation ($r=0.62$, $p<0.001$). BMD at whole body and bone mass had significantly correlation ($r=0.60$, $p<0.001$). BMD at spine and bone mass had significantly correlation ($r=0.49$, $p<0.001$). Bone mass by DEXA (1.9kg) was significantly lower than bone mass by BIA (2.0kg) ($P<0.001$). [Conclusions] There was significantly correlation in bone mass by BIA and BMD by DEXA. Bone mass by BIA and BMD at total hip had the most correlation. Bone mass by BIA is likely to overestimate. So we evaluate that with adequate caution.

P3-007

Does a family history of RA influence the clinical presentation and treatment response in RA? -ANSWER Cohort-

Koichi Murata^{1,2}, Motomu Hashimoto¹, Yonsu Son³, Hideki Amuro³, Koji Nagai⁴, Tohru Takeuchi⁴, Masaki Katayama⁵, Kosuke Ebina⁶, Yuichi Maeda⁷, Ryota Hara⁸, Akira Onishi⁹, Sadao Jinno⁹, Wataru Yamamoto^{1,10}, Kosaku Murakami¹¹, Masao Tanaka¹, Hiromu Ito², Tsuneyo Mimori¹¹, Shuichi Matsuda²

¹Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ²Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ³First Department of Internal Medicine, Kansai Medical University, Osaka, Japan, ⁴Department of Internal Medicine IV, Osaka Medical College, ⁵Department of Rheumatology, Osaka Red Cross Hospital, ⁶Department of Orthopaedic Surgery, Osaka University, Graduate School of Medicine, ⁷Department of Respiratory Medicine, Allergy and Rheumatic Disease, Graduate School of Medicine, Osaka University, ⁸The Center for Rheumatic Diseases, Nara Medical University, ⁹Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, ¹⁰Department of Health Information Management, Kurashiki Sweet Hospital, ¹¹Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University

Conflict of interest: None

[Object] The family history of rheumatoid arthritis (RA) is a strong risk factor for developing RA, affecting both genetically and environmentally, and is routinely assessed. In this study, we assessed whether family history of RA is associated with clinical presentation of RA. [Methods] In ANSWER (Kansai consortium for well-being of rheumatic disease patients) cohort data, 339 untreated patients were diagnosed as RA from 2011 to 2018, and family history of RA were recorded in 259 patients. We evaluated demographic data and disease activity at baseline and 1 year after onset. [Results] 38 patients (15%) had family history of RA within second degree. Between patients with and without family history of RA, no significant difference was recognized between age at onset, symptom duration, gender, positivity or value of rheumatism factor or ACPA, or disease activity. However, in ACPA-positive patients ($n=168$), patients with a family history ($n=23$) showed significantly lower ESR, disease activity at baseline. There was no significant difference in ESR, CRP, or disease activity after 1 year. [Conclusions] Disease activity of ACPA-positive RA patients with a family history of RA is lower at onset, but there is no difference in disease activity after 1 year.

P3-008

Does dietary inflammation exist in rheumatoid arthritis?

Yuto Kobayashi¹, Eri Narita¹, Kentaro Inui², Yuko Sugioka², Tadashi Okano³, Kenji Mamoto², Masahiro Tada³, Tatsuya Koike¹

¹Shirahama Hamayu Hospital, ²Osaka City University Medical School Hospital, ³Osaka City General Hospital

Conflict of interest: None

[Objective] The dietary inflammatory index (DII) is a tool to evaluate the inflammation caused by diet and has been used for predicting low-grade chronic inflammation. We examined whether DII can predict inflammation in rheumatoid arthritis (RA). [Methods] Food nutrition data of 201 RA and age-, sex- matched 201 volunteers (Vo) in a cohort study (TOMORROW, UMIN000003876) were used. DII is a score of nutrients promoting inflammation and the larger value means the higher inflammation. Evaluation items were age, use of biological agents (Bio) or steroid (PSL) and Disease activity score 28 (DAS 28) in RA group. [Results] The mean age was 59.0 y (female 84.6%) in RA, 57.9 (female 84.7%) in Vo. DII was significantly higher in RA compared to Vo ($Vo - 1.13 \pm 1.92$, $RA - 0.60 \pm 1.90$, $P = 0.010$). Among three groups of Bio user, Bio non-user, and Vo, DII was significantly higher in the Bio user in RA by ANOVA ($P = 0.015$). Even when divided into 3 groups of PSL user in RA, PSL non-user in RA and Vo, DII was significantly higher ($P = 0.016$) in the RA group with PSL than the Vo. DAS 28 was significantly higher in PSL user than non-user. [Conclusion] RA inflammation might be affected by dietary intake contents, and Bio and PSL might be used for patients with more inflammation induced by diet.

P3-009

Survey on the relation between meal content and appearance of autoantibodies in general population

Hiroshi Fujii¹, Ichiro Mizushima¹, Masahiro Konishi¹, Hajime Sanada¹, Nobuhiro Suzuki⁷, Misaki Yoshida⁸, Kazuyuki Suzuki¹, Yoshinori Takahashi⁵, Akari Takeji¹, Yuhei Fujisawa⁶, Shunsuke Tsuge⁹, Shigeto Horita⁴, Takahiro Matsunaga⁴, Takeshi Zoshima¹, Hiromi Nuka⁸, Satoshi Hara¹, Yasunori Suzuki³, Kiyooki Ito¹, Kazunori Yamada¹, Satoshi Nakazaki², Mitsuhiro Kawano¹

¹Department of Rheumatology, Kanazawa University Hospital, ²Department of Rheumatology, Kanazawa Johoku Hospital, ³Internal Medicine, Kaga Medical Center, ⁴Department of Rheumatology, Ishikawa Prefectural Hospital, ⁵Department of Infectious Diseases, Kameda Medical Center, ⁶Internal Medicine, Saiseikai Kanazawa Hospital, ⁷Internal Medicine, Wajima Municipal Hospital, ⁸Department of Rheumatology, Fukui Prefectural Hospital, ⁹Department of Rheumatology, Toyama Red Cross Hospital

Conflict of interest: None

[Objective] To conduct survey of diet in general residents, investigate whether specific foods or nutrients influence the appearance of autoantibodies. [Methods] Between 2013 and 2017, a diet survey was conducted using 595 people living in Shika Town, Ishikawa Prefecture using brief-type self-administered diet history questionnaire (BDHQ). Anti - nuclear antibody (ANA), rheumatoid factor (RF), anti - CCP antibody (ACPA), and anti - SSA antibody were measured, and analyzed by binomial logistic analysis whether it relates to specific food and estimated nutrient intake and autoantibody appearance. [Results] Of the 595 patients, 14 ANAs, 24 RFs, 6 ACPAs and 16 anti-SSA antibodies were positive. For foods already reported to be associated with RA such as alcohol, fish intake, vegetables / fruits, meat, salt, etc., there was no consistent and significant association in any of the antibodies. In addition, the number of smokers and smoking duration were not significantly related in this survey. [Conclusions] There was no association between dietary content and the positive rate of autoantibodies. Although there are possibilities that no significant results were obtained due to the small number of cases, other factors may be more important for the appearance of autoantibodies.

P3-010

Titer of anti CCP antibody has changed to positive in a patient with rheumatoid arthritis: A case report

Gen Momoyama¹, Nobuyuki Suzuki¹, Hidekazu Tanaka¹, Yasunobu

Takizawa², Seiji Kobayashi³

¹Department of Orthopedic Surgery, Itakura Hospital, ²Department of Rheumatology, Itakura Hospital, ³Department of Rheumatology and Collagen Diseases, Nippon Medical School

Conflict of interest: None

Clinical history: A 75 years old female presented with swelling, arthralgia of her left ankle joint and right hand joint from August 2017. Serum antibody titer of rheumatoid factor (RF) and anti CCP antibody were less than 3 IU/mL and less than 0.6 U/mL, respectively. She was treated as seronegative RA with methotrexate (MTX) and prednisolone. Since the effect of MTX was poor, she was administered of certolizumab pegol. While maintaining low disease activity, she suddenly had swelling, local heat of her right knee joint in April 2018. Synovial fluid of right knee joint was negative for bacteria and Mycobacterium culture tests and no crystals were detected. She was injected methylprednisolone acetate into her right knee joint, but symptoms did not subsidence. So she underwent surgical synovectomy. At that time, titer of anti CCP antibody in serum and synovial fluid were 423 U/mL and 379 U/mL, respectively and RF was 243 IU/mL in serum. **Clinical significance:** Anti CCP antibody titer is not considered to reflect the disease state and there are few reports on changes over time. We report a rare case where titer of anti CCP antibody were negative and disease activity worsened during treatment with anti TNF inhibitor and the antibody titer has changed to positive.

P3-011

A case of rheumatoid arthritis initiated by focal bronchiectasis

Hideyasu Sugimoto^{1,2}, Masaki Yoshizawa³

¹Respiratory Medicine, Yamato Tokushukai Hospital, ²Respiratory Medicine, Shonan Kamakura General Hospital, ³Department of Rheumatology, Shonan Kamakura General Hospital

Conflict of interest: None

[Case] 66 years old, male (nonsmoker) [clinical course] Blood sputum appeared in March two years ago, The bronchiectasis was pointed in the left lung basal segment as a sequela of pneumonia suffered in childhood. The bronchial artery embolization was performed twice for recurrent blood sputum in November last year, but not effective. Polyarthrits suddenly appeared in June and RF/anti-CCP antibody were strongly positive, so we diagnosed as rheumatoid arthritis (RA) by ACR/EULAR 2010 classification criteria. Before using DMARDs left lung basal segment resection was performed in August in consideration of risk of infection exacerbation. Histopathological findings of resected lungs widely recognized the findings of follicular bronchiolitis with lymphoid follicles developed around the bronchi. We started MTX from 2 months after surgery and are maintaining remission. [Discussion] It is reported that ACPA, which plays an important role in the pathogenesis of RA, is produced in lymphoid follicles in the lungs. In this case, it was confirmed that RF was high titer before arthritis symptoms occurred, and it was inferred that immune abnormality such as ACPA production preceded the onset of RA, and pathological findings also showed RA onset concerned with bronchiectasis.

P3-012

The role of Formyl Peptide Receptor 2 (FPR2) + CD4⁺ T cells in rheumatoid arthritis

Isao Murakami¹, Kosaku Murakami¹, Akiko Yoshida¹, Takashi Usui¹, Shuji Akizuki¹, Ran Nakashima¹, Motomu Hashimoto², Hajime Yoshifuji¹, Masao Tanaka², Koichiro Ohmura¹, Tsuneyo Mimori¹

¹Department of Rheumatology and Clinical Immunology, Kyoto University Hospital, Kyoto, Japan, ²Rheumatic Disease Center, Kyoto University Hospital, Kyoto, Japan

Conflict of interest: None

[Object] FPR2 is the receptor of Resolvin and Lipoxin A4, which are collectively called Specialized Proresolving Mediators (SPMs). Our study aim is to clarify the role of FPR2⁺ CD4⁺ T cells in RA. [Methods] Peripheral blood was collected from RA patients and healthy controls. The surface expression of SPM receptors (FPR2, BLT1, CMKLR1) on

white blood cells was analyzed by flow cytometry. Peripheral blood mononuclear cells (PBMCs) and naïve CD4⁺ T cells from healthy controls were stimulated in vitro and FPR2 expression was examined. We also examined the influence of Resolvin D1 on the production of IFN γ from CD4⁺ T cells in PBMCs stimulated by α CD3/ α CD28. [Results] The expression of FPR2 on T cells was high in part of RA patients. FPR2 expression of CD4⁺ T cells from ESR-high RA patients tended to be higher than from ESR-low patients. After PBMCs from healthy controls were stimulated in vitro by α CD3/ α CD28, FPR2 expression of CD4⁺ T cells were elevated. Addition of Resolvin D1 decreased the production of IFN- γ from CD4⁺ T cells in PBMCs stimulated by α CD3/ α CD28. Naïve CD4⁺ T cells were differentiated to Th0 and Th1, but FPR2 was not expressed in those cells. [Conclusions] FPR2⁺CD4⁺ T cell possibly plays a certain role in RA.

P3-013

Successful use of colchicine for treating a case of polyarthritis with MEFV mutation

Suzuna Sugi, Naomi Yoshida, Daisuke Wakasugi, Satoshi Yamasaki, Munetoshi Nakashima

Division of Rheumatology, Kurume University Medical Center, Fukuoka, Japan

Conflict of interest: Yes

An 82-year-old man visited our hospital because of joint swelling of the hand and feet with tenderness in the proximal extremities. Tests for both rheumatoid factor and anti-citrullinated peptide antibody were positive, but synovitis was not observed upon ultrasonographic (US) examination of the joints. He was treated with 20 mg/day of prednisolone (PSL), which relieved his symptoms, and the PSL dose was reduced to 5 mg/day. 1 year and 4 months later, he experienced swollen and tender fingers of both hands. The PSL dose was escalated to 15 mg/day, with no response after 7 months of treatment. He met the EULAR classification criteria for rheumatoid arthritis (RA). Synovitis was detected by US but his symptoms were not typical of RA, as his clinical course was similar to polymyalgia rheumatica and the recurrent arthritis was refractory to 15 mg/day of PSL. We included familial Mediterranean fever as a differential diagnosis and started colchicine, which resolved his symptoms. US examination confirmed the resolution of synovitis. Gene analysis revealed two mutations, P369S/R408Q, in *MEFV*. Some reports shows colchicine or IL-1 β blockers are useful for treating RA with *MEFV* mutations. Our case also suggests that *MEFV* mutations modulated the RA disease process.

P3-014

Search for RA-susceptibility genes using genetic difference between RA children and non-RA parents

Marowa Hashimoto¹, Keiko Funahashi^{1,2}, Kosuke Okuda², Koji Fukuda³, Shinya Hayashi³, Tsukasa Matsubara^{1,2}

¹Research Institute of Joint Diseases, Kobe, Japan, ²Matsubara Mayflower Hospital, Kato, Japan, ³Department of Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan

Conflict of interest: None

[Object] It seems that analyzing genome between parent and child to search for disease-susceptibility genes is useful because of similarity in both genetic backgrounds. In this study, we searched for RA-susceptibility genes by analyzing genome using genome wide association study (GWAS) among RA children and non-RA parents. [Methods] The subjects were 9 RA children and the each 9 non-RA parents. Illumina HumanHap300K or HumanOmniExpress chip were used for genotyping. SNPs used in this study were common among these chips and were 178,753 SNPs. Case-control study was carried out between RA children and non-RA parents using Chi-Squared test in Recessive Model. [Results] As the result of GWAS, rs959976 ($p = 10^{-3.2}$) on *TRPA1* (Transient Receptor Potential cation channel, subfamily A, member 1) was found among SNPs with comparative lower P value. Rs959976 on *TRPA1* was missense mutation with amino acid substitution (p. His1018Arg). [Conclusions] It has been suggested that the expression of TRPA1 on peripheral blood leukocytes correlate with RA progression. Thus, rs959976 on

TRPA1 may also be involved in the onset of RA. We will continue to search for RA-susceptibility genes by increasing sample sizes.

P3-015

Study of the factor which has on influence on the rheumatoid arthritis synovium

Koji Tateishi¹, Ken Takebe¹, Yasuhiro Terashima¹, Noriaki Yo², Takashi Yamane², Teppei Hashimoto³

¹Department of Orthopaedic Surgery, Kohnan Kakogawa Hospital, ²Kakogawa City Hospital Organization, ³Hyogo College Of Medicine

Conflict of interest: None

[Object] In late years disease control of the rheumatoid arthritis (following RA) is improved drastically by the spread of biological preparation. It is not a rare case which only a single joint pain remains in even if we gave the medical treatment with any drug are not only rare. Because I weighed the factor which has an influence on the synovium in the arms joint of RA and the lower leg joint, I report it. [Methods] The synovial membrane samples were obtained from 17 wrist joints undergoing wrist synovectomy surgery and 17 knee joints undergoing knee arthroplasty. We evaluated CRP, DAS-28, MMP-3, RF, ACPA, having MTX or not, PSL dose. The evaluation of the RA synovium checks many cell surface antigens emerging on Rooney score and the antigen presenting cell surface. [Results] There was no significant difference between two groups except CD56, CD34. [Conclusions] It has been already reported that sustained positive of the bloodstream in the intraarticular synovium appears from the early stage when joint swelling is not apparent to there being an association between progress of a bone, the joint destruction and it and the bloodstream in the synovium. It is thought that a further study will be necessary in future based on this findings.

P3-016

Role of ADAM12 and regulation by miRNA-29b in synovial cell proliferation of rheumatoid arthritis

Masahito Watanabe¹, Keiichiro Nishida¹, Yoshihisa Nasu², Ryuichi Nakahara³, Hideki Ohashi¹, Shunji Okita¹, Yohei Kiso¹, Minami Matsushashi¹, Toshifumi Ozaki¹

¹Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Japan, ²Department of Medical Materials for Musculoskeletal Reconstruction, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Japan, ³Department of Intelligent Orthopaedic System, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Japan

Conflict of interest: None

[Introduction] ADAM12 is a member of a disintegrin and metalloproteinase family and has been reported to participate in the development of variety of tumors by degrading ECM and shed precursors, thus promoting cell proliferation, invasion and metastasis. ADAM12-L is a direct target of the miR-29 families in breast cancer. In the current study, we investigated the expression of ADAM12-L in synovial tissue of rheumatoid arthritis (RA), and examined the potential role of miRNA-29b in regulation of ADAM12. [Methods] The expression of ADAM12-L in RA synovium was examined by immunohistochemistry. The cultured synovial fibroblasts obtained from RA patients at the surgery (RASf) were stimulated by TNF- α and IL-6, and the expression of ADAM12-L was examined by real-time PCR. The expression of ADAM12-L, HDAC4, CDK4 and CDK6 was examined by real-time PCR after miR-29b transfection. [Results] ADAM12-L was highly expressed in RA synovial tissue. Stimulation by TNF- α resulted in upregulation of ADAM12-L, HDAC4 and CDK6 in RASf. Transfection of miR-29b mimics decreased mRNA levels of ADAM12-L, HDAC4 and CDK6 in RASf. [Conclusion] ADAM12-L might be involved in the cell proliferation of RASf. miR-29b might have a role in the reduction of cell proliferation via regulation of ADAM12-L, HDAC4 and CDK6.

P3-017

A case of rheumatoid arthritis on maintenance hemodialysis relapsed with the arteriovenous fistula side arthritis

Koji Harada

Department of Nephrology, Diabetes and Renal Replacement Therapy, Nishinara Central Hospital, Nara, Japan

Conflict of interest: None

Case report: 76 year-old man was diagnosed as rheumatoid arthritis (RA) at the age of 72 and disease activity was stable with salazosulfapyridine (SASP). Hemodialysis (HD) was initiated due to polycystic kidney disease at the age of 74. Then, SASP was discontinued by skin eruption and prednisolone 7.5 mg/day was administered. Refractory arthritis in arteriovenous fistula (AVF) side was continued and celecoxib was added. Because disease activity management was difficult, abatacept (ABT) was started. After the administration of ABT arthritis was disappeared and prednisolone could be discontinued. However, uncontrolled arthritis in AVF side was appeared after 5 months. ABT was switched to tocilizumab (TOC), however, uncontrolled AVF side arthritis was relapsed 5 months after the switch to TOC. Golimumab was started, and then disease activity has been steady. Conclusion: A case of RA on maintenance HD relapsed with the arteriovenous fistula side arthritis has not been reported previously and we report this case with literature review of clinical feature of dialysis patients with RA.

P3-018

Two cases of Rheumatoid Arthritis Manifested as Monoarthritis

Hiroo Hashimoto¹, Kiichi Koumoto¹, Kazuhiko Moriwaki¹, Fumio Otsuka²

¹Internal Medicine, Innoshima General Hospital, Onomichi, Japan, ²Department of General Medicine, Okayama University Hospital

Conflict of interest: None

Case 1: 73-yo male had suffered left elbow pain and swelling since Jan 201X. RF: 27 IU/ml, CCP-Ab: 86.8 U/ml, CRP: 1.5 mg/dl. MRI detected bone erosion, bone marrow edema and synovial membrane swelling in the left elbow joint. Ultrasonography showed synovial membrane swelling of the left elbow, meeting classification criteria: 5/10. Since the patient was diagnosed as RA, PSL (5mg), MTX (8mg/w) and Igaratimod (25mg) were administered. Case 2: 71-yo female had suffered right knee joint pain and swelling, and had left elbow joint and forearm pain since Jun 201X. RF: 15 IU/ml, CCP-Ab: 12.1 U/ml, CRP: 5.2 mg/dl. MRI showed destruction of medial meniscus and anterior cruciate ligament in the right knee and detected bone sclerosis and osteophytes. Ultrasonography showed swelling of synovial membrane in bilateral knee, right 3,4-MCP and 4-PIP joints. She also suffered left knee, right 3,4-MCP and 4-PIP joints pain and swelling, meeting classification criteria: 5-7/10. Since RA, osteoarthritis, destruction of medial meniscus and anterior cruciate ligament were detected, PSL (5mg) and salazosulfapyridine (0.5g) were administered. Conclusion: We report two elderly RA cases manifesting monoarthritis, by showing the differential diagnosis and clinical significance based on the literature.

P3-019

Discrepancy between ultrasound and clinical assessment of enthesitis in patients with psoriatic arthritis

Yutaro Yamada^{1,2}, Kentaro Inui¹, Tadashi Okano¹, Koji Mandai^{1,3}, Kenji Mamoto¹, Yuko Sugioka⁴, Tatsuya Koike⁴, Chiharu Tateishi⁵, Daisuke Tsuruta⁵, Hiroaki Nakamura¹

¹Department of Orthopedics, Osaka City University Graduate School of Medicine, ²Department of Orthopedics, Yodogawa Christian Hospital, ³Department of Orthopedics, Osaka Social Care Center, ⁴Center for Senile Degenerative Disorders (CSDD), Osaka City University Graduate School of Medicine, ⁵Department of Dermatology, Osaka City University Graduate School of Medicine

Conflict of interest: None

[Object] Psoriatic arthritis is classified by CASPAR which requires

arthritis, spondylitis and enthesitis on basis. The enthesitis assessed by physician has somewhat variance. On the other hand, ultrasound examination (US) is sensitive and easy to evaluate enthesitis. We investigated the utility of US for assessing enthesitis in patients with PsA. [Methods] 47 patients with PsA had US at humeral medial epicondyle, triceps, distal quadriceps, proximal/distal patella, Achilles tendon and plantar fascia. These entheses are clinically evaluated by tenderness. US and clinical evaluation are compared. Their associations with disease activity and axial symptoms were investigated. [Results] 37 patients showed US enthesitis and 23 patients showed clinical enthesitis. There was no correlation between them ($r=0.15$, $p=0.30$). DAS28-CRP was associated with clinical enthesitis ($r=0.45$, $p=0.001$), but not with US enthesitis ($r=-0.07$, $p=0.63$). Both US ($r=-0.24$, $p=0.125$) and clinical enthesitis ($r=0.02$, $p=0.90$) were not associated with axial symptoms. [Conclusions] US can detect potential inflammation in the entheses without tenderness. Since this study is cross-sectional, we will investigate association between progression of joint destruction and them prospectively.

P3-020

Significance of MMP-3 in patients with psoriatic arthritis and inflammatory bowel disease related arthritis

Hitoshi Yoshimura¹, Kentaro Inui², Tadashi Okano², Koji Mandai⁵, Yutaro Yamada⁶, Daisuke Tsuruta⁷, Chiharu Tateishi⁷, Yuko Sugioka³, Tatsuya Koike^{3,4}, Hiroaki Nakamura²

¹Department of Orthopaedic Surgery, Osaka Saiseikai Nakatsu Hospital, ²Department of Orthopaedic Surgery, Osaka City University Graduate School of Medicine, ³Department of Orthopaedic Surgery, Center for Senile Degenerative Disorders, Osaka City University Medical School, Osaka, Japan, ⁴Department of Orthopaedic Surgery, Search Institute for Bone and Arthritis Disease, Wakayama, Japan, ⁵Department of Orthopaedic Surgery, Osaka Social Medical Center, Osaka, Japan, ⁶Department of Orthopaedic Surgery, Yodogawa Christian Hospital, Osaka, Japan, ⁷Department of Dermatology, Osaka City University Graduate School of Medicine

Conflict of interest: None

Purpose: Although psoriatic arthritis (PsA) and inflammatory bowel disease related arthritis (IBD-SpA) are classified as spondyloarthritis (SpA), difference of clinical features is not well understood. The purpose of this study is to compare the clinical features of PsA with IBD-SpA, and to clarify the significance of MMP-3 in SpA. **Methods:** One hundred and eighty nine patients with PsA and 81 with IBD-SpA were referred to our department to evaluate musculoskeletal symptoms. Classifications of PsA and IBD-SpA were performed using CAPAR and ASAS criteria with musculoskeletal ultrasounds. Proportion of peripheral, axial and mixed disease, swollen joint counts (SJC), tender joint counts (TJC), DAS-28CRP and blood examinations (RF, ACPA, MMP-3) were evaluated. **Results:** Among referred patients, 116 patients were classified as SpA (PsA: 81, IBD-SpA:35). There was no significant difference between SpA and non-SpA in MMP-3 positivity. Proportion of disease type was significantly different between PsA and IBD-SpA (PsA: per 90.1 ax 8.6, IBD-SpA: per 57.1 ax 17.1%; $p<0.01$). There was weak but significant correlation between MMP-3 and SJC in PsA. **Conclusions:** Proportion of peripheral disease was significantly common in patients with PsA. There was significant correlation between MMP-3 and SJC in PsA.

P3-021

Correlation with body mass index and musculoskeletal condition in patients with psoriasis

Koji Mandai¹, Kentaro Inui², Tadashi Okano², Yutaro Yamada^{2,3}, Daisuke Tsuruta⁴, Chiharu Tateishi⁴, Hitoshi Yoshimura⁵, Yuko Sugioka⁶, Tatsuya Koike^{6,7}, Masahiro Tada⁸, Hiroaki Nakamura²

¹Department of Orthopaedics, Osaka Social Medical Center, ²Department of Orthopedics, Osaka City University Graduate School of Medicine, ³Department of Orthopaedic, Yodogawa Christian Hospital, ⁴Department of Dermatology, Osaka City University Graduate School of Medicine, ⁵Department of Orthopaedics, Osaka Saiseikai Nakatsu Hospital, ⁶Center for Senile Degenerative Disorders, Osaka City University Graduate School of Medicine, ⁷Department of Orthopaedic, Search Institute for Bone and Arthritis Disease, ⁸Department of Orthopaedic, Osaka City General Hospital

Conflict of interest: None

[Object] We investigated the correlation with body mass index (BMI) and musculoskeletal condition in patients with psoriasis (PsO). [Methods] Overall, 48 patients with PsO and 46 patients with Psoriatic Arthritis (PsA) were referred to our department to assess Spondyloarthritis (SpA) from department of dermatology. Diagnosis of PsA was performed using the CASPAR criteria, assisting with ultrasound. The patients were evaluated for Psoriasis Area and Severity Index (PASI), BMI, DAS28-CRP, biologics use, Psoriatic Arthritis Screening and Evaluation (PASE). [Results] The mean age was 58.4 ± 14.7 years, women 36%, mean DAS28-CRP was 2.6 ± 1.3 , Biologics was using in 27 (29%). The mean BMI was 23.9 ± 4.3 in PsA, 24.4 ± 4.3 in PsO ($p=0.59$). The median PASI score was 4.65 (2.1, 8.7) in PsA, 8.7 (2.7, 13.1) in PsO ($p=0.09$). Biologics was using 40% in PsA, 17% in PsO ($p=0.02$). There was no independent factor of BMI in multiple regression analysis. [Conclusions] There was no significant difference in BMI between PsA and PsO, and among PsA patients, there were no correlation between BMI and DAS28-CRP.

P3-022

Functional impairment measurement in psoriatic arthritis in real world

Shoko Tateishi^{1,2}, Hiroko Kanda^{1,2}, Mariko Inoue^{1,2}, Kumiko Ono³, Jun Hirose⁴, Ayumi Yoshizaki⁵, Yoshihide Asano⁵, Shinichi Sato⁵, Sakae Tanaka⁴, Keishi Fujio²

¹Department of Immunotherapy Management, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, ²Department of Allergy and Rheumatology, The University of Tokyo Hospital, ³Department of Joint Surgery, The Institute of Medical Science The University of Tokyo, ⁴Department of Orthopaedic Surgery Faculty of Medicine, The University of Tokyo Hospital, ⁵Department of Dermatology and Photolaser Medicine, The University of Tokyo Hospital

Conflict of interest: Yes

[Objective] We use HAQ-DI, BASFI and SF 36 (PCS) to assess functional impairment in Psoriatic arthritis (PsA). but these measurements are not developed for PsA. We evaluated about these functional measurements in PsA in the real-life. [Methods] Enrolled fifty-four patients with PsA were classified into with ($n=26$) or without ($n=28$) biologics. We compared with change rate of clinical assessment: TJ, SJ, enthesitis, dactylitis, skin, ASDAS, BASMI and functional measurements with or without biologics. And we also assessed correlation between clinical feature and functional measurements. [Results] Clinical feature, skin, peripheral and axial feature were improved with biologics. But three functional measurements were not significantly improved. The strength of correlation was $HAQ>BASFI>SF36$ (PCS). There was no correlation between CRP, skin, dactylitis and HAQ. [Conclusions] In real world, HAQ was more useful in functional measurement in PsA.

P3-023

Partially retrospective observational special drug-use investigation to evaluate long-term safety and efficacy of secukinumab in psoriasis vulgaris and PsA patients- interim analysis

Kazuko Matsumoto
Novartis Pharma.K.K.

Conflict of interest: Yes

[Object] Surveillance objective was to collect partially retrospective data on the long-term safety and efficacy of secukinumab subcutaneous injection in clinical use in psoriasis vulgaris (PsV) and PsA patients in whom this product was started before the conclusion of a contract for surveillance [Methods] This study included patients with PsV or PsA who were not adequately responding to conventional therapies and then received secukinumab for the first time between the market release and the conclusion of the surveillance contract and until April 30, 2016 [Results] 167 patients were assessed as safety set (average period of observation \pm SD: 327.2 ± 68.25 days). The overall incidence rate of adverse reaction was 19.16%. Nasopharyngitis, oral candidiasis and psoriasis were observed in 4 patients each as most frequent adverse reaction. Serious adverse reactions were noted in 9 (5.39%) of 167 patients in the

safety analysis population. In all cases, the patients recovered or were recovering from the events. At W24, the rate of PASI change (average±SE) from baseline was $-84.58 \pm 2.84\%$ (88 patients). VAS change of patient and doctor were -39.5 ± 8.49 (10 doctors), -34.6 ± 13.21 (11 patients), respectively. [Conclusions] Since this report is based on interim data, the results has not been discussed.

P3-024

A case of acute exacerbating psoriasis vulgaris and onset of psoriatic arthritis by cutaneous infection

Misaki Yoshida, Hiromi Nuka, Kunihiro Ogane, Hideo Araki
Department of Nephrology and Rheumatology, Fukui Prefectural Hospital

Conflict of interest: None

A 49-year old man was hospitalized for cutaneous infection, acute exacerbating psoriasis vulgaris and onset of psoriatic arthritis. He was diagnosed as psoriasis vulgaris by skin biopsy 30 years ago. A week after he injured his right leg, he had exacerbated psoriasis and onseted of multiple joint pain. He was diagnosed as acute exacerbating psoriasis vulgaris, onset of psoriatic arthritis and cutaneous infection. He was administered antibacterial drugs. After infection improvement, he was administered Steroidal anti-inflammatory agent, Non-steroidal anti-inflammatory drug and PDE4 inhibitor. Psoriasis was improved, but a right shoulder pain persisted, so he was administered Infliximab. His shoulder pain improved after Infliximab administration and was discharged. This case was stable psoriasis with skin lesion only for 30 years from diagnosis. But he was exacerbated psoriasis and onset of psoriatic arthritis by cutaneous infection. Infection was reported as an environmental factor of psoriatic arthritis. Because TNF α production is promoted in blood infection, it was suggested that possibility of involvement of TNF α in the acute exacerbated psoriasis vulgaris and onset of psoriatic arthritis after infection. I also report that Therapeutic effect with TNF α inhibitor in this case.

P3-025

High frequency of HLA-B40 (B60, B61), B54 and B46 among 12 patients with axial spondyloarthritis exhibiting bamboo spine

Akihiro Toujima, Ai Suzue
Department of Internal Medicine, Anankyo Hospital Tokushima Prefectural Federation of Agricultural Cooperatives for Health and Welfare

Conflict of interest: None

[Object] We examined the effects of the presence of the HLA-B alleles on the progression of spinal lesions in patients with different types of axial spondyloarthritis, such as the ankylosing spondylitis and axial psoriatic arthritis treated at our hospital. [Methods] We examined the clinical features of 12 patients who exhibited bamboo spine and the patients with the same HLA-B variant allele, among 72 patients diagnosed with axial-SpA at our hospital. [Results] Among the 72 patients with axial-SpA, we found 29 with B61, indicating an overall high frequency at 40.2%. Nine out of the 12 patients with bamboo spine were positive for B60 and B61, the major subtypes of B40, whereas 5 patients were positive for B54, and 4 for B46. Among the 72 patients with axial-SpA, HLA-B (54,61) was observed in 6 patients, HLA-B (51,61) in 5 patients, HLA-B (35,61) in 4 patients, and HLA-B (7,51) in 4 patients. These patients were diagnosed with axial PsA or SAPHO syndrome, and b-DMDARD and NSAIDs were effective in these patients. [Conclusions] Based on our findings, it is possible that HLA-B40 (60, 61), found at a high frequency in axial-SpA, and B51, B54, and B7 that are known to be the susceptibility genes of other autoimmune diseases in Japanese people, may contribute to the severity of spinal lesions.

P3-026

Characteristics of the patients with Spondyloarthritis (SpA) in our division

Hitoshi Kodera, Yoshifuji Matsumoto
Kuwana City Medical Center

Conflict of interest: None

[Background] The prevalence of SpA in Japan is thought to be higher than previously reported. There may be some SpA patients without appropriate diagnosis. [Object] To analysis the characteristics of SpA patients (including SAPHO syndrome) diagnosed in our division. [Results] The axSpA was 23 cases, the average age at diagnosis was 44.3 years old (female 69.6 %). The frequency of AS among axSpA was 34.8 %, the average age at diagnosis was 36.8 years old (female 37.5 %). HLA was checked in 52.2 % of patients in the axSpA, of which 75 % were positive. The PsA was 8 cases, the average age at diagnosis was 60.1 years old (female 50 %). The uSpA was 5 cases, the average age at diagnosis was 50.6 years old (female 80 %). The IBD-SpA was 4 cases, the average age at diagnosis was 41 years old (female 50 %). The ReA was 2 cases, the average age at diagnosis was 37 years old (female 0 %). The SAPHO was 8 cases, the average age at diagnosis was 48.1 years old (female 12.5 %). Coexistence of fibromyalgia was found in 26 % of all cases. [Conclusions] The clinical feature of the SpA in our division tended to differ from previously reported cases. This may suggest the possibility of some undiagnosed patients in our area, and the necessity of appropriate collaboration among medical divisions.

P3-027

Ankylosing spondylitis or SAPHO syndrome? A case with remarkable bone erosion and osteoproliferative lesion of the sacroiliac, sternoclavicular joint

Toshihide Shuto
Department of Orthopedics and Rheumatology, Chiyoda Hospital, Miyazaki, Japan

Conflict of interest: None

[Clinical relevance] It is sometime difficult to distinguish SAPHO syndrome from ankylosing spondylitis (AS) without skin lesion. Here we report a case in which it is difficult to distinguish AS and SAPHO syndrome with remarkable bone erosion and osteoproliferative lesion on both sides of the sacroiliac joint and sternoclavicular joint. [Case] Male in his 30s. complained back pain, bilateral knee and shoulder pain appearing about 3 years before the initial visit to our department. Pain was gradually increased, leading to his disability. Very high inflammatory reaction was pointed out, and he was admitted to our department. He showed restriction of thoracic expansion, restriction of the range of motion of the spine. X-rays/CT showed bone proliferative changes accompanied by marked bone erosion on the sternoclavicular joint and sacroiliac joint, and both sacroiliac joints were ankylosed. In addition, unilateral non-marginal syndesmodi was found between L1/2 and the facet joints were bilaterally ankylosed with bony hyperostosis, but vertebral body was not ankylosed. He met both the modified New York criteria of AS and the classification criteria of SAPHO of Benhamou. Infliximab with csDMARDs lessened his inflammation, back pain and arthralgia.

P3-028

Respiratory function and human leukocyte antigens in diffuse idiopathic skeletal hyperostosis

Taketoshi Yasuda, Hiraku Motomura, Isao Matsushita, Yoshiharu Kawaguchi, Tomoatsu Kimura
University of Toyama, Faculty of Medicine

Conflict of interest: None

[Object] In the spine, the bone formation in diffuse idiopathic skeletal hyperostosis (DISH) is sometimes resembles ankylosing spondylitis (AS). The purpose of this study is to investigate the ankylosing level, respiratory function and type of human leukocyte antigen (HLA) in DISH patients to clarify similarities and differences between DISH and AS. [Methods] Nine patients who are satisfied the Resnick criteria for spinal DISH and similar spine ankylosis to AS were enrolled in this study. All cases are male, the average age was 76.3 years old. The level of ankylosis, loss of chest expansion, type of airway disorders and HLA type are investigated in DISH. The respiratory function was examined in % vital capacity (% VC) and forced expiratory volume 1.0 second % (FEV1.0%). [Results] The ankylosing levels were from T2 to L2 in all cases. The loss of chest

expansion was recognized in all cases. Regarding with respiratory function, the average of %VC was 87.7% and the average of FEV1.0% was 75.4%, respectively. The types of airway disorder were normal in 3, restrictive in 6 and obstructive in 1. HLA-B27 was recognized in only 1 case. [Conclusions] DISH and AS were similar in spinal ankylosis and respiratory disorders. These findings may be suggested the presence of AS carry over in DISH.

P3-029

Ankylosing spondylitis with femoral head osteonecrosis treated by vascularized fibular graft and anti-TNF antibody preparation: a case report

Kohei Naito¹, Akihiro Fukui¹, Takuro Ozaki²

¹Department of Orthopedics, Nishinokyo Hospital, ²Department of Rheumatology, Nishinokyo Hospital

Conflict of interest: None

[Introduction] A case report: Ankylosing spondylitis with femoral head osteonecrosis treated by vascularized fibular graft and anti-TNF antibody preparation [Case Presentation] A thirty seven year old male in for consultation due to low back pain and hip pain. X-ray showed ankylosing spondylitis. MRI showed aseptic osteonecrosis of femoral head. He was treated with vascularized fibular graft and anti-TNF α antibody preparation (adalimumab, infliximab) with MTX. Patient keeps good condition for four years after two treatments.

P3-030

Two female cases of Andersson lesion of SpA

Kazuhiro Hatta, Hiroyuki Akebo, Hirofumi Miyake, Ryuichi Sada, Hiroyasu Ishimaru

Department of General Internal Medicine, Tenri Hospital

Conflict of interest: None

Case1. A 59-year-old female came to our OPD clinic because of further exam of subtle CRP elevation. Physical Exam were almost within normal limit except for decreased chest expansion. In addition to Chest x-ray, abdominal x-ray was taken, it showed Andersson lesion in her lumbar spine. Case2. A 60-year-old female was transferred to our OPD because of lumbago relieved with corticosteroid was thought to due to collagen disease. X-ray examination revealed Andersson lesion. Andersson lesion was rare complication of SpA. Among seemingly male dominant SpA, we experienced two female cases of Andersson lesion. Moreover, keys to the correct diagnosis were very suggestive and instructive in real clinical situation in both cases.

P3-031

A case of pustulotic arthro-osteitis who exhibited multiple paradoxical reactions to TNF-alpha inhibitors and was treated with secukinumab

Tatsuo Mori, Naoto Yokogawa, Naoki Tanomogi, Masahiro Iida, Yusuke Nakamichi, Shuhei Sano, Michiru Kina, Nanase Honda, Eisuke Takamasu, Kae Onishi, Yuji Miyoshi, Takayasu Kise, Masako Utsunomiya, Yoshiki Nagai, Kota Shimada, Shoji Sugii

Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan

Conflict of interest: None

Case: a 53-year-old woman with pustulotic arthro-osteitis. She started infliximab (IFX) at age 49. From the age of 50 psoriasis-like rash as a paradoxical reaction appeared. IFX was switched to adalimumab (ADA). Multiple oral ulcers, abdominal pain, diarrhea appeared. Gastroscopy revealed longitudinal multiple ulcers at esophagus. Drug-induced inflammatory bowel disease due to ADA was suspected. ADA was stopped and gastrointestinal symptoms relieved. At the age of 52, certolizumab pegol was started against aggravation of arthritis. Multiple oral ulcers again appeared. We started secukinumab for her arthritis. Her axial arthritis and skin rash improved without adverse events. Discussion: Imbalance of cytokines is assumed as a mechanism of paradoxical reaction of biological

products (Toussiro et al.) In our case two paradoxical reactions made it difficult to continue TNF- α inhibitors. The second-line biologics against spondyloarthritis (SpA) is IL-17 inhibitor (van der Heijde et al.). There is no report using IL-17 inhibitors for SpA patient who can't use TNF- α inhibitor due to paradoxical reactions. This case suggests that IL-17 inhibitors are useful option for patients with SpA who can't use TNF- α inhibitors due to the paradoxical reaction.

P3-032

A case of SAPHO syndrome requiring differentiation from multiple myeloma

Masami Ogasawara, Satoshi Inotani, Tatsuki Matsumoto, Yoshiko Shimamura, Kosuke Inoue, Taro Horino, Yoshio Terada

Department of Endocrinology, Metabolism and Nephrology, Kochi Medical School, Kochi University

Conflict of interest: None

A 76-year-old Japanese male with half-year history of appetite loss, weight loss and stiffness of hands was admitted to our hospital. When he visited another hospital before admission, MGUS was diagnosed by bone marrow biopsy because of monoclonal gammopathy. Physical examination revealed polyarthralgia in the MP and PIP joints and deformities in the thoracic joints. Laboratory examination revealed the elevated level of CRP (7.5 mg/dL), negative rheumatoid factor and negative anti-CCP antibody. Serum and urine proteinogram detected monoclonal gammopathy (IgG κ) and BJP, respectively. Gallium scintigraphy and bone scintigraphy revealed abnormal accumulation in thoracic joints and spinal osteophytes. MRI showed high intensity signal in the thoracic joints. Based on above findings, SAPHO syndrome associated with MGUS was diagnosed. Treatment started with SASP 0.5 g / day and then continued at 1 g / day without relapse. Lots of diseases associated with arthralgia, such as blood diseases and autoimmune diseases, are found in diseases that recognize M protein. However, to our knowledge, there has been no report that M protein was confirmed in SAPHO syndrome. Herein we experienced a rare case of SAPHO syndrome associated with MGUS, so we will report including literature review.

P3-033

Evaluation of patients with psoriatic arthritis in Dermatology and Rheumatology

Natsumi Ikumi^{1,2}, Takamasa Nozaki¹, Hidetaka Shiraiwa¹, Hitomi Haraoka¹, Noboru Kitamura¹, Hideki Fujita², Masami Takei¹

¹Department of Rheumatology, Nihon University School of Medicine,

²Department of Dermatology, Nihon University School of Medicine

Conflict of interest: Yes

[Object] Psoriatic arthritis (PsA) has recently been seen in various clinical departments including dermatology, rheumatology or orthopedics. To determine if there are differences in treatment and disease activity in each department. [Methods] 36 PsA patients fulfilling the CASPAR criteria and attending a dermatology clinic and/or a rheumatology clinic during December 2017 to May 2018 were recruited. The characteristics, treatments, and disease activity of patients were compared using the Fisher's Exact test and t test. [Results] 12 patients with PsA in dermatology (D group), 10 patients in rheumatology (R group) and 14 patients in both departments (B group) were evaluated. The duration of psoriasis and PsA, the activity of arthritis were similar. A number of patients with PASI ≤ 3 in the R group had was significantly (50% vs. 90%, p value 0.04). The rate of achievement of PASI Clear in the B group was significantly lower compared to the D group and the R group (0% vs. 25% and 40%, respectively, p-value 0.02, 0.004). MTX was significantly more common treatment in the R group compared to the D group (42% vs. 90%, p value 0.01). [Conclusions] Although there was no significant difference in the disease activity of arthritis between treatment in dermatology and rheumatology in our study.

P3-034

The study of the therapeutic effect of IL-17A inhibitor on psoriatic arthritis

Takuya Izumiya, Yu Mori, Eiji Itoi

Department of Orthopaedic Surgery, Graduate School of Medicine, Tohoku University, Miyagi, Japan

Conflict of interest: None

[Objective] The aim of this study was to assess the efficacy of IL-17A inhibitors in Japanese patients with active psoriatic arthritis. [Methods] We retrospectively investigated 15 patients who fulfilled the Classification criteria for Psoriatic Arthritis (CASPAR) for the efficacy of IL-17A inhibitors. We assessed the visual analog scale (VAS) score, C-reactive protein-based disease activity score in 28 joints (DAS28), swollen joint count (0 - 66), tender joint count (0 - 68), health assessment questionnaire score and C-reactive protein level at baseline, week 24 and week 52. [Results] Of the 15 patients, 8 were male and 7 were female, with a mean age of 55.6 ± 2.6 years. In the group treated with IL-17A inhibitors, the tender joint count declined from 4.7 ± 2.1 to 1.5 ± 0.8 at week 24 and 1.3 ± 0.8 at week 52, the VAS score declined from 34 ± 6.4 to 32 ± 7.3 at week 24 and 23 ± 5.6 at week 52, and the DAS28 declined from 2.8 ± 0.5 to 2.1 ± 0.3 and 2.1 ± 0.2 at week 52. [Conclusion] Our study demonstrated IL-17A inhibitors are effective for the treatment of active psoriatic arthritis in Japanese patients.

P3-035

Clinical outcome of the anti-IL-17 inhibitor for patients with psoriatic arthritis

Akiko Suda, Yuji Uzawa, Yuji Yoshioka, Daisuke Kanai, Shohei Nagaoka
Yokohama Minamikyousai Hospital

Conflict of interest: None

[Object] To evaluate the efficacy and safety of anti-IL-17 monoclonal antibody in psoriatic arthritis (PsA) patients in our hospital. [Methods] Included in the present study were 10 patients followed up for at least 12 weeks of treatment with anti-IL-17 monoclonal antibody from March 2015 in our hospital, including 9 women (mean age: 58.4 years; mean duration of illness: 5.1 years). [Results] Onset of cutaneous manifestations occurred at a mean age of 40.3 years, whereas that of articular manifestations occurred at a mean age of 52.2 years. Seven patients were peripheral arthritis types, axial types were 3. The former preceded the latter by a mean of 15.7 years. The laboratory findings at the initial visit included a mean C-reactive protein level of 0.79 mg/dl. Drug therapy had been performed in all patients. The administered drugs were methotrexate in 8 patients, infliximab, adalimumab, and prednisolone in 3, and apremilast in 2. Cutaneous manifestations improved in all patient without one. The continuation rate at Weeks 12 and 24 was 72.7% and 54.5%, respectively. It was discontinued in one patient due to inefficacy and in 2 due to side effects, and another one patients due to request of patient. [Conclusions] Therapeutic responses were favorable in a real-world clinical setting.

P3-036

A case of psoriatic arthritis in which syndesmophytes appeared at the cervical spine C1 / 2

Shigeyoshi Tsuji¹, Mari Higashiyama², Jun Hashimoto¹, Tetsuya Tomita³
¹NHO Osaka Minami Medical Center, ²Nissay Hospital, ³Osaka University Orthopedic Biomaterial Science

Conflict of interest: None

Case A 58-year-old female Chief complaint limiting rotating range of motion of cervical vertebra Psoriasis developed at the age of 30 years. Posterior neck pain and cervical spine rotation disorder appeared at the age of 57years. The range of motion of the cervical vertebra was restricted markedly as 20 degrees of right rotation and 30 degrees of left rotation. ACPA negative, RF negative, CRP 0.01mg /dl, MMP3 67ng/ml in the blood biochemical test. A Xray image revealed an irregular image around the denth (C2). CT revealed syndesmophytes between C1/2. In MRI (STIR), high intensity change was observed in the C1/2 area, and

findings strongly suggesting synovitis or osteitis were observed. Clinical Significance It is reported that spondylitis emerges in approximately one third of cases of psoriatic arthritis. When restricting range of motion with rotation of the cervical region is recognized along with neck pain, it is necessary to conduct image search of the cervical spine C1/2 and perform appropriate therapeutic intervention to prevent ankylosing C1/2

P3-037

A case of psoriatic arthritis diagnosed as unexplained or somatoform disorder for a long period of time, with no rash other than nail lesion

Satsuki Aochi¹, Rieko Murakami², Saho Honda²

¹Japan Self Defense Forces Sapporo Hospital, ²JR Sapporo Hospital

Conflict of interest: None

Case 24-year-old female had pain in the neck, back, and lumber region exacerbating since teens. she visited various hospitals but it did not lead to the cause. So she was introduced to our department, at first she depressed in the nail of both hands and toes, there was line of the lateral groove, and a tenderness of an adhesion. However there was no typical psoriasis eruption besides the nail. Bone scintigraphy showed bilaterally asymmetric accumulation in the tendon attachment part and the sacroiliac joint lower part of 2/3. Think of psoriasis, we took her anti-TNF α formulation. After that, symptoms gradually improved. Clinical Significance Psoriatic symptoms cause ADL disorder, work disorder and markedly lower the patients quality of life. if the skin lesion of psoriasis is confirmed to the nail only as in this example, it is overlooked as unknown cause or mental illness. As a lessonful and rae example, report with some literature consideration.

P3-038

Early childhood-onset ankylosing spondylitis with ankylosis of cervical facet joint

Utako Kaneko¹, Naoki Kondo², Junichi Fujisawa²

¹Department of Pediatrics, Niigata University, Niigata, Japan, ²Division of Orthopedic Surgery, Niigata University, Niigata, Japan

Conflict of interest: None

Ankylosing spondylitis (AS) is a chronic rheumatic disease characterized by inflammation and structural changes in the axial skeleton. However, spine and sacroiliac joint involvement are seldom present in childhood and adolescent patients at disease onset. We present a very rare case of early childhood onset AS with rapid progress of ankylosis of cervical facet joint. A 5-years-old Japanese male was referred to our hospital due to neck pain. He was suffering from limited range of motion of cervical right rotation, and retroflexion. There is no abnormal finding on X ray radiography of cervical spine. MRI showed effusion and erosion of right atlanto-occipital joint and dens axis. Laboratory finding showed subtle inflammation. Initial diagnosis was retro-odontoid pseudo tumor, and he was followed by regularly assessment of X ray radiography of cervical spine. At the age of 6, ankylosis of cervical facet joint of C3 to C6 was observed in X ray radiography, and cervical CT scan. Furthermore, X ray radiography of sacroiliac (SI) joint showed osteosclerosis and obscuration. MRI findings of SI joint showed erosion and joint space dilatation. He was diagnosed as having AS, and started adalimumab, which induced improvement of clinical symptom and bone erosion.

P3-039

A clinical study of the assessment of the lesions of peripheral enthesitis and sternoclavicular arthritis by ultrasonography

Hirofumi Ohsaki

Internal Medicine, Ohsaki Clinic

Conflict of interest: None

[Object] There are the cases of causing the anterior chest pain in spondyloarthritis (SpA). Enthesitis are common conditions to SpA, but also SpA cases often go with the sternoclavicular arthritis. Therefore, I examined the relevance of Madrid Sonographic Enthesis Index (MASEI) score and sternoclavicular arthritis by ultrasonography. [Methods] The

subjects were SpA or SpA suspected cases (16 males, 79 females) who underwent joint ultrasonic examination at my clinic from June to September 2018. Tendon structure, bone erosion, bursitis, calcification, Power Doppler signal for peripheral entheses were examined and the MASEI score was calculated and sternoclavicular arthritis was evaluated. [Results] The sternoclavicular arthritis positive were 19 cases, the average MASEI score was 18.1, the score 18 or more were 52.6%. On the other hand, the cases of the sternoclavicular arthritis negative were 76 cases, the average MASEI score was 11.5, score 18 or more was 19.7%. [Conclusions] In this study, the number of cases with a MASEI score of 18 or more was 2.7 times that of cases with SpA or SpA suspected and those with positive sternoclavicular arthritis compared with negative cases. That the sternoclavicular arthritis and the peripheral enthesitis has some strong relevance was suggested.

P3-040

SAPHO syndrome complicated with multiple sclerosis successfully treated with IL-17 receptor antagonist, Brodalumab: A Case Report
Masahide Funabiki, Seiko Kondo, Naho Ayuzawa, Hidetoshi Yanagida
Department of Rheumatology, National Hospital Organization Utano Hospital, Kyoto, Japan

Conflict of interest: None

Case Report: 40 years-old male with 8-year history of optic neuritis and palmoplantar pustulosis was referred to us for neck pain and polyarthralgia persisted for 15 years. He had treated with oral NSAIDs, corticosteroid and MTX for 4 years without remission. He consulted our department of neurology for cervical cord lesion incidentally found in MRI. At the first visit, multiple pustules were observed at palms and soles. Wrists and knees were swollen and painful. Cervical ROM was restricted and the X-ray showed assimilation of C3-5 vertebrae. In sacroiliac MRI, bone marrow edema, JSN and synovial fluid retention were detected. Further, bone scintigraphy with ^{99m}Tc-HMDP demonstrated avid uptake in sternoclavicular joints and lower cervical to lumbar vertebrae. In laboratory test, CRP and ESR were elevated, RF and anti-CCP antibody were negative and HLA-B27 was positive. He was diagnosed with SAPHO syndrome complicated with multiple sclerosis (MS). For the presence of MS, Brodalumab was introduced. BASDAI improved from 5.3 to 1.3 at the 50th week after treatment. Aggravation of MS was not observed over the period. Conclusions: In case anti-TNF α inhibitor is contraindicated, anti-IL-17 receptor antagonist could be a potent therapeutic option for DMARDs resistant SAPHO syndrome.

P3-041

A case of SAPHO syndrome with the chief complaint of severe headache
Tamao Nakashita, Akira Yoshida, Akira Jibatake, Shinji Motojima
Rheumatology and Allergy, Kameda Medical Center, Kamogawa, Japan

Conflict of interest: None

The well-known osteoarticular lesions of SAPHO syndrome are sternoclavicular joint, sacroiliac joint, and pubic joint. However, when skull is involved, patients frequently complain of severe headache. We report a case of SAPHO syndrome whose chief complaint was severe headache. A case was 45 years-old woman. From half year before consultation she noticed low grade fever, weight loss and severe headache of left frontal region. She consulted with a neurosurgeon who recognized a subcutaneous tumor with a diameter of 3cm. FDG-PET showed melting skull, thickening of periosteum and meninges. PSL at the dose of 20mg was started and it was effective, but on tapering her headache relapsed. At this time, pustulosis on her hands, lumbar pain and pain on sternoclavicular joint developed. Biopsy of the tumor revealed thickening of meninges and inflammation was found. Dermatologist diagnosed as PPP and she was referred to us. We diagnosed her skull lesion as a manifestation of SAPHO syndrome. MTX was added and the symptom improved. We suggest that SAPHO syndrome should be included in a differential diagnosis of severe headache.

P3-042

Successful diagnosis and treatment of SAPHO syndrome with Diffuse sclerosing osteomyelitis of the Mandible (DSOM): a case report
Yuichiro Nakanishi¹, Takahiro Seno², Shunya Kaneshita², Kazuki Fujioka², Makoto Wada², Masataka Kohno², Yutaka Kawahito²
¹Internal Medicine, Kumihama Municipal Hospital, Kyoto, Japan, ²Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

Conflict of interest: None

[Rationale] A case is presented of SAPHO syndrome in a 39-year-old man suspected to have DSOM who was initially treated with prednisolone, and successfully treated with NSAIDs, methotrexate, bisphosphonate. After intervention and evaluation with the collaboration of physician and oral surgeon, prednisolone was gradually tapered. [Case] 39-year-old male was referred for swelling and pain of the right mandibular area due to osteomyelitis of the mandible. He had no family history of rheumatic and inflammatory diseases. Although culture test was negative, infectious osteomyelitis was initially suspected and he underwent a long-term antibacterial therapy and an oral surgical procedure, but it did not effective. After 4 years, he complained of pain and difficulty of swelling again. Bone scintigraphy revealed uptake for the right mandibular and the first right sternocostal articulation. He had acne, knee and heel and shoulder pain due to enthesitis. He was diagnosed as SAPHO syndrome. [Outcomes] NSAIDs and MTX therapy was started and it was effective, and it enabled to taper prednisolone. [Conclusion] Collaboration with dentists is important for diagnosis and evaluation of treatment in SAPHO syndrome with osteomyelitis of the mandible.

P3-043

A case of SLE that exacerbated with skin vasculitis and resulted in hemophagocytic syndrome and intestinal microperforation during treatment
Shiori Hiroumi, Yuka Hyodo, Kota Azuma, Yuko Kashihara, Makoto Terada
Itami City Hospital, Hyogo, Japan

Conflict of interest: None

[Case] A 40-year-old woman was diagnosed as SLE at 27-year-old and was taking PSL14 mg/day orally. From early March, exacerbations of exanthema were observed. In the biopsy pathology of skin lesions, there was clear formation of IgA, IgM, complement, and findings of SLE vasculitis were confirmed. Treatment with increasing PSL (20mg/day) and HCQ 300mg/day showed a tendency to improve eruption, but on 17 May, shivering and fever were recognized. There were no findings supporting infectious disease, but pancytopenia and high ferritinemia (13407ng/ml) were recognized. We diagnosed HPS associated with SLE and started administration of mPSL (500mg/day) and IVCY (500mg/m²). Treatment was successful and PSL gradually decreased progressively (PSL30mg/day), but on July 3, fever and shivering were recognized again, and free air was observed around the ascending colon mesencephalon at CT, suspected of supranuclear puncture, the same day operation was performed. Under intraoperative findings, there was no macroscopically apparent puncture site and intraperitoneal irrigation drainage was performed, and relief was performed only with conservative treatment. [Discussion] We report literature considerations on vasculitis, HPS and intestinal perforation with SLE.

P3-044

A case of autoimmune hypophysitis presenting as central diabetes insipidus associated with Systemic Lupus Erythematosus
Satoshi Kawai, Sho Ishigaki, Mayu Nagata, Yuto Takakura, Yoshiro Kanayama, Ryohei Nagata, Hiroshi Takei, Megumi Iwasaki, Ryo Hazue, Hiroaki Taguchi, Yasuo Ohsone, Yutaka Okano
Department of Rheumatology, Kawasaki Municipal Hospital

Conflict of interest: None

A 73-years-old woman noticed polyarthralgia in June X-1. Laboratory studies showed lymphopenia, positive anti-nuclear antibody, anti-DNA

antibody, and hypocomplementemia. So she was diagnosed as Systemic Lupus Erythematosus (SLE). She received prednisolone (PSL) 10mg/day and hydroxychloroquine 200mg/day and PSL was tapered to 5mg/day. But in April X, the patient admitted to our hospital with polydipsia and nausea. Gastro intestinal endoscopy and abdominal CT Scan didn't revealed any digestive system disease. After admission, Urine volume was 3900ml/day, and urinary osmotic pressure was 131mOsm/kg. MRI of the head demonstrated thickening of the pituitary stalk. 5% saline load test and vasopressin load test were positive. Because MRI with administration of gadolinium showed no findings of malignancy, we didn't histopathological examination. On the above mentioned results, she diagnosed autoimmune hypophysitis presenting as secondary central diabetes insipidus associated with SLE. The patient received methylprednisolone pulse therapy and followed by PSL 1mg/kg/day and oral desmopressin. Urine volume gradually decreased and this patient was able to discontinued desmopressin. Followed up MRI showed decreased size of the pituitary stalk. Autoimmune hypophysitis is rare complication with SLE.

P3-045

A case of SLE like symptoms presented during prostate cancer hormone therapy

Masahiro Minoda, Kiyoharu Muranaka
Suwa Central Hospital Chino, Nagano, Japan

Conflict of interest: None

[Case] A 75-year-old man presented to our hospital with facial erythema. He had received hormonal therapy with Leuproin and bicalutamide in the urology department for prostate cancer from 2 months ago. Three weeks before the visit, after working outdoors, he noticed face was flushing. On the patient's presentation to that hospital, he appeared mild erythema on both cheeks and livedo reticularis on both legs. No other abnormal findings were observed. Urine or blood cell abnormality was not observed, CRP 0.26 mg / dl, ESR 1 hour value 41 mm, no complement reduction, 40 times antinuclear antibody, 21 IU / ml anti-ds-DNA antibody, 8.6 U / ml anti-Sm antibody, SS-A antibody <1.9 U / ml and anti-RNP antibody <2.0 U / ml. Follow up with hormone therapy discontinuation and ray exposure avoidance. After that, the skin eruption gradually improved, and blood test reexamination was carried out 6 months later, anti-ds-DNA antibody <10 IU / ml was negative. [Clinical Significance] It is considered that autoantibody appears by the antiandrogen preparation and GnRH agonist as the suppression of the immune cell activity and that it is activated by light stimulation and transiently exhibited the SLE-like finding. We report SLE-like immune response accompanying prostate cancer hormone therapy.

P3-046

A case of recurrent strokes caused by APS and NPSLE

Aiko Hirano, Hiroaki Kusuoka, Hironori Inoue, Keitaro Saito, Aki Sakashita, Yu Isoda, Risa Sagawa, Kazuki Fujioka, Hidetake Nagahara, Makoto Wada, Masataka Kohno, Yutaka Kawahito
Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

Conflict of interest: None

A 62-year-old female diagnosed as SLE was treated with PSL 5mg/day and mizoribine. After herpes zoster infection, she had spike fever and leg edema. Renal biopsy showed type 3 (A/C)+5 lupus nephritis and we raised the dose of PSL to 50mg/day, but her symptoms didn't improve. Increase of the number of cells and proteins was seen in the cerebrospinal fluid and contrast-enhanced brain MRI showed multiple asymptomatic cerebral infarction, subarachnoid hemorrhage and meningitis simultaneously. So we diagnosed her as NPSLE and started administration of intravenous cyclophosphamide (IVCY) biweekly, but acute strokes still occurred. After we changed the antiplatelet treatment to an anticoagulant therapy, she suffered a massive brain hemorrhage, so we had to stop the anticoagulant therapy. However, after keeping the IVCY for 2 months, a new event didn't occur. In this case, the immunosuppressive therapy was effective for the cerebrovascular disease caused by APS and NPSLE. We report our experience along with some literature review.

P3-047

A case of reversibility occipital lobe leukoencephalopathy (PRES) of SLE patient

Takamasa Nozaki, Masashi Oshima, Yutaka Tanikawa, Shoei Yoshizawa, Hiroshi Tsuzuki, Yosuke Nagasawa, Kaita Sugiyama, Atsuma Nishiwaki, Natsumi Ikumi, Isamu Yokoe, Mitsuhiro Iwata, Hitomi Haraoka, Noboru Kitamura, Masami Takei

Division of Hematology and Rheumatology, Department of Medicine, Nihon University School of Medicine

Conflict of interest: None

The Patient is 28 years old woman. Two years ago, she was diagnosed with SLE by lupus nephritis, CNS lupus and pleurisy. She had a cold and legs edema in July. In August Hypertension (sBP150-180) and face edema appeared. She admitted with renal dysfunction, urine protein, urine occult blood for the medical treatment. Blood chemical analysis showed anti ds-DNA antibody (+), immunocomplex (+), reduce of complement activity and urine protein 5.93g/day. We diagnosed of rapidly progressive glomerulonephritis and nephrotic syndrome. We treated with steroid pulse therapy and prednisolone (PSL) of 1 mg/kg and plasma exchange. She developed convulsive seizure on day 30. MRI revealed abnormal signal level mainly on both sides occipital lobe. We continued same therapy, brain damage was remission on day 40. We diagnosed it with reversibility occipital lobe leukoencephalopathy (PRES) from progress. It was induced by renal damage, hypertension and CY. The patient became remission by mycophenolate mofetil afterwards. PRES is introduced by pregnancy, drug, hypertension, collagen disease, renal damage. There is few case reports which caused PRES treated with CY.

P3-048

SLE with anti RNP antibody positive may get worse by trimethoprim-sulfamethoxazole administration : 2 case reports

Tohru Nishizawa^{1,3}, Kai Imai^{2,3}, Minoru Shigesaka^{2,3}, Saki Tsujimoto^{2,3}, Nobuyasu Ishii^{1,3}, Akihiro Tanaka^{2,3}, Keiko Shimamoto^{2,3}, Hideki Amuro^{1,3}, Yonsu Son^{2,3}, Yoshio Ozaki^{2,3}, Shosaku Nomura³

¹Rheumatology and Clinical Immunology, Kansai Medical University Medical Center, ²Rheumatology and Clinical Immunology, Kansai Medical University Hospital, ³1st Department of Internal Medicine, Kansai Medical University

Conflict of interest: None

[Introduction] Trimethoprim-sulfamethoxazole (ST) often prescribe to SLE patients for PCP prevention. Some reports suggest that SLE with anti RNP antibody positive may get worse by ST administration. <Case 1> A 26-year-old female presented with fever and joint pain. She was diagnosed as SLE with lymphadenopathy, arthritis, pleuritis, lymphopenia and ANA positivity (RNP+). Prednisolone and ST were prescribed. Clinical course was improved, but on 9th day these symptoms got worse. Despite of steroid pulse, plasma exchange and MMF administration, clinical course was not improved. When ST was stopped, the symptoms improved on the next day. When ST was prescribed again, the same symptoms appeared within a few hours. <Case 2> A 25-year-old female presented with rash. She was diagnosed as SLE with fever, rash, lymphopenia, hypocomplementemia and ANA positivity (RNP+). Prednisolone was prescribed, and ST was done on-every-other-day. On 8th day, she had fever, headache and pantalgia intermittently. When ST was stopped, the symptom improved on the next day. These symptoms have not appear. [Consideration] The rash and bone marrow suppression are well known by the adverse effect of ST. When the SLE symptom with anti RNP antibody positive patient get worse, ST may be the etiology.

P3-049

A case of asymptomatic retinal vasculitis with systemic lupus erythematosus

Yumiko Mizuno, Masayuki Nishide, Akane Watanabe, Yuta Yamaguchi, Mayu Yagita, Yusuke Manabe, Takayoshi Morita, Yuichi Maeda, Hyota Takamatsu, Toru Hirano, Masashi Narazaki, Atsushi Kumanogoh

Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University

Conflict of interest: None

[Case presentation] A 37-year-old Japanese man was diagnosed with systemic lupus erythematosus (SLE) based on malar rash, wrist arthralgia, leukocytopenia, and positive anti-nuclear antibody and anti-double strand DNA antibody titers. He had no ocular complaints, however, ophthalmological examination prior to hydroxychloroquine (HCQ) therapy incidentally found retinal vasculitis. He was initially treated with 30 mg of oral prednisolone. However, he rapidly developed bilateral photophobia. A branch of the retinal vein was occluded. Moreover, headache and manic-depressive disorder appeared. We diagnosed that retinal vasculitis was highly active and exacerbated, complicated with neuropsychiatric SLE. Pulse methylprednisolone therapy and pulse cyclophosphamide therapy were performed, followed by oral prednisolone at 60 mg/day. Headache abated and his mental status stabilized. His photophobia resolved after 5 months. [Clinical importance] HCQ is widely used in SLE patients, and the number of patients with SLE who undergo ophthalmological screening has been increasing. Asymptomatic retinal vasculitis may be found in more SLE patients. Patients with abnormal eye findings should be closely followed even if asymptomatic, keeping in mind the possibility of neuropsychiatric SLE.

P3-050

A case of APS complicated by SLE who developed by migratory thoracoabdominal and back pain

Kazuma Nishisaka, Shinya Ichikawa, Kyosuke Abe, Goichi Kageyama
Department of Rheumatology, Hyogo Prefectural Amagasaki General Medical Center

Conflict of interest: None

A 23-year-old woman with chief complaint of left back pain, epigastralgia, vomiting, visited ER of our hospital. The contrast-enhanced CT has no abnormality. She was getting better with symptomatic treatment and discharged. But she revisited ER of our hospital again, with chief complaint of right thoracoabdominal pain and vomiting. She was diagnosed as possibly having SLE and APS from serological findings. We suspected that her migratory chest and abdominal pain may be caused by lupus serositis. However, there is no evidence supporting the existence of lupus serositis. An MRI examination of the brain showed multiple cerebral infarctions. We treated her with high dose glucocorticoid, intravenous cyclophosphamide, hydroxychloroquine, and aspirin. After the initiation of therapy, almost all symptoms disappeared. After reviewing the contrast-enhanced CT on admission, we recognized that she had the bilateral adrenal infarctions. We diagnosed that her migratory chest and abdominal pain was caused by adrenal infarctions. Although APS can cause thrombosis in both arteries and veins, there are few cases with adrenal infarction. We experienced a case of APS complicated by SLE which was difficult to diagnose adrenal infarction as a cause of migratory thoracoabdominal and back pain.

P3-051

Acute myocardial infarction in a patient with systemic lupus erythematosus and secondary antiphospholipid antibody syndrome

Shuji Shimomura¹, Yukimasa Hisada¹, Shiori Nakagawa², Kengo Furuichi², Takashi Wada²

¹Internal Medicine, Japanese Red Cross Kanazawa Hospital, ²Department of Nephrology, Kanazawa University Hospital

Conflict of interest: None

[Background] The frequency of ischemic heart disease is low in antiphospholipid antibody syndrome (APS) [1]. 40 cases of acute myocardial infarction (AMI) due to APS were reported. [2] [Case] 32-year-old, female patient. She has a history of taking low dose pills. She was conscious of erythema on the face since March X. In July and September, she had chest pain and ST elevation in ECG and increase of CK were observed. No significant stenosis of coronary artery was found in CAG in July, but in September AMI due to the thrombus of the right coronary artery was confirmed. ANA was positive and ds-DNA antibody was high. Lymphocytopenia (1200/mm³) and serositis (pleural thickening and pericardial effusion in chest CT) were observed. She was diagnosed with

SLE. Anti-cardiolipin antibody IgG (68 U/mL), anti-cardiolipin β 2 GPI antibody (113 U/mL) and lupus anticoagulant were positive and APS was diagnosed. Since SLEDAI score was low (2), she was treated with only antiplatelet and anticoagulation therapy. [Summary] We report a case of AMI associated with SLE and APS. When young women are diagnosed with AMI, the possibility of APS should be considered.

P3-052

A case of recurrent acute subdural hematoma due to vasculitis in systemic lupus erythematosus and antiphospholipid antibody syndrome

Koji Mishima¹, Masahiro Ayano¹, Tomofumi Tatsutani¹, Shoichiro Inokuchi¹, Yasutaka Kimoto², Hiroki Mitoma¹, Mitsuteru Akahoshi¹, Yojiro Arinobu¹, Koichi Akashi¹, Takahiko Horiuchi², Hiroaki Niino³

¹Department of Medicine and Biosystemic Science, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan, ²Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, ³Department of Medical Education, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan

Conflict of interest: None

This case was a 53-year-old woman who diagnosed with systemic lupus erythematosus (SLE) and antiphospholipid antibody syndrome (APS) two years ago. Although the activity of thrombocytopenia and renal dysfunction remained after 40 mg of prednisolone (PSL) was started, this was improved after warfarin was started. She was stable on treatment with PSL 5mg and warfarin (target PT-INR 2 to 3). Eight months ago, she developed the first acute subdural hematoma of the right cerebellar tent. The activity of SLE was not indicated and PT-INR was strictly adjusted to about 2 after this event. However, she repeated hemorrhage at the same site three times. Cerebral angiography examination performed during the course could not identify organic abnormalities such as aneurysm and vascular malformation. Because FDG-PET/CT showed increased FDG accumulation in the right occipital lobe and cerebrospinal fluid examination revealed IL-6 elevation (25.7 pg/mL), we assumed vasculitis as a cause of the recurrent hemorrhage and performed additional immunosuppressive therapy (PSL 30mg+IVCY). There was no episode of hemorrhage during the follow-up period of two months. We report a case in whom vasculitis, in addition to thrombocytopenia and APS, was suspected as a cause of cerebral hemorrhage.

P3-053

An autopsy case of catastrophic antiphospholipid syndrome with multiple cerebral infarction, renal failure, acute hepatitis and pancreatitis

Fumiaki Kondo, Fumihito Suzuki

Department of Rheumatology, JA Toride Medical Center

Conflict of interest: None

A sixty-eight female was diagnosed with antiphospholipid syndrome (APS) based on cerebral infarction (CI) and positive antiphospholipid antibodies on 2008. Aspirin was administrated. She admitted to our hospital for further treatment of chronic kidney disease of unknown etiology on 2015. She received hemodialysis since 2016. Her cognitive function declined and gait disorder appeared since February 2017. Brain MRI depicted multiple CI, SPECT revealed cerebral blood flow decrease in ACA-MCA lesion. Since her cognitive dysfunction advanced, she became in need for medical restraint. She was transported to our hospital due to consciousness disturbance on September 2017. Blood test revealed thrombocytopenia and elevated levels of liver enzymes and amylase. Brain MRI depicted multiple acute CI. Under the diagnosis of catastrophic APS (CAPS), methylprednisolone pulse therapy, continuous heparin infusion, oral prednisolone 40mg/day, and intravenous immunoglobulin were administrated. She died with aspiration pneumonia during the clinical course. Autopsy revealed microvascular thrombosis to the multiple organs, indicating CAPS. If multiple organ dysfunction with thrombocytopenia was observed in rheumatic patients, we should consider CAPS.

P3-054

Non-Hodgkin's Lymphoma in Systemic Lupus Erythematosus; 2 case reports

Takanori Ichikawa, Noriko Sakaguchi, Satoru Ushiyama, Kenichi Ueno, Dai Kishida, Yasuhiro Shimojima, Yoshiki Sekijima
Division of Neurology and Rheumatology, Department of Internal Medicine, Shinshu University

Conflict of interest: None

We present two patients demonstrating malignant lymphoma (ML) which developed in their clinical course of SLE. Case 1: 34-year-old female with a 7-year history of SLE had repeated relapse despite administering prednisolone (PSL) together with immune suppressants. Massive lesions with advanced edema in the right frontal lobe was found on brain MRI which was performed when she indicated convulsive seizure. Brain biopsy revealed EB virus positive central nervous system primary B cell lymphoma. Partial remission was obtained after surgical resection as well as radiotherapy and rituximab administration. Case 2: 33-year-old female, who had 10-year history of SLE as well as anti-phospholipid antibody syndrome, had treated with PSL. She had several episodes of severe vascular damage in her visceral organ and extremities. A subcutaneous tumor was found in her abdomen at her 31-year-old. Consecutively, several subcutaneous tumors appeared in her limbs and trunk. Biopsied tissue demonstrated T cell lymphoma. CHOP therapy was administered and remission was achieved. Conclusion: Considering the relationship between high disease activity of SLE and the pathogenesis of ML, it should be concerned that extranodal lymphoma may appear in the long-term and active phase of SLE.

P3-055

The successful treatment for the refractory thrombocytopenia using belimumab in a patient with systemic lupus erythematosus

Hiroki Kobayashi¹, Takuya Tanimoto², Hiroyuki Maeda¹

¹Department of Rheumatology, Hiroshima Prefectural Hospital, Hiroshima, Japan, ²Respiratory Medicine, Hiroshima Prefectural Hospital, Hiroshima, Japan

Conflict of interest: None

A fifteen-year-old woman was referred to our hospital because of nasal bleeding and petechial hemorrhage. She was diagnosed as having systemic lupus erythematosus (SLE) by the presence of the butterfly rash, positive anti-nuclear antibody, positive anti-phospholipid antibody, and thrombocytopenia. Oral prednisolone (PSL, 45 mg/day) was administered, resulting in the improvement of thrombocytopenia. The dosage of PSL was gradually tapered. Thereafter, in addition to the decrees of her platelet count, the abdominal pain occurred. Because of positive antiphospholipid antibody, thrombosis of the abdominal artery was suspected. After the aspirin-heparin treatment, her platelet count gradually increased and the abdominal pain was improved. Despite the using of PSL, tacrolimus, mycophenolate mofetil (MMF) and eltrombopag olamine, a low platelet count persisted decreased, and the platelet transfusions had to be repeated. As a re-induction therapy, belimumab was administered, which resulted in the improvement of thrombocytopenia. We herein report a case of refractory thrombocytopenia that was successfully treated with the addition of belimumab and discuss the efficacy and the safety in regard to the using of belimumab in SLE.

P3-056

A case of linear cutaneous lupus erythematosus treated successfully with hydroxychloroquine

Ryo Tanaka, Akiko Tanikawa

Department of Dermatology, Keio University Hospital, Tokyo, Japan

Conflict of interest: None

17-year-old woman developed a red streak along the nose ridge in October 2017. She was refractory for oral and topical antibiotics. She visited our hospital. Red pruritic papules were arranged linearly along the nose ridge. Histological examination from the papule showed liquefaction and lymphocytic infiltrates around hair follicles and appendages in a

patchy pattern. No extracutaneous symptoms was seen. Anti-ds-DNA antibody, anti-SS-A antibody, anti SS-B antibody and ANA were negative and blood test and urinalysis was unremarkable. She was diagnosed as linear cutaneous lupus erythematosus. Treatment with topical alclomethazone propionate and topical tacrolimus was failed. Hydroxychloroquine was started. One month later, the red papule begins to depigmented gradually. Skin eruption continued to improve over 3 months. In Japan, treatments previously reported for linear cutaneous lupus erythematosus include topical steroid, topical tacrolimus, systemic steroid, diamino diphenyl sulfone, but no reports using hydroxychloroquine have been made. However, antimalarials are used worldwide for cases refractory for topical steroid or tacrolimus. We summarize previous cases of linear cutaneous lupus erythematosus treated with antimalarials and our case.

P3-057

A case of lupus myocarditis treated with steroid and immunosuppressive drugs

Chiai Nakada, Takuya Oshiro, Tomoo Murayama, Eishi Uechi, Yoshiki Shiohira

Department of Rheumatology, Tomishiro Central Hospital

Conflict of interest: None

[Clinical course] A 44-year-old male with a 20-year history of SLE presented with a 3-month history of progressive dyspnea. He had interrupted treatment 7 years ago. The chest X-ray revealed pulmonary congestion, and cardiac dilatation. Cardiac echocardiography revealed 34% left ventricular ejection fraction (LVEF) and wall edema. Coronary angiography showed no significant stenotic lesions and myocarditis was suspected. The blood test revealed high CRP, high Troponin I and high BNP. Although diuretic drug improved dyspnea, LVEF decline continued. We diagnosed lupus myocarditis and he was treated with steroid pulse on the 10th disease day. LVEF improved to 60% on the 16th disease day. Cyclophosphamide (IVCY) was also used on the 17th disease day. And there was also hematuria and urine protein and we diagnosed as lupus nephritis (LN) by renal biopsy. LN worsened on the 57th disease day. PSL was increased and immunosuppression was switched to the combination of Tacrolimus and Mizoribine. After that, PSL was gradually tapered to low-dose without recurrence of lupus myocarditis. [Clinical significance] SLE-related myocarditis is rare, but life-threatening. There are few prospective studies, and management is based on small-series reports. We reported the patient with literatures.

P3-058

A case of systemic lupus erythematosus with pulmonary hypertension (SLE-PAH) for long-term management

Yuko Kurihara, Shimpei Ohnari, Takahiro Suzuki

Kawasaki Municipal Ida Hospital

Conflict of interest: None

A 73-year old woman with SLE-PAH was admitted to our hospital because of progressive dyspnea. The patient had been diagnosed with SLE 40 years earlier. 25 years earlier pulmonary hypertension developed and she was treated with prednisolone 60 mg daily, and she responded. 16 years earlier, beraprost sodium was started. 10 years earlier the systolic pulmonary arterial pressure (SPAP) was estimated at 70 mmHg by Doppler echocardiography. Oxygen therapy and bosentan was started against progressive hypoxemia. 6 years earlier right heart catheterization revealed mean PAP of 60/30 mmHg. 4 years earlier the SPAP was estimated at 95 mmHg. Sildenafil was started. However sildenafil was switched to tadalafil. Her dyspnea deteriorated and she was admitted to our hospital. She developed congestive heart failure. Spironolactone was started and the patient was discharged with improve. One month after this admission the patient died suddenly. Post mortem examination of the vasculature revealed findings consist with Fibroelastic intimal thickening and medial thickening of the pulmonary arterial branches were found without evidence of vasculitis, fibrinoid necrosis, or thromboemboli. This case suggested the benefit of glucocorticoids and pulmonary vasodilators in patients with severe SLE-PAH.

P3-059

Combined usage of tacrolimus and rituximab in systemic lupus erythematosus patient with severe immune thrombocytopenia: A case report

Hideyuki Watanabe, Nobuhisa Hirase
Kyushu Rosai Hospital

Conflict of interest: None

A 65-year-old woman was admitted because of mucocutaneous bleeding involving the skin, oral cavity. Laboratory data revealed thrombocytopenia and immunological abnormalities, suggesting elevated disease activity. She was assessed and diagnosed as having systemic lupus erythematosus based on immune thrombocytopenia, positive antinuclear antibody and antiphospholipid antibody, low C3 levels and direct Coombs test in the absence of hemolytic anemia. Prednisolone, eltrombopag, *Helicobacter pylori* eradication and intravenous immunoglobulin therapy failed to improve the thrombocytopenia. Tacrolimus at 2-3mg/day and 4 doses of rituximab 375mg/m² weekly were added to the prednisolone regimen. Eventually, the thrombocytopenia improved and prednisolone could be effectively tapered. Combination of tacrolimus and rituximab could be an additional or alternative modality for treating refractory immune thrombocytopenia associated with systemic lupus erythematosus.

P3-060

A case of systemic lupus erythematosus with Pseudo-pseudo Meigs syndrome

Saki Tsujimoto^{1,2}, Hideki Amuro^{1,2}, Nobuyasu Ishii^{1,2}, Tohru Nishizawa^{1,2}, Shosaku Nomura²

¹Rheumatology and Clinical Immunology, Kansai Medical University Medical Center, Moriguchi, Japan, ²First Department of Internal Medicine, Kansai Medical University, Hirakata, Japan

Conflict of interest: None

Case: A 32 year-old female suffered with abdominal bloating and facial edema for a month. She was admitted to our hospital. She had malar rash, leukopenia, renal disorder and positive anti-nuclear antibody and anti-Smith antibody. We made a diagnosis of systemic lupus erythematosus (SLE). Chest and abdominal CT showed pleural effusion and ascites. Pleural effusion increased rapidly, that caused orthopnea. We ruled out SLE serositis, hypoalbuminemia, or gynecological malignancies. So her CA-125 was elevated, we made a diagnosis of Pseudo-pseudo Meigs syndrome (PPMS). The patient was treated with methylprednisolone 1000mg/day for three days, followed by prednisolone 1mg/kg/day. Pleural effusion and ascites were improved, and CA-125 level normalized. PPMS syndrome described as a disease of pleural effusion, ascites, and elevated CA-125 level in patients with SLE. The mechanism of this syndrome has not become clear. PPMS should therefore be considered in the differential diagnosis of a patient presenting with ascites and pleural effusions in patients with SLE.

P3-061

Worsening of central serous chorioretinopathy after steroid administration in a patient with protein-losing gastroenteropathy due to systemic lupus erythematosus

Arata Hibi, Yuto Kasahara
Department of Nephrology and Rheumatology, Rakuwakai Otowa Hospital, Kyoto, Japan

Conflict of interest: None

A 56-year-old Japanese woman was referred to the hospital because of persistent diarrhea and worsening systemic edema. Computed tomography showed bilateral pleural effusion, ascites, and a small amount of pericardial effusion. Blood test results showed hypoalbuminemia; mild anemia with positive direct Coombs test; thrombocytopenia; as well as positive antinuclear antibody, antiphospholipid antibodies, and anti SS-A antibody. Nephrotic syndrome was ruled out using urinalysis. The antrum of the stomach and the duodenal bulb were suspected as protein-losing sites with ^{99m}Tc human serum albumin diethylenetriamine pentaacetic

acid scintigraphy. As per these test results, protein-losing gastroenteropathy (PLGE) due to systemic lupus erythematosus (SLE) was suspected. Fundoscopy was performed prior to steroid administration and revealed central serous chorioretinopathy (CSC) on the right eye. Although PLGE responded well to steroid therapy, we were required to consider tapering steroids because the CSC worsened after steroid administration. Although PLGE is a rare manifestation of SLE, it generally achieves good therapeutic response to steroid monotherapy. However, in a patient with CSC, we should be aware of the risk of worsening the eye symptoms due to steroid administration.

P3-062

A case of severe lupus myocarditis

Chizuru Abe¹, Nozomi Iwanaga¹, Midori Akagi¹, Chieko Kawahara¹, Yoshiro Horai¹, Yasumori Izumi¹, Atsushi Kawakami²

¹Department of Rheumatology and General Internal Medicine, National Hospital Nagasaki Medical Center, ²Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Science

Conflict of interest: None

A 61-year-old woman with a 20-year history of systemic lupus erythematosus (SLE) and lupus nephritis was admitted to a neighboring hospital due to slight fever, general malaise and renal dysfunction. She developed heart failure and alveolar hemorrhage, for which steroid pulse therapy, tracheal intubation and artificial ventilation were performed. She was then transferred to our hospital. Interdigital erythema with erosion and a positive anti-DNA antibody test reflected SLE disease activity. Elevated Cardiac Troponin T and diffuse high signal intensity of her left ventricular wall revealed by MRI-short inversion time inversion recovery suggested the presence of lupus myocarditis (LM). Steroid pulse therapy was followed by administration of 40 mg/day prednisolone and intravenous cyclophosphamide, which resolved heart failure and alveolar hemorrhage and the tracheal tube was removed. However, she then developed perianal cutaneous vasculitis, lupus colitis, brain infarction due to antiphospholipid syndrome and cytomegalovirus infection. Considering her general condition, we avoided additional immunosuppressive therapy and she died just after the transfer to a palliative care unit. This is a rare case of LM which occurred after the onset of SLE and lupus nephritis.

P3-063

A case of steroid-induced diabetic SLE patient who disclosed a gradual renal dysfunction probably due to the treatment with biguanide

Yuta Ibayashi¹, Tetsushin Murakami¹, Yasutaka Kimoto¹, Daisuke Oryoji¹, Masahiro Ayano², Yojiro Arinobu², Hiroaki Niiro³, Koichi Akashi², Takahiko Horiuchi¹

¹Kyushu University Beppu Hospital Internal Medicine, ²Department of Medicine and Biosystemic Science, Kyushu University Hospital, ³Department of Medical Education, Kyushu University Graduate School of Medical Sciences

Conflict of interest: None

In January of X-31 year, 28 year old woman was hospitalized by unknown fever and dyspnea and was diagnosed as cardiac tamponade accompanying lupus endocarditis. During the course, she got a diagnosis as central nerve lupus, then a temporary remission being observed with steroid therapy thereafter. Since the year of X-7, she has been prescribed the daily doses of 15mg of prednisolone, 3 mg of tacrolimus, 150 mg of brelinin. There revealed overeating and obesity due to side effects of steroids, HbA1c was in the range of 6.5 to 6.9%, and α GI formulation was started as type 2 diabetes in X-2 year. From June of X-1 year, HbA1c worsened to 7.1%, so she was introduced to the department of diabetes medicine. Biguanide preparation / DPP-4 inhibitor were added from the same month. HbA1c was stabilized at 6.5%, but gradually worsened the kidney dysfunction. The deterioration of SLE per se was also taken into consideration, probably due to the drug-related nephritis, so we discontinued Metgluco from July X, followed by the prompt improvement of creatinine level. Metgluco is a good indication from the point of view by diabetes medicine, but it might be necessary to consider very carefully when prescribing biguanide in patients with renal dysfunction.

P3-064

Lupus-associated pulmonary hypertension: Long-term response to combination of immunosuppressive and vasoactive therapy

Koichiro Shinoda, Hiroyuki Hounoki, Reina Tsuda, Hirofumi Taki, Kazuyuki Tobe

First Department of Internal Medicine, University of Toyama Japan

Conflict of interest: None

[Case] 34-years-old female was admitted to our hospital, because of dyspnea on effort. She was diagnosed systemic lupus erythematosus [SLE] at the age of 13, and was treated with prednisolone [PSL] 30 mg/day. She complicated with lupus nephritis at the age of 26 and treated with PSL and cyclosporin A [CsA]. She first admitted to our hospital at the age of 33 for exacerbation of lupus nephritis and successfully treated with PSL and tacrolimus [TAC]. UltrasoundCardioGraphy [UCG] demonstrated slightly higher transtricuspid pressure gradient [TRPG] of 35 mmHg. Her anti-ds-DNA antibody was gradually elevated, and she admitted. ECG detected right heart load findings, TRPG 82.8 mmHg at UCG, mean PAP 53 mmHg, PCWP 6 mmHg at right heart catheter. Pulmonary embolism was never detected by imaging examination. She was diagnosed pulmonary arterial hypertension [PAH] complicated with SLE. Oxygen inhalation and steroid pulse therapy were initiated and we changed to azathioprine from TAC. As a vasodilatation therapy, beraprost, bosentan [now macitentan] and sildenafil were used. Currently 9 years after the onset of PAH, her condition was improved. [Clinical Significance]: Immunosuppressive therapy including IVCY early in onset is effective for PAH that is combined with SLE and MCTD.

P3-065

A case of Systemic Lupus Erythematosus (SLE) treating with Belimumab

Sachiko Fukumi, Keiichiro Matsunaga

Department of Internal Medicine, Yokosuka General Hospital Uwamachi

Conflict of interest: None

Fifty-eight years old woman, who was diagnosed as Systemic Lupus erythematosus (SLE) with malar and discoid rash, photosensitivity and nonerosive arthritis nineteen years ago, was treated with prednisone (PSL). One year later her skin symptoms were worse, so she received administration of mizoribine (MZR) and intravenous methylprednisolone (IVMP). Four years later she got renal symptom, so we enforced renal biopsy. The result was ISN/RPS Class III, so she received intravenous cyclophosphamide and we also used PSL, MZR and tacrolimus (TAC) as maintenance therapy. She complicated with hemophagocytic syndrome three years ago and treated with IVMP with intravenous immunoglobulin (IVIg). Until three month ago her symptom was stable, we maintained with PSL and TAC, but her compliment level was decreased and anti-dsDNA Ab was sustained positive, so we introduced her belimumab. Belimumab, which is anti-BLys monoclonal antibody, respond to improvement of clinical symptom. We report and consider our case on basis of literature.

P3-066

HCQ efficacy for comorbidities of SLE

Junya Ajiro, Katsumitsu Arai

Niigata Prefectural Central Hospital

Conflict of interest: None

[Object] Prognosis dramatically improved with steroid treatment in SLE patients. On the other hand, there are many comorbidities such as hypertension and femoral head necrosis, improvement of QOL of SLE patients is an important subject. In Japan, HCQ was approved for skin lupus erythematosus, systemic lupus erythematosus indication. HCQ has been approved in more than 70 countries including Europe and is positioned as a standard treatment for SLE abroad, since was approved in the US in 1955 Although the effectiveness of HCQ to SLE is obvious, it is expected that comorbidities caused by steroid administration will be alleviated. We examined the effect of HCQ on comorbidities. [Methods] we investigated steroid dosage, blood pressure, HbA1c, HDL and LDL retro-

spectively for SLE patients undergoing maintenance therapy before and after HCQ treatment. [Results] Improvement was found in the reduction of the dosage of steroids and the several items. [Conclusions] In addition to the effect of SLE on the disease itself, HCQ can also be expected to have an effect on indirect co-morbidities.

P3-067

Systemic sclerosis complicated by idiopathic portal hypertension

Hajime Sanada¹, Satoshi Hara¹, Masahiro Konishi¹, Kazuyuki Suzuki¹, Takeshi Zoshima¹, Ichiro Mizushima¹, Takashi Kawane², Hiroshi Fujii¹, Kazunori Yamada¹, Mitsuhiro Kawano¹

¹Department of Rheumatology, Kanazawa University Hospital, ²Department of Nephrology, Rheumatology, Infection, Toyama Red Cross Hospital

Conflict of interest: None

A 68-year-old woman admitted to our hospital because of hyperglobulinemia 4 years before. A diagnosis of Sjogren's syndrome was made from sicca syndrome, chronic sialadenitis in lip biopsy, and positive anti-SSA antibodies. In addition, she was also diagnosed with diffuse cutaneous systemic sclerosis (SSc) because of wide range of skin sclerosis and positive anti-centromere antibodies. She has been prescribed pulmonary vasodilators for pulmonary hypertension and estimated pressure of pulmonary artery remained 50 mmHg. She was admitted to our hospital because acute chest pain and dyspnea have developed for 7 days, and diagnosed with pneumothorax. Massive ascites was also observed, and it remained after pneumothorax resolved. Serum-ascites albumin gradient was 1.4 g/dL, so her ascites was transudative and would be caused by portal hypertension (IPH). Her ascites was not responded to diuretics, so she needed to be punctured her abdomen or to receive cell-free concentrated ascites refusion therapy third times per two weeks. IPH rarely associated with SSc. Pathological findings of liver are very similar to those of skin sclerosis in SSc with IPH: dense fibrosis, and vascular obstruction. When SSc patients develop refractory ascites, we should consider IPH as a differential diagnosis.

P3-068

A case of the scleroderma that an ureter cancer and bladder cancer were able to be diagnosed with urinalysis abnormality

Yasunori Tsubouchi, Amane Nakabayashi

Division of Internal Medicine, Kyoto Kuramaguchi Medical Center

Conflict of interest: None

[Case] The patient was 73-year-old woman who had a scleroderma. Urine occult bleeding, leukocyte positive lasted. Urine cytodiagnosis was class V, urinary tract epithelial cancer were detected. Abdominal CT showed soft shadow, cranial ureter, renal pelvis expansion in right lower part ureter. She was hospitalized in urology department. Tumors in the right ureter, an ureter oral region bladder were detected by ureteroscopy. Transitional cell carcinoma was diagnosed by biopsy. A transurethral bladder tumor resection was enforced under lumbar anesthesia. Laparoscopic right kidney ureter total extraction was enforced under general anesthesia. After seven years, progress is good without a recurrence and metastasis. [Clinical significance] Kidney crises may cause a renal function disorder on scleroderma, urine occult bleeding and protein become often positive. In this case, occult bleeding was positive, but protein was negative. Urine white blood cell was positive due to hydronephrosis. Urinalysis abnormality became the decisive factor of ureter and bladder cancer diagnosis. When we accept microscopic hematuria without proteinuria in menopause women, even collagen disease except dermatomyositis has to consider the possibility of the malignant tumor of urinary tract origin.

P3-069

Efficacy of LDL apheresis in systemic scleroderma with arteriosclerosis obliterans

Makio Kusaoi, Takuya Nemoto, Shota Sakuma, Yoshiyuki Abe, Go Murayama, Michihiro Ogasawara, Kazuhisa Nozawa, Ken Yamaji, Naoto Tamura

Department of Internal Medicine and Rheumatology., Juntendo University School of Medicine.

Conflict of interest: None

[Case report] A 75-year-old woman has suffered from systemic scleroderma since at the age of 55. From at the age of 73, skin ulcer was found on the right fifth toe and the sole. she complained foot pain even in at rest, and walking difficulty. She was diagnosed complications with arteriosclerosis obliterans (ASO) in the right lower limb arteriography. Percutaneous angioplasty and balloon dilatation were performed for severe ischemia of the right lower limb, but after a while, re-occlusion was recognized. Also, a severe ulcer gradually appeared on the left toe, she was referred to our hospital for ineffectiveness of Bosentan and Tadalafil administration. We performed LDL apheresis twice a week (a total of 10 times procedures) for ASO. At the end of the course of treatment, the right foot skin ulcers were completely cured and a remarkable improvement of the skin ulcer of the left side. [Discussion] The mechanisms of the efficacy of LDL apheresis were presumed to increasing production of bradykinin, nitrogen monoxide, and functional improvement of vascular endothelial cells in the previously reports. [Conclusion] LDL apheresis may effective for the refractory peripheral artery disease even if there are rheumatic disease in the basic complications in addition to ASO as in this case.

P3-070

A Case of Systemic Sclerosis with Systemic Multiple and Huge Calcinoses

Akitsu Yoshida, Mari Tochihara, Akira Nishino, Shinya Hirahara, Hirokazu Nishina, Masanori Hanaoka, Yasuhiro Katsumata, Yasushi Kawaguchi, Hisashi Yamanaka

Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Case] A woman in her 40s was diagnosed as diffuse cutaneous systemic sclerosis (SSc) 15 years ago, based on her Raynaud's phenomenon, skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints, interstitial lung disease, and positive anti-Scl-70 antibodies. She was treated for her skin and lung involvement with glucocorticoids, intravenous cyclophosphamide, intravenous immunoglobulin, and tocilizumab, but their effect was limited. Her modified total skin score reached 40 points a year ago. Her pain in the shoulder and hip and their joint range of motion limitations deteriorated several years ago, and her X-ray and CT showed multiple and huge calcinoses around her shoulder and hip joints. Serum level of calcium, phosphate and intact-PTH were within normal ranges. Generally, surgical intervention should be considered for severe, refractory calcinosis. However, it was avoided due to her poor general conditions. [Clinical Significance] Calcinosis affects 25% of SSc patients. Although pathogenesis is unknown, there is evidence supporting local trauma, chronic inflammation, vascular hypoxia, and dysregulation of bone matrix proteins as potential mechanisms. There is a very limited evidence base for the management of calcinosis.

P3-071

A case of the anti-RNA polymerase III antibody (Ab) positive systemic sclerosis (SSc) complicated with double cancer

Ichiro Mori, Saori Inui, Tomofumi Takeda, Kei Fujioka, Tatsuo Ishizuka
Center of General Internal Medicine and Rheumatology, Gifu Municipal Hospital

Conflict of interest: None

A 75 years old man was diagnosed SSc because of the skin sclerosis and skin biopsy at 60 years old. He was introduced to our department in order to treat interstitial pneumonia by 7.5 mg prednisolone at 72 years old. However, anti-RNA polymerase III Ab was pointed out. When He was hospitalized with bacterial pneumonia at 73 years old, he complicated pollakisuria with high PSA levels. Histological examination after biopsy revealed prostate cancer. Chemotherapy started because of accumu-

lation of lumbar vertebrae indicated by bone scintigraphy. Then he showed anorexia with Na 118mEq/l at 75 years old. Chest X-rays showed increase of the left hilar shadow. He consulted respiratory medicine. Bronchoscopic biopsy revealed pulmonary small cell carcinoma. The anti-RNA polymerase III Ab is detected in approximately 5% of SSc. This positive cases of antibody showed rapid progression, extended lesion of skin sclerosis and contractures, and low incidence of IP and high incidence of renal crisis. It is also reported that the incidence of the malignant tumor is higher-frequency than 20-30% compared with other SSc-associated antibody-positive cases. We have reported SSc with double cancers such as prostate cancer and small cell lung carcinoma with anti-RNA polymerase III Ab positive.

P3-072

A Case report of multiple tooth resorption in SSc patients

Takumi Memida¹, Shinji Matsuda¹, Kazuhisa Ouhara¹, Yusuke Yoshida², Shintaro Hirata², Eiji Sugiyama², Hidemi Kurihara¹

¹Department of Periodontitis, Hiroshima University, Hiroshima, Japan,

²Department of Clinical Immunology and Rheumatology, Hiroshima University, Hiroshima, Japan

Conflict of interest: None

A systemic sclerosis (SSc) patient who visited department of periodontics in Hiroshima university hospital has multiple unexplained tooth resorptions (MUTR). MUTR is first report in Japan, whereas only one case has been reported in Spanish patient in 2017. We examined systemic and oral conditions in SSc patient collaborating with department of Clinical Immunology and Rheumatology. Twenty-four patients participated to the examination, and MUTR were found in 3 patients including first case. Systemic conditions differed in three patients although their maxillofacial conditions were in high homogeneity. One, they have exhibited MUTR, and they have some calcinosis of an anterior nasal spine. In addition, their mouth is limited opening because of facial skin fibrosis. These common points suggest pathologic physiology of 3 patients is similar. The histological analysis of fraction of the tooth in first patient revealed it was bone replacing resorption in tooth. We found novel symptoms, MUTR, in SSc patients. Disease-specific iPS cells from these patients can be revealed mechanisms of MUTR. In the future, these studies would make understanding the mechanism of pathogenesis of SSc.

P3-073

A case of suspected pulmonary veno-occlusive lesion with centromere positive systemic sclerosis

Ayana Okazaki, Kenichiro Hata, Takao Kiboshi, Hidehiko Makino, Shogo Matsuda, Youhei Fujiki, Reiko Wakura, Takuya Kotani, Tohru Takeuchi, Shigeki Arawaka

Division of Rheumatology, Department of Internal Medicine IV, Osaka Medical College

Conflict of interest: None

76 years old female was diagnosed as systemic sclerosis 10 years ago because of skin sclerosis, anti-centromere antibody positive, Raynaud phenomenon. She suffered from dyspnea on effort one years ago, and dyspnea was gradually worsened. She was suspected pulmonary hypertension because TR-PG was 65mmHg by Echocardiography. Right heart catheterization revealed mean pulmonary artery pressure (mPAP) 52mmHg, pulmonary capillary wedge pressure (PCWP) 6mmHg and pulmonary vascular resistance (PVR) 14.7wood unit. Her HRCT presented thickened septal lines, centrilobular ground-glass opacity, and mediastinal lymph node enlargement. %DLCO and 6MWD were 16.1% and 70m respectively. She was diagnosed as pulmonary artery hypertension associated with systemic sclerosis, and suspected that pulmonary veno-occlusive lesion was complicated. She was treated with Tadalafil (20mg) and Macitentan (5mg) with diuretic agent. mPAP and PVR improved to 38mmHg and 12 wood unit 4 weeks after the therapy. Three months later, she was admitted to our hospital because of right heart failure. Her symptom was improved after diuretic agent was added on. We reported a rare case with three CT signs of pulmonary veno-occlusive lesion complicated with systemic sclerosis.

P3-074

The use of nailfold videocapillaroscopy to assess for Raynaud's phenomenon associated with hand-arm vibration syndrome

Nanase Honda, Naoki Tanomogi, Masahiro Iida, Yusuke Nakamichi, Shuhei Sano, Tatsuo Mori, Michiru Kina, Eisuke Takamasu, Kae Onishi, Takayasu Kise, Yuji Miyoshi, Masako Utsunomiya, Yoshiki Nagai, Naoto Yokogawa, Kota Shimada, Shoji Sugii

Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center

Conflict of interest: None

[Introduction] Hand-arm vibration syndrome (HAVS) is an occupational disease affecting workers in multiple industries in which hand-held vibration tools are used. Its vascular component is a type of secondary Raynaud's phenomenon. [Case] A 42-year-old man had Raynaud's phenomenon and digital ulcers in his fingers. He had diagnosed as systemic lupus erythematosus. Immunosuppressive and vasodilator therapy had no effect on Raynaud's phenomenon. In nailfold videocapillaroscopy (NVC), avascular areas without giant capillaries or neoangiogenesis were observed in all fingers. At the age of 48, ischemia of the right index finger led to osteomyelitis and the amputation was needed. The occupational history was obtained that the patient was engaged in handling vibration tools for 32 years. Hand-arm vibration syndrome was suspected. Reduction of vibration exposure and smoking cessation improved Raynaud's phenomenon markedly and then the number and the form of capillaries became normal in NVC. [Discussion] It is important to recognize the possibility of hand-arm vibration syndrome as a potentially curable cause of Raynaud's phenomenon even in rheumatic diseases. Improvement of microvascular damage was observed in NVC after reduction of vibration exposure.

P3-075

Two cases of treatment-resistant systemic sclerosis-related interstitial lung disease (SSc-ILD) who were treated with mycophenolate mofetil (MMF)

Tamao Nakashita, Akira Yoshida, Akira Jibatake, Shinji Motojima
Rheumatology and Allergy, Kameda Medical Center, Kamogawa, Japan

Conflict of interest: None

ILD is an important cause of death in patients with SSc. Recently, there are reports in which MMF was administered successfully for the treatment of standard -regimen resistant SSc-ILD. We here report 2 cases of severe resistant SSc-ILD for whom MMF was administered. Case 1 is a 61-year-old female with diffuse SSc. The remission induction for ILD was done by the combination of PSL and IVCY and maintenance therapy was done by PSL and AZA. However, AZA was stopped because of hepatotoxicity. Afterwards, ILD exacerbated and IVCY was re-introduced, but stopped because of nausea and others. MMF was introduced with dose of 1g/day and increased to 2g/day. After 21 months use of MMF, FVC and DLCO did not decrease, and HRCT score improved slightly. Case 2 is a 49-years-old female with the initial symptom of severe digital ulcer. The remission induction and the maintenance of SSc-ILD were done by the same regimen as in the Case 1. However, ILD progressed gradually and pneumothorax developed several times. AZA was changed to MMF 1.5g. day and the HRCT did not worsen after 12 months. We suggest that MMF can be a treatment option for SSc-ILD.

P3-076

A case of pulmonary arterial hypertension with mixed connective tissue disease

Takafumi Onose, Reina Tsuda, Naonori Sugishita, Miho Yamazaki, Ryoko Asano, Toshiki Kido, Hiroyuki Hounoki, Koichiro Shinoda, Hirofumi Taki, Kazuyuki Tobe
University of Toyama

Conflict of interest: None

A 58 year old woman was diagnosed as scleroderma in 2006 and PAH (pulmonary arterial hypertension) in 2015. She had a palpitation and dyspnea in progression. Finally, she could not do any activities of dai-

ly living due to dyspnea. She was diagnosed as exasperation of PAH and referred to our hospital. She was newly diagnosed as MCTD (mixed connective tissue disease) due to elevated anti U1-RNP antibodies and SLE-like symptoms. Echocardiography and right cardiac catheterization showed no evidence of left heart failure and pulmonary perfusion scintigraphy denied chronic thromboembolic pulmonary hypertension. Therefore she was diagnosed PAH, which was IV degree in WHO-PH classification, and right heart failure due to MCTD. Vasodilator agents, catecholamine and methylprednisolone pulse therapy made her better immediately. After improvement of PAH and heart failure, she was prescribed IVCY therapy additionally. Combination of vasodilator agent, corticosteroid and immunosuppressive agent can improve prognosis (*Arthritis Rheum.* 2008;58 (2):521-31), therefore we should start treatment as soon as possible.

P3-077

A case of Scleroderma Rheumatoid arthritis Systemic lupus erythematosus overlap syndrome

Mai Yamashita¹, Takaichi Okano², Yoko Nose¹, Yo Ueda¹, Sho Sendo¹, Kengo Akashi¹, Akira Onishi¹, Jun Saegusa², Akio Morinobu¹

¹Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, ²Clinical Laboratory, Kobe University Hospital, Kobe, Japan

Conflict of interest: None

[Back ground] Overlap syndrome (OS) is difficult, heterogenous disease concept. We report a patient who has various symptoms, and fulfilled criteria of systemic sclerosis (SSc), Rheumatoid arthritis (RA), and systemic lupus erythematosus (SLE). [Case description] A 74-year-old man was consulted us for fever and subacute pleuritis. He presented sclerodactyly distal to wrist, nail fold bleeding, NSIP in lower lung. ANA was 2560 fields (homogeneous and nucleolar pattern), and anti-topoisomerase -I antibody (Scl-70) was positive. Thus he was diagnosed with SSc. In addition, he had arthralgia one year before, elevated RF (17IU/ml), and active synovitis in ultrasonography, so he also diagnosed with RA. Furthermore, he had positive Direct Coombs'test, so he met criteria of SLE. We treated him with prednisolone 0.6mg/kg according to treatment protocol of pleuritis in RA or SLE. Pleruritis decreased, but NSIP didn't improve, and he needed home oxygen therapy after discharge. [Discussion] In the literature review, 20% in SSc patients are OS. In this case, positive Scl-70 indicated typical pure SSc, but pleuritis, fever, and arthritis suggested OS. And SSc-RA-SLE OS has not been reported previously. Here we have brief discussion about SSc-RA-SLE OS.

P3-078

A case of systemic sclerosis repeating digital ulcers complicated dermatomyositis

Yoshinori Harada¹, Yasutaka Okita¹, Eri Oguro¹, Kentaro Kuzuya¹, Hidetoshi Matsuoka¹, Satoru Teshigawara¹, Maiko Yoshimura¹, Yuji Yoshida¹, Kentaro Isoda¹, Jun Hashimoto¹, Shiro Ohshima¹, Yukihiko Saeki²

¹Department of Rheumatology & Allergology, National Hospital Organization Osaka Minami Medical Center, ²Department of Clinical Research, National Hospital Organization Osaka Minami Medical Center

Conflict of interest: None

Case: 44-year-old female Course: She presented bilateral digital pain in Dec of 2015 and was diagnosed systemic sclerosis (SSc) with interstitial pneumonia (IP). Digital ulcers worsening, beraprost sodium 0.12mg was started. Transferred to our hospital in Mar of 2016, sarpogrelate hydrochloride 300mg was added. Digital ulcers worsening in Jan of 2017, alprostadil alfadex ointment was effective. She presented both thighs and popliteals pain in Mar of 2018, followed by bilateral back pain with difficult motion. She revealed serum myogenic enzymes increase, fever, myalgia and positive anti-ARS antibody. She was hospitalized on 6th of Aug. No limb hypotonia, skin ulcers of right ear and right fingers, Gottron signs of right elbow and both knees, and mechanic hands were observed. EMG developed myogenic pattern. UCG developed no myocardial dysfunction and no pulmonary hypertention. IP deteriorated by imaging and function. No malignancy was found. Diagnosed dermatomy-

ositis (anti-ARS syndrome), prednisolone 30mg and tacrolimus 2mg was started, with remarkable effect. Prednisolone is gradually decreased visit by visit. Discussion: In case of SSc skin lesion worsening, we should consider not only original disease recurrence but also dermatomyositis complication, and in indication, we should use steroids actively.

P3-079

A case report of successful immunosuppressive therapy for Ogilvie's syndrome due to scleroderma

Junya Suzuki, Shotaro Kojima, Ayako Matsuki, Kentaro Takahashi, Takeshi Umibe
Matsudo City General Hospital

Conflict of interest: None

A 53-year-old woman with hand swelling and exertional dyspnea during a year, was diagnosed as scleroderma because of sclerotic change from fingers to the elbows, interstitial pneumonia and positive anti-RNA polymerase III antibody half a year before her admission to our hospital. She had a fever and chest discomfort from the previous week, and was diagnosed with pleuritis and pericarditis. Despite administration of PSL 30 mg, a new abdominal distension and pain appeared. CT showed luminal dilation of the right semicolon without obstruction. We diagnosed it was an intestinal pseudo-obstruction. Pleuritis and pericarditis also tended to deteriorate, so we increased PSL dose to 60 mg. Transanal decompression was also performed. However, her fever, abdominal symptoms and chest symptoms remained. Therefore, IVCY (cyclophosphamide intravenous therapy) was performed. Her fever fell down quickly and abdominal symptoms disappeared. CT showed improvement of intestinal dilation, pleuritis and pericarditis. Intestinal pseudo-obstruction due to scleroderma is generally a chronic course, and the fibrosis of the intestinal tract is considered to be irreversible. Acute colonic pseudo-obstruction is classified as Ogilvie's syndrome. Little has been reported on Ogilvie's syndrome due to scleroderma.

P3-080

A Case of Systemic Sclerosis Associated with Nephrotic Syndrome

Masashi Mizuno¹, Koji Uehara², Taio Naniwa², Michio Fukuda¹
¹Department of Cardio-Renal Medicine and Hypertension, Nagoya City University Graduate School of Medical Sciences, ²Department of Respiratory Medicine, Allergy and Clinical Immunology, Nagoya City University Graduate School of Medical Sciences

Conflict of interest: None

A case of 28-year-old man who had suffered from nephrotic syndrome was reported. The patient had developed digital ulcers in 2006 and had been treated methotrexate under diagnosis of systemic sclerosis. However, he then had developed sclerosis of skin. Proteinuria had appeared in June 2018. His blood showed hypoproteinemia. A renal biopsy was judged to be at high risk due to the problem of arthrogyrosis, and considering the acute onset of nephrotic syndrome, steroid treatment (oral prednisolone 50 mg/day) started without histological diagnosis. However, he had an incomplete remission by the steroid therapy. Then a renal biopsy was performed and showed no spiking or bubbling was found on periodic acid methenamine silver staining. His renal biopsy revealed the minimal change glomerular lesion microscopically. Improvement in urinary protein and serum albumin was insufficient, so focal glomerulosclerosis was also presumed from the clinical course. Since such renal diseases were rarely observed in systemic sclerosis, we herein report the interesting case suggesting immune system abnormality.

P3-081

The use of nailfold videocapillaroscopy to assess Raynaud's phenomenon secondary to dermatomyositis

Nanase Honda, Naoki Tanomogi, Masahiro Iida, Yusuke Nakamichi, Shuhei Sano, Tatsuo Mori, Michiru Kina, Eisuke Takamasu, Kae Onishi, Takayasu Kise, Yuji Miyoshi, Masako Utsunomiya, Yoshiki Nagai, Naoto Yokogawa, Kota Shimada, Shoji Sugii
Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center

Conflict of interest: None

[Introduction] Nailfold videocapillaroscopy (NVC) is useful in the evaluation of microvascular damage in systemic sclerosis. Recently, the significance of nailfold microvascular abnormalities in dermatomyositis was reported. [Case] A 29-year-old woman with proximal muscle weakness, rash over cheek and neck, periungual erythema and Raynaud's phenomenon was admitted. Creatine kinase was elevated and myositis-specific antibodies were negative. Electromyography showed signs of myopathy and muscle pathology showed perifascicular atrophy. In NVC, giant capillaries, microhemorrhages and loss of capillary density were observed. The patient was diagnosed as dermatomyositis and started on glucocorticoid and azathioprine. 3 months later, muscle weakness, rash and Raynaud's phenomenon improved and creatine kinase normalized. 9 months later, NVC showed remarkable bushy and ramifying capillaries with a decrease of giant capillaries and an increase in capillary density. [Discussion] In systemic sclerosis, Raynaud's phenomenon is refractory and slowly progressive microvascular damage can be observed in NVC. In dermatomyositis, Raynaud's phenomenon improves and in the presented case the severe microvasculopathy at the onset and the remodeling of microvascular after treatment were observed by NVC.

P3-082

Usefulness of muscle echo in polymyositis and dermatomyositis

Chie Ogita, Kazuteru Noguchi, Maki Shibamoto, Mai Nakano, Rei Tadokoro, Kazuyuki Tsuboi, Mei Tani, Tetsuya Furukawa, Masao Tamura, Takahiro Yoshikawa, Teppei Hashimoto, Mai Morimoto, Naoto Azuma, Masayasu Kitano, Kiyoshi Matsui
Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine

Conflict of interest: None

[Object] MRI has been widely used as a morphological evaluation of neuromuscular diseases, and in recent years the utility of muscle echo has also been reported. Muscle echo is an aid in the diagnosis of inclusion body myositis and myosarcoma. Inflammatory findings of polymyositis (PM) and dermatomyositis (DM) can also be evaluated on muscle echo. This time, we evaluated muscle of inflammatory myopathy using muscle echo. [Methods] We used a high frequency probe (7 - 12 MHz) and examined the patient in a sitting position. Regardless of the presence or absence of muscle pain or muscle weakness, we made the observation sites of all cases into quadriceps femoris and biceps brachii muscle. We evaluated both short and long axis images. [Results] Compared with healthy muscles at the same site, PM patients showed an increase in muscle brightness, and in short-axis images there was conspicuous irregularity of the muscle bundle. DM Patients had predominantly myofascial thickening and necrotizing myopathy patients had marked muscle atrophy. [Conclusions] Diagnosis of inflammatory myopathy and evaluation of disease condition are possible by using muscle echo. To evaluate accurately it is important to use muscle echo under the same conditions on the same machine.

P3-083

Practice investigation of polymyositis, dermatomyositis in our hospital

Shin Furukawa, Hirohiko Kitakawa
Internal Medicine, Kushiro Red Cross Hospital

Conflict of interest: None

[Object] In conformity with "polymyositis, dermatomyositis treatment guidelines issued in 2015," we grasp the practice situation of the case of previously treated polymyositis / dermatomyositis in the past 20 years in this hospital and examine clinical problems. [Methods] We searched polymyositis, dermatomyositis and a diagnosed case (27) on an electronic chart from October, 1998 to October, 2018. In conformity with "the diagnostic criteria, practice guidelines on polymyositis, dermatomyositis," we received the analysis of various complications, therapies, age, sex, examination data of the target cases. [Results] Sex: Seven men: 20 women, Age at investigation 54.2±13.4 years old, Age at onset 50.1±14.2 years old, Polymyositis / dermatomyositis:11/16, Interstitial pneumo-

nia:12, Malignant tumor⁴, Autoimmune disease¹⁵ (MCTD⁴, SjS, SSc each³), aJo-1 Ab (+)², aARS Ab (+)¹, aMDA5 Ab (+)¹, Treatment regimen: Steroid 27 (oral Predonine 27, Steroid pulse 3), Cyclosporine 2, Tacrolimus 6, IVIG 2, MTX³. Outcome: Remission 20, Recurrence 5, Death 2. [Conclusions] As for the treatment that we received, approximately adapted treatment was performed in new guidelines. The cases that a periodical search was not accomplished appeared about the complications such as interstitial pneumonia or the malignant tumor.

P3-084

Predictive serum biomarkers for mortality and relapse in idiopathic inflammatory myopathies-associated interstitial lung disease

Yoko Nakagome, Yasushi Kondo, Kazuki Hirano, Takayoshi Kurabayashi, Sho Sasaki, Yasushi Koyama, Mai Sugiyama, Yuto Izumi, Chiho Yamada, Shinji Sato
Department of Rheumatology, Tokai University

Conflict of interest: None

[Object] To identify predictive serum biomarkers of mortality and recurrence in idiopathic inflammatory myopathies (IIM)-associated ILD. [Methods] A total of 125 of IIM-associated ILD patients were enrolled. The risk of mortality and relapse were examined using the recent predictive model that combined the serum biomarkers (including serum ferritin, CRP, KL-6 levels and anti-MDA5 antibody positivity). [Results] 28 patients were positive for anti-MDA5 antibody and 75 patients had anti-ARS antibody. During the observation period (median 42 months), Death related to ILD was observed in 31 patients. The mortality of ILD was significantly associated with positive numbers of serum biomarkers of predictive risk model for PM/DM-ILD. Univariate analysis showed that serum ferritin and CRP levels were correlated with mortality although they were not associated with recurrence of ILD. Only serum KL-6 level was significantly associated with recurrence of ILD. [Conclusions] The predictive risk model of the combined evaluation of autoantibodies and serum biomarkers is useful for assessing the prediction of mortality in IIM-associated ILD. Only serum KL-6 was associated with relapse of IIM-associated ILD. To identify predictive serum biomarkers of poor survival and recurrence in myositis-associated ILD.

P3-085

The involvement of type I interferon in pathophysiology of dermatomyositis

Jeong Hoon Park^{1,2}, Hachirou Konaka^{2,3}, Eri Itotagawa^{2,3}, Yasuhiro Kato^{2,3,4}, Hyota Takamatsu^{2,3}, Atsushi Kumanogoh^{2,3}

¹Osaka University Faculty of Medicine, ²Department of Immunopathology, World Premier International Research Center Immunology Frontier Research Center, ³Department of Respiratory Medicine and Clinical Immunology, Osaka University Graduate School of Medicine, ⁴Division of Allergy, Rheumatology and Connective Tissue Disease, NTT West Osaka Hospital

Conflict of interest: None

[Object] Expression of interferon-stimulated genes (ISGs) has been reported in polymyositis/dermatomyositis (PM/DM). However, only a few studies have directly measured type I interferon (IFN-I) in patients. Here, we evaluated IFN-I in the serum of PM/DM and studied its clinical significance. [Methods] Sera from PM/DM (n=40) and healthy controls (HC; n=37) were collected to measure IFN-I bioactivity and ISG-inducing activity using a cell-based reporter system. To identify the molecular mechanisms of IFN-I production, knockout reporter cells were generated. [Results] IFN-I bioactivity and ISG-inducing activity were significantly higher in DM than PM or HC. Elevated IFN-I was observed almost exclusively in DM patients with anti-MDA5 antibody and associated with clinical manifestation. The ISG-inducing activity was completely diminished in IFNAR2-knockout reporter cells. [Conclusions] Anti-MDA5 antibody-positive DM patients with high IFN-I levels tended to have severe disease manifestation. Diminished ISG-inducing activity in IFNAR2-knockout reporter cells suggested that it was induced by IFN-I itself and not by other extracellular factors, implying IFN-I overproduction by cell-intrinsic abnormalities. Our data indicate that IFN-I signaling may be a promising therapeutic target for DM.

P3-086

The study on prognostic factor for anti-MDA5-antibody positive DM patients

Toshiki Kido, Hiroyuki Hounoki, Takafumi Onose, Naonori Sugishita, Miho Yamazaki, Ryoko Asano, Reina Tsuda, Koichiro Shinoda, Hirofumi Taki, Kazuyuki Tobe
The First Division of Internal Medicine, Toyama University Hospital, Toyama, Japan

Conflict of interest: None

[Object] The aim of this study is to retrospectively review the clinical practice of our institution and to evaluate the clinical manifestation and prognostic factors in patients with interstitial pneumonia (IP) associated with anti-melanoma differentiation-associated gene 5 (MDA5) antibody (Ab) positive dermatomyositis (DM). [Methods] Subject comprised 7 patients who presented with DM positive for anti-MDA5 Ab. Base line characteristics, clinical manifestations, parameters and outcomes were recorded (5 survived, 2 died). [Results] We analysed continuous variables such as highest serum ferritin, LDH, anti-MDA5 Ab titer and age of diagnosis, which had no significance in two groups of survived group and that with fatal outcome. We also considered IP involvement in right middle lobe, bacteremia and pneumomediastinum during treatment course, and we found the last two factors were more frequently in the group with outcome of death. [Conclusions] Bacteremia and pneumomediastinum seems to be important factors which contribute to poor outcome in MDA5 Ab positive DM patients.

P3-087

Initial predictors of poor survival in anti-melanoma differentiation-associated gene 5 antibody-associated dermatomyositis and rapidly progressive interstitial lung disease

Kazuki Hirano, Yasushi Kondo, Yoko Nakagome, Mai Sugiyama, Yuto Izumi, Sho Sasaki, Takayoshi Kurabayashi, Yasushi Koyama, Chiho Yamada, Shinji Sato
Department of Rheumatology, Tokai University

Conflict of interest: None

Initial predictors of poor survival in anti-melanoma differentiation-associated gene 5 antibody-associated dermatomyositis and rapidly progressive interstitial lung disease

[Objective] To identify initial predictors of poor survival in patients with anti-melanoma differentiation-associated gene 5 antibody (anti-MDA5 ab) associated dermatomyositis (DM) and rapidly progressive interstitial lung disease (RP-ILD). [Methods] Twenty-eight patients with anti-MDA5ab associated DM and RP-ILD were enrolled. We retrospectively collected clinical data at the time of diagnosis and their outcome. we analyzed associations between them by univariate and multivariate analyses. [Results] The mean age of 28 patients was 56.3±10.4 years. During the observation period (median: 22 months), 14 patients died (50%) due to RP-ILD. Univariate analysis revealed that age at onset, serum levels of ferritin, CRP and SP-D were significantly associated with mortality. Subsequently we performed multivariate analysis and identified the elevation of serum SP-D as independent risk factor for mortality due to RP-ILD: (p <0.01; HR 1.02, 95%CI 1.01-1.04) [Conclusion] High serum SP-D concentration at baseline might be an independent predictor of poor survival in patients with anti-MDA5ab associated DM and RP-ILD.

P3-088

Clinical characteristics and prognostic factors in patients with anti-MDA5 antibody positive dermatomyositis

Shun Nomura, Ryosuke Hara, Wataru Ishii
Division of Rheumatology, Nagano Red Cross Hospital

Conflict of interest: None

[Object] Anti-MDA5 (melanoma differentiation-associated gene5) antibody positive dermatomyositis patients show rapidly progressive interstitial pneumonia. The aim of this study is to elucidate clinical characteristics and prognostic factors in patients with anti-MDA5 positive dermatomyositis. [Methods] We retrospectively examined clinical data,

treatment and outcome of anti-MDA5 antibody positive dermatomyositis patients who were admitted to our hospital between April 2015 and October 2018. [Results] Ten patients were enrolled in this study. Six patients survived and 4 patients died. Interval between onset of disease and commencement of treatment was 102 days in survival group and 29 days in fatal group. Serum ferritin, KL-6 and CRP were higher in fatal group than survival group. All patients were treated with oral prednisolone in combination with calcineurin inhibitors. All patients in fatal group were treated with methylprednisolone pulse therapy and intravenous cyclophosphamide (IVCY). On the other hand, only 3 patients in survival group were treated with IVCY. [Conclusions] Anti-MDA5 antibody positive dermatomyositis is fatal disease. Early combination therapy of immunosuppressants improved the prognosis, but it is not enough. We need to find out new effective treatment.

P3-089

Transition of ferritin value during initial treatment in anti-MDA5 antibody positive interstitial pneumonia and anti-synthetase syndrome

Satoshi Omura, Takuya Yanagida, Masatoshi Kadoya, Atsushi Omoto, Wataru Fukuda

Center for Rheumatic Disease, Japanese Red Cross Kyoto Daiichi Hospital

Conflict of interest: None

[Object] Although it is known that high levels of ferritin before treatment start with Anti-synthetase syndrome (ASS) and anti-MDA5 antibody-positive interstitial pneumonia become prognostic exacerbating factors, there are few reports reported. We investigated the trend of ferritin value at the beginning of treatment. [Methods] A case of each disease diagnosed at our hospital and receiving initial treatment was taken from January 2007 to October 2018. Patients measuring ferritin levels at least twice before treatment and 1 to 4 weeks after treatment were selected from among them and examined for the course of ferritin values from the start of treatment to 4 weeks. [Results] The each case satisfying the above was 6 cases and 4 cases. The median ferritin values before treatment were 690.5 ng / mL and 564 ng / mL, respectively. Except for one case of ASS, the ferritin value increased after treatment started. In all cases, the ferritin level peaked within 4 weeks. The median peak-out of ferritin levels in 6 surviving cases in total was 14 days and in dead cases it was 25.5 days. [Conclusions] It was suggested that the length of the period required for peak out of ferritin value may be a factor of prognostic prediction.

P3-090

Necessity of triple therapy for anti-MDA5 antibody positive dermatomyositis

Takayasu Ando, Takeshi Suzuki, Harunobu Iida, Kanako Suzuki, Yutaka Goto, Marina Uchida, Yusa Asari, Hisae Fujimoto, Shoshi Shinagawa, Kana Ishimori, Keiichi Sakurai, Tomofumi Kiyokawa, Hiromi Matsushita, Yukiko Takakuwa, Kumiko Tonooka, Mitsuru Imamura, Yoshioki Yamasaki, Seido Ooka, Hiroko Nagafuchi, Kimito Kawahata
Division of Rheumatology and Allergology, St. Marianna University School of Medicine

Conflict of interest: None

[Object] To evaluate necessity of triple therapy for anti-MDA5 antibody (aMDA5 Ab) positive dermatomyositis (DM). [Methods] The data of aMDA5 Ab positive patients were retrospectively collected from clinical records. These patients were classified triple therapy group and double therapy group as induction therapy. We compared both groups of clinical characteristics, prognosis and existence of interstitial pneumonia (IP) recurrence. Rapidly progressive IP (RP-IP) was defined as developing respiratory symptoms within 1 month after its onset. [Results] All 10 patients were female and mean age was 50.5±10.8. Six patients were triple therapy group (IVCY+Tac:4, IVCY+CsA:2) and 4 were double therapy group (PSL+IVCY:2, PSL+Tac:2). Survival rate in all patients was 90%. Baseline characteristics were not significantly different between two groups, but cytomegaloviremia was significantly increased in triple therapy group ($p < 0.01$). In double therapy group, 2 patients complicated RP-

IP, and one of them died of infections, but another 3 patients survive without recurrence of IP. [Conclusion] Both aMDA5 Ab positive DM patients treated with triple and double therapy had good survival rate compared with previous reports. Triple therapy will not be necessary for all aMDA5 Ab positive DM patients.

P3-091

Usefulness of Combined Immunosuppressive Therapy in Anti-MDA5-Positive Dermatomyositis with Interstitial Lung Disease

Hideaki Tsuji¹, Ran Nakashima¹, Yuji Hosono², Yoshitaka Imura³, Masato Yagita³, Hajime Yoshifuji¹, Shintaro Hirata⁴, Takaki Nojima⁴, Eiji Sugiyama⁴, Kazuhiro Hatta⁵, Yoshio Taguchi⁶, Masaki Katayama⁷, Kiminobu Tanizawa⁸, Tomohiro Handa⁸, Takeshi Kubo⁹, Shuji Akizuki¹, Kosaku Murakami¹, Motomu Hashimoto¹⁰, Masao Tanaka¹⁰, Koichiro Ohmura¹, Tsuneyo Mimori¹

¹Department of Rheumatology and Clinical Immunology, Kyoto University Graduate School of Medicine, ²National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, ³Department of Clinical Immunology and Rheumatology, The Tazuke-Kofukai Medical Research Institute, Kitano Hospital, ⁴Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, ⁵Department of General Medicine, Tenri Hospital, ⁶Department of Respiratory Medicine, Tenri Hospital, ⁷Department of Rheumatology and Clinical Immunology, Osaka Red Cross Hospital, ⁸Department of Respiratory Medicine, Kyoto University Hospital, ⁹Department of Diagnostic Imaging and Nuclear Medicine, Kyoto University Hospital, ¹⁰Department of Advanced Medicine for Rheumatic Diseases, Kyoto University Hospital

Conflict of interest: None

[Object] Since the standard treatment had not been established for rapidly progressive interstitial lung disease (RP-ILD) in anti-MDA5-positive dermatomyositis (DM), we prospectively evaluated the efficacy of combined immunosuppressive therapy. [Methods] Newly onset adult Japanese anti-MDA5-positive DM patients with ILD received combined immunosuppressive regimen with glucocorticoids, tacrolimus, and intravenous cyclophosphamide (IVCY) and/or plasmapheresis (PE). We set a historical control with step-up treatment of immunosuppressants. The primary endpoint was 6-month survival and 2nd endpoint was analyzing transition of laboratory data during 52 weeks. [Results] Combined immunosuppressive regimen (n=29) received IVCY about 20days earlier with shorter intervals and received PE more frequently than step-up treatment (n=15). Six-month survival rates were 89% and 33%, respectively ($p < 0.0001$). At week 52, the levels of anti-MDA5, ferritin, and %VC were improved. Cytomegalovirus reactivation was frequently observed during 52 weeks. [Conclusions] Early combined immunosuppressive therapy is effective for anti-MDA5-positive DM with ILD, and in intractable cases, additional effect can be expected in PE. Opportunistic infections should be monitored during treatment.

P3-092

Clinical features of anti-MDA5 antibody positive amyopathic dermatomyositis patients

Kazuma Ino, Takayuki Hoshiyama, Takumi Muramatsu, Yasuhiro Hasegawa, Junichi Kondo, Toshihiro Tono, Yoshiyuki Arinuma, Tatsuo Nagai, Sumiaki Tanaka, Kunihiro Yamaoka
Rheumatology and Infectious Diseases, Kitasato University School of Medicine, Sagamihara, Kanagawa, Japan

Conflict of interest: None

[Object] In order to understand its clinical features, we examined anti-MDA-5 (melanoma differentiation-associated gene 5) antibody positive amyopathic dermatomyositis (ADM) experienced at our hospital. [Methods] We retrospectively examined initial ADM patients who hospitalized in our department and were confirmed as positive for anti-MDA5 antibody (including anti-CADM140 antibody) after March 2013. [Results] 13 patients had anti-MDA 5 antibody positive. The mean age was 51.7 years, sex was 4 males and 9 females, all cases had skin rash, 12 cases had interstitial pneumonia, myositis such as muscle weakness were observed in 3 cases. There were 10 surviving and 3 deaths. The average ferritin and KL-6 values were 505 ng/mL and 740.1 U/mL respectively. 11

patients survived and 3 patients were dead. Since October 2016 when anti-MDA-5 antibody measurement was covered in insurance, There were no deaths (n=6). [conclusions] Measurement of anti-MDA5 antibody may sample the rapid progressive dermatomyositis early and contribute to improvement prognosis by strong immunosuppressive therapy.

P3-093

Three cases of hemophagocytic syndrome in dermatomyositis with anti-MDA-5 autoantibody

Manabu Honda¹, Mayuko Moriyama¹, Masahiro Kondo¹, Shunichi Kumakura², Yoshiko Sumita¹, Yohko Murakawa^{1,2}

¹Department of Rheumatology, Shimane University, ²Department of Medical Education and Research, Shimane University

Conflict of interest: None

Hemophagocytic syndrome (HPS) is a rare complication but exhibits poor prognosis in dermatomyositis (DM). We describe here three cases with HPS in DM with anti-MDA-5 autoantibody. Case 1: A 63-year-old woman was admitted to our hospital with high fever, muscle weakness, Gottron's papule, mechanic's hands. Laboratory tests showed elevated serum muscle enzymes, thrombocytopenia and hyperferritinemia. Bone marrow aspiration and biopsy revealed hemophagocytosis. She was diagnosed as DM with HPS. After she died of interstitial pneumonia, it found that anti-MDA5 autoantibody was positive. Case 2: A 50-year-old man was admitted to our hospital with high fever, dysphagia, facial erythema, mechanic's hand, leukopenia and hyperferritinemia. Anti-MDA5 autoantibody was positive. He was diagnosed as amyopathic DM. Bone marrow examinations revealed hemophagocytosis. Case 3: A 57-year-old woman was admitted to our hospital with arthralgia, muscle weakness, facial erythema, heliotrope eruption, shawl and V neck signs, elevated serum muscle enzymes, pancytopenia and hyperferritinemia. Anti-MDA5 autoantibody was positive. She was diagnosed as DM. She was also diagnosed as HPS with bone marrow examinations. Thus, our cases indicated that anti-MDA-5 autoantibody might be associated with HPS.

P3-094

Three cases with dermatomyositis of anti-MDA5 antibody which followed various processes

Maki Shibamoto, Mai Morimoto, Tetsuya Furukawa, Kazuteru Noguchi, Rei Tadokoro, Kazuyuki Tsuboi, Mei Tani, Chie Ogita, Takahiro Yoshikawa, Masao Tamura, Tepei Hashimoto, Naoto Azuma, Masayasu Kitano, Kiyoshi Matsui

Division of Rheumatology, Hyogo College of Medicine Department of Internal Medicine

Conflict of interest: None

We report three cases with interstitial lung disease (ILD) of anti-MDA5 antibody positive. The first patient was 31-year-old man, who had gottron's sign and ferritin's elevation. CT showed ground-glass opacification (GGO) in both lower lungs. He was received methylprednisolone (mPSL) pulse therapy following prednisolone (PSL) 1mg/kg/day, tacrolimus (TAC) and intravenous cyclophosphamide (IVCY). Later, gottron's sign was disappeared, ferritin level decreased. The second patient was 37-year-old woman, who had gottron's sign and ferritin's elevation. CT showed random GGO in both lungs. She was received PSL0.8mg/kg/day, TAC and IVCY. However, she had steroid psychosis and could not receive intravenous treatment. We changed to oral cyclophosphamide, and gottron's sign was disappeared, ferritin level decreased. The third patient was 82-year-old man, who had the erythema in finger, elbow joint stretch side and back. CT showed diffuse GGO in both lungs. He was received mPSL pulse therapy following PSL1mg/kg/day, TAC and IVCY. However, he had sigmoid colon piercing and underwent abdominal surgery. After oxygenation had got worse, and he died. We experienced three cases which followed various processes, and report with literature consideration.

P3-095

Clinical features of anti-MDA5 antibody-positive clinically amyopathic dermatomyositis that caused repeated aggravation of interstitial pneumonia

Satoshi Suzuki¹, Takuya Nishi¹, Shota Sakuma¹, Keigo Ikeda¹, Ken Yamaji², Naoto Tamura², Shinji Morimoto¹

¹Department of Internal Medicine and Rheumatology, Juntendo University, Urayasu Hospital, ²Department of Internal Medicine and Rheumatology, Faculty of Medicine, Juntendo University

Conflict of interest: None

Anti-MDA5 antibody-positive clinically amyopathic dermatomyositis (CADM) often accompanies rapidly progressive interstitial pneumonia (RP-ILD). However, relapse is reported to be infrequent if the treatment is successful, although the long-term prognosis is unclear. We examined the clinical features of three cases of CADM with recurrences of ILD. In case 1, developed CADM at 44 years of age and was treated with steroid pulse therapy (IVmPSL) and 50 mg/day but was hospitalized with ILD aggravation at 47 and 51 years of age. In case 2, developed CADM at 54 years of age and was treated with IVmPSL and 40 mg/day of PSL with cyclosporin (CyA); ILD was aggravated at 61 years of age and cyclophosphamide pulse therapy (IVCY). ILD was aggravated for the third time at 66 years of age, and the patient died. In case 3, developed CADM at 60 years of age. IVmPSL was initiated with 50 mg/day of PSL; CyA was also added. However, ILD recurred at 67 years of age; thus, CyA was replaced with tacrolimus, and IVCY was introduced. Although cases of recurring CADM are rare, they do exist and can sometimes be fatal. The prognosis for CADM has improved over time owing to its establishment as a disease. However, further accumulation of research is needed to ascertain its long-term prognosis.

P3-096

Clinical significance in the early induction of IVCY in patients with anti-MDA5 antibody-positive DM associated with interstitial lung disease

Takuma Koga, Yumi Yoshida, Makiko Hayashi, Kyoko Fujimoto, Satoshi Sakamoto, Yukiko Hidaka, Masaki Okamoto, Shinjiro Kaieda, Masaki Tominaga, Tomoaki Hoshino, Hiroaki Ida

Division of Rheumatology, Department of Medicine, Kurume University School of Medicine

Conflict of interest: None

Background: Intensive immunosuppressive therapy including steroids, calcinurin inhibitor and IVCY has been reported to be improved poor prognosis in anti-MDA-5 antibody positive DM associated rapidly progressive interstitial lung disease (RP-ILD). We examined whether the early induction of IVCY may improve prognosis. Methods: A total of fifteen patients diagnosed as having anti-MDA-5 antibody-positive DM with ILD from 2007 to 2018 were enrolled. All patients received intensive immunotherapy including IVCY. In addition, respiratory function was analyzed in anti-MDA-5 ab or anti-ARS ab positive ILD during chronic phase. Results: Seven patients were received IVCY within 28days after ILD diagnosis and only one patient was killed by RP-ILD. Four out of eight patient, who received IVCY after 28 days ILD diagnosis, died. In the chronic phase, forced vital capacity (FVC) tended to be improved in anti-MDA-5 ab positive ILD. In contrast, FVC was decreased in anti-ARS ab-positive ILD in the long observation period. Conclusion: Early induction of IVCY may improve poor prognosis caused by RP-ILD. In the chronic phase of anti MDA-5 antibody positive DM patients with ILD, pulmonary function test results were well maintained and had a good clinical course.

P3-097

Three clinically amyopathic dermatomyositis cases with anti MDA5 antibody who were treated with hydroxychloroquine

Nobuyuki Ono, Mariko Sakai, Yoshinobu Nakao, Yuri Sadanaga, Akihito Maruyama, Syuichi Koarada, Yoshifumi Tada

Department of Rheumatology, Saga University Hospital

Conflict of interest: None

The usefulness of hydroxychloroquine (HCQ) has also been reported in dermatomyositis (DM), but its use is limited due to its myotoxicity. We reported three cases using HCQ for anti-MDA5 antibody positive amyopathic dermatomyositis (CADM). Case 1: A 74-year-old male was suffered from skin symptoms with multiple ulcers and subacute interstitial pneumonia with elevated ferritin (948 mg / ml) and anti-MDA 5 antibody. His refractory skin ulcers for the three-drug combination therapy was improved by additional HCQ treatment. Case 2: 82-year-old female with progressive interstitial pneumonia appeared during treatment of NP-SLE was diagnosed as CADM from Gottron's sign, elevated ferritin (1395 mg / ml), and anti-MDA 5 antibody. The triple combination therapy with HCQ improved her respiratory symptoms. Case 3: A 74-year-old female, with Gottron's sign, subacute interstitial pneumonia, elevated ferritin (719 mg / ml) and MDA 5 antibody was diagnosed as CADM. The skin symptoms and high ferritinemia were refractory for the triple combination therapy. Additional HCQ treatment improved them. (Discussion) Anti-MDA5 antibody positive dermatomyositis is known to have high type 1-IFN activity, suggesting that HCQ may be useful for the remission induction and maintenance therapy.

P3-098

A case of successful treatment of combination with plasma exchange and rituximab for rapid progressive interstitial lung disease with anti MDA-5 antibody positive dermatomyositis

Hiroshi Hamada¹, Masao Katayama², Kahori Oshima², Nobuyoshi Minemura², Eiji Nagasawa², Kyoko Takano², Michita Suzuki², Kumiko Umemura², Syunsuke Yokoi², Takakazu Hasegawa², Mayu Sugiyama²

¹General Medicine, Nagoya Medical Center, ²Department of Rheumatology, Nagoya Medical Center

Conflict of interest: None

A 54-year-old female has had rash on face since one month ago, and on both hands from the end of the same month. Since she has had fever and muscle pain in proximal limbs. She saw previous doctor and chest CT revealed ground-glass appearance, so she was suspected of DM. After that She was referred to our hospital for purpose of treatment. After hospitalization we found anti-MDA5 antibody was positive, for Steroid pulse, tacrolimus and endoxan were performed. The interstitial shadow progressed was observed even after additional treatment with Endotoxin adsorption, immunoglobulin therapy. So rituximab and plasma exchange were introduced. So respiratory state improved, and titer of anti-MDA5 antibody and ferritin declined. And she was discharged on 156th day. (Discussion) It is known interstitial lung disease with anti-MDA5 antibody positive DM is refractory to treatment and poor prognosis. There is no definitive treatment, In this case, there was a possibility that plasma exchange and rituximab could lead to good result. Further investigation is necessary in the future.

P3-099

A case of that was able to inhibit progress by IVIg and RTX administration for the immunosuppressive therapy anti MDA-5 antibody-positive treatment-resistant interstitial pneumonia

Masami Mizuno, Ken Takao, Takuo Hirota, Yukio Horikawa
Department of Diabetes and Endocrinology, Gifu University Hospital

Conflict of interest: None

[Case] We report the case of a patient who was hospitalized for dermatomyositis in 2017. The diagnosis was based on the presence of anti-MDA-5 antibody and a mild ground glass shadow appearance on laboratory investigations. Prednisolone 55 mg and tacrolimus were subsequently initiated. Although there was no evidence of exacerbation with the ground glass shadow evaluation, KL-6, lactate dehydrogenase, ferritin, and PaO₂ values suggested otherwise. High dose cyclophosphamide was administered intravenously from April. A diagnosis of rapidly progressive interstitial lung disease (RP-ILD) was made by the end of May. The patient was subsequently admitted to our department and steroid pulse therapy was initiated. However, RP-ILD aggravated following which rituximab (RTX) and intravenous immunoglobulin (IVIg) therapy was added. The patient was stable subsequently. Markers such as KL-6, SP-D, and antiMDA-5 antibody suggested improvement. However, RP-

ILD aggravated abruptly by June end and the patient succumbed to septic shock. [Discussion] The management of advanced RP-ILD with positive antiMDA-5 antibody is unclear. Although IVIg and RTX were partially effective, further evidence is necessary to prove its safety and efficacy.

P3-100

A case of anti-MDA5 antibody positive amyopathic dermatomyositis with refractory eruption and chronic interstitial lung disease managed by introduction of triple therapy

Yuki Mizutani, Kentaro Noda, Naohiro Sugitani, Yasuo Suzuki, Ayako Nakajima

Center for Rheumatic Diseases, Tsu, Japan, Mie University Hospital

Conflict of interest: None

[Case presentation] A 43-years-old female complained fever and joint pain from 1 month before hospitalization. She had no muscle weakness nor elevated CK, but had heliotrope rash and Gottron's purpura. Biopsy from her hand skin revealed liquefactive degeneration of the epidermis. She was diagnosed as having amyopathic dermatomyositis (CADM). Interstitial lung disease (ILD) was confirmed on CT and the anti-MDA5 antibody titer was 143 index. Since ferritin was slightly high at 222 ng/mL and she had no respiratory symptom at her first visit, treatment with prednisolone 30 mg/day and tacrolimus 3 mg/day was started. Fatigue and joint pain improved, however, erythema remained and ferritin increased. On the 10th day of treatment, she received cyclophosphamide intravenous injection therapy (IVCY). By continuation of IVCY every 2 weeks, ferritin decreased, erythema and lung slightly improved. [Clinical significance] In this case, initial ferritin level was not high enough, however, we needed 3 agents to manage refractory erythema and ILD. We emphasize that it is necessary to treat such patient with 3 agents intensively from the early stage of CADM.

P3-101

Early detection of rapidly progressive interstitial lung disease with anti-MDA5 antibody-positive clinically amyopathic dermatomyositis after caused by exacerbation of skin rash

Naoya Matsuoka, Akimasa Asai, Mayumi Ito, Makoto Yamaguchi, Shiho Iwagaitsu, Hironobu Nobata, Takayuki Katsuno, Shogo Banno, Yasuhiko Ito

Aichi Medical University

Conflict of interest: None

In June 2018, a 57-year-old Japanese woman was diagnosed with hemophagocytic syndrome and clinically amyopathic dermatomyositis (CADM) based on the findings of rash on the fingers and legs, pancytopenia and a high titer of anti-MDA5 antibody (158 index). We administered 500mg of methyl-prednisolone (m-PSL) pulse therapy followed by prednisolone (PSL) 50mg/day with tapering and add on tacrolimus (TAC), and symptoms were improved. However, after three month, she presented exacerbation of erythemas, and a chest computed tomography (CT) showed diffuse ground-glass opacities with path cures of consolidations in both the middle and lower lung fields. We diagnosed rapidly progressive interstitial lung disease (RP-ILD). We successfully treated with 500mg of m-PSL pulse and intravenous cyclophosphamide therapy followed by PSL and TAC. The patient's skin symptoms and lung abnormal shadows decreased. This case suggests that careful physical examinations and monitoring the serum makers are important. Exacerbation of skin rash could be one of the symptoms of early detection of lung involvement with dermatomyositis.

P3-102

A markedly effective multi-agent immunosuppressive therapy and plasma exchange for Clinical Amyopathic Dermatomyositis (CADM) accompanied by interstitial Pneumonia exhibiting anti-MDA5 antibody positivity and high ferritin levels: A Case Report

Kazuyuki Suzuki¹, Kiyooki Ito¹, Misaki Yoshida², Kunihiro Ogane², Masahiro Konishi¹, Hajime Sanada¹, Takeshi Zoshima¹, Satoshi Hara¹, Ichiro Mizushima¹, Hiroshi Fujii¹, Kazunori Yamada¹, Mitsuhiro Kawano¹

Conflict of interest: None

[Case] A 50-year-old man presented at a local clinic with fever and fatigability. He had had rubefaction around the eyelids erythema of the fingertips from 4 months before. He had typical skin findings such as heliotrope rash and Gottron's sign. Blood tests revealed no muscular symptoms and elevated CK level. Thus, a diagnosis of CADM was made. Blood test revealed anti-MDA5 antibody positivity and high ferritin levels and CT showed interstitial Pneumonia. Owing to his high risk of RP-ILD, he was treated with 60mg/day PSL, 3mg/day Tac, and IVCY. The interstitial pneumonia shadows improved but reexacerbated with respiratory symptoms after PSL dose attenuation. Owing to the high anti-MDA5 antibody titer levels and persistent markedly high ferritin levels (10,182 ng/ml), he was transferred to our hospital. Plasma exchange (PE) was conducted in addition to the multi-agent immunosuppressive therapy. After PE, anti-MDA5 antibody titer and ferritin levels markedly decreased. His respiratory symptoms improved, and the PSL dose was reduced to 30mg/day. [Discussion] Anti-MDA5 antibody titer and ferritin levels are strongly associated with poor prognosis in CADM accompanied by RP-ILD. Therefore, patients with high anti-MDA5 antibody titer and ferritin levels require early intensive therapy.

P3-103

Successful treatment of single filtration plasmapheresis for anti-MDA5 antibody positive dermatomyositis that developed pneumocystis pneumonia during treatment for rapidly progressive ILD

Masahiro Kogami, Yoshiyuki Abe, Kurisu Tada, Ken Yamaji, Naoto Tamura

Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine

Conflict of interest: None

The patient is a 66 years old woman. On May, she presented with finger joint arthralgia, skin rash and dry cough. Because these symptoms weren't improved, she was hospitalized on June. Anti-MDA5 antibody was positive, and she had Gottron's sign and rapidly progressive ILD. She received methylprednisolone pulse therapy from day 1 to day 3, and intravenous cyclophosphamide therapy (IVCY) on day 4 and tacrolimus (TAC) from day 5. After these treatments, her respiratory condition was improved but image of CT scan was not improved. We added single filtration plasmapheresis (SFPP) on day 21, however, she complicated with anaphylactic shock for FFP, then SFPP was discontinued. On day 35, her respiratory condition was suddenly worse, it was difficult to distinguish ILD exacerbation from pneumocystis pneumonia by image of CT scan. We resumed methylprednisolone pulse with TMPco, and TAC and IVCY was discontinued. In addition, we started SFPP again to ILD from day 39, and SFPP was done total 16 times. On day 76, oxygen therapy was no longer necessary because of respiratory status improved, and she discharged from hospital on day 101. We report that the effective of SFPP for anti-MDA5 antibody positive dermatomyositis with some literature review.

P3-104

A case of anti-MDA5 antibody-positive dermatomyositis complicating rapidly progressive interstitial lung disease and pneumomediastinum successfully treated with multidisciplinary therapy including tofacitinib

Manami Kato, Kei Ikeda, Takahiro Kageyama, Tadamichi Kasuya, Takashi Kumagai, Hiroki Furuya, Shunsuke Furuta, Tomohiro Tamachi, Akira Suto, Kotaro Suzuki, Hiroshi Nakajima

Department of Allergy and Clinical Immunology, Chiba University Hospital, Chiba, Japan

Conflict of interest: None

The prognosis of rapidly progressive interstitial lung disease (ILD) that is associated with anti-MDA5 antibody-positive dermatomyositis is poor and early intervention with high-dose corticosteroids and combined multiple immunosuppressive agents is recommended. However, treat-

ment strategy for refractory cases has not been established. Here, we describe a 44-year-old man with anti-MDA5 antibody-positive dermatomyositis complicating rapidly progressive ILD. His ILD was progressive and accompanied by pneumomediastinum despite receiving the combination of high-dose corticosteroids, calcineurin inhibitors, and cyclophosphamide. While double filtration plasmapheresis was not effective either, multidisciplinary therapy including plasma exchange and tofacitinib improved his life-threatening conditions. His ILD and dermatomyositis are stable with no signs of infection on prednisolone 5 mg daily, cyclosporine 100 mg twice daily, and tofacitinib 5 mg twice daily one year after discharge. Tofacitinib merits further investigation as a novel treatment option for refractory cases of this disease.

P3-105

Successful treatment with tofacitinib for anti-MDA5 antibody-positive dermatomyositis with interstitial pneumonia complicated with rheumatoid arthritis, and throughout the treatment course tofacitinib could be discontinued

Yuki Ueno¹, Katsuhiko Oda¹, Koji Nagai², Hideyuki Shiba¹, Masakazu Sugino¹

¹Department of Internal Medicine, Aino Hospital, Osaka, Japan, ²Department of Internal Medicine IV, Osaka Medical College, Osaka, Japan

Conflict of interest: Yes

[Introduction] In JCR 2018, we reported a case of successful treatment with tofacitinib (TOF) for anti-MDA5 antibody-positive dermatomyositis with acute interstitial pneumonia (DM-AIP) complicated with rheumatoid arthritis (RA). We additionally report that TOF can be discontinued during remission maintenance period. [Case] A 41-year-old female was diagnosed with RA and anti-MDA5 antibody-positive DM-AIP in 2017. She was treated with prednisolone (PDN), cyclosporine (CSA) and intravenous cyclophosphamide pluse therapy. Chest CT showed that consolidation/ground-glass opacity had partially improved. However, her respiratory condition was getting worse. And, she still suffered from polyarthritis. Informed consent was obtained from patient and family, we additionally administered TOF. After the TOF treatment, not only polyarthritis, but also IP improved. The dosage of PDN was decreased to 5 mg/day, and we discontinued TOF on 11 months after the TOF administration. After, polyarthritis and IP had not exacerbated. Side effects were renal dysfunction due to CSA, herpes zoster, and skin and soft tissue infection. [discussion] Our case suggest in JCR 2018 and 2019 that TOF may be useful for remission induction treatment and can be discontinued during remission maintenance period.

P3-106

An autopsy case of anti-MDA5 antibody positive dermatomyositis with rapid progressive interstitial pneumonia

Naofumi Chinen¹, Tatsuo Mori²

¹Department of Internal Medicine, Tamnanbu Chi-iki Hospital, ²Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center

Conflict of interest: None

A-78-year old man who had a past history of surgery for gastric and colon cancer was admitted to other hospital with pneumonia. He was treated with antibiotics, but his respiratory condition was worsen. After two weeks, he was transferred to our hospital. Gottron's papules and periungual erythemas were found. He did not complain of arthralgia and myalgia, but weakness of both quadriceps muscle was recognized. Laboratory findings showed normal CK level (139 U/mL) and slightly elevation of aldolase (10.3 U/L). CT scan showed diffuse ground glass appearance and infiltration in both lung. Skin biopsy from elbow showed vacuolization of dermoepidermal junction and perivascular lymphocytic infiltration. He was diagnosed with dermatomyositis with interstitial pneumonia. He was treated with mPSL pulse therapy, but died of respiratory failure after 7 days. At later date, there was proved to be positive of anti-MDA5 antibody (index 210). Autopsy findings of lung demonstrated diffuse alveolar damage with prominent hyaline membrane lining alveolar sac with edema of alveolar septae. Occasionally intra-alveolar hemorrhage and fibrin thrombi were seen. These findings was compatible to diffuse alveolar damage. Here we report a valuable autopsy case of anti-

P3-107

An autopsy case of anti-MDA5 antibody-positive dermatomyositis

Tsuyoshi Watanabe¹, Tatsuya Arai¹, Hiroyuki Yoshida², Yoshihiro Nakamura¹, Hiroki Ikai¹, Fumiya Kitamura², Mari Yamamoto¹, Yukari Murai², Koji Takasugi², Naoho Takizawa¹, Waka Kokuryo¹, Yoshiro Fujita^{1,2}

¹Department of Rheumatology, Chubu Rosai Hospital, ²Department of Nephrology, Chubu Rosai Hospital

Conflict of interest: None

[Case] A 72-year-old man presented with three weeks of decreased appetite and one week of erythema with pruritus on his back. He was emergently admitted due to persistent poor dietary intake and difficulty standing. Chest computed tomography revealed consolidation in the left lung and a pneumococcal urinary antigen test was positive. He was admitted with the initial diagnosis of bacterial pneumonia; however, his respiratory status did not improve after 5 days of antibiotics. Physical examination revealed blood blister-like palmar papules on his hand and flagellate erythema on his back. We considered dermatomyositis in the differential diagnosis, and pulsed intravenous methylprednisolone and cyclophosphamide with oral tacrolimus were started on day 5. On day 7, the presence of anti-MDA5 antibody was confirmed, and the patient was diagnosed with anti-MDA5 antibody-positive dermatomyositis. His respiratory status worsened rapidly and he died on day 14, despite intensive care. An autopsy was performed. [Clinical significance] In this case, we immediately started combination therapy with immunosuppressant agents for dermatomyositis after failure of antibiotic therapy; however, the patient eventually died. We present this case with the results of autopsy. Conflict of interest: None

P3-108

A case of interstitial pneumonia with dermatomyositis. Rapid inspection of anti-MDA 5 antibody is useful for early diagnosis and determination of therapy

Tomohiko Koboyama, Youhei Fujiki, Takuya Kotani, Koji Nagai, Kenichiro Hata, Tohru Takeuchi, Shigeki Arawaka
Osaka Medical College Hospital

Conflict of interest: None

A 35-year-old woman was admitted to our hospital with a 3-month history of muscle pain, erythematous eruptions, and dyspnea. A general examination revealed Gottron's papules, palmar papules, erythemas on the elbows and knees joints. Muscle weakness (MMT4) in the proximal muscle of the limbs were observed. Fine crackles were noted in the bilateral lower lung fields. Laboratory findings showed aldolase 8.7 U/L, CK 450 U/L, KL-6 464 U/mL, and ferritin 346 ng/mL. Anti-MDA5 antibody positive was found immediately. Chest high-resolution computed tomography (HRCT) scanning showed linear opacities, consolidations, and ground-glass opacities in the lower lobes. She was diagnosed as having rapid progressive interstitial pneumonia (RPIP) associated with anti-MDA5 antibody-positive dermatomyositis (DM). We started combination therapy including prednisolone, cyclosporine, and intravenous pulse cyclophosphamide (IVCY) on day 1. However, her IP resisted treatment. Thereafter we added mycophenolate mofetil with IVCY repeated intermittently. After these treatments, the serum ferritin level and radiologic findings gradually improved. Her RP-ILD has remained in remission. The anti-MDA5 antibody rapid test using ELISA kit (MESACUP™) in house was useful for diagnosis and determination of treatment.

P3-109

Anti-MDA5 antibody-positive dermatomyositis-associated interstitial pneumonia who had anti-ARS antibody positive on ELISA, but negative on RNA immunoprecipitation: A case report

Yoichi Nakayama¹, Saki Minoda¹, Hiroyuki Akebo¹, Hirofumi Miyake¹, Ryuichi Sada¹, Hiroyasu Ishimaru¹, Ran Nakashima², Tsuneyo Mimori², Kazuhiro Hatta¹

¹Department of General Internal Medicine, Tenri Hospital, Tenri, Japan,

Conflict of interest: None

Case A 54-year-old woman was admitted with bilateral thigh pain and weakness, and erythema of her face, chest, and hands. Physical examinations revealed proximal muscle weakness, heliotrope rash, and inverse Gottron's papules. Laboratory results were as follows: CK, 402 U/L; aldolase, 23.7 U/L; KL-6, 425 U/mL; and ferritin, 1586 ng/mL. Chest CT showed faint ground glass opacity (GGO) on the left upper lobe. Anti-ARS antibody (ARS-Ab) and anti-MDA5 antibody (MDA5-Ab) were reported to be positive on day 7 and 14, respectively. Follow-up CT showed exacerbation of GGO. We started multi-immunosuppressive therapy including pulse steroid therapy, IVCY, and tacrolimus (Tac). Moreover, we added plasma exchange, rituximab, and IVIg for the deterioration of her lung. The treatment led her stable disease state, and she kept treatment with 7mg of PSL and 3mg of Tac over a year. **Discussion** MDA5-Ab-positive DM often leads fatal interstitial pneumonia (IP). In our case, the patient was initially diagnosed as anti-synthetase syndrome, but ARS-Ab was negative on RNA precipitation. The positive finding of MDA5-Ab led us induction of early strong immunosuppressive therapy. **Conclusion** We need to consider existence of MDA5-Ab, if ARS-Ab is positive on ELISA assay in a patient with DM-associated IP.

P3-110

Muscle strength recovery progress from baseline in anti-ARS antibody syndrome

Naoki Mugii¹, Mitsuhiro Kawano², Takashi Matsushita³, Kazuhiko Takehara³

¹Department of Rehabilitation, Kanazawa University Hospital, Ishikawa, Japan, ²Division of Rheumatology, Department of Internal Medicine, Kanazawa University Hospital, Ishikawa, Japan, ³Department of Dermatology, Faculty of Medicine, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, Ishikawa, Japan

Conflict of interest: None

[Object] Muscle strength recovery have been reported in dermatomyositis/polymyositis patients after the start of therapeutic intervention, but no studies compared the recovery from the baseline. We aimed to analyze the muscle strength changes from the baseline until the stage of treatment as outpatient. [Methods] Twelve anti-ARS antibody syndrome patients with muscle weakness and elevated serum muscle enzymes joined the study at the baseline before the therapeutic intervention start. Quadriceps Femoris muscle strength was measured at 4 timeline points: baseline, within 1 week after the start of treatment (<1w), at discharge and as outpatient. We measured the muscle strength using a hand held dynamometer and obtained the percentage compared to the age-matched data from previous studies in healthy individuals. Serum Creatine Kinase (CK) was also investigated. [Results] The mean muscular strength were 70% (baseline), 75.2% (<1w), 84.7% (discharge), and significantly higher in outpatient point reaching 105.3% (p<0.05). Serum CK mean values were chronologically 2813, 1065, 88.2 and, 54.8. [Conclusions] The muscular strength and CK mean values showed considerable improvement throughout the treatment. The Quadriceps strength was fully recovered based in healthy individuals data.

P3-111

Coexistence of anti-SRP and anti-SS-A/Ro antibodies in inflammatory myopathy: Does the association occur by chance?

Tadashi Nakamura¹, Naoki Shiraishi², Seiyu Honda³

¹Clinical Rheumatology, Sakurajyuji Hospital, Kumamoto, Japan, ²Clinical Nephrology, Sakurajyuji Hospital, Kumamoto, Japan, ³Department of Rheumatology, Honda Clinic Office, Uto, Japan

Conflict of interest: None

[Object] Myositis-related autoantibodies are tools for the diagnosis in idiopathic inflammatory myopathies and placed into two groups: myositis-specific antibodies (MSAs) and myositis-associated antibodies (MAAs). Of the MSAs, anti-signal recognition particle (SRP) antibodies

are found in inflammatory myopathy (anti-SRP myopathy), being said to be an immune-mediated necrotizing myopathy. The significance of the association of MSAs and MAAs in inflammatory myopathies has not yet been discussed, so considering the clinical importance of a coexistence of MSAs and MAAs may be useful. [Methods] Through our experience with anti-SRP myopathy with typical clinical signs and anti-SS-A/Ro antibodies, we reviewed the literature related to this antibody combination and evaluated the coexistence of MSAs and MAAs in inflammatory myopathy. [Results] The prevalence of anti-SRP antibody was 0.45% in a cohort of Japanese patients with autoimmune diseases and anti-SS-A/Ro antibody is the most prevalent MAA found in more than 30% of patients. [Conclusions] Our experience with anti-SRP myopathy indicates that clinical investigation of inflammatory myopathy with coexistence of MSAs and MAAs will lead to clarification of clinical subsets and new understanding of the mechanisms of inflammatory myopathy.

P3-112

Two cases of polymyositis/myopathy with anti-signal recognition particle (SRP) antibody complicating interstitial pneumonia

Shuntaro Miyoshi¹, Hirofumi Watanabe¹, Rie Sasaki¹, Mitsuhiro Iwahashi¹, Jiro Yamana¹, Seizo Yamana¹, Hiroki Kobayashi², Takuya Tanimoto², Hiroyuki Maeda²

¹Higashi Hiroshima Memorial Hospital, ²Hiroshima Prefectural Hospital

Conflict of interest: None

In cases of polymyositis with anti-signal recognition particle (SRP) antibody those clinical course are myositis. But those pathological findings are myopathy. There are rarely complicated by interstitial pneumonia. [Case 1] A 56 year old women saw near doctor because of muscle weakness. Her examination showed CPK high, she was referred and entered our hospital. her chest CT showed obscured glass. MRI showed her muscle was caused by the inflammation. The electromyogram also showed low amplitude. So we performed muscle biopsy and that showed no myositis but muscle necrosis. Her blood test showed SRP antibody. We diagnosed polymyositis/myopathy with SRP antibody. [Case 2] A 57 year old man has smoking history. He saw near doctor because of lower limbs muscle weakness. His examination showed CPK high, he was referred and entered our hospital. His chest CT showed fibrotic lesion. MRI showed his muscle was caused by the inflammation. In EUROLINE his blood test showed SRP antibody. We diagnosed polymyositis/myopathy with SRP antibody. They have treated by corticosteroid and immunosuppressive drugs. Their interstitial pneumonia are also not worse. We report those rare cases with some literature review because sometimes this polymyositis are different in terms of treatment progress.

P3-113

Clinical investigation regarding anti-TIF1-gamma antibody in inflammatory myositis patients

Daisuke Hirano, Shusaku Fukaya, Natsuko Watanabe, Masashi Suzuki, Tatsuki Naganawa, Ai Umeda, Konomi Ashihara, Megumi Kurumizawa, Takako Hashimoto, Jo Nishino, Shunji Yoshida, Hidekata Yasuoka
Division of Rheumatology, Department of Internal Medicine, Fujita Health University School of Medicine

Conflict of interest: None

[Object] To investigate the clinical significance of anti-TIF1- γ antibody (Ab) in inflammatory myositis (IM). [Methods] In 31 patients with inflammatory myositis diagnosed between October 2016 and October 2018, we investigated clinical features stratified by anti-TIF1- γ Ab. [Results] Anti-TIF1- γ -Ab were positive in 4 of the 31 patients. 2 of 4 in the anti-TIF1- γ -Ab positive groups complicated of malignancy within 1 year after onset. In the anti-TIF1- γ -Ab negative group, malignancy within 1 year after onset was complicated in 5 of 27 cases. In the anti-TIF1- γ -Ab positive group, 3 of 4 cases had dysphagia. In the anti-TIF1- γ -Ab negative group, only 2 of 27 patients had dysphagia ($P=0.008$). In the anti-TIF1- γ -Ab negative group, 19 of 27 patients had complication of interstitial lung disease (ILD), whereas no patient had complication of ILD in the anti-TIF1- γ -Ab positive group. [Conclusions] In patients with anti-TIF1- γ -Ab positive IM, dysphagia were many cases. In contrast, it was suggested that ILD is less prevalent in anti-TIF1- γ -Ab positive cases

($P=0.015$).

P3-114

Phenotype and the therapy of anti-TIF1gamma antibody positive dermatomyositis (TNF1g-DM)

Yoshikazu Fujikawa, Kengo Akashi, Motoko Katayama, Mai Yamashita, Yoko Nose, Takumi Nagamoto, Yuzuru Yamamoto, Hiroataka Yamada, Yoshihide Ichise, Ikuko Naka, Takaichi Okano, Yo Ueda, Sho Sendo, Akira Onishi, Jun Saegusa, Akio Morinobu
Rheumatology and Clinical Immunology, Kobe University Hospital, Kobe, Japan

Conflict of interest: None

[Object] Phenotype and the therapy of anti-TIF1 γ antibody positive dermatomyositis (TNF1g-DM) [Methods] We investigated the phenotype and the outcome of the treatment in the myositis that we treated in our hospital. [Results] We treated 148 cases of idiopathic inflammatory myositis in our hospital, of which 9 were TNF1g-DM. Average age at onset was 63 years old. In all cases, patients had distinctive skin rash and muscle weakness and in 7 cases, they had dysphagia. In 3 cases with cancer, the average of serum creatine kinase (CK) was 2385U/l. We administered 1mg/kg of prednisolon in 8 cases. Four cases were treated with immunosuppressants, and seven cases with intravenous immunoglobulin. In 5 of 6 cases with elevated serum CK, serum CK was normalized within a month. But in comparison with serum CK, the improvement of muscle weakness, especially esophageal dysmotility, was poor. [Conclusions] In our investigation, TNF1g-DM patients showed good response with treatment in serology, but dysphagia, which was associated with the prognosis, was poorly improved. So it is controversial whether the improvement of elevated levels of muscle enzymes is one of the goals of the treatment in TNF1g-DM. We report our investigation of the phenotype and treatment of TNF1g-DM.

P3-115

The case series study of anti-TIF1gamma antibody-positive patients with dermatomyositis

Masatoshi Kimura, Ayako Aizawa, Kunihiko Umekita, Chihiro Iwao, Yuki Rikitake, Kosho Iwao, Mao Rikitake, Takeshi Kawaguchi, Yumi Kariya, Motohiro Matsuda, Shunichi Miyauchi, Katoko Takajo, Ichiro Takajo, Akihiko Okayama
Department of Rheumatology, Infectious Diseases, and Laboratory Medicine, University of Miyazaki, Miyazaki, Japan

Conflict of interest: None

[Object] The aim of this study is to evaluate the clinical characteristics of anti-TIF1 γ antibody (TIF1 γ ab)-positive patients with dermatomyositis (TIF1 γ -DM). [Methods] Five cases were diagnosed as TIF1 γ -DM in our department from April 2012 to July 2018. The physical findings, malignancies, therapeutic regimens were evaluated. In addition, we analyzed the changes of TIF1- γ ab levels before and after treatment for malignancies. [Results] Four patients were female. The average age was 66 years old at the onset of TIF1 γ -DM. All patients showed typical clinical findings of DM such as muscle weakness and skin rash. Four patients showed dysphagia. Three patients had malignant lesion such as laryngeal cancer, breast cancer, and lymphoma, respectively. Immunosuppressive treatment was administered in TIF1 γ -DM patients without malignancy. On the other hands, treatment for malignancies including radiotherapy, surgical operation and chemotherapy was administered in patients with malignancy-associated DM (MDM) prior to immunosuppressive treatment. In 2 patients of MDM, the levels of anti-TIF1 γ ab were decreased after treatment for malignancy. [Conclusions] More clinical researches with large number participants are necessary to clarify the characteristics and the pathogenesis of TIF1 γ -DM.

P3-116

A case of anti-TIF1-gamma antibody and anti-ARS antibody positive interstitial pneumonia combined with gastric cancer

Akihiro Tanaka^{1,2}, Nobuyasu Ishii², Keiko Shimamoto^{1,2}, Hideki Amuro², Tohru Nishizawa², Yonsu Son^{1,2}, Yoshio Ozaki^{1,2}, Tomoki Ito², Shosaku

Nomura²

¹Rheumatology and Clinical Immunology, Kansai Medical University Hospital, Hirakata, Japan, ²First Department of Internal Medicine, Kansai Medical University, Hirakata, Japan

Conflict of interest: None

[Case] An 84-year-old man. He visited a nearby hospital with respiratory distress, and diagnosed as anti-ARS antibody positive interstitial pneumonia. He was introduced to our department for scrutiny and treatment. Treatment started with prednisolone 0.5 mg/kg from the first hospital day, but chest X-ray examination showed decreased permeability of both lungs, and prednisolone 1 mg/kg was started from 4th hospital day. Since new lesions were found in chest CT, steroid pulse therapy was added from the 9th hospital day, but no improvement was observed. Anti-TIF1-gamma antibody was positive, and upper gastrointestinal endoscopy was performed on the 15th hospital day. Gastric tumor was found, and the pathological result was adenocarcinoma. [Discussion] In this case, since it was anti-ARS antibody positive, we started treatment of interstitial pneumonia with moderate amount of prednisolone. However, it was refractory to treatment, resulting in anti-TIF1- γ antibody positive and gastric cancer combined. Anti-ARS antibody positive interstitial pneumonia is said to have good steroid reactivity. In cases where initial treatment does not respond or when some anti-TIF1-gamma antibody is positive, screening tests of malignant tumors should be conducted as the condition permits.

P3-117

Successful treatment with tocilizumab for refractory antisynthetase syndrome

Takumi Matsumoto, Takao Katsuragawa, Hitoha Nomura, Hiroaki Tamura
Rheumatology Center, Department of Rheumatology, Kin-ikyo Chuo Hospital

Conflict of interest: None

[Case] 67-year-old-female with rheumatoid arthritis and Sjögren's syndrome was diagnosed with interstitial pneumonia (IP) in April 2003 in our hospital, and treated with 60mg prednisolone (PSL). She was making good progress, but suffered from dermatomyositis with muscle weakness, Gottron's sign, elevation of creatine kinase, body weight loss, and positive test for anti-Jo-1 antibodies while tapering the dose of PSL (16mg) in March 2004. Her myositis and IP remitted by PSL of 30mg, but relapsed while tapering the dose of PSL (19mg) in April 2005. Her myositis and IP ameliorated by azathioprine (50mg) and PSL (30mg). But she repeated the recurrences of myositis and IP while tapering the dose of PSL in spite of combination therapy with cyclosporine (240mg/33kg = 7.3mg/kg, trough=235ng/ml, C2=523ng/ml), abatacept (125mg/week, subcutaneously), cyclophosphamide (600mg/body/month, 6 months), and tacrolimus (4mg/body, trough=9.66ng/ml). Her myositis and IP remitted successfully with tocilizumab (162mg/2 weeks, subcutaneously), tacrolimus (3mg/body), and PSL (9mg) since December 2017. [Conclusions] Treatment of antisynthetase syndrome refractory to corticosteroids and immunosuppressants is yet to be established. We will discuss about preceding reports about efficacy of biologics.

P3-118

Anti-TIF1-gamma autoantibodies-positive dermatomyositis with diffuse large B-cell lymphoma ameliorated by R-CHOP therapy: a case report

Yasutaka Okita¹, Eri Oguro¹, Kentaro Kuzuya¹, Hidetoshi Matsuoka¹, Satoru Teshigawara¹, Maiko Yoshimura¹, Yuji Yoshida¹, Kentaro Isoda¹, Yoshinori Harada¹, Yoshihiko Hoshida³, Shiro Ohshima¹, Yukihiko Saeki^{1,2}

¹Department of Rheumatology and Allergology, NHO Osaka Minami Medical Center, Osaka, Japan, ²Department of Clinical Research, NHO Osaka Minami Medical Center, Osaka, Japan, ³Department of Clinical Laboratory, NHO Osaka Minami Medical Center, Osaka, Japan

Conflict of interest: None

Dermatomyositis is related to malignancies compared to the general population. Especially the anti-TIF1- γ antibody is strongly correlated with prevalence of malignancies. The type of malignant tumor varies depending on race and region. In Japan, there is a high proportion of adenocarcinomas such as gastric cancer. We report a case of anti-TIF1- γ antibody positive dermatomyositis complicated with diffuse large B-cell lymphoma. A 70-year-old man presented with a 3-month history of general pruritic erythema rash, axillary mass, fever. There was no muscle weakness, dyspnea on exertion or joint pain. On physical examination, he had Gottron's sign, periungual erythema and axillary lymph nodes swelling. His blood tests showed elevated CPK, LDH, sIL-2R and anti-TIF1- γ antibody titer. MRI revealed lymph nodes enlargement and findings suggestive of myositis. There were no findings suspected of interstitial pneumonia. The results of skin biopsy showed infiltration of mononuclear cells around the vessels. The results of axillary lymph node biopsy showed proliferation of large neoplastic B lymphoid cells with a large nuclear size. He was diagnosed with dermatomyositis complicated with DLBCL. He was treated with 6 courses of R-CHOP therapy. DLBCL and dermatomyositis were ameliorated.

P3-119

Double Cancer of the Oropharynx and Prostate Occurring in an Anti-TIF1-gamma Antibody-Positive Dermatomyositis Patient: A Case Report

Yuko Asanuma¹, Takayuki Kon², Kurisu Tada¹, Kazuhisa Nozawa¹, Ken Yamaji¹, Naoto Tamura¹

¹Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan, ²Department of Internal Medicine and Rheumatology, Juntendo University Nerima Hospital, Tokyo, Japan

Conflict of interest: None

A 66-year-old man, who has had radical neck dissection and chemotherapy for oropharyngeal cancer 2 years ago, presented with arthralgia, myalgia and skin rash. He had weakness and tenderness in both upper and lower extremities, and a skin rash on his face and arms that resembled heliotrope rash, Gottron's papules, V-neck sign and shawl sign. At first, we suspected paraneoplastic syndrome, but after further examination, we found that anti-TIF1-gamma antibody was positive. Also, MRI, electromyography, and skin biopsy showed findings compatible with dermatomyositis, so we diagnosed him as anti-TIF1-gamma antibody-positive dermatomyositis. After we started oral prednisolone (30mg/day), his rash and myalgia improved, so he was discharged. While he was hospitalized, we found that his mediastinal lymph nodes were enlarged, and started chemotherapy for recurrent oropharyngeal cancer. Also, we found adenocarcinoma in his prostate through biopsy, so we started hormone therapy for that as well. This case report shows that it is important to consider the possibility of not only paraneoplastic syndrome, but also recurrent or multiple cancer, when we diagnose anti-TIF1-gamma antibody-positive dermatomyositis.

P3-120

A case of anti-Ro52 antibody positive dermatomyositis complicated with systemic capillary leak syndrome (SCLS)

Motohiko Sato, Daisuke Kawata, Takuji Itakura, Ayaka Maeda, Hiroyuki Hagiya

Department of Rheumatology, Yokohama City Minato Red Cross Hospital

Conflict of interest: None

A 40-year-old man was referred to our hospital due to fever, walking difficulty, and polyarthralgia. His physical findings revealed proximal muscle weakness with myalgia, Heliotrope eruption and V-neck sign. Myogenic enzymes were elevated, MRI showed high signal intensity areas with STIR sequences on thigh muscles. Electromyography was compatible with inflammatory myositis. According to the Bohan and Peter criteria, he was diagnosed as dermatomyositis. Prednisolone (PSL) 60mg/day was started. His skin eruptions promptly improved, but CPK level was elevated and muscle strength was further reduced. He became almost bedridden. Although mPSL pulse therapy was added, he suffered from hypovolemic shock, acute respiratory and renal failure, and entered inten-

sive care unit. Furthermore, he developed anasarca especially in the thigh with markedly elevated CPK level (65,000U/L). He was thought to be in SCLS and compartment syndrome with rhabdomyolysis. Accordingly, we added IVIG and tacrolimus. Then his symptoms gradually improved. After two months of rehabilitation, he can walk by himself, and he was discharged home. We report a rare case of dermatomyositis complicated with SCLS.

P3-121

A case of myositis localized to the neck with positive for the anti-titin antibody induced by pembrolizumab

Saki Mukohara, Soshi Takahashi, Norihiko Amano, Yasuhiro Nohda, Katsuhiko Yoneda, Miwa Nishida, Saori Hatachi, Shunichi Kumagai
Department of Rheumatic Disease, Shinko Kinen Hospital

Conflict of interest: None

[Case report] 76-year-old woman, who developed advanced urothelial cancer with focal recurrence and inversion, was treated with pembrolizumab from April 2018. After the three cycles of pembrolizumab, she felt general malaise and laboratory test showed creatine kinase (CK) level of 2537 U/L and she rapidly developed dropped head syndrome. An electromyogram revealed myogenic change in cervical muscles. Magnetic resonance imaging (MRI) demonstrated the presence of focal changes of myositis and fasciitis involving the muscles around the cervical spine. An electrophysiologic did not demonstrate positive waning on repetitive stimulation and she was diagnosed as immune checkpoint inhibitor-related myositis (irMyositis). On laboratory test, only anti-titin antibody, which is one of anti-striated muscle antibody, was positive. From elevation of cardiac enzyme and negative change of T wave in electrocardiogram, we considered that she also developed myocarditis. She received prednisolone therapy and immediately levels of CK was decreased and abnormal wave in ECG improved. [Discussion] There are many unclear points in the immune-related adverse events (irAE). This is the first case of the irMyositis showing anti-titin antibody positive.

P3-122

A case of interstitial pneumonia associated with anti-PL-7 antibody positive dermatomyositis with thrombotic thrombocytopenic purpura

Hidehiko Makino, Kenichiro Hata, Takaaki Ishida, Tomohiko Kuboyama, Shogo Matsuda, Takao Kiboshi, Youhei Fujiki, Koji Nagai, Takuya Kotani, Maki Kagitani, Tohru Takeuchi, Shigeki Arawaka
Department of Internal Medicine IV, Osaka Medical College

Conflict of interest: None

We report a case of 30s-year-old woman, she noticed an itch and erythema of the skin from May of the X year and caused pain of the proximal muscle and intermittent fever of the 37 degrees level from the middle of June. At the end of July she was revealed a rise in CK and liver enzymes when the uterine content removal was performed in the diagnosis of a progressive miscarriage, and she was transported to a former hospital. Although treated with steroids because it did not improve by observation, the interstitial pneumonia in the chest CT in the middle of August and the Gottlon's sign were pointed out, and it became transference to our hospital because the dermatomyositis was suspected. We diagnosed dermatomyositis from anti-ARS Ab positive. The anti-ARS Ab was later found to be an anti-PL-7 Ab. We started treatment with prednisolone, cyclosporine, cyclophosphamide, but on 3rd day the patient showed disturbance of consciousness and TTP was suspected. We used plasma exchange in combination, but the condition did not improve, and the patient died on the 7th day. Anti-PL-7 Ab positive cases have characteristics such as TTP and alveolar hemorrhage may be complicated, and long-term prognosis is bad. However, it is rare to follow a rapid turning point and report it including past cases.

P3-123

A case of anti-Ro-52 antibody positive-dermatomyositis with preceding panniculitis, followed by cutaneous leukocytoclastic vasculitis

Daisuke Nakatsubo, Yoshimasa Hamano, Michihito Katayama, Hitoshi

Deguchi

Department of Immunology, Kinki Central Hospital of Mutual Aid Association of Public Teachers

Conflict of interest: None

We report a rare case of 76 year-old female with dermatomyositis having an onset from panniculitis. She consulted the department of dermatology of our hospital due to painful erythema on her right thigh, which was diagnosed as panniculitis, followed by muscles pains and at bilateral upper arms and thighs. She was hospitalized in our department with proximal extremity muscle weakness and polyarthralgia. CPK elevation and specific histological findings led to the diagnosis of dermatomyositis with panniculitis. Neither specific skin manifestation nor interstitial pneumonia was observed. Anti-Ro-52 antibody was detected by the comprehensive screening of autoantibodies. Her subjective symptoms and radiological findings were improved by the dairy oral corticosteroid therapy (1mg per kg of prednisolone). She took 20mg of prednisolone per day in gradual decreasing when propable purpura was seen and diagnosed as cutaneous leukocytoclastic vasculitis. The purpura was improved by rest and oral colchicine without re-increasing of corticosteroid. We present this case with some literature review.

P3-124

A case with dermatomyositis positive for anti-NXP2 antibody suggested from granular type of anti-nuclear antibody

Kentaro Noda¹, Yuki Mizutani¹, Yasuo Suzuki¹, Naohiro Sugitani¹, Masataka Kuwana², Ayako Nakajima¹

¹Center for Rheumatic Diseases, Tsu, Mie, Japan, Mie University Hospital, ²Department of Allergy and Rheumatology, Nippon Medical School, Graduate School of Medicine

Conflict of interest: None

[Case] A 70-year-old female complained muscle weakness and erythema on her upper limbs. The Gottron papule, V neck sign, shawl sign, and weakness of neck flexor and deltoid muscles with elevated CK at titer of 2491 U/l were detected. The muscle of both upper arms and thigh appeared as hyperintense in T2-weighted MR images. The biopsy of skin showed liquefactive degeneration of epidermis and lymphocyte infiltration around the vasculature. HE staining of a biopsied muscle showed perivascular inflammation. With the diagnosis dermatomyositis, 40 mg/day of PSL and 3 mg/day of TAC were started, resulting good response except muscle weakness of neck flexor. The type of ANA in this patient was granular type and myositis specific antibody was negative. Positivity of Anti-NXP2 antibody was confirmed by immunoprecipitation and immunoblotting. [Clinical Significance] Detection of granular type of ANA itself is rare. Granular pattern is known as atypical speckled and staining pattern of anti-NXP2 antibody is supposed to be atypical speckled. In this case, we supposed anti-NXP2 antibody was positive from this ANA pattern. It is significance that we could expect the presence of anti-NXP2 antibody from the pattern of ANA pattern.

P3-125

Report on treatment experience with high-dose calcineurin inhibitor for acute / subacute interstitial pneumonia associated with dermatomyositis

Takayasu Suzuka¹, Takuya Kotani¹, Kenichiro Hata¹, Youhei Fujiki¹, Takaaki Ishida¹, Takao Kiboshi¹, Hidehiko Makino¹, Tomohiko Kuboyama¹, Tohru Takeuchi¹, Shigeki Makino², Shigeki Arawaka¹

¹Department of Internal Medicine IV, Osaka Medical College, ²Osaka Medical College Mishima-Minami Hospital

Conflict of interest: None

[Objective] We report a treatment experience with high-dose calcineurin inhibitor for acute/ subacute interstitial pneumonia (A/SIP) associated with dermatomyositis (DM). [Method] 30 patients with DM-A/SIP were treated with calcineurin inhibitor at a high dose in addition to steroids. We assessed the treatment effect in the observation period of 6 months after the start of treatment. The cyclosporine (CSA) dose was adjusted to maintain the peak levels (C2) above 1500 ng/mL, and the tacro-

limus (TAC) dose was adjusted to maintain the trough levels (C12) within a range of 15–20 ng/mL. [Results] CSA and TAC were administered to 19 and 11 patients, respectively. CSA was selected for more severe cases. In the 6-month observation period, 14 patients in the CSA group survived (8 improvement, 5 stability, 1 exacerbation) and 4 died due to exacerbation of IP. One patient was transferred to another hospital, so the course could not be followed. In the TAC group, 10 patients survived (improvement 8 cases, stable 2 cases), 1 case died due to suspected viral encephalitis though IP improved. We cannot compare because the disease severity differs between the two groups, but report the treatment experience of DM-A/SIP with high concentration calcineurin inhibitor with literature consideration.

P3-126

Refractory polymyositis, induction of remission with rituximab for dermatomyositis

Hisae Fujimoto, Seido Ooka, Yutaka Goto, Kanako Suzuki, Harunobu Iida, Takayasu Ando, Yusa Asari, Marina Uchida, Kana Ishimori, Hiromi Matsushita, Keiichi Sakurai, Tomofumi Kiyokawa, Yukiko Takakuwa, Kumiko Tonooka, Takeshi Suzuki, Mitsuru Imamura, Yoshioki Yamasaki, Hiroko Nagafuchi, Kimito Kawahata

Division of Rheumatology and Allergology, St. Marianna University School of Medicine

Conflict of interest: None

[Background] In dermatomyositis (DM) polymyositis (PM), there are the patients who are resistant to typical treatment. For refractory myositis, we report on four patients using rituximab (RTX). [Case 1] A 33 years old, men with DM. This patients were treated in azathioprine (AZA), tacrolimus (Tac), mycophenolate mofetil (MMF), but were treated with intravenous cyclophosphamide (IVCY) because interstitial pneumonia (ILD) worsened. The myositis was improved by RTX. [Case 2] A 47 years old woman with DM. For ILD, was treated in IVCY, but it is discontinued by a liver damage. ILD and the myositis were improved by RTX. [case 3] A 61 years old woman with PM. This patients was treated with AZA, CyA, methotrexate (MTX), MMF, were ineffective. The myositis was improved by RTX. [Case 4] A 55 years old woman with antiMDA5 antibody-positive DM. This patients was treated in IVCY, and ILD remitted. However, cutaneous ulcer aggravated it in maintenance therapy in Tac. The cutaneous ulcer was improved remarkably by RTX.

P3-127

Clinical features related to cytomegalovirus infection after immunosuppressive therapy in polymyositis and dermatomyositis

Kenichi Ueno, Satoru Ushiyama, Dai Kishida, Yasuhiro Shimojima, Yoshiki Sekijima

Division of Neurology and Rheumatology, Department of Internal Medicine, Shinshu University School of Medicine

Conflict of interest: None

[Objectives] To investigate the clinical characteristics associated with the induction of cytomegalovirus (CMV) infection after initiating immunosuppressive therapy in patients with polymyositis (PM) and dermatomyositis (DM). [Methods] We reviewed the clinical records of 42 patients with PM/DM in whom CMV pp65 antigen test were performed after starting treatment. [Results] CMV infection was shown in 17 patients (CMV positive), and their mean age was 63 ± 13 years; meanwhile, that of patients without CMV infection (CMV negative) was 50 ± 13 years, suggesting patients in CMV positive were elder than those in CMV negative. Serum albumin levels and circulating lymphocyte counts in CMV positive were significantly lower than in CMV negative. Methylprednisolone pulse therapy (mPSL) was administered to 12 patients in CMV positive, whereas 6 patients in CMV negative were treated with mPSL. The complication of other infection was frequently demonstrated in CMV positive. [Conclusion] CMV infection in patients with PM/DM may be implicated in the features including old age, low levels of serum albumin and lymphocytes counts, as well as mPSL administration. It was also concerned that multiple infection could occur in patients having CMV infection.

P3-128

Two cases of myositis syndrome with anti-PM/Scl antibodies

Hironori Inoue, Hiroaki Kusuoka, Keitaro Saito, Aki Sakashita, Aiko Hirano, Yu Isoda, Risa Sagawa, Kazuki Fujioka, Hidetake Nagahara, Makoto Wada, Masataka Kohno, Yutaka Kawahito
Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

Conflict of interest: None

Background: Anti-PM/Scl antibodies are generally detected in polymyositis/systemic sclerosis overlap syndromes in European and North American patients, but it is rare in Japanese ones. Case 1: A 50-year-old female, suffered from systemic muscle pain especially lower limbs from 4 years ago. Anti-PM/Scl-75 antibody was 1+ and anti-PM/Scl-100 antibody was negative. Muscle weakness was observed but interstitial pneumonia (IP) and skin symptoms were not detected. We started to treat with 50 mg/day of prednisolone (PSL), 6 mg/week of Methotrexate and the symptoms improved. Case 2: A 68-year-old female suffered from fatigue from half a year ago. She complained shortness of breath on exertion. Anti-PM/Scl-75 antibody was 3+ and anti-PM/Scl-100 antibody was 3+. Mechanic's hands, IP and muscle weakness were observed. We started to treat with 50 mg/day of PSL, 2 mg/day of tacrolimus and the symptoms improved. Discussion: In our two cases, scleroderma-specific skin lesions were not appeared, and muscular weakness dominated iliopsoas muscle. They had different characteristics from the cases reported from Europe or North America. We report two cases of myositis syndrome with anti-PM/Scl antibodies with some literature review.

P3-129

A case of anti-Ku antibody-positive polymyositis which needed combined modality therapy for hemophagocytic syndrome

Takuya Nishi¹, Satoshi Suzuki¹, Mai Yoshida^{1,2}, Yuki Matsuoka¹, Keigo Ikeda¹, Ken Yamaji², Naoto Tamura², Shinji Morimoto¹

¹Department of Internal Medicine and Rheumatology, Juntendo University Urayasu Hospital, Chiba, Japan, ²Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan

Conflict of interest: None

A 40-years-old man presented arthralgia of both knee, decrease in grip strength on August 2017, anti-nuclear antibody titer over 2560 times and high levels of serum CK on November. Anti-Ku antibody was detected besides high levels of myogenic enzyme, myogenic change, non-destructive arthritis, systemic inflammation, diagnosed polymyositis. Presenting anti-U1-RNP, anti-Sm antibody and leukopenia, overlap syndrome of SLE and myositis was suspected although no nephropathy or cutis symptom. Starting 35 mg of PSL on January 2018, but showed fever, shaking chill, liver dysfunction, thrombocytopenia, high level of serum ferritin, urgently hospitalized. Bone marrow examination showed increase of histiocytes with phagocytosis of all blood corpuscles, diagnosed hemophagocytic syndrome. Not improved though steroid semi-pulse, simple plasma exchange performed for 3 days, with cyclosporine. The treatment succeeded, discharged by tapering PSL to 45 mg. Anti-Ku antibody has high positive rate in overlap syndrome in Japan, shows reactivity to steroid, good prognosis. The case led to HPS, presumed to caused by overlap of SLE such as anti-Sm antibody and hypocomplementaemia. This case suggested need of systemic examination including searching of other autoantibodies and evaluation of organ complications in these patients.

P3-130

Myositis-specific or -related antibodies were frequently found in patients other than mastitis

Ryutaro Yamazaki, Kazuhiro Kurasawa, Yuta Takamura, Tomoyuki Miyao, Ayae Tanaka, Satoko Arai, Takayoshi Owada, Reika Maezawa, Masafumi Arima

Dokkyo Medical University

Conflict of interest: None

Purpose: To clarify the clinical features of patients with myositis-spe-

cific or -related antibodies, particularly underlying diseases. Methods: Subjects were 974 patients whose serum were examined for myositis-specific or -related antibodies using Euroline Myositis profile3. Medical records of patients with positive results were reviewed to examine clinical features. Results: Of 974 patients who were suspected CTD, 145 (14.9%) were positive for anti-ARS, -SRP, -Mi2, KU, and PM-Scl (70 or 100) Abs. Of 68 patients with anti-ARS Ab (ant-OJ; 1, EJ;15, PL-12; 13, PL-7; 8, Jo-1; 31), 38 were myositis (DM; 17, PM21), and idiopathic interstitial pneumonia (IIP) and Sjogren syndrome (pSS) were 14 and 10, respectively. Myositis was found in 9 of 17 anti-SRP Ab+ patients (DM; 4, PM; 5) and in 5 of anti-Mi2 Ab+ patients (DM; 4, PM1). In patients with these Abs, there were RA and IIP. Of 32 patients with anti-KU Ab, 14 were myositis (DM; 6, PM8), 7, 6 and 3 were SLE, pSS and IIP, but none were scleroderma. Of 23 patients with anti-PM-Scl Abs, 7 were myositis (DM;4, PM3), RA and pSS were 5, and only 2 cases were SSc. Conclusion: Myositis-specific or -related antibodies were frequently found in patients other than myositis.

P3-131

The improvement of nailfold videocapillaroscopy abnormalities in 2 patients with dermatomyositis

Kei Araki, Hiroki Kohno, Kazutoshi Yukawa, Tatsuomi Kuranobu, Tadahiro Tokunaga, Yusuke Yoshida, Tomohiro Sugimoto, Katsuhiro Ohi, Sho Mokuda, Keisuke Oda, Takaki Nojima, Shintaro Hirata, Eiji Sugiyama

Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital

Conflict of interest: None

[Background] In dermatomyositis (DM) patients, nailfold videocapillaroscopy (NVC) abnormalities are found in some cases, but the change after the treatment is not fully understood. From the beginning of treatment, we observed NVC abnormalities in two DM patients every 2 weeks. [Case1] A 37-year-old man was diagnosed as DM with skin eruption and cough. Blood tests showed elevated creatine phosphokinase (CK), hyperferritinemia, anti-melanoma differentiation associated gene 5 (MDA5) antibody positive, and computed tomography (CT) revealed interstitial pneumonia. He was treated with three drugs of prednisolone, tacrolimus, cyclophosphamide. [Case2] A 68-year-old woman was diagnosed as DM due to skin eruption, muscle pain and muscle weakness. Blood test showed CK elevation and anti-Mi-2 antibody positive. She was treated with glucocorticoids and azathioprine. In both cases, there were NVC abnormalities at the initiation of treatment, but those changed into almost normal findings after 8 weeks. [Clinical significance] In two cases of DM, NVC abnormalities improved along with underlying diseases. The degree of NVC abnormalities may be related to the severity of myositis, skin eruption, or interstitial pneumonia, and it may be an indicator of the treatment response.

P3-132

Seronegative necrotizing myopathy associated with Rosuvastatin: a case report

Yuto Nakakubo, Masaaki Fujita, Toshiki Nakajima, Yumiko Nakano, Yoshitaka Imura

Department of Clinical Immunology and Rheumatology, The Tazuke-Kofukai Medical Research Institute, Kitano Hospital, Osaka, Japan

Conflict of interest: None

[Case] A 41-year-old woman presented with myalgia and reddish urine, 4 months after starting rosuvastatin. Laboratory tests showed a marked increase of creatine kinase: CK (206100U/L), serum myoglobin (19714.1ng/mL). She was hospitalized with diagnosis of ladbomyolysis. Although we continued fluid therapy, CK was still elevated remarkably. Anti-ARS antibody, anti-TIF1- γ antibody, anti-Mi-2 antibody, anti-MDA-5 antibody, anti-HMGCR antibody, anti-mitochondria M2 antibody, and anti-SRP antibody were negative. MRI showed symmetrical STIR high signals in bilateral tibialis anterior muscles, rectus femoris muscles and so on. Biopsy from right rectus femoris supported immune-mediated necrotizing myopathy, with active necrosis of muscle fibers and regenerative changes in HE and expression of HLAABC and MAC depo-

sition on sarcolemmal membrane in immunological staining. Prednisolone 40mg/day (0.6mg/kgBW/day) was started. Because of insufficient CK decrease, we added methotrexate 8mg/week and tacrolimus 3mg/day and CK decreased. [Clinical significance] Anti-HMGCR antibody and Anti-SRP antibody are known as disease-specific antibodies of necrotizing myopathy. However, cases in which no antibody was detected were seldom reported. We report our experience with some literature review.

P3-133

A case of Good syndrome complicated with dermatomyositis, Sjögren's syndrome, and neuromyelitis optica

Shotaro Masuoka, Hiroshi Sato, Keiko Koshiba, Mai Kawazoe, Soichi Yamada, Satoshi Mizutani, Kotaro Shikano, Sei Muraoka, Toshihiro Nanki

Division of Rheumatology, Department of Internal Medicine, Toho University School of Medicine

Conflict of interest: None

Good syndrome (GS) is characterized by thymoma with immunocompromised condition. Several cases in GS with autoimmune diseases have been reported. [Case] A 48-year-old male developed GS three years ago. Seven months ago, skin rash, muscle weakness and increase of CK level were observed. MRI and electromyogram revealed myositis findings, and he was diagnosed with dermatomyositis. Sjögren's syndrome was also suspected because of dry eye and mouse. He was treated with 50 mg/day of prednisolone (PSL), and the symptoms were improved. However, thrombocytopenia and visual loss appeared. Based on the presence of pancytopenia and elevation of ferritin level, hemophagocytic syndrome was suspected. Intravenous glucocorticoid pulse therapy was administered before switching 60 mg/day of PSL and cyclosporine. However, the visual impairment progressed. Lower limb weakness and bladder rectal disturbance also appeared. MRI revealed optic neuritis and myelitis. We then performed plasma exchange and administration of rituximab, nevertheless, the symptoms were not improved. At five months later, he died because of pneumonia. Autopsy revealed demyelination in optic nerve and spinal cord. We reported rare GS case complicated with dermatomyositis, Sjögren's syndrome and neuromyelitis optica.

P3-134

A case of long-term course of polymyositis confirmed by follow-up FDG-PET-CT after pancreatic cancer surgery

Tatsuki Matsumoto, Taro Horino, Satoshi Inotani, Hirofumi Nishikawa, Yoshiko Shimamura, Kosuke Inoue, Yoshio Terada

Department of Endocrinology, Metabolism, Nephrology, Kochi Medical School, Kochi University

Conflict of interest: None

A 51-year-old Japanese woman presented with myalgia and muscle weakness was admitted to our hospital. Six years before, she was diagnosed pancreatic tail cancer and resection of pancreatic body and tail was performed. Seven years before, hyper-CPK-emia had persisted. Although FDG-PET-CT was performed once a year for follow-up after surgery, recurrence of pancreatic cancer was not pointed out. Laboratory examination revealed the elevated levels of CRP, CPK, and positive anti-cytoplasmic antibody. Based on findings of muscle biopsy specimen of biceps, polymyositis was diagnosed. The levels of CPK and CRP normalized, myalgia also improved with treatment started with PSL 20 mg/day. When confirming the past FDG-PET-CT backwards, they showed that FDG accumulation increased over time to the proximal muscles such as the upper arm, thigh, and so on, from when the elevated levels of CPK was initially observed. Furthermore, after the treatment, disappearance of FDG accumulation was observed. In our case, it was suspected that polymyositis was progressing more slowly than pancreatic tail cancer surgery based on the sequential FDG-PET-CT findings. It was suggested that FDG-PET-CT is effective for diagnosis, follow-up and treatment effect determination of polymyositis.

P3-135

A case of dermatomyositis complicated by rheumatoid arthritis treated with abatacept

Shotaro Kojima, Junya Suzuki, Ayako Matsuki, Kentaro Takahashi, Takeshi Umibe
Matsudo City General Hospital, Matsudo, Japan

Conflict of interest: None

A 56-year-old male was diagnosed with rheumatoid arthritis at previous hospital. He was treated with 5mg/day of prednisolone and 1000mg/day of salazosulfapyridine. In December 201X-3, he had muscle weakness, muscle pain, and Gottron signs. He was diagnosed as dermatomyositis with an elevation of CK, inflammation findings at MRI and electromyogram. He had no malignancies. He was treated with 60mg/day of prednisolone, 400mg/day of cyclosporine, and intravenous immunoglobulin. Then the symptoms were improved. In April 201X, when the dose of prednisolone was tapered to 12.5mg/day, he had a relapse of dermatomyositis with an elevation of CK. He was treated with 40mg/day of prednisolone and 10mg/week of methotrexate, but the symptoms were not improved. There were no symptoms which suggest the relapse of rheumatoid arthritis, but we introduced abatacept with diagnosis as dermatomyositis complicated by rheumatoid arthritis. Then the symptoms of dermatomyositis were improved. In October 201X +1, the dose of prednisolone is tapered to 7mg/day. In Japan Abatacept is not generally used as the therapy of dermatomyositis, but there are some reports which suggest the efficacy of abatacept against dermatomyositis. This case suggests that abatacept may be effective against dermatomyositis.

P3-136

Alveolar hemorrhage in a patient with dermatomyositis

Yuji Uzawa, Yuji Yoshioka, Daisuke Kanai, Akiko Suda, Shohei Nagaoka
Yokohamaminamikyosai Hospital

Conflict of interest: None

A 66-year-old woman was admitted to our hospital because of dyspnea. She was diagnosed with dermatomyositis based on biopsied specimen and clinical symptoms and positive for anti Jo-1 antibody 12 years ago. Thoracic computed tomography (CT) showed new ground-glass pattern in bilateral lung fields. We did bronchoscopy for diagnosis. Alveolar hemorrhage was strongly suspected since bronchoalveolar lavage fluid (BALF) was bloody. Cytologic studies for her BALF detected hemosiderin-laden macrophages. Pulse therapy with methylprednisolone improved alveolar hemorrhage. It is said that patients with dermatomyositis complicate alveolar hemorrhage very rarely. This patient is the rare case of dermatomyositis with alveolar hemorrhage.

P3-137

A case of focal eosinophilic myositis of the hand

Sayuri Yamashita, Hidenaga Kawasumi, Atsuko Murota, Makiko Kimura, Manabu Tanabe, Takashi Ogasawara, Mutsuto Tateishi
Department of Rheumatology, Tokyo Metropolitan Ohtsuka Hospital

Conflict of interest: None

A 30-year-old woman with 4-year history of ulcerative colitis was referred to our hospital to evaluate a swollen lesion on the left hand. She noticed a swollen lesion on the first web space of the left hand 2 weeks before her visit. Physical examination showed that vital signs were normal. Her thenar was swollen with no tenderness. She had no skin eruption or muscle weakness. Laboratory studies showed that the white blood cell count was 15,800/uL (reference range, 3,300-8,600/uL) with eosinophilia at 66% (reference range 0.2-7.3%). Muscle enzymes were also elevated (CK 262 U/L, aldolase 7.7 U/L). Magnetic resonance imaging of the left hand demonstrated high intensity lesions in adductor pollicis muscle with fat-suppressed T2 weighted image. Muscle biopsy from the left adductor pollicis muscle showed marked infiltration of eosinophils. She was diagnosed as having focal eosinophilic myositis. Two months after her first visit, symptoms resolved spontaneously. This case suggest that physicians should consider the possibility of eosinophilic myositis if isolated myositis is seen in patients with peripheral blood eosinophilia.

P3-138

A patient with Takayasu arteritis with right pulmonary artery obstruction and recurrent right lung field infection was safely treated with total right lung resection and tocilizumab administration

Yoshihiro Yoshida, Mayumi Matsuda, Yoshinobu Nakao, Takashi Maruyama, Kazuhiro Yokota, Hiroshi Kajiyama, Kojiro Sato, Yu Funakubo, Toshihide Mimura
Department of Rheumatology and Applied Immunology, Saitama Medical University

Conflict of interest: Yes

Case A 57 year-old female was diagnosed as a right pulmonary infection. The symptom was once improved, but she suffered from the recurrence after 2 months. A chest contrast-enhanced CT scan revealed an occlusion and wall thickening of right main pulmonary artery. Takayasu arteritis was suspected due to a wall-thickening of aortic arch. The diagnosis was confirmed by PET-CT. The treatment with prednisolone 0.8mg/kg did not induce favorable response. Additional administration of tacrolimus, steroid pulse, increase amount of prednisolone (1.0 mg/kg) or methotrexate did ameliorate the disease activity. Angioplasty of right pulmonary artery was considered risky because no angiographical information was obtained on the distal side. Finally, because she had pulmonary Aspergillus infection and complicated pneumothorax, total right pulmonary resection was performed after 5 months. Additional Tocilizumab administration caused CRP complete negative and immunosuppressants unnecessary and prednisolone decreased without any adverse events. **Clinical significance** Since there have been only a few case-reports describing requirement of total unilateral pulmonary resection for Takayasu arteritis, here along with some literature review we report our case, which is believed educative for rheumatologists.

P3-139

Inflammatory Subclavian artery aneurysm with Takayasu Arthritis : Successful Surgical Treatment with Tocilizumab

Mari Yamamoto
Department of Rheumatology and Nephrology, Chubu-Rosai Hospital, Aichi, Japan

Conflict of interest: None

48-year-old woman presented to our hospital with fever and headache. Same symptoms developed since she was 20-year-old and she was diagnosed with Takayasu arthritis. Since the onset of symptoms prednisolone was started for providing symptomatic relief and she could not reduce prednisolone less than 10mg per day. She had no other past medical history. When she came to our hospital, she took 8mg per day prednisolone. She never takes another immunosuppressive agents. On physical exam, her blood pressure was 110/78mmHg in both arms. A cardiovascular examination revealed a left subclavian bruit and mild aortic regurgitation. She had also 30mm left subclavian artery aneurysm. Since treatment with methotrexate (MTX) was difficult with PSL dose reduction, tocilizumab (TCZ) combination therapy was started. When she could successful of weaning off PSL 5mg/day, left common carotid artery - left subclavian artery bypass and chest stent graft interpolation were performed and the postoperative course is unevenful. [Discussion] Takayasu arteritis is one of the major vasculitis, causing stenosis of blood vessels and aneurysm. There are only few reports of TCZ therapy with Takayasu's arteritis aneurysm. We report as a successful surgical treatment case by TCZ combination.

P3-140

Repeated physical examination in a patient with fever of unknown origin revealed carotid bruit after 4 weeks from onset and confirmed diagnosis of Takayasu's arteritis: a case report

Yasunori Suzuki^{1,2}, Kazuyuki Suzuki², Kiyooki Ito², Kazuaki Mizutomi¹, Mitsuhiro Kawano²

¹Department of Internal Medicine, Division of Rheumatology and Nephrology, Kaga Medical Center, Kaga, Japan, ²Department of Internal Medicine, Division of Rheumatology, Kanazawa University Hospital, Kanazawa, Japan

Conflict of interest: None

[Background] In diagnosis of fever of unknown origin, thorough history taking and physical examination are essential but sometimes hints of diagnosis become clinically evident lately. [Case report] The patient was a 48-year-old woman who presented 5 days fever without any associated symptoms. After 3 weeks from onset contrast enhanced CT showed pulmonary infiltrative shadow in the left lingular segment. Antibiotics did not work. Finally, repeated physical examination revealed newly carotid bruit on 4 weeks from onset. She was diagnosed as Takayasu's arteritis by PET-CT. [Conclusion] Repeated physical examination could give a clue for diagnosis in a patient with fever of unknown origin.

P3-141

Long-term efficacy and safety of abatacept in an elderly patient with large vessel vasculitis

Miki Murata, Atsuo Uefuji, Ryosuke Yoshihara, Natsuko Nakagawa, Yasushi Tanaka, Kazuko Shiozawa
Rheumatology & Collagen Disease Center, Hyogo Prefecture Kakogawa Medical Center

Conflict of interest: None

A 83-year-old female case. It was diagnosed as rheumatoid arthritis in 2012. From around 2013, a strong inflammatory response not related to the degree of arthritis was observed in the blood test. Takayasu arteritis diagnosis with MRI and PET-CT. Aortic dissection also accompanied during the course. High inflammation continued, when combined with Abatacept, inflammatory response and back pain improved. Improvement was also seen in contrast MRI and PET-CT. Even now, there are few reports that large angiitis has been treated with ABT, as it is a rare case, we will examine and report it.

P3-142

Three cases of reactive aortitis appeared after infection

Yoshinobu Nakao, Mariko Sakai, Yuri Sadanaga, Akihito Maruyama, Nobuyuki Ono, Syuichi Koarada, Yoshifumi Tada
Saga University Hospital

Conflict of interest: None

[Case 1] Sixty-eight-year-old man experienced fever, dyspnea and chest pain a week after his improvement of pneumococcus pneumonia. CT scan and MRI showed thickening of the blood vessel wall and fat around the blood vessel from the aortic arch to abdominal aorta. His fever and radiographic changes were improved spontaneously. [case2] Sixty-six-year-old man experienced fever and dyspnea after the improvement of infectious enteritis. CT scan showed thickening of the blood vessel wall and fat around the blood vessel from the aortic arch to thoracic aorta. His fever and radiographic changes were improved spontaneously. [Case3] Seventy-seven-year-old woman with ovarian cancer had fever and cough after G-CSF treatment during her chemotherapy. After improvement of her bronchitis, she became febrile again. CT scan showed thickening of the blood vessel wall and fat around the blood vessel in the aortic arch. Fever and the inflammatory response were improved spontaneously. [Discussion] We experienced 3 cases of aortitis that developed after infection leading to spontaneous remission. We supposed that these cases were associated with reactive arthritis.

P3-143

A case of Crohn's disease complicated with large vasculitis with asymptomatic right internal carotid artery occlusion

Kaori Ishimura, Yuji Nozaki, Hiroki Akazawa, Chisato Ashida, Fusayo Ikeda, Atsuhiko Yamamoto, Tetsu Itami, Kenji Sakai, Asuka Inoue, Shinkai Ri, Toshihiko Shiga, Kazuya Kishimoto, Koji Kinoshita, Masanori Funauchi, Itaru Matsumura
Kindai University Hospital Osaka Japan

Conflict of interest: None

[Case] 14-year old man [Chief complaint] Right brachial pain [Histo-

ry of present illness] He was receiving mesalazine and infliximab on diagnosis of Crohn's disease. He was referred to our hospital 7 months after diagnosis of Crohn's disease due to an inflammatory reaction increase and right upper limb pain. [Passage] A difference in left-right blood pressure was recognized, so contrast CT was performed. A stenosis of the right brachial artery was observed and diagnosed as large arteritis. The left internal carotid artery occlusion was confirmed by the carotid pulse echo performed as a screening test, and occlusion was confirmed by the MRA at the origin of the left internal carotid artery. But the flow of the left internal carotid artery from the eight internal carotid artery or vertebral basilar artery was maintained. Prednisolone 30 mg / day and aspirin 100 mg / day started. Inflammatory response and right brachial artery stenosis improved. Azathioprine 25 mg / day was used in combination and discharged. [Consideration] In this case, echo made it possible for him to get medical treatment earlier before cerebrovascular accident occurred. Thus, aggressive blood vessel evaluation using contrast CT, echo and so on regarding systemic vasculitis is important.

P3-144

Abdominal aortitis after using pegfilgrastim during the lung cancer chemotherapy

Nao Oguro, Tomoki Hayashi, Mika Hatano, Ryo Takahashi
Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan

Conflict of interest: None

A 49-year-old man was diagnosed with advanced stage 4 lung small cell carcinoma and started chemotherapy. Patient received 3.6mg pegfilgrastim as prophylaxis for neutropenia. 11days after the administration of pegfilgrastim, patient developed abdominal pain and high fever. Initial laboratory test revealed white blood cell count of 28800/ μ l and C-reactive protein 18.52mg/dl. Computed tomography:CT scan showed thickness of the soft tissue around abdominal aorta and Magnetic resonance imaging showed the wall thickness and contrast enhancement. We excluded the Takayasu arteritis and giant cell aortitis from the clinical history and physical examination. There was no elevation of IgG4 and no sign of infection. G-CSF associated aortitis were strongly suspected and 40mg prednisolone was started. High fever and inflammatory marker were rapidly improved. A week after the treatment, CT scan showed complete resolution of soft tissue thickness. There were 6 reported case of G-CSF associated aortitis and 2 of them were induced by pegfilgrastim. Underlying diseases varied, and most of the case treated by corticosteroid and rapidly improved. It seemed to be important to reveal the mechanism, treatment necessity and risk factors of the disease by accumulating the case.

P3-145

A case of aortitis complicated by ischemic colitis

Hiroyuki Teruya, Ko Sudo, Hiroyuki Yano, Mitsuyo Kinjo
Okinawa Chubu Hospital, Okinawa, Japan

Conflict of interest: None

Chief complaint: Abdominal pain, hematochezia **History of present illness:** A 86 year-old woman with history of advanced rheumatoid arthritis on low dose prednisone and diabetes, who presented with 2 months duration of headache, and lower abdominal pain associated with hematochezia for one day. **Clinical course:** An abdominal CT scan with contrast revealed findings suggestive of ischemic colitis in splenic flexure to descending colon, and thickened abdominal aortic wall. As abdominal pain persisted, repeated abdominal CT scan 8 days later revealed expanding inflammation around abdominal wall. Prednisolone 40mg daily was started for large vessel vasculitis. Biopsy of temporal artery was suboptimal. The patient developed steroid psychosis and deferred all oral medications. Subcutaneous tocilizumab successfully controlled her symptoms and inflammation. **Clinical significance:** Persistent abdominal pain and inflammation were the keys to diagnose aortitis in this case. Aortitis can cause hematochezia by mesenteric ischemia which may be life-threatening. Early detection of vasculitis is important to improve prognosis.

P3-146

A case of primary Sjögren Syndrome comorbid with large vessel vasculitis

Takahisa Suzuki¹, Yoshikazu Nakashima², Akitomo Okada², Atsushi Kawakami³

¹Sasebo City General Hospital, Sasebo, Japan, ²Nagasaki Genbaku Hospital, Nagasaki, Japan, ³First Department of Internal Medicine, Nagasaki University Hospital

Conflict of interest: None

Case report The patient was 63-year-old, female. She developed dry eye, dry mouth, and polyarthritis at age 57. She was diagnosed with primary Sjögren Syndrome, on the basis of keratoconjunctivitis sicca and presence of anti-Ro/SS-A antibody and anti-La/SS-B antibody. Because she comorbid interstitial nephritis and arthropathy refractory to NSAIDs treatment, she had a low dose of prednisolone. In X-year mid of June, she visited our hospital and presented with a fever over 38 degrees Celsius continued for a week and myalgia. Plain CT scan could not presented cause of fever. Laboratory test showed elevation of CRP (25.88mg/dL). Since the origin of the fever was still unknown, she was examined by FDG-PET/CT. The exam indicated she developed large vessel vasculitis. Although we planned to remission induction therapy, thereafter she rapidly declined fever, reduced CRP levels, and diminished lymph nodes swelling in the natural course. Follow up FDG-PET / CT exam in mid of July revealed improvement of the large vessel vasculitis. **Clinical Significance** For the vasculitis associated with Sjogren's syndrome, large vessel vasculitis considered to be rare. We experienced a case thought to be the large vasculitis taking selfremiting course, so we reported this case with literature review.

P3-147

Aortitis associated with SLE

Hiroyuki Akebo, Yoichi Nakayama, Saki Minoda, Hirofumi Miyake, Ryuichi Sada, Hiroyasu Ishimaru, Kazuhiro Hatta
General Internal Medicine, Tenri Hospital

Conflict of interest: None

A 49-year-old female complained of an 1-week history of bilateral shoulder pain followed by a 3-day history of anterior chest pain, dyspnea and fever of 38°C. SLE was diagnosed 35 years ago, followed by 5 times of relapse with pericarditis or pleurisy. She was successfully treated with prednisolone (PSL) 0.5 mg/ kg/ day in those times. On admission to our hospital she was treated with PSL 8 mg/ day. The investigations showed elevated CRP 9.4 mg/ dl, ESR 89 mm/ h and ds-DNA 13 U/ ml, without pleural effusion or pericardial effusion and ECG abnormality. Contrast CT showed aortic wall thickness between ascending region and arch with periaortic soft tissue inflammation. Two sets of blood culture were negative. There was no sign or symptom suggesting that coexistence of antiphospholipid syndrome, Behcet syndrome and temporal arteritis. She was diagnosed as Lupus aortitis and administered PSL 0.5 mg/ kg/ day. Her symptom, laboratory abnormality and aortic wall thickness improved. She is maintained with PSL 10 mg/ day without relapse. There are only 13 reports of Lupus aortitis. The therapeutic approach is unclear in the situation. In this case, we have retried the regimen of PSL with which her relapse had been controlled, and gotten good response.

P3-148

A Case of "Limb Restricted Arteritis": Presenting Large Vessel Giant Cell Arteritis Like Symptoms and Diagnosed by PET-CT

Isao Matsuura¹, Shohei Nakamura^{1,2}, Yohei Seto^{1,2}

¹Department of Rheumatology, Tokyo Women's Medical University Yachiyo Medical Center, ²Department of Rheumatology, Institute of Rheumatology, Tokyo Women's Medical University

Conflict of interest: None

A 70-year-old man was referred to our institution for a 20-day history of persistent fever and high level of CRP. He had claudication of lower limb, but denied myalgia, arthralgia and any craniocervical symptom. Large Vessel Giant Cell Arteritis (GCA) was suspected from his age and

history. Contrast CT from his neck to pelvis did not show any organ and vessel lesion. PET-CT was performed and increased FDG uptake was not observed in any large arteries but bilateral brachial and femoral arteries. Therefore, he was diagnosed with limb restricted arteritis. Forty mg of prednisolone was commenced and his symptoms were resolved promptly. GCA with extracranial large vessels and with first branches of aorta reportedly occupies 20-30% and 10-20% of total GCA respectively. In contrast, a few studies have reported regarding limb arteritis which is restricted to the arteries distal to aorta and these epidemiological data is scarce. Additionally, limb restricted arteritis distal to first branches of Aorta which are out of CT imaging range may have been much overlooked like our case. Hence, PET-CT and vascular ultrasound would be preferable for diagnosis. We discuss the pathology of limb restricted arteritis and the diagnosis with imaging modalities referring to literature.

P3-149

A Case of Microscopic Polyangiitis Complicated by large vessel Lesions

Tepei Kamikawa¹, Akari Kato¹, Teruchika Yamada², Yuichi Handa¹, Masanobu Horikoshi¹

¹Division of Rheumatology, Saitama Red Cross Hospital, ²Oomiya Clinic

Conflict of interest: None

[Case] 62-yo male [Clinical course] The patient was diagnosed with MPA based on IP, RPGN, the high titer of MPO-ANCA in October, X-2. Treatment using PSL and IVCY was administered. In June of the X-1, lung cancer was suspected, and in August of the same year, the right lower lobe was excised. It was diagnosed as pulmonary adenocarcinoma. With postoperative CRP being 4-7 mg / dl, prolongation of inflammatory reaction was observed. In the PET, accumulation promotion was observed on the vessel wall from the abdominal aorta to the bilateral iliac artery, and inflammation of the large artery was suspected. Few subjective symptoms appeared due to the post cancer operative condition. Therefore, the follow-up observation was conducted without treatment. For about one year from that time to the present, symptoms have not been observed. In addition, MRI shows narrowing of vascular lumen has not progressed. [Conclusion] In ANCA-related angiitis, the complication of macrovascular lesions has been considered rare. However, it has been suggested that in the case inflammation of unknown origin is prolonged like in this case, it is necessary to consider it as a disease state requiring differential diagnosis.

P3-150

A case of thromboangiitis obliterans in a never-smoking woman of middle age

Natsuki Shima¹, Yoichiro Akiyama¹, Ayako Kokuzawa¹, Katsuya Nagatani¹, Masahiro Iwamoto^{1,2}, Seiji Minota¹

¹Division of Rheumatology and Clinical Immunology, Department of Medicine, Jichi Medical University, ²Department of Rheumatology, Tochigi Medical Center Shimotsuga

Conflict of interest: None

A 48-year-old woman with severe pain and numbness in her right leg and foot was admitted to our hospital. Pulsation in the right popliteal artery was normal, whereas that in the right dorsal pedis artery reduced. Pulsations in the left popliteal, left dorsal pedis, bilateral brachial, and radial arteries were normal. White blood cell count was 10,800/μl, CRP was 0.65 mg/dl, lupus anticoagulant was 2.35 and anti-cardiolipin IgG was 11.9 U/ml. MPO-ANCA and other autoantibodies were negative. CT angiography showed obstruction in the right anterior tibial artery and disruption in the right tibial and fibular arteries. Polyarteritis nodosa and anti-phospholipid syndrome were in the differential diagnosis. The combination therapy with methylprednisolone pulse therapy, intravenous cyclophosphamide, some vasodilators and anticoagulants was ineffective. Gangrene developed in her right toes, and amputation was mandatory. Pathological findings of the amputated leg revealed thromboangiitis obliterans (TAO, Buerger's disease). She had never smoked, and she had little exposure to passive smoking. We should expand differential diagnosis up to TAO in patients who show refractory to conventional therapy for vasculitis even if their clinical characteristics do not match the typical

epidemiology.

P3-151

Presence and significance of NETs in the necrotic lesion of ANCA-associated vasculitis

Sakiko Masuda^{1,2}, Yuka Nishibata¹, Daigo Nakazawa², Utano Tomaru³, Tamihiko Kawakami⁴, Tatsuya Atsumi², Akihiro Ishizu¹

¹Department of Medical Laboratory Science, Faculty of Health Sciences, Hokkaido University, ²Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, ³Department of Pathology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, ⁴Department of Dermatology, School of Medicine, Tohoku Medical and Pharmaceutical University

Conflict of interest: None

[Object] Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is characterized by production of ANCAs and systemic necrotizing vasculitis in small vessels. Recent studies have revealed that disordered regulation of neutrophil extracellular traps (NETs) is critically involved in the pathogenesis of AAV. [Methods] We examined the amounts of NETs in formalin-fixed paraffin-embedded tissue sections and compared the results for AAV with the results for diseases that should be distinguished from AAV. [Results] NETs were more abundant in necrotizing vasculitis of AAV than in non-AAV, such as polyarteritis nodosa and cutaneous arteritis, or in granulomatous angiitis of giant cell arteritis. We next focused on pulmonary granulomas in AAV and non-ANCA-associated diseases. The amount of NETs was significantly greater in necrotizing granulomas of AAV than in granulomas of sarcoidosis without necrosis. Although NETs were formed in necrotizing granulomas of tuberculosis equivalently to those formed in AAV, they were more susceptible to degradation by DNase I than were NETs in AAV. [Conclusions] In AAV, DNase I-resistant NETs were deposited in necrotic lesions.

P3-152

Classification of ANCA-associated vasculitis by Epithelial Cell-Derived Cytokines

Kyoko Otsuka¹, Kensuke Irino¹, Yojiro Arinobu¹, Nobuyuki Ono², Yasushi Inoue³, Masahiro Ayano^{1,4}, Yasutaka Kimoto⁵, Hiroki Mitoma¹, Mitsuteru Akahoshi¹, Koichi Akashi¹, Takahiko Horiuchi⁵, Hiroaki Niino^{1,6}

¹Department of Clinical Immunology and Rheumatology / Infectious Disease, Kyushu University, ²Department of Rheumatology, Saga University, ³Department of Rheumatology, Japanese Red Cross Fukuoka Hospital, ⁴Department of Stem Cell Biology and Medicine, Faculty of Medical Science, Kyushu University, ⁵Department of Internal Medicine, Kyushu University Beppu Hospital, ⁶Faculty of Medical Sciences Medical Education, Kyushu University

Conflict of interest: None

[Object] IL-25 and IL-33 classified as epithelial cell-derived cytokines are produced from vascular endothelial cells and epithelial cells. Recently, serum IL-25 levels were reported to be elevated in active eosinophilic granulomatosis with polyangiitis (EGPA). A correlation between IL-33 and large vessel vasculitis has also been reported. ANCA-associated vasculitis (AAV) has many common clinical signs and it is required to raise the accuracy of diagnosis and disease classification. In this study, we examined the correlation between AAV type or organ involvement and serum IL-25 and IL-33 concentrations. [Methods] We measured serum IL-25, IL-33 concentrations of 22 patients with AAV (8 patients with EGPA, 8 patients with granulomatosis with polyangiitis (GPA), 6 patients with microscopic polyangiitis (MPA)) at the initial examination by Multiplex Assays, and examined relationship with laboratory and clinical findings. [Results] IL-25 levels were elevated in 12 patients, all cases expressed higher levels of IL-33. Factors related to elevation of IL-25 include BVAS score at diagnosis, skin vasculitis, and presence of neurological manifestations. [Conclusions] It is possible that IL-25 is involved in some pathology of AAV and is useful for diagnosis and classification.

P3-153

Five cases of AAV cases in newly established the department of Rheumatology in our hospital

Hideki Shimizu

Funabashi Municipal Medical Center

Conflict of interest: None

[Background] ANCA-related vasculitis (AAV) has been gradually recognized as a representative vasculitis. However, initial approach has not been sufficient. [Object/Methods] To examine the actual clinical aspect, we retrospectively summarize the medical records in our 5 cases of AAV. [Results] Total 5 cases of AAV was 2 males and 3 female, and average age was 74.2 ± 11.12 years. Its category was 4 cases of MPA and 1 case of GPA. All cases were positive for MPO-ANCA, and one case was also positive for PR3-ANCA. Disease onset were 8 years in one case, 5 months in 2 cases and initial diagnosed cases were remained 2 cases. Initial approach for AAV patients performed as an each doctors of respiratory, neurology, nephrology and orthopedics. The initial treatments of all cases were mainly selected glucocorticoids, and only one case of an alveolar bleeding were also combined immunosuppressive drugs. [Discussion/Conclusions] Much cases of ours which had not been sufficient for the initial use of immunosuppressive drugs were retained disease activity, except for newly diagnosed cases. AAV is also desirable for early diagnosis, and after then its patients should be selected appropriate immunosuppressive therapy according the degree of disease progression.

P3-154

Analysis of Six Cases of ANCA Associated Vasculitis with Intestinal Perforation in Our Institution

Takamasa Murosaki, Takeo Sato, Akiko Miyanaga, Ayako Kokuzawa, Yoichiro Akiyama, Katsuya Nagatani, Takao Nagashima, Masahiro Iwamoto, Seiji Minota

Division of Rheumatology and Clinical Immunology, Jichi Medical University

Conflict of interest: None

[Object] To investigate the backgrounds of intestinal perforation in ANCA associated vasculitis (AAV) because of the difficulty of judging whether it is derived from vasculitis. [Methods] We examined 162 AAV cases in our division from 2005 to 2016. [Results] Intestinal perforation: n = 6 (3.7%), female: n = 3 (50.0%), age: 67.5 (year, mean), MPO-ANCA positive: n = 5, PR3-ANCA positive: n = 2, MPA: n = 4, GPA: n = 1, EGPA: n = 1, small intestine: n = 2, descending colon: n = 1, sigmoid colon: n = 3. All events occurred after starting glucocorticoid {duration: 18.5 (0.1 - 73.7) [month, median (range)]}. Pathology were examined in four. Two had biopsy-proven vasculitis of small intestine with short duration {0.9 (0.1 - 1.7)}. Four had colon involvement, with no vasculitis, from diverticulum (n = 3), long duration {41.8 (16.6 - 73.7)}. In Swedish cohort with 202 AAV cases; perforation: n = 5, post-medication: n = 4, small intestine: n = 2 (improved after reinforce), ascending colon: n = 1 (pre-medication, biopsy-proven vasculitis, improved), sigmoid colon: n = 2 (dead). [conclusions] In our institution, vasculitides were proved in small intestine perforations and its duration of medication was short. The cause of perforation is due to vasculitis in small intestine, but various in colon.

P3-155

A case of acute pancreatitis and hemoperitoneum associated with microscopic polyangiitis

Kazuya Tsuji, Kaoru Arai

Japanese Red Cross Kochi Hospital

Conflict of interest: None

A 54-year-old woman exhibited malaise and reduction of urine output was referred to our hospital because of renal function deterioration with glomerulonephritis feature. After examination, she was suspected rapid progressive glomerulonephritis. She underwent renal biopsy, we diagnosed microscopic polyangiitis (MPA) with MPO-ANCA positive and renal biopsy specimen findings. We administered prednisolone. She com-

plained epigastric pain after admission and gradually deteriorated. We performed computed tomography (CT), revealed acute pancreatitis (AP). Pancreatic specimen on EUS-FNA showed no malignancy. Considering AP associated with MPA, we selected pulse cyclophosphamide therapy adding to pulse steroid therapy. However she suddenly failed into shock state, she was detected extravasation in pancreas tail's arteries on contrast CT. We diagnosed hemorrhage in pseudocyst associated with AP caused hemoperitoneum. She underwent emergency transcatheter arterial embolization, succeeded in hemostasis. After that, abdominal symptoms ameliorated in parallel with nephritis findings. In light of the clinical course, we diagnosed AP associated with MPA. <Conclusion>Symptomatic pancreatic involvement in cases of MPA is rare. We add review of the literatures.

P3-156

Microscopic polyangiitis presenting hemorrhagic shock due to gastric artery aneurysm rupture: A case report

Kenji Funakoshi¹, Takeshi Kaneko¹, Tomomi Tada¹, Shinichiro Nameki¹, Jun Fukui¹, Takashi Hosokawa¹, Yuji Yoshida², Hiroshi Fujiwara¹
¹Osaka General Medical Center, ²National Hospital Organization Osaka Minami Medical Center

Conflict of interest: None

A 73-year-old man was admitted to a previous hospital with a 1-month history of fever and a high serum C-reactive protein (CRP) level. Thorough investigation did not reveal infection. He was transferred to our hospital for further examination. We diagnosed him with microscopic polyangiitis from acute progressive glomerulonephritis and a high serum titer of myeloperoxidase anti-neutrophil cytoplasmic antibody. Methylprednisolone pulse therapy followed by the administration of high-dose steroid rapidly improved his fever and lowered the elevated serum CRP levels. On day 5 after initiating treatment, he developed sudden cardiopulmonary arrest; however, successful cardiopulmonary resuscitation was performed. Contrast-enhanced computed tomography (CECT) revealed rupture of a left gastric artery aneurysm and multiple aneurysms of the intra-abdominal arteries. Transcatheter arterial embolization of the left gastric artery stabilized his vital signs. He was treated with intravenous cyclophosphamide pulse therapy in addition to high-dose steroid. CECT performed a month later did not reveal any intra-abdominal aneurysm. Subsequently, his general condition and renal function showed improvement. This case report describes and analyzes the possible causes of gastric artery rupture.

P3-157

A case of ANCA-associated vasculitis with bilateral perirenal hematoma

Masako Kusakabe¹, Takaaki Ishida¹, Tomohiko Kuboyama¹, Takao Kiboshi¹, Youhei Fujiki¹, Kenichiro Hata¹, Maki Kagitani², Tohru Takeuchi¹, Shigeki Arawaka¹

¹Department of Internal Medicine IV, Osaka Medical College, Osaka, Japan, ²Blood Purification Center, Osaka Medical College Hospital, Osaka, Japan

Conflict of interest: None

A 73-year-old woman presented with right secretory otitis media since January and with fever and cough since February. She transferred to our hospital on March 27 and diagnosed with ANCA-associated vasculitis (AAV) due to CRP 13.26 mg/dl, creatinine 4.67 mg/dl, MPO-ANCA >300 U/ml, microscopic hematuria, and proteinuria. Because of rapidly progressive glomerulonephritis, she was treated with prednisolone 60mg, intravenous cyclophosphamide (IVCY), plasma exchange, hemodialysis (HD), and intravenous heparin. On April 3, she suddenly complained of right back pain and hematuria. Abdominal CT showed right perirenal hematoma. She discontinued heparin and had blood transfusion. However, in the next morning, she complained of left back pain, and abdominal CT showed left perirenal hematoma. Because of hypotension and depressed level of consciousness, she was admitted to the intensive care unit and treated with steroid pulse therapy and IVCY undergoing continuous hemodiafiltration. Increasingly, her consciousness and renal impairment improved without obviously rebleeding episode, so she dis-

continued HD on March 18 and transferred on July 27. It is important to consider perirenal hematoma when back pain and hypotension appeared, although AAV with perirenal hematoma is a rare case.

P3-158

Simple plasma exchange therapy for microscopic polyangiitis with diffuse alveolar hemorrhage and rapidly progressive glomerulonephritis: a case report

Shinya Seki

Department of Internal Medicine, Asama General Hospital, Saku, Nagano, Japan

Conflict of interest: None

An 80-years-old male. He was diagnosed with pneumonia and hospitalized on 8th August X. Computer tomography showed ground-glass opacity, consolidation, and patchy shadow on the both lungs. Ampicillin/sulbactam was started, but it was changed to Levofloxacin and Clindamycin on day 5, and Micafungin was added on day 7. He had blood sputum from day 8, and his renal function declined. On day 16, MPO-ANCA was higher than 300U/ml. I became his doctor on day 17, and diagnosed as microscopic polyangiitis (MPA) with diffuse alveolar hemorrhage and rapidly progressive glomerulonephritis. As his SpO₂ was 90 % (reservoir mask oxygen 8L/min), a ventilator was started. Pulse steroid therapy, prednisolone (0.8mg/kg/ day) was started. From day 21, simple plasma exchange therapy was carried out for 3 days. On day 24, intravenous cyclophosphamide (IVCY, 260mg/m²) was carried out. He tended to improve, and withdrew from a ventilator on day 27. eGFR improved from 24 to 81 mL/min/1.73m². On day 43, he withdrew oxygen therapy and was reduced steroid. On day 55, IVCY was carried out. He didn't have any infection. On day 71 (abstract registration date), prednisolone is 25mg/day, and rehabilitation is continued to return his home. I report plasma exchange therapy's possibility of treating sever MPA.

P3-159

2 cases of Hypertrophic pachymeningitis with anti-neutrophil antibody

Hiroyuki Ohashi, Tamaki Sagisaka
Omaezaki Municipal Hospital

Conflict of interest: None

Hypertrophic pachymeningitis is a rare clinical disorder involving thickening of the dura mater which is often associated with ANCA-related vasculitis. Case1: 74 year-old female. She complaints of headache, numbness and edema of both legs, fever and taste disorder. In Aug.,2011, she performed renal biopsy and its result revealed only hypertensive changes. Whereas, μ PSL was administered from Oct., 2011. because of high fever. She suffered from a headache and walking disturbance. Her skull MRI showed an extensive hypertrophic pachymeningitis and laboratory data showed CRP 1.37 mg/dl, MPO-ANCA 23.2 U/ml. She treated with PSL+IVCY, then her symptoms improved. Case2: 79 year-old male: He complaints of arthralgia of both fingers, severe headache and taste disturbance in March, 2018. In May his skull MRI showed an extensive hypertrophic pachymeningitis and data showed CRP 9.0 mg/dl and PR3-ANCA 4.3 U/ml. He was treated with PSL+IVCY, and rituximab but not induced a remission. Thus MMF was administered, then he developed a remission. Discussion: ANCA-positive Hypertrophic pachymeningitis is considered a localized of the ANCA-related vasculitis, A combination of PSL+IVCY is reported less recurrence than PSL alone. However, flare up case used with PSL+IVCY is needed by another immunosuppression.

P3-160

Microscopic polyangiitis presenting drooping hands and feet

Takanori Ito, Mizuki Kato, Yoichiro Haji
Rheumatology Department, Daido Hospital

Conflict of interest: None

[Clinical significance] Vasculitic neuropathy (VN) is typically refractory and lower patient's ADL. Microvascular injury and ischemia pro-

voke damage of myelinated sensory and motor long tract nerve and cause peripheral VN that presents mononeuritis multiplex or distal symmetric polyneuropathy. In this case, we treated early microscopic polyangiitis (MPA) presenting drooping hands and feet and distal symmetric dysesthesia and hypesthesia by corticosteroid (CS) pulse, intravenous immunoglobulin (IVIG) and intravenous cyclophosphamide (IVCY). The peripheral nerve symptoms and life function are improved dramatically. [Case presentation] Seventy-year-old woman, she had blood feces and was hospitalized in other as diverticular hemorrhage two days later. It disappeared slowly, but dysesthesia of her hands and feet appeared and had been worse rapidly. Day 4, she had drooping hands and feet and distal symmetric hypesthesia, became bedridden. Day 6, MPO-ANCA was high titer, she was diagnosed with MPA. Day 8, she was transferred our hospital, treated by methylprednisolone pulse and high dose CS, IVIG and IVCY for induction therapy. Her symptoms improved and MPO-ANCA became negative. After four months, we started maintenance therapy by azathioprine, she could walk with support and return home.

P3-161

A case of ischemic optic neuropathy associated with microscopic polyangiitis (MPA)

Makiko Higuchi, Tomoya Miyamura, Kenji Tamagawa, Tomoaki Iwanaga, Motoko Ishida, Soichiro Takahama, Rumi Minami, Masahiro Yamamoto, Eiichi Suematsu

Department of Internal Medicine and Rheumatology, Clinical Research Institute, National Hospital Organization Kyusyu Medical Center

Conflict of interest: None

A 74-year-old man was diagnosed with combined pulmonary fibrosis and emphysema (CPFE) at the age of 71. He was treated with respiratory department. On 1 July 20XX he suddenly realized the vision loss and visual field defects of the right eye. He visited an ophthalmologist. He was diagnosed with ischemic optic neuropathy, because of a central scotoma by visual field examination, pallor of the optic nerve head, decrease in perfusion of right optic nerve head temperature by fundus examination. Laboratory examination showed an elevated CRP. He had a possibility of arteritis and was introduced to our department. Laboratory examination showed CRP 4.32mg/dl, ESR 66mm, and MPO-ANCA ≥ 300 U/ml. Chest CT examination showed CPFE. He was diagnosed to suspected MPA. Treatment with pulsed methyl-prednisolone and aspirin 100mg/day was started, followed by PSL 50mg/day and Azathioprine 100mg/day. Inflammation improved promptly and, his eyesight recovered. Although the scotoma remains in the visual field examination, the swelling of the optic disc has disappeared. There have been reports of MPA positive cases with ischemic optic neuropathy, and steroid therapy is effective. In case of diagnosis ischemic optic neuropathy, it is necessary to distinguish MPA for early diagnosis and treatment.

P3-162

A case of diffuse alveolar hemorrhage caused by ANCA-associated vasculitis successfully treated with endoscopic bronchial occlusion and APRV (Airway Pressure Release ventilation)

Noriya Momoki, Kei Hirose, Manami Hirata, Akiko Ueno, Masahiro Yamamura

Department of Rheumatology, Okayama Saiseikai General Hospital

Conflict of interest: None

[Background] Typically, a patient with refractory pneumothorax or local bleeding of lung can be treated with endoscopic bronchial occlusion. we are making this report because we can successfully treat a patient suffered from dyspnea due to diffuse alveolar hemorrhage caused by ANCA-associated vasculitis with endoscopic bronchial occlusion and APRV. [Case] A 75-year-old man was admitted to our hospital because of bloody sputum and fever. After admission, He had been treated with antibiotics and tranexamic acid. On the 3rd hospital day, blood sputum and dyspnea had exacerbated drastically, so he was intubated emergently in ICU. We started methylprednisolone pulse therapy and performed plasma exchange. But blood sputum and dyspnea hadn't been improved, therefore, we treat him with endoscopic bronchial occlusion and ARPV. After that, diffuse alveolar hemorrhage and dyspnea had been improved, so he

could be weaned from ventilator and discharged from the ICU. And then immunosuppressants were administered in a general ward. He could be discharged from hospital. [Conclusions] APRV and a bronchial occlusion are useful for diffuse alveolar hemorrhage when it is uncontrollable with only immunosuppressive therapy.

P3-163

Two case of elderly patient with ANCA-associated vasculitis

Yukiko Asami

Yokosuka City Hospital, Yokosuka, Japan

Conflict of interest: None

Patient 1 was a 82-year-old woman, suffering from leg edema, fever-up, general fatigue, and difficulty in motion. Renal biopsy showed pauci immune crescentic glomerulonephritis and tubulointerstitial nephritis, leading to a diagnosis of AAV with positive MPO-ANCA serology. She received prednisolone (PSL) therapy, however presented with progressive renal insufficiency. She was added plasma exchange (PE), but suffered from catheter occlusion, deep venous thrombosis, and multiple hemorrhages, and then died from cytomegalovirus (CMV) infection and gastrointestinal perforation. Patient 2 was a 88-year-old woman, developing numbness and weakness in limb with fever-up. She was diagnosed with AAV, following a positive result for MPO-ANCA, interstitial pneumonia, renal dysfunction, and peripheral neuropathy in a 'stocking-glove' pattern. During the therapy with PSL and a single dose of rituximab followed by PE, she suffered from renal and hepatic insufficiency and CMV infection, but finally improved. The management of AAV in elderly patients continues to present significant therapeutic challenges, since both prevention of comorbidity and management of complication are difficult. PE with the single RTX injection may improve the prognosis of elderly AAV.

P3-164

A case report of difficult diagnosis in the patient with microscopic polyangiitis

Yuki Mizutani, Mayu Sugiyama, Kahori Oshima, Takakazu Hasegawa, Syunsuke Yokoi, Kumiko Umemura, Michita Suzuki, Kyoko Takano, Eiji Nagasawa, Nobuyoshi Minemura, Masao Katayama

Division of Rheumatology, Department of Internal Medicine, National Hospital Organization Nagoya Medical Center, Nagoya, Japan

Conflict of interest: None

[Case] A 88-year-old female [Chief complaint] Fever [Present illness] She had pneumonia and was administered antibiotics because she had high fever and cough, left chest pain around late July. It was not improved by antibiotics. The serum IgG4 was elevated, so she was transferred to our hospital. She had fever, the elevation of CRP and pleurisy. We suspected drug-induced vasculitis, so we stopped some drugs and changed some drugs. After that, she had high fever once a week. Pleurisy was improved and the serum CRP was decreased. We didn't find the focus of inflammation and tumor. The serum IgG4 was elevated, but we didn't find IgG4-related disease. She had arthritis of left hand and ground glass opacity in X-ray. That was not improved by antibiotics. We diagnosed microscopic polyangiitis because urine occult blood, MPO-ANCA and PR3-ANCA were positive. She took prednisolone 30 mg/day, and the symptom was improved. [Discussion] After drugs was stopped and changed, the symptom was improving. We diagnosed microscopic polyangiitis because she had the arthritis, urine occult blood and MPO-ANCA was positive. We reported this noteworthy case because it is difficult to diagnose in the cause of fever of unknown origin.

P3-165

An example of the anti Ku antibody-positive AAV

Kyoko Ozaki, Hirota Itoh, Masaki Katayama

Rheumatology and Clinical Immunology, Osaka Red Cross Hospital

Conflict of interest: None

The case is 38 years old, a woman. A cough develops from X-4 ten a

year these past months. We had interstitial pneumonia pointed out in X-2 two a year month and showed CK increase, antiKu antibody positive and diagnosed it with overlap syndrome of myositis scleroderma and were under the medical treatment by steroid mass therapy. After that we tapered a steroid and became the follow-up. Fever develops from the middle of January in X year. MPO-ANCA was positive and, in acknowledgment of interstitial pneumonia exacerbation and multiple mononeuritis, had a diagnosis of AAV and performed medical treatment in steroid mass therapy and a cyclophosphamide pulse. Headache, fever, lingual left side ectopia develop from the end of July in X year. We showed hypertrophic cranial pachymeningitis and the cystography effect augmentation around the left hypoglossal canal by MRI and were under the medical treatment by steroid mass therapy and rituximab administration for multiple mononeuritis and thought, AAV. After medical treatment initiation, the symptom was improved. The disorder plurally included disease-specific auto-antibody, and each affected it separately, and myositis clinical condition, pulmonary disease, a neurologic lesion were thought to develop over time, respectively.

P3-166

Role of rheumatoid factor in clinical manifestation of microscopic polyangiitis

Keishi Etori, Yosuke Toda, Yoko Yabe, Kensuke Suga, Takayuki Nakamura, Daisuke Kashiwakuma, Shin-ichiro Kagami
Research Center for Allergy and Clinical Immunology, Asahi General Hospital

Conflict of interest: None

[Object] The aim of this study is to investigate the association between the presence of rheumatoid factor (RF) and clinical features of microscopic polyangiitis (MPA). [Methods] We retrospectively reviewed the medical records of 42 patients who were diagnosed as MPA and measured RF titer from January 2007 to January 2017 in our hospital. Of 42 patients, 28 patients had RF positive (RF-positive group). We compared clinical features including BVAS version 3 and VDI (3, 6 and 12 months later after initial treatment) in RF-positive group and RF-negative group. [Results] There were no significant differences in age, sex and disease duration before initial treatment in both groups. General and nervous manifestation at diagnosis were more frequently involved in the RF-positive group ($p=0.036$ and $p=0.049$, respectively). The titer of ANCA at diagnosis had no significant difference. However, the level of CRP were higher in the RF-positive group than RF-negative group ($p=0.04$). Additionally, serum levels of C4, CH50 and Alb had a significant negative correlation with the RF titers ($p=0.02$ $R=-0.35$, $p=0.02$ $R=-0.35$ and $p=0.01$ $R=-0.36$, respectively). VDI at each time point had no differences. [Conclusions] The presence of RF could be associated with general and nervous manifestation in MPA.

P3-167

A Case of Microscopic Polyangiitis Complicated with Established Rheumatoid Arthritis

Kotaro Hashimoto, Mari Tochihiro, Hirokazu Nishina, Shinya Hirahara, Akira Nishino, Masanori Hanaoka, Yasuhiro Katsumata, Masayoshi Harigai, Hisashi Yamanaka
Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Case] Six months before admission, a woman in her 60's with rheumatoid arthritis (RA) presented with proteinuria, RBC cast, granular cast and her serum creatinine levels elevated. A month before, she complained of edema of legs and intermittent left chest pain. Consulting a doctor, anemia worsened and consolidation was in left lower lobe on chest X-ray and CT. On admission, physical examination revealed pitting-edema and palpable purpura of her both legs. Laboratory tests showed Cr 1.04 mg/dl, CRP 7.68 mg/dl, MPO-ANCA 804 U/ml and protein-to-creatinine ratio in spot urine 0.57 g/gCr. Rapidly progressive glomerulonephritis was suspected. Hemosiderin-laden macrophages were in bronchoalveolar lavage fluid, so she was diagnosed as pulmonary hemorrhage and received a diagnosis of definite microscopic polyangiitis. By the induction therapy

(oral prednisolone 40 mg/day, pulse methylprednisolone 1g and rituximab 375 mg/m² 4 times), her symptoms improved. The dosage of prednisolone was tapered. [Clinical significance] In the review paper about an overlap between RA and ANCA associated vasculitis (AAV), 15 articles were published from 1976 to 2015 and 35 case reports were described. We thought it was worth sharing the rare knowledge that AAV could develop in patients with established RA.

P3-168

Two patients with ANCA-associated vasculitis, showing a decrease in visual acuity

Ryota Takamatsu, Takanori Ichikawa, Masayuki Matsuda
Department of Rheumatology, Saku Central Hospital

Conflict of interest: None

ANCA-associated vasculitis sometimes affects nervous systems. We report 2 patients with ANCA-associated vasculitis, showing a decrease in visual acuity. [Case 1] A 77-year-old man noticed a decrease in the right visual acuity, which gradually worsened in 2 months. After cataract surgery, he lost right visual acuity. MPO-ANCA was positive. MRI revealed diffuse pachymeningitis and an enhancement effect around the right optic nerve and cavernous sinus. After starting steroid therapy, his right visual acuity quickly improved. [Case 2] An 82-year-old woman gradually showed a decrease in the left visual acuity and field defect, while being treated with low-dose steroid for MPO-ANCA positive microscopic polyangiitis. She had a past history of the right ischemic optic neuritis. MRI revealed enhancement effects around the bilateral optic nerves and cavernous sinuses. Her left visual acuity quickly improved after administrations of rituximab following steroid pulse therapy. Cranial nerve involvement, such as a decrease in visual acuity, produces a serious damage to activity of daily living in patients with ANCA-associated vasculitis. To avoid neurological sequelae, early treatment including rituximab is important and should be actively considered.

P3-169

Microscopic polyangiitis mimicking Temporal arteritis

Kyosuke Yamamoto¹, Kensuke Nakanishi²
¹Okinawa Prefectural Nanbu Medical Center & Children's Medical Center Minamidaitou Clinic, ²Department of General Internal Medicine, Okinawa Prefectural Hokubu Hospital

Conflict of interest: None

[Case report] A 69 year-old man with chronic obstructive pulmonary disease, presented with fatigue, dry cough and dyspnea on exertion. 18 days before, he had the influenza. His fever was gone in a few days, but other symptoms did not improve. On examination, his blood pressure was 124/68 mmHg; heart rate, 127 beats/min; temperature, 38.0°C; respiratory rate, 24 beats/min; oxygen saturation (on room air) 91%. Auscultation of the chest revealed bibasilar crackles. Laboratory test revealed elevated C-reactive protein and computed tomography showed traction bronchiectasis and emphysema. Despite of broad-spectrum antibiotics therapy, his fever persisted. Additional history taking and laboratory study revealed bilateral jaw claudication and positive MPO-ANCA. Superficial temporal artery biopsy was performed, which showed small vessel vasculitis, in which inflammation was limited to small periadventitial vessels, with sparing of the temporal artery. We diagnosed with microscopic polyangiitis (MPA) and administered prednisolone 60mg/day. He was discharged on the 20th day without fever or jaw claudication. It was reported that MPA occurred symptoms like temporal arteritis. Detailed history taking and biopsy were useful for diagnosis.

P3-170

A case of ANCA associated vasculitis with GCA like symptoms, clinical course and isolated granulomatous small vessel vasculitis around temporal artery

Keitaro Saito, Hiroaki Kusuoka, Hironori Inoue, Aki Sakashita, Aiko Hirano, Yu Isoda, Risa Sagawa, Kazuki Fujioka, Hidetake Nagahara, Makoto Wada, Masataka Kohno, Yutaka Kawahito
Inflammation and Immunology, Graduate School of Medical Science,

Conflict of interest: None

[Case] 75-year-old female [chief complaint] fever, purpura, shoulder pain, and jaw claudication [Present illness] A 75 years old female presented with fever, purpura, shoulder pain, and jaw claudication, which had continued for 2 months in Nov 2017. Laboratory data showed that WBC was 16000 / μ L, CRP 17.03 mg/dL, and MPO-ANCA was positive (22.0 U/mL). Ultrasonography showed halo sign on the temporal artery, where no specific finding was seen on CTA and 18F-FDG-PET. A biopsy of skin purpura showed neutrophilic and leukocytoclastic vasculitis and temporal artery biopsy provided small vessel vasculitis and aggregation of macrophages, which did not infiltrate into temporal artery although there was intimal hyperplasia in it. This patient might be diagnosed not as GCA but as granulomatosis with polyangiitis (GPA) by CHCC 2012. We commenced high dose of glucocorticoid monotherapy (PSL50 mg/day) and tapered it to maintenance dose without relapse for a year. [Consideration] We report a case of ANCA associated vasculitis (AAV) which had GCA like symptoms with pathological findings which showed isolated granulomatous small vessel vasculitis around the temporal artery. On this case it was difficult to make a differential diagnosis as GCA or AAV.

P3-171

Successful management of a patient developing renal and cardiac amyloidosis during treatment of Microscopic polyangiitis [MPA] with Giant cell arteritis [GCA] with Tocilizumab

Serina Koto¹, Sosuke Tsuji¹, Yushiro Endo¹, Ayuko Takatani¹, Takashi Igawa¹, Toshimasa Shimizu¹, Remi Sumiyoshi¹, Tomohiro Koga¹, Shinya Kawashiri¹, Naoki Iwamoto¹, Kunihiro Ichinose¹, Hideki Nakamura¹, Tomoki Origuchi², Atsushi Kawakami¹

¹Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ²Department of Rehabilitation Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: None

A 61-year-old woman with conjunctival hyperemia, headache since September X, presented to her primary care physician with engorgement and tenderness of bilateral temporal arteries. She was admitted to our hospital in November X. Gadolinium-enhanced MRI showed an enhancement of blood vessel wall of temporal arteries. Interstitial pneumonia on CT, scleritis, positivity for MPO-ANCA led to the diagnosis of MPA complicated with GCA. Her symptoms and inflammatory reaction improved by prednisolone [PSL] and azathioprine. Almost two years later, her renal function got worse. Furthermore, heart enlargement appeared on Chest X-ray, and echocardiography revealed cardiac hypofunction. Because of renal function getting worse, renal biopsy was performed. Pathological results showed deposition of AA amyloid without vasculitis. Echocardiography showed abnormal myocardial reflectivity of left ventricular wall, and we diagnosed renal and cardiac amyloidosis. Because of her alveolar hemorrhage, she was treated by increase of PSL and Intravenous cyclophosphamide [IVCY]. After 2 course of IVCY, we changed to Tocilizumab. After that it kept renal function, improved inflammatory reaction, and reduced PSL. This case suggested that tocilizumab can have an effect on MPA with GCA and amyloidosis.

P3-172

Multiple ulcerative colitis and uveitis as initial presentations in a patient with HLA-A*26 positive granulomatosis with polyangiitis

Norikazu Hinamoto¹, Ken-ei Sada², Keiji Ohashi², Yoshinori Matsumoto²

¹Department of Medicine, Chugoku Central Hospital, Fukuyama, Hiroshima, Japan, ²Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University, Okayama, Japan

Conflict of interest: None

[Case] A 44-year-old man visited a physician because of watery stool for 2 weeks and fever for one week. He was diagnosed with right uveitis, and treated with instillation of steroids 3 months before. Thickening of

colon wall at CT scan and high CRP levels were found, so antibiotics was administrated. His symptoms did not improve, and then he was referred to our hospital. He had no aphthous ulcer and erythema nodosum, but each ocular pain and right ptosis developed 2 days before referral. His PR3-ANCA was positive, and HLA A26 was also positive. Orbital mass and multiple ulcers of colon were found, then granulomatosis with polyangiitis (GPA) was made finally. After initiation of daily dose of 70mg of prednisolone after methylprednisolone therapy, his symptoms immediately improved. [Clinical significance] Previous report showed that ocular involvement was found in 30-50% of patients with GPA, and uveitis was 25% of ocular involvements. On the other hands, gastrointestinal involvement was found in 7% of patients with microscopic polyangiitis and GPA were reported and related to fatal outcome. Uveitis and colitis in this patient might relate to HLA-A26 as the disease-susceptibility gene for Bechet disease.

P3-173

One case that we can diagnose by a skin biopsy GPA complicated with systemic scleroderma

Rei Tadokoro, Kazuteru Noguchi, Mai Nakano, Chie Ogita, Masao Tamura, Teppei Hashimoto, Masayasu Kitano, Maki Shibamoto, Kazuyuki Tsuboi, Mei Tani, Mai Morimoto, Tetsuya Furukawa, Takahiro Yoshikawa, Naoto Azuma, Kiyoshi Matsui

Division of Rheumatology Department of Internal Medicine Hyogo College of Medicine

Conflict of interest: None

She went to hospital for systemic scleroderma and interstitial pneumonia. She had arthralgia and CRP increased, she began to take PSL5mg. She was hospitalized because MPO-ANCA was positive and CRP was not improved though she took PSL15mg. There were no abnormal findings though we searched an infection and the malignant tumor. She was diagnosed GPA because she had otitis media and interstitial pneumonia, and biopsy of right palmar eruption showed necrotizing granulomatous vasculitis. When we prescribed her PSL30mg inflammatory reaction was improved, so we prescribed her AZP and discharged. But there was exacerbation of nasal soreness, nose mass increase and a cough symptom. We discontinued AZP because drug hepatopathy was detected from June, CRP gradually rose, and so she was hospitalized again. Head CT showed a high absorption range to both maxillary antra, ethmoid sinuses and frontal sinuses, chest CT showed a large number of nodular shadow to both embryonate newly and so we diagnosed her with relapse of GPA. We gave RTX to her but CRP was not improved, We added MTX6mg. Then it was showed nose mass reduction, the improvement of the cough symptom. That systemic scleroderma was mixed with GPA is very rare. According to Derrett-Smith, anti U3-RNP antibody may suggest merger of AAV.

P3-174

Granulomatosis with polyangiitis presenting as a renal mass

Ayano Watanabe, Kaneshige Sasaki

Department of Rheumatology Medicine, Kainan Hospital Aichi Prefectural Welfare Federation of Agricultural Cooperatives, Japan

Conflict of interest: None

A 67-year-old man was presented with weight loss, frequent urination. His medical histories were Sjogren's syndrome, recurrent acute otitis media, hypertension and hyperlipidemia. Computed tomography (CT) showed a left renal abnormal lesion. 8 months later, this lesion had expanded to 65mm and para-aortic lymphadenopathies were revealed. Renal biopsy revealed inflamed tissue comprising mixed inflammatory cells including lymphocytes and plasma cells. Malignant lesions were not observed. A nephrectomy was performed that demonstrated necrotizing granulomatous lesions and vasculitis. MPO-ANCA testing was positive (10.4 U/mL). No pulmonary symptoms were presented. CT of the chest did not detect nodular lesions. Based on these findings, he was diagnosed with granulomatosis with polyangiitis. He received predonisolone (30mg/day), which resulted in improvement of fatigue. The presentation of GPA as a renal mass is rare and about fifteen cases have been reported in the literature. In conclusion, GPA can present as an inflammatory mass in the

kidney and should be considered in the differential diagnoses.

P3-175

PR3-ANCA associated vasculitis with secondary membranous nephropathy

Shunichiro Hanai^{1,2}, Yoshiaki Kobayashi^{1,2}, Yurika Tatsuno^{1,2}, Chisaki Ajima^{1,2}, Kimie Harama^{1,2}, Kei Kobayashi^{1,2}, Rei Koh^{1,2}, Daiki Nakagomi^{1,2}, Kenichiro Kitamura^{1,2}

¹Third Department of Internal Medicine, University of Yamanashi, Yamanashi, Japan, ²Center for Clinical Immunology and Rheumatology, University of Yamanashi Hospital, Yamanashi, Japan

Conflict of interest: None

A 73-year-old woman developed ophthalmalgia and congestion of her left eye a month earlier. She was referred to our hospital for further assessment. Serum creatinine level was 0.91 mg/dL, urine protein/creatinine ratio was 2.6 g/gCr (UPCR), occult blood test and PR3-ANCA was positive. Computed tomography of the lung revealed bilateral ground-glass opacity. Renal biopsy showed membranous nephropathy (MN) with bubbly appearance of basement membrane on the outer surface of the capillary wall by light microscopy. There was no signs of necrotizing vasculitis. Immunofluorescence microscopy revealed granular deposits of IgG along the outer surfaces of all capillary walls. Anti-phospholipase A2 receptor antibody was negative. She was diagnosed with PR3-ANCA associated vasculitis (AAV), and received oral prednisolone 25mg per day, four infusion of rituximab (375mg/m²) at a week interval. UPCR was reduced, and other symptoms were improved immediately. Renal involvement of AAV typically shows pauci-immune glomerulonephritis, but immune-complex glomerulopathy was also reported. Some literatures suggest that MN associated with AAV is a poor prognosis factor of the renal function. Early treatment may be needed for MN associated AAV.

P3-176

A case of otitis media with ANCA associated vasculitis (OMAAV) with anti-aminoacyl tRNA synthetase antibody syndrome

Hiroki Matsuzawa, Kazuaki Katsumata, Tetsuya Hoshi, Satsuki Aochi
Department of Rheumatology, Teine Keijinkai Hospital

Conflict of interest: None

[Case] A 73-year old women visited us for consultation due to bilateral shoulder and hip pain of one month. She had been taking prednisolone (PSL) 3mg/day for anti-aminoacyl tRNA synthetase (ARS) antibody syndrome with interstitial lung disease (ILD) for 5years. Her symptom was evaluated as a flare of anti ARS antibody syndrome, and the dose of PSL was increased to 15mg/day. Then, her symptoms resolved completely. After 3months, she noticed difficulty of hearing. Laboratory test revealed positive MPO-ANCA (147U/mL), and otoscopy showed right otitis media with granuloma exists in the middle ear, then she was diagnosed with otitis media with ANCA associated vasculitis (OMAAV). Shortly after treatment with PSL 60 mg/day, her ear symptoms disappeared and MPO-ANCA became negative. While PSL was tapered, Azathioprine (AZA) 50mg/day was started, but stopped for agranulocytosis. Since then she has been only on PSL without any relapse. [Clinical importance] OMAAV is a disease concept transmitted from Japan and is one of important differential diseases of refractory otitis media. Although ANCA sometimes becomes positive in dermatomyositis/polymyositis, very few reports showed the occurrence of ANCA associated vasculitis (AAV). Especially this case is probably first report of OMAAV with anti-ARS antibody syndrome.

P3-177

Otitis media with ANCA-associated vasculitis (OMAAV) with extra-axial granulation tissue formed in the left middle cranial fossa

Keisuke Saito, Katsuya Nagatani, Takeo Sato, Yoichiro Akiyama, Hiroi Kusaka, Ayako Kokuzawa, Akiko Miyanaga, Takamasa Murosaki, Masahiro Iwamoto, Seiji Minota

Division of Rheumatology and Clinical Immunology, Jichi Medical University Hospital, Shimotsuke, Tochigi, Japan

Conflict of interest: None

[Case] A 65-year-old woman had reported left ear closure and deafness two years earlier and was diagnosed as having left otitis media with effusion at an otolaryngology clinic. She was positive for MPO-ANCA and antibiotic treatment was not effective for her otitis media. Inflammatory granulation tissue was observed in the middle ear biopsy, but findings of vasculitis were not clear. We made the diagnosis of OMAAV, and remission was achieved with PSL and IVCY therapy. 10 days ago she visited our department with dizziness, headache, vomiting. MRI revealed tumor formation in the extra-axial region of the left middle cranial fossa. The pathology examination of the mass in the biopsy showed inflammatory granulation tissue, but no obvious vasculitis was observed. We concluded that her OMAAV had relapsed, and we administered steroid pulse therapy. The tumor clearly shrunk, and remission is maintained at present by rituximab. [Clinical significance] In Japan, only 16% of OMAAV cases manifest the pathological findings of typical vasculitis. At 31% of OMAAV, complications are observed during the course. An early clinical diagnosis of OMAAV should be made and early treatment should be started even if clear pathological findings of vasculitis are not obtained.

P3-178

Efficacy and safety of azathioprine in induction therapy of microscopic polyangiitis

Chisato Ashida, Toshihiko Shiga, Yuji Nozaki, Tetsu Itami, Kaori Ishimura, Hiroki Akazawa, Fusayo Ikeda, Atsuhiko Yamamoto, Kenji Sakai, Asuka Inoue, Shinkai Ri, Kazuya Kishimoto, Koji Kinoshita, Masanori Funauchi, Itaru Matsumura
Kindai University Hospital Osaka Japan

Conflict of interest: None

[Object] Although cyclophosphamide (CY) is proposed as a remission induction therapy for microscopic polyangiitis (MPA), there are cases in which cannot receive CY. [Methods] Here we analyzed retrospectively the clinical features, renal histopathology findings, survival, relapse rate of 24 consecutive patients with MPA, including 8 patients who was received CY and 11 who was received AZP. [Results] We found that in patients no significant differences between the two groups in terms of the patient's background, BVAS, renal disorder, serology and urine findings. Tubulointerstitial disorder was more advanced at patients who received CY. Serum creatinine showed a declining trend in the CY group 6 months after the start of treatment, but it decreased significantly in the patients who received AZP 24 months after the treatment. There was no significant difference between the two groups regarding life prognosis, side effect occurrence rate, relapse rate. [Conclusions] These observations indicate that AZP could be considered to use for induction therapy in MPA cases with 50% or less of the tubulointerstitial disorder. The possibility of using AZP for induction of remission has been shown. Further study is required for long-term prognosis of induction therapy using AZP.

P3-179

Japanese patients with MPO-ANCA positive microscopic polyangiitis may not require the administration of immunosuppressants for an induction therapy

Mizuho Morooka, Junji Oyama, Kazuhiro Yoshikawa, Izaya Nakaya
Iwate Prefectural Central Hospital

Conflict of interest: None

[Object] Most Japanese patients with microscopic polyangiitis (MPA) are treated with glucocorticoid (GC) alone in contrast to European treated with GC and cyclophosphamide (CY) or rituximab. We investigated prognosis of MPA treated with GC alone. [Methods] This retrospective study included 42 patients with MPO-ANCA-positive MPA newly-diagnosed between 2010 and 2017. Patients with serum creatinine level >500 mmol/L were excluded and analyzed using the Kaplan-Meier method. [Results] The mean age, the mean Birmingham vasculitis activity score and median follow-up period was 72.8 years, 15.0 and 21 months. Of 42 cases, 38 cases were treated with GC alone, and only four added CY owing to inadequate response to GC. All patients treated with GC alone, ex-

cept for one who died from uremia, reached remission. Of the 38 cases with GC alone, five developed end stage renal disease and six died. The survival and renal survival rates of the 38 cases treated with GC alone at 1 and 3 years were 0.97 and 0.87, and 0.92 and 0.73, respectively. [Conclusions] The overall survival rate of the Japanese MPO-ANCA-positive MPA treated with GC alone was good. Additional immunosuppressants may not be required.

P3-180

A case of rapidly progressive glomerulonephritis with double positive MPO-ANCA and anti-glomerular basement membrane antibody : successful treatment with plasma exchange and rituximab

Naonori Sugishita, Hiroyuki Hounoki, Takafumi Onose, Miho Yamazaki, Ryoko Asano, Toshiaki Kido, Atsushi Matsui, Reina Tsuda, Koichiro Shinoda, Hirofumi Taki, Kazuyuki Tobe
University of Toyama, Japan

Conflict of interest: None

[Case] A 69 year old woman introduced our hospital with fever, pulmonary nodule, hematuria and overt proteinuria. We diagnosed rapidly progressive glomerulonephritis (RPGN). MPO-ANCA was positive and steroid therapy was performed prior to renal biopsy as ANCA associated vasculitis. Anti-glomerular basement membrane (GBM) antibody was also positive. Plasma exchange and rituximab were performed, her renal function improved. Renal biopsy was performed, and peritubular capillary flame and the IgG deposition of the linear pattern were confirmed, then both MPO-ANCA and anti-GBM antibody were thought to be involved in clinical condition. [Discussion] It is reported that anti-GBM antibody becomes positive in about 5% in ANCA-related vasculitis. The mechanism by which an immune response to the glomerular basement membrane occurs following the glomerular injury due to ANCA associated vasculitis and anti-GBM antibody appears has been proposed. This is a first case of rituximab in cases with double-positive ANCA and anti-GBM antibody.

P3-181

Three cases suspected of rituximab induced acute thrombocytopenia during remission induction therapy for ANCA-associated vasculitis

Yoko Nose, Yo Ueda, Motoko Katayama, Mai Yamashita, Takaichi Okano, Sho Sendo, Kengo Akashi, Akira Onishi, Jun Saegusa, Akio Morinobu

Department of Rheumatology and Clinical Immunology, Kobe University Hospital, Kobe, Japan

Conflict of interest: None

BACKGROUND: The number of ANCA-associated vasculitis (AAV) patients treated with rituximab (RTX) for remission induction therapy is increasing. Although RTX induced acute thrombocytopenia (RIAT) has been reported as a rare complication in patients with malignant lymphoma (ML), there are few reports about RIAT in patients with AAV. **METHODS:** We reviewed AAV patients treated with RTX in our department. We clarified the clinical features of suspicious cases of RIAT and compared with those in ML. **RESULTS:** There were three cases of suspicious cases of RIAT. Among them, thrombocytopenia occurred acutely and severely within several days after third or fourth administration of RTX. Although it needed to distinguish from the reactivation of cytomegalovirus or other drug-induced thrombocytopenia, the rapid decrease after RTX administration and the recovery after discontinuation or extension of next RTX administration were the common feature. Thinking from that most RIAT cases in ML occurred after the first administration of RTX, the mechanism of RIAT may be different between ML and AAV. On the other hand, thrombocytopenia after re-administration of RTX didn't recur in one patient as well as most cases in ML. **CONCLUSIONS:** We should pay attention to thrombocytopenia after RTX administration.

P3-182

A case of rituximab induced acute thrombocytopenia (RIAT) in granulomatosis with polyangiitis

Ryoko Asano, Hiroyuki Hounoki, Takafumi Onose, Naonori Sugishita, Miho Yamazaki, Toshiaki Kido, Atsushi Matsui, Reina Tsuda, Koichiro Shinoda, Hirofumi Taki, Kazuyuki Tobe

First Department of Internal Medicine, University of Toyama

Conflict of interest: None

[Case] A 62 year old man admitted to our hospital because of gait disorder due to hypertrophic lesion in spinal cord. Although anti-neutrophil cytoplasmic antibody (ANCA) was negative, he was diagnosed as granulomatosis with polyangiitis (GPA) because of saddle nose, hypertrophic spinal pachymeningiitis and necrotizing angiitis on a nasal mucosal biopsy. He improved after methylprednisolone pulse therapy, but he relapsed with sinusitis five months later. We initiated rituximab (RTX) therapy and after third RTX administration, thrombocytopenia and hypocomplementemia was observed, and we diagnosed rituximab induced acute thrombocytopenia (RIAT). He was improved for a year, but he developed sinusitis again. We determined re-infusion of RTX under his consent, but RIAT was observed after second RTX administration. [Discussion] RIAT develops within several days of RTX administration and has been reported as a rare adverse event occurring during the treatment of lymphoma, on the other hand, there are few reports in the autoimmune disease. Rheumatologists should consider RIAT as we have more opportunities to use RTX. We report our case, along with the relevant literature.

P3-183

A case of single administration of rituximab to ANCA-associated vasculitis in hemodialysis patients and introducing remission

Tatsuaki Amano

Yokkaichi Municipal Hospital

Conflict of interest: None

[Case] A 68-year-old man. In X - 8 year, he was diagnosed with rheumatoid arthritis and remission was maintained by MTX, but he was self - discontinued from November, X - 1. Fever, sore throat, otic pain, eating disorders appeared in April X, and he visited our hospital. Highly renal dysfunction was recognized (Cr 14 mg/dL), and emergency dialysis was introduced. PR-3ANCA positive, pharyngeal granuloma, renal biopsy confirmed Hemispheric forming glomerulonephritis, confirmed as GPA. After steroid pulse therapy as induction of remission, we continued PSL at 50 mg / day, and administered rituximab at 500 mg only once. Vasculitis findings other than kidney were promptly improved, and we reduced the dose of PSL to 20 mg in 4 weeks after the start of treatment. Although hemodialysis could not be withdrawn, remission has been maintained without adverse events. [Discussion] In introducing remission to ANCA-associated vasculitis in dialysis patients, a single administration of rituximab can be one of safe and effective treatments that enables early loss of steroids.

P3-184

Granulomatosis with polyangiitis (GPA) with multiple tumor lesions in the choroid plexus successfully treated with rituximab

Mai Suhara, Yasushi Kondo, Yoko Nakagome, Kazuki Hirano, Yuto Izumi, Takayoshi Kurabayashi, Sho Sasaki, Yasushi Koyama, Chiho Yamada, Shinji Sato

Tokai University Hospital, Isehara, Japan

Conflict of interest: None

A 36-year-old female had recurrent nasal bleeding with chronic sinusitis since 2003 and developed to nasal septal defect. Mucosal biopsy from sinuses showed noncaseating granuloma and the chest CT demonstrated cavitary lesions in the both lungs. We diagnosed her as granulomatosis with polyangiitis (GPA) and high-dose prednisolone (PSL) with cyclophosphamide (IVCY) was initiated. However, retrobulbar neuritis optica was arisen with PR3-ANCA positivity after initial remission induction therapy. She suffered frequent relapse of lung and upper tract involvements for many years, although she received intensive treatment

with combination of PSL, IVCY and MTX. In September 2016, she began to notice headache, nausea, and double vision and head MRI showed multiple, contrast enhanced tumor lesions in the choroid plexus. For the first time, she was introduced received rituximab (RTX) for this refractory disease. Soon after that, and neurological focal signs were resolved and MRI revealed significant regression of choroid plexus lesions. We continued to use RTX as a maintenance therapy and we could reduce the daily PSL dose to 5 mg so far. This case was recurrent and refractory GPA who showed rare neurologic manifestation of choroid plexus lesion and successfully treated and managed with RTX.

P3-185

A study on the number of rituximab initial doses for ANCA-related vasculitis cases in our hospital

Kazuyuki Tsuboi¹, Takahiro Yoshikawa¹, Chie Ogita¹, Mei Tani¹, Masao Tamura¹, Yuichi Yokoyama², Masahiro Sekiguchi², Atsushi Saito³, Aki Nishioka⁴, Shinichiro Tsunoda³, Mai Morimoto¹, Tepei Hashimoto¹, Naoto Azuma¹, Masayasu Kitano¹, Hajime Sano⁶, Kiyoshi Matsui¹

¹Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, ²Division of Rheumatology, Hyogo Prefectural Nishinomiya Hospital, ³Department of Nephrology, Sakai Rumi Clinic, ⁴Division of Rheumatology, Nishinomiya Watanabe Hospital, ⁵Division of Rheumatology, Sumitomo Hospital, ⁶Division of Rheumatology, Kyoto Okamoto Memorial Hospital

Conflict of interest: None

[Background] Rituximab (RTX) administration method for ANCA-related vasculitis (AAV) is 4 times the initial dose of 375 mg / m² / week, which is previously confirmed in guidelines for B cell lymphoma. The optimal dosing regimen for AAV is still under discussion. [Purpose] We examined the number of first RTX administration therapy for intractable / recurrent AAV and the presence or absence of relapse of AAV pathology in 3 years after administration. [Object] 29 patients (8 men, 21 females, average age 68.9 ± 12.7 years old). Clinical diagnosis was 16 cases of Granulomatosis with Polyangiitis (GPA), 11 cases of Microscopic Polyangiitis (MPA), 2 cases of Eosinophilic Granulomatosis with Polyangiitis (EGPA). The number of RTX initial doses was 2 times in 8 cases and 4 times in 21 cases. [Methods] We examined the existence of AAV relapse for 3 years after administration in 25 patients excluding 4 cases of death. AAV relapse was defined as clinical symptoms or blood test findings or image findings was exacerbated. [Results] 10 cases (2 times in 1 case, 4 times in 9 cases) was relapsed. There was no difference in relapse rate between the two groups in the Kaplan-Meier method. [Conclusion] There was no difference in relapse rate between the first RTX 2 and 4 times for AAV in 3 years.

P3-186

The efficacy and safety of rituximab on relapsing granulomatosis with polyangiitis

Makiko Hayashi, Kyoko Fujimoto, Shinjiro Kaieda, Yumi Yoshida, Suzuna Sugi, Takuma Koga, Yukiko Hidaka, Tomoaki Hoshino, Hiroaki Ida

Division of Respiratory, Neurology and Rheumatology, Department of Medicine, Kurume University School of Medicine, Japan

Conflict of interest: None

[Objectives] To evaluate the efficacy and safety of rituximab (RTX) therapy in patients with relapsing granulomatosis with polyangiitis (GPA) in our hospital. [Methods] Nine patients with GPA were administrated with RTX. Efficacy and safety of RTX were evaluated for six months. The efficacy was determined as follows; 1) reduction of BVAS score was more than 30%. 2) dosage of steroids was reduced. Eight patients with GPA were already given by CY. Five patients relapsed after discontinuation of CY. Three patients were refractory to GPA by conventional therapy including CY. RTX was administered weekly for consecutive 4 weeks. The average follow-up periods were 18 months. [Results] Five patients treated with RTX achieved clinical remission for all observation period. One patient maintained clinical remission for eighteen months and relapsed. Although two patients developed allergic reactions and discontinued RTX, infectious disease and cytopenia were not observed in all cases.

[Conclusion] Compared to CY therapy, efficacy and safety of RTX therapy for the patients with GPA was indicated. Attention to acute allergic infusion reaction is needed.

P3-187

A case of microscopic polyangiitis which plasma exchange was effective

Yuki Miyaguchi, Shie Ichihara, Norihiro Suga
Nagoya City West Medical Center

Conflict of interest: None

[Case] A 69-year-old woman had cough and bilateral joint pain since 1 month before. Although antibiotic drugs were taken, the fever and general malaise continued. As purple spot appeared, she visited our hospital. We diagnosed rapidly progressive glomerulonephritis (RPGN) from proteinuria and hematuria, her serum creatinine (2.46mg/dL). The MPO-ANCA titer increased to 776IU/mL. We started steroid pulse therapy (methylprednisolone 0.5g/day) and oral administration of prednisolone 30mg/day. Histological findings on renal biopsy showed diffuse paucimmune cellular crescentic glomerulonephritis, diagnosed as RPGN by microscopic polyangiitis. Intravenous cyclophosphamide 250mg/day and the second steroid pulse therapy was administered, but since the renal function progressively deteriorates, plasma exchange therapy (PE) was used in combination. Renal function remarkably improved after the start of PE, MPO-ANCA decreased to 5.6IU/mL. [Conclusions] It is expected that PE will be useful in cases where it is difficult to administer immunosuppressive drugs due to side effects or severe cases with progressive organ disorder. This case was a case in which progressive renal dysfunction could be suppressed by combined use of PE.

P3-188

Attainment of steroid free remission in ANCA associated vasculitis

Kouji Kobayashi¹, Yumiko Sugiyama¹, Shigeru Ohno¹, Hideaki Nakajima²

¹Center for Rheumatic Diseases, Yokohama City University Medical Center, ²Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine

Conflict of interest: None

Objectives: To determine the frequency of steroid free remission and to define disease characteristics of ANCA associated vasculitis patients achieving steroid-free remission. Methods: We retrospectively reviewed clinical charts of 44 consecutive patients (age 71.3±13y.o., female 70%, disease duration 8.1±6.7years, MPA:23, EGPA:12, GPA:9) who met each of Ministry of Health, Labor and Welfare Diagnostic Criteria followed in our hospital. Steroid free remission was defined as a 3-month consecutive period of no disease activity without corticosteroid treatment. Clinical characteristics, BVAS, corticosteroid use, immunosuppressant medicines were examined and compared between patients groups with and without present steroid use. Results: 10 patients (22.7%) achieved steroid free remission. There were no differences in onset of age, disease duration, sex, co-administration of immunosuppressants, initial dose of steroid, CRP and ANCA at baseline between two groups. Patients with less than two damaged organs (p=0.001), lower baseline BVAS (p=0.05), and without nephritis (p=0.02) led to higher rates of steroid discontinuation. Conclusion: Steroid-free remission might be a realistic goal in some patients with ANCA associated vasculitis.

P3-189

Clinical features of eosinophilic granulomatosis with polyangiitis

Shinichiro Nameki, Takeshi Kaneko, Tomomi Tada, Kenji Funakoshi, Jun Fukui, Takashi Hosokawa, Hiroshi Fujiwara
Division of Rheumatology, Osaka General Medical Center

Conflict of interest: None

OBJECTIVE: We aimed to determine the clinical features of eosinophilic granulomatosis with polyangiitis (EGPA). METHOD: This retrospective study analyzed data obtained from 11 patients diagnosed with

EGPA and treated at our center between April 2011 and September 2017. RESULTS: All patients reported a history of bronchial asthma, 7 showed a positive serum myeloperoxidase anti-neutrophil cytoplasmic antibody test, and 5 showed a positive rheumatoid factor test. Neurological and pulmonary involvement occurred in 9 patients each. The Five Factor Score was 0, 1, 2, and 3 in 4, 5, 1, and 1 patient, respectively. The mean Birmingham Vasculitis Activity Score at the time of diagnosis was 14.1. All patients received corticosteroid therapy. Intravenous immunoglobulin, azathioprine, and cyclophosphamide were administered to 5, 4, and 3 patients, respectively. Induction therapy improved ear, nose, throat, and pulmonary involvement in all patients; however, neurological symptoms persisted in 8 patients. No patient developed relapse or died of vasculitis within a year. CONCLUSIONS: Patients with EGPA tend to develop neurological and/or pulmonary involvement. Residual symptoms persisted in 89% of the patients with neurological involvement a year after induction therapy.

P3-190

Clinical pictures of Eosinophilic Granulomatosis with Polyangiitis patients in our department

Takumi Muramatsu, Kazuma Ino, Yasuhiro Hasegawa, Junichi Kondo, Yu Matsueda, Takayuki Hoshiyama, Toshihiro Tono, Yoshiyuki Arinuma, Tatsuhiko Wada, Tatsuo Nagai, Sumiaki Tanaka, Kunihiro Yamaoka
Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine

Conflict of interest: None

[Object] The aim of this study is to optimize treatment for patients with eosinophilic granulomatosis with polyangiitis (EGPA) by analyzing clinical features from EGPA patients in our university hospital. [Methods] We examined 14 inception EGPA patients admitted to our hospital since December 2012. [Result] 6 patients were positive for myeloperoxidase-anti-neutrophil cytoplasmic antibody (ANCA), 1 patient was positive for proteinase-3-ANCA and 7 patients were negative. All patients had peripheral neuropathy and 11 patients had sinus lesions. In patients positive or negative for ANCA, mean age was 45.3 year-old or 56.4, initial eosinophil count was 9055/ μ L and 7140, total IgE was 2144 IU/mL and 1073, C-reactive protein was 10.03 mg/dL and 3.70, respectively. 4 patients with ANCA and 2 patients without ANCA had pulmonary lesions. Only 4 patients with ANCA had renal lesions. Cardiac lesions were involved in 3 patients with ANCA and 4 patients without ANCA. Of 5 patients who received intravenous cyclophosphamide treatment (IVCY), 1 patient experienced relapse, while 5 of 9 patients who did not received IVCY experienced relapse. [Discussion] Pulmonary and renal lesions were related to ANCA positivity. Initial IVCY could reduce relapses.

P3-191

A case of eosinophilic granulomatous polyangiitis complicated by bilateral calcified urethral stenosis

Masaki Itagane, Hiroyuki Yano, Mitsuyo Kinjo
Department of Rheumatology, Okinawa Chubu Hospital

Conflict of interest: None

Case 39 y.o male **Chief complaint** Right lower abdominal pain **History of present illness** Eosinophilic granulomatous polyangiitis (EGPA) was diagnosed 3 months earlier when the patient presented with numbness, weakness in lower extremities, difficulty walking, and eosinophilia with eosinophilic vasculitis in the skin biopsy. He was started on prednisolone 40mg daily. Right lower abdominal pain developed 2 days earlier, and physical examination was remarkable for right lower abdominal tenderness, skin ulcers with necrotic changes in fingertips and legs, asymmetrical distal motor and sensory neuropathy findings consistent with mononeuritis multiplex. Postrenal acute kidney injury was attributed to bilateral urethral stenosis, and the patient underwent bilateral nephropathy with prompt recovery of renal function. Prednisolone increased to 60mg and intravenous cyclophosphamide pulse therapy abated neurological symptoms and skin ulcer. **Discussion** This case illustrated EGPA with severe dermatological and neurological manifestations complicated by uncommon findings of progressive bilateral calcified urethral stenosis. We reviewed literature on urological presentation of ANCA vasculitis in-

cluding EGPA.

P3-192

Eosinophilic Granulomatosis with Polyangiitis (EGPA) with Eosinophilic Myocarditis (EMC)-a Case Report

Masahiro Konishi¹, Ichiro Mizushima¹, Hajime Sanada¹, Kazuyuki Suzuki¹, Akari Takeji¹, Satoshi Hara¹, Kiyooki Ito¹, Takashi Kawane², Hiroshi Fujii¹, Kazunori Yamada¹, Mitsuhiro Kawano¹

¹Division of Rheumatology, Kanazawa University Hospital, ²Department of Rheumatology, Toyama Red Cross Hospital

Conflict of interest: None

[Case] A 66-years-old woman had received antiasthmatic agents to treat her chronic cough from 3 years before the current admission. Two months before the current admission, dyspnea on exertion appeared. Because her dyspnea was exacerbated and eosinophilia and bilateral lung infiltrates were detected, she was referred to our hospital as suspected eosinophilic pneumonia. On admission, she complained of dysesthesia of legs. Laboratory data showed marked eosinophilia despite the negativities of PR3-ANCA and MPO-ANCA, and CT showed cardiac enlargement, pericardial effusion, and pleural effusion. Skin and myocardial biopsy revealed cutaneous vasculitis with eosinophil infiltration and the findings compatible with eosinophilic myocarditis (EMC), respectively. Based on the diagnosis of EGPA with EMC, 40 mg/day of prednisolone (PSL) was started. Then, the dosage of PSL was gradually tapered. Glucocorticoid improved her dyspnea, laboratory data, and imaging findings. Because improvement of leg dysesthesia was not sufficient, IVCY was added and she was discharged from our hospital. [Discussion] In EGPA cases, the complication of EMC is generally considered to be a factor of poor prognosis. The present case in which EMC was well improved suggested the importance of early treatment.

P3-193

The case of EGPA complicated by serositis

Marina Shinoura², Satoshi Suzuki², Takuya Nishi², Shota Sakuma², Keigo Ikeda², Shinji Morimoto², Ken Yamaji¹, Naoto Tamura¹

¹Department of Rheumatology, Juntendo University School of Medicine, ²Department of Rheumatology, Juntendo University Urayasu Hospital

Conflict of interest: None

[Case] The patient was a 27-year-old man who had a childhood history of asthma. He presented with a month of tiredness, lower leg edema, skin rash and fever. He first had a feeling of tiredness and edema from scrotum to lower legs in May 201X. From the following month, he developed a fever. At the first visit he had purpura, numbness of whole body. The number of eosinophils in the blood was greatly increased and total serum IgE was elevated. Eosinophilic Granulomatosis with Polyangiitis (EGPA) was suspected, so he was referred to the department of rheumatology. MPO-ANCA was negative. A chest X-ray showed bilateral pleural effusion that was revealed Eosinophilic and exudative by thoracentesis. The result of skin biopsy was compatible with EGPA. On the 2nd hospital day administration of prednisolone (PSL) 60mg was began, but pleural effusion was increased. So he was treated by steroid semi pulse therapy. Then pleural effusion, the number of eosinophils and purpura were improved. [Conclusion] We experienced the case of EGPA with bilateral pleural effusion responded to corticosteroid therapy. Relatively rare case of EGPA complicated by serositis is reported along with some literature review.

P3-194

A Case of Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss) with subepidermal blister

Eri Shishido, Yukiya Iimura, Junichi Kurashina, Masahiro Yasumura, Tomoki Tanaka, Seiichi Ono, Fusazo Urano, Sadahiro Suzuki
Shinonoi General Hospital, Nagano, Japan

Conflict of interest: None

The patient is a 49-year-old man. His past medical history is signifi-

cant for asthma, eosinophilic sinusitis and nasal polyp. He developed skin erosion on his limbs one month previously and treated as contact dermatitis, but the rash worsened and vesicles and Bullae appeared. A week previously, he developed pains, peripheral neuropathy and swelling in lower extremities. He was admitted to hospital with EGPA. The skin biopsy revealed the presence of multiple intraepidermal vesicles and subepidermal blisters, with eosinophilic infiltrate, eosinophilic vasculitis and granuloma formation. Subsequent direct immunofluorescence microscopy did not show any immunoglobulin or complement deposits in the lesional skin. Blood test revealed an eosinophil count of 4790 / μ L (40.4%), negative anti-neutrophil cytoplasmic antibody (ANCA) and negative anti-BP180 antibody. The patient was subsequently treated with oral prednisolone (1 mg/kg per day) and cyclophosphamide followed (500 mg), followed by courses of azathioprine (50 mg), which resolved the bullous skin lesions, as well as reduced the pain and pruritus for several days. He is currently under regular surveillance. EGPA with subepidermal blister is rarely reported in the literature. We report our case, along with the relevant literature.

P3-195

A case of eosinophilic polyangiitis granulomatosis (EGPA) which was difficult to treat MPO-ANCA positive where propylthiouracil seemed to be a trigger

Hideki Yamanaka, Yusuke Hanioka, Kaori Seki, Ryota Nakamura, Tomoyuki Nakamura, Keiko Yamagami, Hitoshi Goto
Internal Medicine, Osaka City General Hospital

Conflict of interest: None

She was diagnosed as Graves' disease x-12 years ago and was treated with thiamazole. There was hope of birth and was changed to propylthiouracil from x-3 years after birth. There are numbness and weakness from the left shoulder to the elbow from the middle of April x, and edema of the lower limb increased. EGPA was diagnosed as a history of asthma / sinusitis, eosinophilia, muscle weakness and peripheral neuropathy, MPO - ANCA 196 U / mL. She has been treated with 1000 mg/day of Methylprednisolone and 30mg/day of prednisolone. However, abdominal pain and numbness appeared and the eosinophil count increased. In the lower endoscopic examination, there was a finding of vasculitis and the neurological symptoms were deteriorated. Immunoglobulin high dose therapy (IVIG) 20000 mg / day x 5 days was done. PSL increased to 40 mg / day and azathioprine and tacrolimus were added. There was no increase in eosinophils and abdominal symptoms also improved. PSL was gradually decreased, the immunosuppressant was continued, and eosinophil count did not rise by introducing mepolizumab, but the numbness symptoms remained elapsed. Propylthiouracil has been reported to induce vasculitis and reports that IVIG therapy at the remission phase is effective.

P3-196

A patient with eosinophilic granulomatosis with polyangiitis treated only with mepolizumab and intravenous immunoglobulin

Yukihiko Ikeda, Hiromichi Tamaki, Sho Fukui, Haruki Sawada, Ayako Kitada, Mitsuru Watanabe, Yuko Kataoka, Rui Kawato, Masei Suda, Haruyuki Yanaoka, Ryo Rokutanda, Yuri Ohara, Hisanori Shimizu, Tokutaro Tsuda, Mitsumasa Kishimoto, Ken-ichi Yamaguchi, Masato Okada
Immuno-Rheumatology Center, St Luke's International Hospital

Conflict of interest: None

(Case) A 78 year-old woman with a history of adult-onset asthma presented with dyspnea on exertion for 2 months. Additionally she complained of bilateral lower limb edema and numbness for 2 weeks. On physical examination, she had pitting edema on the bilateral lower extremities and paresthesia on the distal one third of the lateral lower legs. Laboratory data revealed eosinophilia of 6360/ μ L, C-reactive protein of 10.72 mg/dl, positive troponin T. Anti-neutrophil cytoplasmic antibody was negative. Her chest X-ray showed pulmonary edema and cardiomegaly. The ejection fraction (EF) on echocardiogram decreased to 38%. A biopsy of myocardium was non diagnostic. She was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA). Due to the patient's preference, intravenous immunoglobulin (IVIG) and mepolizumab

(MEPO) were initiated without glucocorticoids (GC). Her dyspnea gradually improved and the EF recovered to 45% in 2 weeks. Her paresthesia also improved but remained mildly. Her disease activity remained in remission with mepolizumab thereafter. (Conclusion) To our knowledge, this is the first reported case of EGPA successfully treated with MEPO and IVIG but without GC. This case may suggest possibility of GC-free regimen in a certain fraction of patients with EGPA.

P3-197

Clinical features and outcomes of the patients with IgA vasculitis experienced in our hospital

Norihiro Nagamura

Rheumatology and Allergy, Shimane Prefectural Central Hospital

Conflict of interest: None

Object: IgA vasculitis is immune-complex mediated small vessel vasculitis, and is less common in adults. Though the disease course is usually benign, gastrointestinal and renal involvements sometimes become fatal. We analyzed the clinical features and outcomes of the patients in our hospital and considered the prognosis. Methods: 13 patients with IgA vasculitis fulfilled the classification criteria of ACR 1990 or EULAR 2008 from April 2011 to April 2018 were included. Results: There were male of 62% and female of 38% patients with the mean age of 45.5 years. All patients had palpable purpura, 69% with nephritis, 54% with gastroenteritis, 31% with both. The prednisolone (PSL)-therapy was initiated with the mean dose of 0.92 mg/kg for the median period of 9.3 months in 11 patients, and resulted in good response and stopping the therapy in all patients. In the observational period, only 1 patient recurred. Conclusions: The patients with renal involvement caused by IgA vasculitis were reported to have a 30% risk for progression to renal insufficiency. Though the management for IgA vasculitis is still controversial, long-term PSL therapy for more than a half year might be favorable for IgA vasculitis-nephritis outcome in addition to the relief from the gastrointestinal symptoms.

P3-198

A case report of IgA vasculitis which was difficult to distinguish from MPA

Yuki Iizuka, Yohei Kirino, Chiharu Hidekawa, Natsuki Sakurai, Masaki Mitsushashi, Daiga Kishimoto, Reikou Kamiyama, Ryusuke Yoshimi, Hideaki Nakajima

Department of Rheumatology, Yokohama City University, Kanagawa, Japan

Conflict of interest: None

[Case] A 46-year-old male was transported to our hospital with respiratory failure. He had polyarthritis, abdominal pain, hemoptysis and hematuria. Purpura was found on his legs, but it had been diagnosed as IgA vasculitis (IgAV) by skin biopsy performed at the previous hospital. Diffuse ground-glass opacity (GGO) observed on chest CT suggested of alveolar hemorrhage. Even after steroid pulse therapy, GGO deteriorated. Although anti-neutrophil cytoplasmic antibody was negative, we clinically diagnosed him as microscopic polyangiitis (MPA) and administered plasma exchange and intravenous cyclophosphamide. After these treatments, his symptoms improved rapidly. A renal biopsy revealed IgA deposition in the mesangium. IgA deposition in skin and kidney suggested that alveolar hemorrhage was caused by IgAV. He was discharged on day 42. [Discussion] IgAV is rare in adults and the rate of alveolar hemorrhage is reported to be 0.8-5%. Although IgAV with alveolar hemorrhage often results in poor outcomes, the treatment has not been established. We will present the current case along with a literature review.

P3-199

A Case of IgA Vasculitis accompanied with Kidney and Testicular Ischemia

Hideyuki Matsushima, Takayuki Hirai, Shota Minami, Nobuo Negoro
Clinical Immunology, Osaka City University Hospital

Conflict of interest: None

A 41-year-old man, having palpable purpura of the lower legs 2 weeks before, abdominal pain and bleeding 3 days before, was admitted to our hospital with suspected IgA vasculitis. Although skin biopsy did not show IgA deposition, EULAR classification criteria (2010) was satisfied, he was diagnosed as IgA vasculitis. Symptoms improved with prednisolone 60 mg / day. However, left testicular pain and microscopic hematuria on day 14 after hospitalization began. Ultrasonography revealed left testicular bleeding. Angiographic examination revealed irregularities and stenosis of left testicular and renal artery. Diagnosed as complication of polyarteritis nodosa, cyclophosphamide pulse therapy was performed. His pain gradually improved and he was discharged. At 240 day after onset of the disease, purpura and hematuria restarted and he was hospitalized. Renal biopsy showed IgA nephropathy (crescentic glomerulonephritis, ISKDC classification Grade 3), and IgA vasculitis requiring aggressive treatment was confirmed. Because medium-sized vasculitis is also accompanied, his treatment is strengthened such as azathioprine and tonsillectomy. The case suggests us that precious diagnosis including biopsies is important to select the better treatment in patient with complicated vasculitis syndrome.

P3-200

Two cases of the elderly with gastrointestinal manifestation complicated IgA vasculitis

Takahiro Yajima¹, Rie Yamada²

¹Department of Nephrology, Matsunami General Hospital, ²Department of Internal Medicine, Matsunami General Hospital

Conflict of interest: None

[Case 1] A 69-year-old female presented with 3-day palpable purpura on legs. Skin biopsy revealed leukocytoclastic vasculitis. Based on possible diagnosis of IgA vasculitis (IgAV), PSL therapy began orally administered (30mg/day). The purpura disappeared within a week, but recurred on 12th hospital day. She complained of epigastralgia on 15th hospital day. Esophagogastroduodenoscopy (EGD) revealed telangiectasia of stomach and erosion of duodenum. PSL intravenously administered (50mg/day) led disappearance of gastrointestinal symptoms and purpura on 20th hospital day. [Case 2] A 79-year-old male presented with 3-day abdominal pain and purpura on legs. Laboratory data showed elevated inflammatory marker and renal failure. Abdominal CT revealed thickening of the duodenal wall. EGD revealed ulcerative lesions in the duodenum. These findings made the most plausible diagnosis of IgAV. PSL intravenously administered (50mg/day) ameliorated the abdominal pain in a few days. Despite the improvement of EGD findings on 18th hospital day, renal function exacerbated requiring hemodialysis. [Discussion] We report two cases of the elderly gastrointestinal involvement of aged IgAV. Intravenous injection of steroid preempted successful improvement of abdominal symptoms and EGD findings.

P3-201

Two case reports of the intestinal vasculitis who were not determined the definite diagnosis after the operation of the perforation

Yoshiki Shiohira, Takuya Oshiro, Chia Nakata, Tomoo Murayama, Eishi Uechi, Masato Oroku

Department of Nephrology and Rheumatology, Tomishiro Central Hospital, Tomigusuku, Okinawa, Japan

Conflict of interest: None

Case 1: 81-year-old woman was diagnosed left renal pelvic carcinoma and left renal ureterectomy and partial cystectomy was performed. Two weeks later ulcer and penetration of descending colon developed and then left hemi-colectomy and artificial colostomy was done. Five months later acute lymphocytic leukemia occurred, after that she died. Reconfirmation of the pathology revealed a scarring vasculitis of the colon. We diagnosed this case was polyarteritis nodosa combined with malignancy Case 2 is a 73-year-old woman being treated with hypertension. Abdominal pain persisted and she was admitted to our hospital at department of surgery. On the 23rd hospital day intestinal perforation was suspected, and subtotal colectomy, partial resection of the small intestine, and artificial colostomy were done. Proteinuria, hematuria and renal dysfunction were observed on admission, but 6 years later the renal function

deteriorated and was introduced into dialysis. She also complicated a bladder bleeding and abdominal cavity pelvic abscess due to rectal-bladder fistula. Reconfirmation of the pathology of the colon revealed a necrotizing venulitis. It was considered as IgA vasculitis (serum IgA 644 mg/dl). Conclusion: Diagnosis is uncertain Intestinal perforation is caused by vasculitis.

P3-202

A case of IgA vasculitis treated successfully with rituximab

Kazuo Kushimoto¹, Takuya Sawabe², Masahiro Ayano¹, Miki Nakano¹, Yasutaka Kimoto³, Hiroki Mitoma¹, Mitsuteru Akahoshi¹, Yojiro Arinobu¹, Koichi Akashi¹, Takahiko Horiuchi³, Hiroaki Niino⁴

¹Department of Medicine and Biosystemic Science, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan, ²Department of Rheumatology, Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital, Hiroshima, Japan, ³Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, ⁴Department of Medical Education, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan

Conflict of interest: None

A 63-year-old man presented to our hospital with arthralgia of the left knee and right ankle joint and palpable purpura of both lower legs. His serum IgA was elevated (629 mg/dL) and coagulation factor XIII activity was decreased (65%). A skin biopsy of the purpura revealed leukocytoclastic vasculitis, and he was diagnosed with IgA vasculitis based on the criteria provided by the American College of Rheumatology in 1990. We started treatment with corticosteroids (PSL 30 mg/day) because his severe arthritis was resistant to non-steroidal anti-inflammatory drugs. We achieved temporary remission; however, he relapsed with new-onset fever, diarrhea, and mild renal dysfunction when the dose of PSL reached 12.5 mg after tapering. We added mizoribine, but the patient's response was poor. After starting rituximab, he achieved remission and the dose of PSL was tapered to 3 mg/day. The present case demonstrates a good efficacy of RTX for the treatment of IgA vasculitis.

P3-203

Remarkable effect of TNF α inhibitor for refractory lower leg ulcers in patients with malignant rheumatoid arthritis

Asami Akita¹, Yukie Yamaguchi¹, Nobuaki Ikeda¹, Miwa Kanaoka¹, Yasushi Ototake¹, Michiko Aihara¹, Yohei Kirino²

¹Department of Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine, Yokohama, Japan, ²Department of Hematology and Clinical Immunology, Yokohama City University Hospital, Yokohama, Japan

Conflict of interest: None

The first case is a 78-year-old woman, who has been suffering from rheumatoid arthritis (RA) for 33 years being treated with prednisolone and methotrexate (MTX). She visited our hospital due to development of skin ulcers in her leg and toe. DAS28-CRP was 3.09. Skin biopsy revealed necrotizing vasculitis. High dose corticosteroids (CS) and azathioprine were not effective, then Etanercept (ETN) was administered in combinations with L-CAP and negative pressure wound therapy. Finally, the lesion was improved. The second case is an 81-year-old woman, who has been treated of her RA with MTX and salazosulfapyridine for 8 years. Skin biopsy for newly appeared erythema revealed necrotizing vasculitis. High dose CS was failed, then her skin vasculitis got worsen to form deep leg ulcer. DAS28-CRP was 4.05. Finally, the ulcer was improved by ETN. Stasis leg ulcers in RA patients may be commonly observed in daily clinics. However, a refractory leg ulcer may be caused by rheumatoid vasculitis, which sometimes requires aggressive therapy. Even though the disease activity is not high, it may be important to suspect vasculitis in RA patients with a refractory gangrene or ulcers. In addition, a prompt use of TNF α inhibitors may be helpful in cases resistant to CS or immunosuppressive drugs.

P3-204

Rapid improvement of microaneurysms in visceral arteries was confirmed by follow-up angiography in a case of polyarthritis nodosa

Yoshinobu Matsuura¹, Takehiro Hirayama¹, Akihiko Nakabayashi¹, Akira Mega², Yoshinori Katada¹

¹Division of Rheumatology and Clinical Immunology, Sakai City Medical Center, Sakai, Japan, ²Nephrology, Diabetology, Rheumatology, Sakai City Medical Center, Sakai, Japan

Conflict of interest: None

[Introduction] Visceral angiography, a valuable examination for the diagnosis of polyarthritis nodosa (PN), is rarely performed as a follow-up examination in the course of treatment. In this case, we had a chance to perform follow-up angiography, and confirmed marked improvement of microaneurysms only 1 week after initiation of immunosuppressive therapy. [Case] A 74-year old man, who presented with malaise and appetite loss for several days, was admitted to a hospital. He developed retroperitoneal bleeding 13 days after administration, then transferred to our hospital. Visceral angiography revealed microaneurysms, stenosis and obstruction in the branching of both celiac and superior mesenteric artery (SMA). He was treated with coil embolization for aneurysms in the branches of SMA considered as a source of retroperitoneal bleeding. Laboratory tests showed increased CRP (16 mg/dl); MPO-ANCA and PR3-ANCA were negative. He was diagnosed with PN, and treated by corticosteroid pulse therapy and intravenous cyclophosphamide. An enlargement of an aneurysm was confirmed by CT angiography 1 week after corticosteroid pulse therapy, so visceral angiography and coil embolization were performed again, showing dramatically improved microaneurysms, stenosis and obstruction in the visceral arteries.

P3-205

A case of polyarteritis nodosa with myalgia and marked edema of lower limbs

Kyoko Takano¹, Yuki Mizutani¹, Hiroshi Hamada¹, Mayu Sugiyama¹, Kahori Oshima¹, Takakazu Hasegawa¹, Syunsuke Yokoi¹, Kumiko Umemura¹, Michita Suzuki¹, Eiji Nagasawa^{1,2}, Nobuyoshi Minemura¹, Masao Katayama¹

¹Division of Rheumatology, Department of Internal Medicine, National Hospital Organization Nagoya Medical Center, ²Nagasawa Clinic

Conflict of interest: None

[Case] A 7X-year-old woman presented fever and edema and myalgia of bilateral lower limbs. Laboratory tests showed WBC 15200/ μ L, CRP 15.8mg/dL, ESR 56mm/H, CK 37U/L (normal), aldolase 7U/L (slightly elevated). ANA, MPO-ANCA and PR3-ANCA were all negative. MRI revealed increased signal in the bilateral femoral muscles, pectineus, obturator externus and obturator internus on STIR sequences. She was received femoral muscle biopsy because myositis was suspected. The biopsy revealed perivascular inflammatory infiltrate with lymphocytes and histiocytes and fibrinoid necrotic vasculitis. The fasciitis and myositis findings were not clear. She was diagnosed with polyarteritis nodosa (PN). She was treated with 40mg (1mg/kg/day) of prednisolone and 50mg/day of azathioprine. During the course, she complicated of deep vein thrombosis of the lower limbs, so 30mg/day of edoxaban was used. These treatment resulted in immediate improvement of her symptoms and normalization of serum CRP and ESR values. [Discussion] There are some cases of myalgia without CK increase in PN. We reported a case diagnosed as PN by MRI and muscle biopsy. It is important to suspect PN as one of causes of myalgia of lower limbs. MRI and muscle biopsy may be useful for diagnosis of PN in those cases.

P3-206

A case of polyarteritis nodosa begun by meralgia

Shiho Iwagaitsu, Hanako Ito, Masayoshi Toda, Hiroya Tanaka, Naoya Matsuoka, Masako Koshino, Asako Kachi, Akimasa Asai, Nao Asai, Mayumi Ito, Hirokazu Sugiyama, Makoto Yamaguchi, Hironobu Nobata, Takayuki Katsuno, Shogo Banno, Yasuhiko Ito
Department of Internal Medicine, Division of Rheumatology and Nephrology, Aichi Medical University School of Medicine

Conflict of interest: None

Polyarteritis nodosa (PAN) is a medium vessel vasculitis affecting systemic organs. PAN limited to the muscles is rare and typically muscle lesions often appear on the lower leg. We report a case of PAN begun with meralgia. An 83-year-old male presented with meralgia and brachialgia for 4months. Low dose prednisolone (PSL) was administered by his primary care physician in the diagnosis of polymyalgia rheumatica. Brachialgia was improved rapidly, but meralgia were persisted. Laboratory testing showed a low level of creatine kinase and an elevated C-reaction protein (CRP) levels of 18 mg/dL. Lower limbs MRI showed muscle atrophy on the ventral side of the femur and STIR high signal was observed at the same site. Enhanced MRI demonstrated hyperintensities on T1 in the femoral muscles. Muscle biopsy was performed from the quadriceps right muscle, the biopsied specimen revealed thickening of the vessel wall with inflammatory cell infiltration. According to these findings, he was diagnosed with PAN and administered with PSL 40 mg/day, the symptoms of PAN were improved rapidly.

P3-207

A case of polyarthritis nodosa as rashes like cellulitis and myalgia of lower thighs

Miho Yamazaki, Reina Tsuda, Takafumi Onose, Naonori Sugishita, Ryoko Asano, Toshiki Kido, Hiroyuki Hounoki, Koichiro Shinoda, Hirofumi Taki, Kazuyuki Tobe
Department of Internal Medicine 1, Toyama University Hospital

Conflict of interest: None

[Case] A 74-year-old female with hypertension had fever, pain and swelling of lower thighs 3 months ago. She was admitted as cellulitis and treated with six kinds of antibacterial drugs, but CRP level was remained 6 ~ 7 mg/dL. Her symptoms were improved a few, so she left the hospital 2 months ago. However got worse soon, she was admitted and treated with 2 kinds of antibacterial drugs together and NSAIDs during three weeks. CRP level was improved to 2.7 mg/dL from 16.3 mg/dL, but remained. So she was started treating with PSL 5mg/day, left the hospital a month ago. Thereafter, her symptoms got worse again, so she was introduced and admitted to our hospital. She was only positive for RF among autoantibodies. She was negative for serum HBs-antigen and HBV-DNA, but positive for serum HBs-antibody. She was performed a biopsy on the skin, the muscle and fascia. The biopsy showed small arteritis with infiltrating by neutrophil. She was started treating as polyarthritis nodosa with methylprednisolone 500mg/day for three days. After the three days, She was treated from PSL 20mg (0.5mg/kg)/day. Her symptoms were improved, and CRP level became negative. [Clinical significance] We discuss about the case of small arteritis suspected of polyarthritis nodosa with literature review.

P3-208

Lower leg myalgia as the initial symptom in systemic vasculitis

Satoru Ushiyama, Noriko Sakaguchi, Takanori Ichikawa, Kenichi Ueno, Dai Kishida, Yasuhiro Shimojima, Yoshiki Sekijima
The Third Department of Internal Medicine, Shinshu University School of Medicine

Conflict of interest: None

[Object] To investigate the clinical features in patients indicating myalgia as the initial episode of systemic vasculitis. [Methods] By reviewing clinical records of patients with systemic vasculitis, they were classified into two groups dividing patients with or those without myalgia as the initial episode of disease (myalgia or non-myalgia group, respectively). Clinical findings were analyzed between two groups. [Results] We recruited 82 patients (mean age 61 \pm 15, 31 men and 51 women), who were classified into eosinophilic granulomatosis with polyangiitis (n = 7), granulomatosis with polyangiitis (n = 20), microscopic polyangiitis (n = 30), and polyarteritis nodosa (n = 21), as well as 4 patients of unclassifiable. Of them, 22 patients were classified to myalgia group, in which the majority of patients demonstrated lower leg myalgia. Meanwhile, there were no significant differences in mean age and sex distribution between two groups. In myalgia group, administering immunosuppressant togeth-

er with prednisolone (PSL) was required for achieving remission. [Conclusions] Lower leg myalgia can be an initial clinical episode of vasculitis. Even in the case showing myalgia as a principal symptom, concomitant use of immunosuppressive agent may be necessary for achieving favorable outcome.

P3-209

A case showing polyarteritis nodosa like symptom accompanied with thrombocytopenia

Shota Nakano, Harumichi Suma, Atsushi Tanaka, Takuya Sawabe
Department of Rheumatology, Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital, Hiroshima, Japan

Conflict of interest: None

<Case> 67-year-old man <Chief complaint> Fever, general malaise, joint pain, muscle pain <Current medical history> On 6 September, a fever of the order of 38 °C Because there was no improvement, he was introduced to his previous doctor on the 18th. Various infectious disease tests and autoantibody tests were performed, but since there was no abnormality, he was treated with SBT / ABPC and MINO as sepsis. On the 26th he was transferred to our hospital, the inflammatory response high value, platelet reduction of the 60000 / uL range, pleural effusion, pericardial effusion was observed, pleural effusion was exudative. The cause was still unknown, so we administered high-dose steroids and inflammation improved. Polyarteritis nodosa usually involves thrombocytosis, but we observed weight loss, hypertension, purpura, joint pain, muscle pain, and neuropathy in the course of scrutiny, We were to administer an immunosuppressive agent as a polyarteritis nodosa when relapsing symptoms. <Discussion> This case is a course that can not be explained by known single disease, and it is necessary to follow carefully in the future. We report with differentiation such as idiopathic pericarditis, adult onset Still's disease, TAFRO syndrome etc.

P3-210

A suspicion case of primary central nervous system vasculitis with emergency surgery due to cerebral hemorrhage after steroid pulse therapy

Yutaka Tanikawa, Marina Hamaguchi, Masashi Oshima, Shoei Yoshizawa, Hiroshi Tsuzuki, Yosuke Nagasawa, Kaita Sugiyama, Atsuma Nishiwaki, Natsumi Ikumi, Takamasa Nozaki, Mitsuhiro Iwata, Hitomi Haraoka, Noboru Kitamura, Masami Takei

Division of Hematology and Rheumatology, Department of Medicine, Nihon University Itabashi Hospital, Nihon University School of Medicine Itabashi Hospital

Conflict of interest: None

A 81-year-old female, who was treated with common cold by antibiotics, recognized extremities weakness in addition to persisted inflammation. She was referred to our hospital for examination and treatment. On the first day after admission to our hospital, head MRI showed multiple strokes in bilateral cerebral cortex. She started to be treated with heparin. On 13th day of admission, followed-up head MRI showed new multiple strokes in bilateral cerebral cortex on heparin. On 22nd day of admission, head MRI showed cerebral microbleed and subarachnoid hemorrhage. As all the autoantibodies were negative as well as central nervous system lesion had progressed rapidly, which were unable to conduct biopsy, she started to be on steroid pulse therapy with suspicion of primary CNS vasculitis (PCNSV). On 28th day of admission, she had consciousness disturbance, left hemiplegia. Head CT showed right cerebral hemorrhage and she transferred to another hospital for surgery. [Discussion] PCNSV is vasculitis in localized central nervous system. Diagnosis of PCNSV is required to perform brain biopsy. If brain biopsy is unfeasible like this case, it can be considered that treatment at an early stage is required when PCNSV is suspected with progression of central nervous lesion in other examinations.

P3-211

Three cases of suspected muscle localized vasculitis

Kenichi Hiraga, Yoshinori Masui, Naonori Tsuda, Toshikazu Kano

General Internal Medicine, Rheumatology, Kohnodai Hospital, National Center for Global Health and Medicine

Conflict of interest: None

[Background] We report 3 cases of suspected muscle localized vasculitis. In all cases, blood examination showed elevated inflammatory markers, but creatine kinase (CK) was normal and ANCA was negative. [Case 1: An 80-year-old male.] The main complaint was weakness of the lower limb. The inflammation of his muscles of both thighs was revealed with contrast-enhanced MRI and FDG-PET/CT (PET/CT). Muscle biopsy revealed findings of perimysium vasculitis and diagnosed as muscle localized vasculitis. [Case 2: A 69-year-old male.] The chief complaint was a fever. MRI and PET/CT revealed the inflammation of his femoral muscles. Although no abnormal findings were observed in muscle biopsy, we diagnosed as muscle localized vasculitis. [Case 3: A 69-year-old male.] The chief complaint was a fever and weakness of the lower limbs. We recognized the contrast effect with MRI and the accumulation of FDG with PET-CT in the muscle of the lower leg. Muscle biopsy was rejected, so we diagnosed muscle localized vasculitis and started prednisolone. [Conclusions] In cases of the fever of unknown origin with weakness of the lower limbs, it was suggested that we should differentiate muscle localized vasculitis even if CK is within normal limit and ANCA is negative.

P3-212

A case of cutaneous arteritis without inflammatory response: a case report

Yu Isoda, Hiroaki Kusuoka, Hironori Inoue, Keitaro Saito, Aki Sakashita, Aiko Hirano, Risa Sagawa, Kazuki Fujioka, Hidetake Nagahara, Makoto Wada, Masataka Kohno, Yutaka Kawahito

Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

Conflict of interest: None

A 37-year-old woman was admitted with paralysis of the ulnar area of the left in year X-10 and her grip strength declined. She was diagnosed with left ulnar nerve paralysis, so underwent neuro-transposition and the symptoms improved. Two years later, similar symptoms appeared in the opposite ulnar area and the transposition also was done. After that the symptoms once again flared in each hand and she had reoperations. In October of year X-1, paresthesias in the hands and lower thigh appeared intermittently. In September year X, numbness and livedo reticularis on the lower leg appeared, so she was hospitalized for further examination in our hospital the next month. At the time of admission, she had the atrophy of the interosseous muscle of the hands, weak grip strength and a nerve conduction study showed mononeuritis multiplex in limbs. The laboratory exam showed no inflammatory reactions nor specific antibodies. But skin biopsy of the lower limbs revealed fibrinoid necrosis and inflammatory cells on the dermic artery wall, so she was diagnosed as cutaneous arteritis (CA). oral steroid therapy with azathioprine improve neurological symptoms promptly. CA sometimes develops negative inflammatory response, so we should keep it in mind in clinical practice.

P3-213

A Case Report of Angiosarcoma with an Aortic Lesion Diagnosed as Polyarteritis Nodosa Based on Fever, CRP Elevation and Renal Artery Stenosis

Sho Fukui, Hiromichi Tamaki, Haruki Sawada, Mitsuru Watanabe, Yukihiro Ikeda, Ayako Kitada, Rui Kawato, Masei Suda, Haruyuki Yanaoka, Ryo Rokutanda, Hisanori Shimizu, Tokutaro Tsuda, Mitsumasa Kishimoto, Ken-ichi Yamaguchi, Masato Okada

Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan

Conflict of interest: None

A 58-year-old male with diabetes and hypertension due to bilateral renal artery stenosis diagnosed 1.5 year ago was referred to our hospital for refractory PAN. 4 month prior to admission, he stayed at the prior hospital for fever, high CRP, weight loss, and acute renal injury (Cre 2.7

mg/dl). Renal biopsy showed interstitial nephritis and one fibrotic crescent out of 30 glomeruli. Pelvic MRA showed focal dissection of rt common iliac artery. He was diagnosed as PAN and completed steroid pulse therapy twice and IVCY 4 times. His fever, CRP and renal function improved partially, but exacerbated after PSL was tapered to 20 mg a day. He was referred to us after developing left wrist drop and lumbar fractures. Immunosuppression was intensified with mPSL and rituximab for possible vasculitic emergency tentatively. Malignancy was strongly suspected due to his refractory course. PET-CT scan demonstrated increased FDG uptake in L2 vertebra, aortic wall close to rt renal artery, rt femoral head and lt acetabulum. Biopsy from the vertebral lesion revealed angiosarcoma. His fever and high CRP improved dramatically with treatment of weekly paclitaxel. We should consider angiosarcoma as a differential diagnosis of PAN since it was reported to mimic PAN though it is a rare malignancy.

P3-214

IgG4-related disease with eosinophilic dermatosis; A rare case of skin lesions of IgG4-RD

Yusuke Manabe, Yuichi Maeda, Yuta Yamaguchi, Yumiko Mizuno, Mayu Yagita, Masashi Narazaki, Atsushi Kumanogoh

Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University

Conflict of interest: None

A 76-year-old female had recognized swelling of submandibular glands with high titer of IgG4 level (740mg/dl). In the past, she had received corticosteroid due to asthma and eosinophilic pneumonia. She also had swelling of her face and erythema of her neck and limbs which lead her to admission. Contrast-enhanced CT had revealed swelling of tale of pancreas, small nodules and ground-glass opacity of her lung, and swelling of multiple lymph nodes in the mediastinum. They were consistent with IgG4-RD, but skin biopsy had atypical result, which was perivascular eosinophilia with few plasma cells in dermic layer of the skin. She also had eosinophilia (5099/ μ L) so differential diagnosis such as eosinophilic granulomatosis with polyangiitis (EGPA) should be ruled out. As a result of biopsy from other organs, there was rich infiltration of IgG4 positive plasma cells in her lung (IgG4/IgG ratio>45%), whereas in a submandibular gland and lymph nodes in her mediastinum was not. Consequently, we diagnosed her disease as IgG4-RD. After receiving 30mg dose of corticosteroid, her symptoms had improved. The skin lesions of IgG4-RD sometimes take the form of irregular pattern which causes difficulty of diagnosis. This is the rare case of IgG4-RD case with eosinophilic dermatosis.

P3-215

Peripheral blood eosinophils in high IgG4 cases

Reika Maezawa, Kazuhiro Kurasawa, Yuta Takamura, Tomoyuki Miyao, Aya Tanaka, Ryutaro Yamazaki, Satoko Arai, Takayoshi Owada, Masafumi Arima

Department of Rheumatology, Dokkyo Medical University

Conflict of interest: None

[Object] We clarify the relationship between IgG4 level and peripheral blood eosinophils. [Methods] In our hospital, cases with IgG4 of more than 135 mg / dl were extracted and diseases, IgG4 levels, peripheral blood eosinophil counts were examined. [Results] We studied 262 cases in which blood IgG4 was above 135 mg / dL. IgG4RD was 96 cases, and the average IgG4 value was 705.8 ± 604.5 mg / dL. Other diseases were 166 cases, 246.1 ± 456.9 mg / dL. The average number of peripheral blood eosinophils as a whole is $1011.1 / \mu$ L \pm 3310, the maximum value 10880.1 / μ L, the median 221.7 / μ L, the average 535.0 / μ L minus 1282.1 for IgG4 related diseases, the maximum value 29916.6 / μ L, the median 194.7 / μ L Met. When examining the relationship between the IgG4 level and the number of eosinophils, it is roughly classified into an IgG4 single increase group and an eosinophil alone single increase group, and the group that increases both is rare. IgG4RD was the main disease of the IgG4 single increase group. In cases with eosinophils exceeding 2000 / μ L, only 4 cases of IgG4 related disease were found, and most were EGPA. [Conclusions] Although eosinophilia is observed in IgG4-re-

lated diseases, few cases show a marked increase of more than 2000 / μ L.

P3-216

IgG4-related skin disease; two cases of IgG4-RD presented with skin lesions

Akari Kato¹, Teppei Kamikawa¹, Teruchika Yamada², Yuichi Handa¹, Masanobu Horikoshi¹

¹Department of Rheumatology, Japanese Red Cross Saitama Hospital, ²Ohmiya Clinic

Conflict of interest: None

[Background] IgG4-RD can show various type of skin lesions, recently described as IgG4-related skin disease. [Case1] A 78-year-old man with pruritus eruption and elevated serum IgG4 (1510mg/dl) was referred to our hospital. Examinations showed lung infiltration in the left lower lobe on CT, and abnormal uptake in the lung and the prostate on FDG-PET. Although skin biopsy showed little infiltration of IgG4 (+) cells, he was diagnosed for IgG4-RD on the basis of lung and prostate biopsy showing infiltration of IgG4 (+) cells (IgG4 (+)/IgG (+) cells >95%). [Case2] A 54-year-old man with eyelid swelling and erythema was referred to our hospital. Lacrimal gland biopsy had shown marked infiltration of IgG4 (+) cells and he had already been diagnosed for IgG4-RD. The patient also had elevation of serum IgG4 (1610mg/dl). Chest and abdominal CT revealed bronchial and aortic wall thickening and thickening of soft tissue in front of the spine. Skin biopsy showed infiltration of IgG4 (+) cells (>80%). [Discussion] IgG4-related skin disease can be induced by direct infiltration of IgG4 (+) cells or secondary manifestation. Although skin biopsy was nonspecific in case1, we could diagnose him for IgG4-RD based on systemic inspection. IgG4-related skin disease could be a cause of persistent skin lesion.

P3-217

A case of IgG4-related disease with uterine cervical involvement

Yusuke Yamauchi¹, Masahiro Ayano¹, Yasutaka Kimoto², Hiroki Mitoma¹, Mitsuteru Akahoshi¹, Yojiro Arinobu¹, Koichi Akashi¹, Takahiko Horiuchi², Hiroaki Niuro³

¹Department of Medicine and Biosystemic Science, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan, ²Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, ³Department of Medical Education, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan

Conflict of interest: None

A 38-year-old female presented to our hospital with bilateral eyelid swelling, parotid swelling, submaxillary swelling, nasal congestion and chronic sinusitis. On her laboratory examination, serum IgG4 level was elevated (670 mg/dl). A biopsy of right lacrimal gland showed marked infiltration of lymphocytes and plasma cells (IgG4/IgG ratio of 90%) and fibrosis, and she was diagnosed as IgG4-RD. FDG-PET/CT scan demonstrated a high uptake in cervix of uterus as well as in lacrimal gland, parotid gland, submandibular gland, sublingual gland, nasal mucosa, ethmoid sinus and mediastinum/hilar lymph node. After gynecological examination, a cone excision of the cervix was performed. The endocervical tissue also showed histopathologic features supportive of IgG4RD (IgG4/IgG ratio of 80%). Treatment was initiated with prednisolone at a dose of 0.6 mg/kg/day (35mg). One month later, her symptoms disappeared almost entirely by physical examination. CT after 7 months revealed resolution of bilateral eyelid swelling and parotid swelling. MRI after 8 months revealed shrinking of the uterine cervical lesion. This is a rare case of IgG4RD with uterine cervical involvement.

P3-218

Difficulty to differentiate multicentric Castleman's disease from IgG4-related disease : A case report

Harumichi Suma, Shota Nakano, Atsushi Tanaka, Takuya Sawabe
Department of Rheumatology, Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital

Conflict of interest: None

A female in her seventies showed an elevated C-reactive protein level (CRP) of about 1 mg/dl 8 years ago. She experienced no symptoms at all, and was followed by her primary care doctor. Three years ago, her CRP level was raised by 7 mg/dl, and anemia and renal dysfunction occurred. Simultaneously, she presented a polyclonal hypergammaglobulinemia. She remained asymptomatic, however, anemia and renal dysfunction were getting worse. She was referred to our hospital. At the initial visit, she showed no aberration on physical examination. Her blood tests are as follows: CRP 13.1 mg/dl, hemoglobin 6.6 g/dl, creatinine 1.3 mg/dl, immunoglobulin G 7882 mg/dl, immunoglobulin G subclass 4 740 mg/dl, immunoglobulin A 1030 mg/dl, immunoglobulin M 256 mg/dl, and interleukin 6 55.6 pg/ml. Whole-body CT scan showed multiple lymphadenopathy of left infraclavicular, bilateral axillary, mediastinal, and bilateral inguinal regions. It is difficult to distinguish multicentric Castleman's disease (MCD) and IgG4-related disease (IgG4-RD) clinically. Left axillary lymph node biopsy revealed IgG4-positive plasma cell infiltration. We report the characteristics of MCD and IgG4-RD to differentiate themselves, and the course of treatment.

P3-219

A case of "pseudo-meningioma", which was diagnosed as an IgG4-related disease based on the pathological findings

Hikaru Hirose, Shinya Hirahara, Akira Nishino, Mari Tochihiro, Hirokazu Nishina, Masanori Hanaoka, Yasuhiro Katsumata, Hisashi Yamanaka

Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Case] Ten months ago, a woman had a headache and was detected tumor which was not presented before. It spread along the right tent and pushed the brainstem. Tumor was extracted by neurosurgeon six months ago and oppression was canceled. Meningioma was denied from pathology findings. Invasion of prominent B lymphocytes/plasma cells and fibrosis was observed. It could not evaluate "IgG4/IgG positive cells ratio \geq 40%" due to crushed degeneration. IgG4 positive plasma cells exceeded 10/HPF and serum IgG4 was high as 226 mg/dL. So IgG4 related disease was suspected. IgG4-related disease comprehensive diagnostic criteria was not fulfilled and plasmacytoma tumors could not be denied because of large number of κ chain-dominant CD 138 positive plasma cells. Any symptoms disappeared, but a part of the tumor remained, and in consideration of the risk of re-exacerbation without treatment, we started prednisolone at 0.6 mg/kg. Subsequently, the serum IgG4 value rapidly normalized and it did not relapse after the gradual decrease of prednisolone. [Clinical Significance] As rare IgG4-related disease of central nervous system, there are few reports of tumorous lesions similar to meningiomas as in this example. This case was important considering various disease states of IgG4 related diseases.

P3-220

An example of the IgG4-related disease that merged SLE

Kazusato Hara¹, Yoshikazu Nakashima¹, Takahisa Suzuki², Akitomo Okada¹, Atsushi Kawakami³

¹Department of Rheumatology, Japanese Red Cross Nagasaki Genbaku Hospital, ²Department of Immunology and Rheumatology, Sasebo City General Hospital, ³Department of Immunology and Rheumatology, Nagasaki University Hospital

Conflict of interest: None

A case is a 78 year old man. He admitted to the medical department of Hematology, recognizing the pancytopenia. IgG:7150mg/dl and the immunity electrophoresis test was performed, it was multi-clone. No significant findings were observed in the bone marrow test. CT showed lots of lymphadenopathy and the enhancement of soft shadow in the abdominal aorta and the iliac artery. IgG4:704mg/dl was high and IgG4-related diseases were suspected. Anti-nuclear antibodies and anti-Sm antibody positive, low complement blood and white blood cells, renal dysfunction and urinary findings, so we underwent renal biopsy. Interstitial cell infiltration and Hana-like fibrosis, mesangial cell increase, IgG in fluorescence antibody method, IgA, IgM, C3, deposition of C1q, was admitted

deposition of mesangial region in electron microscopy. We diagnosed as IgG4-RD/IgG4 related kidney disease (IgG4-RKD) and systemic lupus erythematosus (SLE)/lupus nephritis (LN) Class II merger. We started prednisolone 40mg for treatment and are decreasing gradually. Both sides submandibular gland swelling and lymphadenopathy, the soft shadow disappear, and IgG4 decreases to the normal range. Also, renal function become normal. The course is good, adding a mycophenolic acid mofetil.

P3-221

A case of MALT lymphoma diagnosed by biopsy of a growing mass around right kidney during therapy of IgG4-related disease

Kahori Oshima, Masao Katayama, Nobuyoshi Minemura, Eiji Nagasawa, Kyoko Takano, Michita Suzuki, Kumiko Umemura, Syunsuke Yokoi, Takakazu Hasegawa, Mayu Sugiyama

National Hospital Organization Nagoya Medical Center

Conflict of interest: None

A 60-year-old man with a history of diffuse large B-cell lymphoma came to the hospital because of left swelling eyelid and right swelling axially lymph node 2 years before. He was diagnosed as IgG4-related disease because the eyelid biopsy histology confirmed it. According to the enhanced CT scan, many lymph nodes throughout the body, including a small mass around the right kidney, were swelling. PET-CT scan and an additional biopsy of neck lymph node were proceeded in order to confirm the diagnosis. Because no evidence of malignancy were found, we finally diagnosed with IgG4-related disease and started on PSL 0.6 mg/kg/day. The response to the treatment was remarkable and almost all lesions were disappeared. However, in spite of under treatment and other lesions were improved, the only mass around the right kidney was growing bigger within one year, so malignancy and lymphoma was considered as a differential diagnosis. The biopsy of the mass was proceeded laparoscopically and its history confirmed MALT lymphoma. We report a case of MALT lymphoma diagnosed by biopsy of a growing mass around right kidney during therapy of IgG4-related disease with some discussion.

P3-222

A case of IgG4-related disease with marked eosinophilia and purpura

Katsunori Nakagawa¹, Hiromasa Kawashima¹, Ryo Yoneima¹, Yoshiaki Tai¹, Emiko Tatsumi¹, Kiyomi Yoshimoto¹, Yasuhiro Akai^{1,2}, Yasuhito Tanaka², Takashi Fujimoto², Kenji Nishio¹

¹Department of General Medicine, Nara Medical University Hospital,

²The Center for Rheumatic Diseases, Nara Medical University Hospital

Conflict of interest: None

A 55-year-old female presented with swelling of salivary and lacrimal glands for 6 months. She was admitted with 10 days history of purpura of lower legs. She had a history of bronchial asthma. Her laboratory results were: peripheral white blood cell count, 17,000 / μ L with 72.0% eosinophils (12,000 / μ L); ESR, 79 mm; CRP, 0.47 mg/dL; IgG, 3,870 mg/dL; IgG4, 2,200 mg/dL; IgE, 1,675 U/mL; and both PR3-ANCA and MPO-ANCA negative. CT showed mediastinal and paraaortic lymphadenopathy, but no findings suggesting pancreas swelling or retroperitoneal fibrosis. The submandibular gland biopsy revealed lymphoplasmacytic infiltration with 70% of IgG4+/IgG+ cell ratio. The skin biopsy of purpura indicated eosinophilic infiltration, but no apparent findings of vasculitis. She was diagnosed with IgG4-related disease (IgG4-RD), as she had no evidence of vasculitis. She was commenced on 0.6 mg/kg (50 mg daily) of prednisolone (PSL), and the swollen salivary and lacrimal glands and purpura resolved completely on the 7th day of treatment. IgG4-RD was reported to have eosinophilia with the eosinophil count of up to 2,000 cells/ μ L. A differential diagnosis between IgG4-RD and eosinophilic granulomatosis with polyangiitis (EGPA) was essential, as she had eosinophilia, purpura and a history of asthma.

P3-223

A case of inflammatory aortic aneurysm which was difficult to decide whether IgG4 related or unrelated

Tohru Michitsuji¹, Haruna Matsuo¹, Takahisa Suzuki¹, Atsushi

Kawakami²

¹Department of Rheumatology, Sasebo City General Hospital, Sasebo, Japan, ²Department of Immunology and Rheumatology, Unit of Translational Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: None

A 90-year-old woman presented with fever and loss of appetite. She visited our hospital and was hospitalized. She was pointed out an abdominal aortic aneurysm (AAA) two years ago. AAA didn't increase but surrounding soft tissue increased. Mantle sign was positive. Her laboratory data showed increase of inflammatory response. We thought it necessary to distinguish IgG4 related disease. Her serum IgG4 levels was not elevated. Gallium scintigraphy showed uptake of gallium in submandibular gland. But she never agreed to biopsy. We judged it necessary to corticosteroid therapy because size of soft tissue was increased at day 20 of the disease. We started Prednisolone 0.6mg/kg/day. Size of soft tissue was reduced and Her C-reactive protein levels was negativeization. Like this case, IAAA without other lesion and not applicable for surgery is difficult to be judged whether IgG4 related or unrelated. We report also including literature considerations.

P3-224

A case of IgA vasculitis combined with IgG4 related disease

Koji Uehara¹, Shin-ichiro Omura¹, Toru Yamabe¹, Shinya Tamechika¹, Shinji Maeda¹, Michio Fukuda², Taio Naniwa¹

¹Department of Respiratory Medicine, Allergy and Clinical Immunology, Nagoya City University Hospital, ²Department of Cardio-Renal Medicine and Hypertension, Nagoya City University Hospital

Conflict of interest: None

[Case] A 50-year-old man was diagnosed IgG4 related disease 5 months ago because of swelling of the submaxillary gland and elevation of IgG4 227 mg/dl. He was observed with no treatment. 20 days before admission, he had a fever, palpable purpura and multiple mononeuropathy. Laboratory data showed creatinine elevation and urine protein increase. CT findings showed thick bronchiolar thickening, enlargement of both kidneys and patchy contrast defect. Renal biopsy showed plasma-cyte infiltration in interstitium without glomerulonephritis and skin biopsy showed IgA deposition on the vessel wall. We diagnosed as a combination of IgG4 related disease and IgA vasculitis. We started steroid therapy and he was discharged from hospital. [Clinical significance] There were few reports of the combination of IgG4 related disease and IgA vasculitis, and in the past reports only 2 cases were reported. Both cases had glomerulonephritis and interstitial lesions in the kidneys and palpable purpura of the skin. We report with some literature review on the combination of IgG4 related disease and IgA vasculitis.

P3-225

Metabolomic analysis in IgG4-related disease

Takafumi Kawanami, Shino Fujimoto, Yoshimasa Fujita, Hiroshi Kawabata, Yasufumi Masaki

Department of Hematology and Immunology, Kanazawa Medical University

Conflict of interest: None

IgG4-related disease is indicated by increased infiltration of IgG4-positive plasma cells, typically elevated IgG4 serum levels and the formation of lymphoplasmacytic infiltrate in one or more organs. We explored the metabolome of >400 small molecules in serum from 10 matched pair IgG4-related disease subjects prior to (PRE) and following (POST) steroid treatment and contrast these profiles with a cohort of 10 normal non-diseased subjects (NORM). The polyunsaturated fatty acid arachidonate is involved in pro-inflammatory activities through its metabolism to the pro-inflammatory prostaglandins via cyclooxygenase activity and HETEs via lipoxygenases. Individuals with PRE IgG4-related disease had elevated arachidonate and the 12-lipoxygenase product, 12-HETE, as compared to NORM subjects. The higher levels of the pro-inflammatory arachidonate and 12-HETE was unaffected by steroid treat-

ment as POST subjects had similar levels of these biochemicals as was observed in PRE subjects.

P3-226

Usefulness of Serum IgG4 in IgG4-Related Disease

Hiroki Ozaki¹, Tomohiro Kameda², Shusaku Nakashima², Hiroaki Shimada², Risa Wakiya², Mikiya Kato², Taichi Miyagi², Hiroaki Dobashi²

¹Department of Rheumatology, KKR Takamatsu Hospital, ²Department of Internal Medicine, Division of Hematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University

Conflict of interest: None

[Object] We evaluated the usefulness of serum IgG4 in diagnosis of IgG4-related disease (IgG4-RD) and monitoring after treatment. [Methods] This study included 37 patients of IgG4-RD and 9 patients of others who showed high levels of serum IgG4. Laboratory data, image findings and the treatment response were analyzed from their medical records retrospectively. Relapse was defined by the new development or return of abnormal findings on physical examination, laboratory tests or imaging studies. [Results] There were 34 cases in men, 12 cases in females. Serum IgG4 was 614±514 mg/dl for IgG4-RD and 178±59 mg/dl for other diseases. In all 26 cases of IgG4-RD treated for more than 1 year, serum IgG4 was decreased after treatment started. 16 of them fell within the reference value range (<135 mg / dl). Relapse was observed in 12 cases, but there was no relation between normalization and re-elevation of serum IgG4 and relapse. In addition, there was only one case in which re-elevation of serum IgG4 was observed before relapse. [Conclusions] Serum IgG4 levels were useful in the differential diagnosis of IgG4-RD. In addition, serum IgG4 was decreased in all cases by treatment, but there was no relation between the transition of serum IgG4 and the presence or absence of relapse thereafter.

P3-227

A case of IgG4-related disease with varied clinical manifestations

Hideaki Sofue, Ken Murakami

Department of Rheumatology, Kyoto Yamashiro General Medical Center

Conflict of interest: None

[Case] 87-year-old man [chief complaint] fever of unknown origin [history] hypertension, chronic obstructive pulmonary disease, history of heavy drinking [current medical history] He was hospitalized due to unknown fever lasting about 1 month. He had leucopenia, normocytic anemia, hyponatremia, hypothyroidism (TSH: 6.49 µIU/mL, FT4: 0.50 ng/mL, FT3: 1.6 pg/mL). Thyradin was started as a treatment of primary hypothyroidism and antibiotics were initiated, but these did not respond. He was introduced to the department of Rheumatology on the 35th hospital day. He had low Serum complement levels, the high serum IgG4 concentration, renal dysfunction, exocrine pancreatic insufficiency, hypopituitarism, retroperitoneal fibrosis, left hydronephrosis, periaortitis, interstitial pneumonia and pure red-cell aplasia. We diagnosed possible IgG4-related disease and started 30mg/day of prednisolone (PSL). We changed PSL to hydrocortisone because hyponatremia did not improve and then hydrocortisone responded. He was discharged on the 79th hospital day. [Clinical significance] This case was difficult to be diagnosed because he had various symptoms. We think this case is valuable.

P3-228

A case of IgG4-Related Disease with multiple organ involvement

Soichiro Adachi, Kazuo Matsui, Atsushi Noguchi, Yoshiharu Amasaki

Department of Rheumatology, Tonan Hospital

Conflict of interest: None

An eighty-three years old man with swelling of parotid glands and high levels of serum IgG and IgG4 was referred to our hospital in May 2017. He developed weight loss and fatigue gradually and was admitted to our hospital in September 2018. Imaging studies revealed multiple organ involvements and the immunohistochemical staining of the right submandibular gland showed numerous IgG4 positive cells. He was diag-

nosed with IgG4-related disease with multiple organ involvement and treatment with oral glucocorticoid was started. The characteristics of imaging findings and the indication of systemic treatment of IgG4-related disease will be discussed.

P3-229

Clinical features of Behçet's disease complicated with joint symptoms

Toshihiro Tono¹, Shunsei Hirohata¹, Hirotohi Kikuchi², Tetsuji Sawada³, Mitsuhiro Takeno⁴, Hiroko Nagafuchi⁵, Yohei Kirino⁶, Ipppei Miyagawa⁷, Yoshiya Tanaka⁷, Kunihiro Yamaoka¹

¹Department of Collagen Disease and Infection Internal Medicine, Kitasato University Hospital, ²Teikyo University Hospital, ³Tokyo Medical University Hospital, ⁴Nippon Medical School Hospital, ⁵St. Marianna University School of Medicine Hospital, ⁶School of Medicine Medical Course Internal Medicine and Clinical Immunology, Yokohama City University, ⁷Hospital of the University of Occupation and Environmental Health, Japan

Conflict of interest: None

[Object] Approximately 60% of Behçet's disease patients have joint symptoms. The present study aimed to clarify the clinical features of these patients in Japan. [Methods] Depending on retrospective medical chart review, 151 cases were collected from 7 cooperative medical institutions treated during 2007 to 2017. Clinical characteristics and treatment regimens were analyzed. [Results] The order of most commonly afflicted joints were, knee, ankle and PIP joints. Among the patients with X-ray imaging joint space narrowing and deformation were observed in 18 joints out of 293 joints. Among those who were treated with steroids as initial treatment, 84% improved and those treated with 10 mg/day or less resulted in lower rate of improvement. There was significantly less relapse of the joint symptoms in patients treated with colchicine and MTX compared to those treated with prednisolone. [Conclusions] These results indicate that PSL should be administered at 10mg or higher for treating joint symptoms in acute phase of Behçet's disease. In addition, colchicine and MTX has the effect of preventing recurrence of joint symptoms of Behçet's disease.

P3-230

Management of pregnancy in patients with Behçet's disease

Shunsuke Uchiyama¹, Mitsuhiro Takeno^{1,2}, Takahisa Gono¹, Masataka Kuwana¹

¹Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, ²Nippon Medical School Musashi Kosugi Hospital, Kanagawa, Japan

Conflict of interest: None

[Object] This study is aimed to investigate clinical outcomes of pregnancy in Behçet's disease (BD) patients. [Methods] We retrospectively reviewed treatments and outcomes of pregnancy in BD patients between July 2014 and October 2018 in our hospitals. [Results] Seven patients had 8 pregnancies including 6 successful delivery and 2 ongoing. Of them, 3 patients had BD flares. Case 1 was a 23-year-old female who developed chronic progressive neuro-BD after discontinuation of colchicine at pregnancy. Case 2 was a 45-year-old female had a flare with skin and ocular symptoms after deliveries, which required colchicine and topical steroids. Case 3 was a 28-year old female who received infliximab (IFX) due to a severe ocular attack at 33 weeks of gestation, though discontinuation of IFX had been planned at 26 weeks. All newborns were fine except suspending live vaccinations for a year in Case 3. [Discussion] Our study suggest that treatment changes are often associated with disease flares during pregnancy in BD patients. Drafts of Japanese guidelines recommend low dose prednisolone, and suggest to use cyclosporine-A, azathioprine, and anti-TNF antibodies if necessary. Colchicine may be used under informed consent. Further study is needed for establishing management for BD during pregnancy.

P3-231

Clinical Features of Our Patients with Behçet's Disease in Saitama Medical Center Jichi Medical University

Tsuyoshi Kobashigawa, Toru Yago, Eri Watanabe, Hiroki Yabe, Shigeru Kotake

Division of Rheumatology, 1st Department of Comprehensive Medicine, Saitama Medical Center, Jichi Medical University

Conflict of interest: None

[Object] To investigate the clinical features of our Behçet's Disease (BD). [Methods] We enrolled 27 BD patients (12 males) in our hospital (Saitama Medical Center, Jichi Medical University) who continued arriving at April 1st, 2018 into this study. We analyzed their age, gender, each symptom of BD, diagnose, treatment, etc, statistically. [Results] The median age was 45 year-old (y/o): quartile, 31 y/o and 56 y/o. The symptoms of BD were as blow: oral aphthous ulcers (OU), 26 (96.3%), genital ulcers, 17 (63.0%); skin lesions, 22 (81.5%) with acneiform eruption, 13 (48.1%), erythema nodosum, 14 (51.9%) and phrenitis, 4 (14.8%); uveitis, 13 (48.1%); arthritis, 23 (85.2%), intestinal lesions, 9 (33.3%); neural lesions, 0 (0%); vascular lesions, 6 (22.2%); positive pathergy test, 2 (7.4%); epididymitis, 0 (0%). The treatments were performed with steroid-pulse to 6 (22.2%) cases; mean dose of oral steroid, 3.2 mg/day, 17 cases out of 27 were exactly taken; CyA, 2 cases; MTX, 3; AZT, 3; 5-ASA, 2; SSZ, 2; IVCY, 2; warfarin, 3; none of biologics. [Conclusions] We analyzed our BD patients. A vascular BD case was absent from OU and none was taken biologics.

P3-232

A Clinical Features of Behçet's Disease Comorbid with MDS with 8 Trisomy: a Review of Literatures

Takahiro Itamiya, Takafumi Tomizuka, Kurumi Asako, Daisuke Tsukui, Yoshitaka Kimura, Hirotohi Kikuchi, Hiroko Oguchi, Zenichiro Honda, Akiteru Takeuchi, Hajime Kono

Teikyo University Hospital, Tokyo, Japan

Conflict of interest: None

[Object] There have been several reports on patients with Behçet's disease accompanied with MDS with 8 trisomy. Most of these are reported from Japan, and a high incidence of intestinal legion and a low incidence of uveitis are pointed out. A pathological relationship between Behçet's disease and MDS with 8 trisomy isn't still fully understood, and it's a chicken or egg situation. [Methods] 65 case reports on Behçet's disease and MDS with 8 trisomy were collected. They were categorized into three groups according to written medical records, Behçet's disease preceded MDS (30 cases), MDS preceded Behçet's disease (19 cases), and these two diseases occurred simultaneously (16 cases). [Results] There was no significant difference in the onset age of Behçet's disease and MDS between the three groups. And there was no significant difference between the three groups in the rate of each symptom or clinical features (oral, genital, skin, uveitis, pathergy, HLA-B51 positive, fever, arthralgia, gastrointestinal, vasculitis, CNS involvement, and sex category). [Conclusions] Regardless of the preceding disease of Behçet's disease or MDS with 8 trisomy, there were no significant differences in the clinical features of Behçet's disease.

P3-233

Recurrent fever and panniculitis with trisomy 8

Sho Fujimoto, Naoyasu Ueda, Sanshiro Inoue, Genichi Tanaka, Koichi Mashiba

Miyazaki Prefectural Miyazaki Hospital

Conflict of interest: None

[Case] 84-year-old male [Chief complaint] fever, recurrent painful erythema [Current medical history] He had recurrent fever and painful erythema on his back from around June X-1 year. His blood examination showed anemia, thrombocytopenia and strong inflammation. He was admitted to our hospital on February X year. His symptom and laboratory data improved spontaneously in about 5 days. Histopathology of skin tissue showed panniculitis. After discharge, similar symptoms and blood test

abnormalities repeated every 14-21 days and spontaneously achieved remission in about 5 days. Erythema appeared the upper limbs and the abdomen as well as the back. Some examinations were performed, and bone-marrow examination revealed trisomy 8. 2.8% of blast cell and less than 10% of the morphological abnormality of erythroid cells and megakaryocytic cells was observed; these did not meet the morphological criteria of myelodysplastic syndrome. Ulcerative lesions were found at the terminal ileum by total colonoscopy. [Discussion] Several cases have been reported mainly from Japan about Behçet's disease-like symptoms coexisting myelodysplastic syndrome with trisomy 8, but it is rare to find trisomy 8 through Behçet's disease-like symptoms before the onset of myelodysplastic syndrome.

P3-234

A case of intestinal Behçet's disease associated with myelodysplastic syndrome (Trisomy 8)

Mariko Harada, Yoshiyuki Abe, Eri Hayashi, Kentaro Minowa, Kurisu Tada, Ken Yamaji, Naoto Tamura
Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan

Conflict of interest: None

The patient is a 40-years-old woman. She was diagnosed incomplete Behçet's disease, since she presented with genital ulceration, oral ulceration, erythema nodosum and elevation of serum IgD level in X-8 year. She was treated with prednisolone and colchicine. In X-1 year, she presented with right lower abdominal pain, and colonoscopy revealed ileocecal ulcers. Because she was diagnosed as MDS (trisomy 8) in X-20 year, we diagnosed her current symptoms as intestinal Behçet's disease associated with MDS (Trisomy 8). Her first-line therapy with adalimumab was discontinued because of secondary failure. Her second-line therapy with infliximab (IFX) was failed with 300mg of IFX at the first time, however succeeded with 600mg of IFX per 8 weeks after the second time. Since she was relapsed 8 months later, we treated her with extreme high dose IFX (600mg of IFX per 4 weeks), after we confirmed negative of Human Anti-Chimeric Antibody in her serum. In present, she showed remission state with extreme high dose IFX and cyclosporin. This disease is intractable and TNF inhibitor is only temporarily effective. We also examine three similar cases experienced in our hospital and literature review.

P3-235

Two patients present with autoinflammatory syndrome like manifestation with trisomy 8 not associated to myelodysplastic syndrome (MDS)

Fangyi Chin, Sayaka Tsuzuki, Hideyuki Takahashi, Keigo Setoguchi
Department of Rheumatology, Komagome Hospital Tokyo Japan

Conflict of interest: None

Case1) 21y.o F. Six years before diagnosis, she had fever, pancytopenia, diagnosis of AOSD was made and treated with steroid. Bone marrow aspiration (BMA) reveal chromosomal abnormality (trisomy 8) without any specific disease. Three years before diagnosis, recurrent aphthous stomatitis, genital ulcer appeared. Finally, she developed ileocecal ulcer and with diagnosis of gastrointestinal Behçet disease (GIBD), Infliximab was administered. Since we couldn't achieve good response, we increment IFX to maximal dose and then she achieved remission. Case2) 51y.o M. The patient present with recurrent fever, pharyngitis, thrombocytopenia and migratory panniculitis four years ago. At that time BMA reveal trisomy 8 without any specific disease. Steroid was used on patient demand at first but during course, inflammation became exacerbated and recurrent multiple gastrointestinal ulcer were developed. We started IFX according to BD treatment but despite increment IFX dose, we can't achieve remission. Clinical significance) BD associated MDS with trisomy 8 has known to GI predominant feature and refractory to conventional treatment. Our cases are not associated to MDS so it could be good opportunity to examine the influence of trisomy 8.

P3-236

Six cases of seronegative spondyloarthropathy with HLA-B51 positive

Ryosuke Yoshihara, Atsuo Uefuji, Miki Murata, Natsuko Nakagawa, Yasushi Tanaka, Kazuko Shiozawa
Rheumatology & Collagen Disease Center, Hyogo Prefectural Kakogawa Medical Center

Conflict of interest: None

[Object] There are some patients with rheumatic symptoms and HLA-B51 positive, who meet neither diagnostic criteria for Behçet's disease nor classification criteria for rheumatoid arthritis or spondyloarthropathy. We examined the clinical manifestation of such cases. [Methods] We analyzed the clinical findings of six patients. [Results] Two men and four women. Average onset age was 55 years. Clinical symptoms were three cases of low back pain, two cases of sternoclavicular pain, three cases of peripheral joint pain, two cases of Achilles tendon pain, a case of upper and lower limb pain and a case of episcleritis. All cases were negative for rheumatoid factor and anti-CCP antibody. Three cases were CRP positive. HLA-A24 was also positive in five cases. As a result of administration of NSAID to five cases, the two remitted but three did not. One patient remitted after using methotrexate because of steroid resistance. [Conclusion] HLA-B51 may be related not only to Behçet's disease but also to spondyloarthropathy with relatively good prognosis. However, it is possible that joint symptoms preceded Behçet's disease. There are also a few similar case reports.

P3-237

Trigeminal neuralgia complicated with acute neuro-Behçet's disease

Tomohiro Kozuki, Yuji Miyoshi, Makoto Sugihara, Miho Ohshima
Department of Rheumatology, Tama-Hokubu Medical Center

Conflict of interest: None

Trigeminal neuralgia (TN) can be seen in autoimmune connective tissue diseases. Headache has been reported to account for 53.9% in acute neuro-Behçet's disease (NBD) patients. However, few case reports presented with TN have been published. A 48 year-old woman with no past medical history presented fever, polyarthralgia and headache lasting for a week. As for her headache, paroxysmal attacks of her left facial sharp pain lasted for a second, with persistence of aching between paroxysms. She had oral and genital ulcers, polyarthritis and erythema nodosum on bilateral legs. Her left facial muscle spasm occurred on her every attack and the rest of neurological findings were unremarkable. Laboratory test was consistent with moderate inflammation in the serum (CRP 10.09mg/dl) and cerebrospinal fluid (Cell count 246/ μ l, IL-6 1400pg/ml). She was negative for anti-CCP antibody, ANA, MPO/PR3-ANCA and HSV/VZV-DNA. MRI of her head showed no abnormalities. Acute NBD manifesting aseptic meningitis with TN was clinically diagnosed. She got afebrile and the headache disappeared soon after intravenous prednisolone 50mg/day. We shall be aware of NBD as differential diagnosis of TN with multiple systemic symptoms. Early treatment of corticosteroid is possibly effective for the TN of acute NBD.

P3-238

Successful treatment of neuro-Behçet's disease with methotrexate and infliximab: a case report

Noriaki Yo¹, Ayaka Inoue¹, Hiroaki Nakagawa¹, Midori Kitayama¹, Takuro Maeda¹, Rimi Iwamoto², Chihiro Tanaka¹, Takashi Yamane¹

¹Department of Rheumatology, Kakogawa Central Hospital, ²Department of Pharmacy, Kakogawa Central Hospital

Conflict of interest: None

A 50 year-old-Japanese man, his vision was impaired one year before, and was diagnosed as uveitis. He was aware of dizziness 6 months before, developed diplopia and gait ataxia, and visited the other hospital one month before. Neurological examinations showed cerebellar ataxia, magnetic resonance imaging revealed his pons stroke, and he was hospitalized. Lumbar puncture was performed. The cerebrospinal fluid (CSF) showed a elevation of cell count and IL-6 levels, and he was suspected

neuro-Beçet's disease and referred to our hospital. We diagnosed as neuro-Beçet's disease by oral aphthous ulcerations, acneiform lesion, uveitis, and neurologic symptoms. We treated him with methylprednisolone pulse therapy, and prednisolone. The CSF cell count and IL-6 levels decreased, and we reduced PSL gradually. When we dosed 0.7mg/kg/body PSL, the CSF cells and IL-6 levels increased again. Therefore we added methotrexate, but the CSF cell count and IL-6 levels didn't decrease. Then we infused infliximab, neurologic symptoms and CSF abnormalities improved. There is no strong evidence for the use of infliximab to treat neuro-Beçet's disease, and it is not clear how long to continue immunosuppressive treatment. We report the efficacy of MTX and infliximab combination therapy.

P3-239

A case of vascular Behçet Disease with an occlusion of right main pulmonary artery

Nozomi Tanaka¹, Hajime Yoshifuji¹, Ran Nakashima¹, Shuji Akizuki¹, Kosaku Murakami¹, Motomu Hashimoto², Masao Tanaka², Koichiro Ohmura¹, Tsuneyo Mimori¹

¹Department of Rheumatology and Clinical Immunology, Kyoto University Hospital, ²Department of Advanced Medicine for Rheumatic Diseases, Kyoto University Hospital

Conflict of interest: None

A 36-year-old woman, who was diagnosed with incomplete Behçet's disease (BD) 7 years before, has presented with dry cough, exertional dyspnea and bloody sputum for 10 months. Chest CT revealed multiple infiltrates in both lungs. Bloody fluid was collected in bronchoalveolar lavage. Contrast enhanced CT showed thickening of walls on the branches of the aortic arch and occlusion of right main pulmonary artery. She was diagnosed with pulmonary infarction with vascular BD. Serum CRP levels were decreased with high dose glucocorticoids (GC). However, vascular lesions were not improved on CT after 4 weeks, and serum CRP levels were slightly elevated. Then, infliximab (5mg/kg) was added and GC was tapered. Chronic pulmonary thromboembolism, Takayasu arthritis (TAK) and vascular BD can cause pulmonary arterial stenosis. In BD, thromboembolism or arterial aneurysm are common, whereas a few cases with pulmonary arterial stenosis have been reported. In our case, it is controversial whether this patient has both TAK and BD or only BD. We discuss treatments and prognoses of patients with pulmonary arterial stenosis, referring our case series and the literatures.

P3-240

Subclavian Artery Aneurysm with Uveitis revealed Behçet's Disease without Oral Aphthous Ulcer

Takehiko Manabe, Tsuyoshi Kobashigawa, Eri Watanabe, Hiroki Yabe, Toru Yago, Shigeru Kotake

Division of General Medicine and Division of Rheumatology, Department of Comprehensive Medicine, Saitama Medical Center, Jichi Medical University

Conflict of interest: None

[Clinical significance] The oral aphthous ulcer was the necessary symptom for classifying Behçet's disease (BD) with the criteria of international study groups for BD. Nowhere, we experienced a 61-year-old male patient with uveitis, acneiform eruption and subclavian artery aneurysm without oral aphthous ulcers, who was diagnosed having BD with Japanese criteria of BD. We report the present case and review of the re-treaters. [Case] A 61-year-old male was performed vitrectomy for cataract due to uveitis of his left eye. One month was passed after the operation, reduced visual acuity on his left eye was occurred with vitreous opacity. At the same period, he complained his left neck pain and disability of raise-up motion on his left arm. MRI of neck was performed and was shown his left subclavian artery aneurysm and the size was 60 millimeter. The vitreous surgery against uveitis was performed. The patient with uveitis and subclavian artery aneurysm was referred to our division. According to dermatologists in our hospital, the present patient was having acneiform eruptions on his abdomen. The HLA analysis showed he is double positive B51 and A26 loci. We diagnosed he was a patient with BD by Japanese criteria of BD; interestingly, he was absent from oral

aphthous ulcers.

P3-241

Refractory pulmonary thrombosis resolved by adalimumab in a patient with Behçet disease: case report

Shuzo Yoshida¹, Yuko Kimura¹, Nobuhisa Shibahara²

¹Department of Immuno-Rheumatology Center, Arisawa General Hospital, Hirakata, Osaka, Japan, ²Department of Urology, Arisawa General Hospital, Hirakata, Osaka, Japan

Conflict of interest: None

[case] 80 years old man. He was admitted in our hospital because of uveitis, arthritis, and erythema nodosum. He was diagnosed with Behçet disease base on clinical symptoms and laboratory findings of C-reactive protein (CRP) positive and HLA-B26 positive. He was treated with prednisolone (30 mg/day) and colchicine. His symptoms improved. However, he noticed arthralgia and uveitis again, and CRP elevated 8.33 mg/ml and D-dimer 2.3 µg/dl. Enhance chest CT revealed pulmonary thrombosis. He was treated with heparin and warfarin. However, pulmonary thrombosis was worsened, and D-dimer elevated to 3.2 µg/dl. He was treated adalimumab (ADA), pulmonary thrombosis was improved. [Clinical significance] ADA may effective refractory pulmonary thrombosis in a patient with Behçet disease.

P3-242

A case of multiple colon ulcer with differential diagnosis with intestinal Behçet's disease or Crohn's disease

Kenichiro Kubo¹, Yoshikata Misaki¹, Noriyuki Yamakawa¹, Kohei Yoshioka²

¹Department of Rheumatology, Kyoto Katsura Hospital, Japan, ²Department of Pediatrics, Kyoto Katsura Hospital, Japan

Conflict of interest: None

A 38-year-old female presented with mild fever, arthralgia, abdominal pain and bilateral erythema on lower leg admitted to our hospital in May 20XX. The skin biopsy revealed the pathological findings consistent with erythema nodosum. Her symptoms had improved without therapy until two months, when exacerbated with high fever, arthralgia, abdominal pain, multiple aphthous oral ulcer and genital ulcer. HLA-B51 was negative. She was diagnosed with having Behçet's disease and was treated with colchicine. Her arthralgia improved but abdominal pain persisted. Although poorly studied on ileocecal and ascending colon because of stenosis, colonoscopy showed entire circumference inflammation on sigmoid and transverse colon accompanied with multiple ulcers of punched-out appearance. Capsule endoscopic examination showed multiple simple ulcer in ileocecal and ascending colon. She was treated with high-dose prednisolone (PSL) 100mg/day and enteric salazosulfapyridine, resulted from clinical improvement. Colonoscopy later revealed residual multiple longitudinal ulcers in ascending colon, suggestive of Crohn's disease. She had been tapered with PSL without recurrence. We report this case with consideration of multiple colon ulcer diagnosed as Intestinal Behçet's disease or Crohn's disease.

P3-243

A case of gastrointestinal Behçet with surgery on refractory ileocecal ulcer

Hiroaki Kusuoka, Keitaro Saito, Hironori Inoue, Aki Sakashita, Aiko Hirano, Yu Isoda, Risa Sagawa, Kazuki Fujioka, Hidetake Nagahara, Makoto Wada, Masataka Kohno, Yutaka Kawahito

Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

Conflict of interest: None

[Case] 25 years old female. [Chief complaint] Abdominal pain [Present illness] She was diagnosed as incomplete type Behçet's disease (BD) from recurrent aphthous stomatitis, genital ulcer and arthritis when she was 20 years old. Arthritis was getting worse and abdominal pain appeared because of ulcerative lesions at ileocecum, so we diagnosed as

gastrointestinal BD when she was 22 years old. She was treated with ADA, methotrexate, colchicine, mesalazine and PSL, and we gradually decreased the dose of PSL. But her right lower abdominal pain was exacerbated in April 2018, so ADA was changed to IFX. One month later, her symptoms and CRP value worsened, contrast CT revealed the thickening of the ileocecal wall, and colonoscopy showed that ulceration lesions at ileocecum did not change significantly. So laparoscopic ileocolic resection were performed, and we found that the ulcer was so deep. Abdominal pain and inflammatory response improved after that surgery. [Discussion] Refractory, deep, and punched-out ulcers are typical in gastrointestinal BD and it is thought that intestinal perforation are often caused by these features. Because it is about to perforate in our case, surgical treatment is to considered positively for intestinal lesion which is resistant to medication.

P3-244

Two cases of multicentric Castleman disease with pulmonary involvement experienced in our department

Tomoyuki Nakamura, Hideki Yamanaka, Kaori Seki, Yusuke Hanioka, Ryouta Nakamura, Keiko Yamagami, Hitoshi Goto
General Medicine, Osaka City General Hospital

Conflict of interest: None

Multicentric Castleman disease (MCD) is a polyclonal lymphoproliferative disorder with inflammatory symptoms. Dysregulated overproduction of IL-6 by enlarged lymph node is implicated in the pathogenesis of MCD. We experienced two cases of MCD with lung lesion. Case 1: 37 y.o. female was admitted because of anemia and hypergammaglobulinemia. She had IgG (4760mg/dl), CRP (5mg/dl) and no respiratory symptom, but CT showed small ground glass nodule (GGN) and histopathologic findings of lung revealed plasma cell-infiltrated lesion by TBLB and those of inguinal lymph node revealed sheets of plasma cells, therefore she was diagnosed MCD and started prednisolone (PSL) 20mg/day. Case 2: 34 y.o. female was admitted because of fever. She had slight cough, IgG (3873mg/dl) and CRP (20mg/dl). CT showed GGN and histopathologic findings of axillary lymph node revealed sheets of plasma cells, therefore she was diagnosed MCD. She started PSL 30mg/day, because SPO2 decreased to 86% by 6 minutes walk test. About half of MCD cases of Japanese were reported to have progressive lung lesion. However the two cases improved with PSL. It is necessary to consider introduction of anti-IL-6 receptor antibody according to clinical course because cyst formation may cause irreversible respiratory failure.

P3-245

Longitudinal analysis of serum cytokine levels in a patient with acute onset neuro-Sweet disease

Hiroi Kusaka, Katsuya Nagatani, Takeo Sato, Seiji Minota
Division of Rheumatology and Clinical Immunology, Department of Medicine, Jichi Medical University Hospital, Shimotsuke, Tochigi, Japan

Conflict of interest: None

[Object] Sweet disease occasionally affects central nervous system (CNS): neuro-Sweet disease (NSD). Aim of this study is to elucidate the pathophysiology of NSD by analyzing longitudinally serum levels of 27 cytokines in a patient with acute onset NSD. [Methods] The serum levels of 27 cytokines from a 55-year-old male NSD patient at the onset of neurological symptoms and at the remission after 8 months of glucocorticoid treatment were assayed by Bio-Plex Pro Human Cytokine Assay Kit (Bio-Rad Laboratories) and compared with those from one healthy control. [Results] Serum levels of the following cytokines were elevated at the onset of neurological symptoms, and returned to those of a healthy control at the remission. The elevated cytokines were categorized into three groups: inflammatory cytokines (IL-1 β , IL-6, and TNF- α); chemoattractants (IL-8/CXCL8 and IP-10/CXCL10); and growth factors (G-CSF, PDGF and VEGF). Especially, IP-10/CXCL10 was elevated by 29.8 times compared with the remission. Th1 cytokines were not elevated in this case. [Conclusions] It was suggested that various cytokines are involved in the pathophysiology of Sweet disease. If we pay attention to the onset of CNS, it is necessary to examine whether there is a difference from Sweet disease without CNS in the future.

P3-246

A case of Sweet Syndrome characterized by neutrophil infiltration into the muscle with difficulty in distinguishing from Statin-Associated Autoimmune Myopathy

Akihiko Nakabayashi¹, Taro Akira¹, Hiroshi Shimagami¹, Michiko Ohashi¹, Masashi Okamoto¹, Takehiro Hirayama¹, Akira Mega², Yoshinobu Matsuura¹, Yoshinori Katada¹

¹Division of Rheumatology and Clinical Immunology, Sakai City Medical Center, Sakai, Japan, ²Nephrology, Diabetology and Rheumatology, Sakai City Medical Center, Sakai, Japan

Conflict of interest: None

[Case] A 77-year-old man was admitted to a hospital 48 months ago, complaining a high fever and polymyalgia with elevated CK 1317 U/L. He had papular rashes and blisters on flexor aspect of his right lower leg. Skin biopsy showed superficial perivascular dermatitis. As he had been taking pitavastatin for a month, statin-associated autoimmune myopathy was suspected. Pitavastatin was stopped and steroid pulse therapy, 80mg of prednisolone (PSL) and 8mg of methotrexate (MTX) were started. 40 months ago, he visited our department for myalgia in left thigh. Immunosuppressive therapy was intensified, resulting in some response. Both 22 months and 17 months ago, he complained myalgia in his left lower leg. As abscess was suspected by MRI, antibiotic was used. 16 months ago, he had myalgia in both lower legs. Muscle biopsy revealed marked infiltration of inflammatory cells dominated by neutrophils. Re-examination of previous specimens revealed similar finding compatible with sweet syndrome. After 1mg of colchicine was added, no relapse was noted, enabling tapering of PSL and MTX. [Discussion] Although sweet syndrome is a rare disease presenting neutrophil infiltration usually into the dermis, neutrophil infiltration into the muscle can occur.

P3-247

Three cases of remitting seronegative symmetrical synovitis with pitting edema syndrome (RS3PE)-like symptoms associated with periodontitis

Hiroshi Okuno¹, Muneo Ota², Hiroaki Ogawa¹, Ichiro Kato², Hisayoshi Inoue¹, Akira Hatakeyama², Katsumi Sato¹

¹Department of Orthopaedic Surgery, Tohoku Rosai Hospital, ²Department of Rheumatology, Tohoku Rosai Hospital

Conflict of interest: None

[Case 1] A 74 y/o man presented to our hospital with local edema, warmth, and redness in his right hand. After admission, he was found to have polyarthritis and pitting edema in both hands, as well as severe periodontitis. Antibiotic administration, several teeth extraction, and oral care improved his symptoms promptly. [Case 2] A 60 y/o man presented to our hospital with pain, swelling, redness and warmth in his right ankle. He was prescribed a course of antibiotics for cellulitis. Subsequently, he developed pain and swelling in his left foot and pitting edema in his right foot. Though his symptoms seemed to improve with antibiotics, he developed bilateral ankle pain and foot edema and was found to have severe periodontitis. Treatment for periodontitis resulted in prompt symptom remission. [Case 3] A 55 y/o man presented to our hospital with edema and stiffness in his right hand, along with polyarthritis. His laboratory tests showed a high white blood cell count, elevated inflammatory markers, and the presence of anti-streptolysin-o antibodies; he also had severe periodontitis. Extraction of his teeth combined with antibiotic treatment improved his symptoms and inflammatory test results. These cases indicate an association between periodontitis and RS3PE syndrome.

P3-248

Serositis and anasarca due to TAFRO syndrome

Satoshi Akao, Hiroyuki Yano, Ko Sudo, Hitoshi Miyasato, Mitsuyo Kinjo
Department of Rheumatology, Okinawa Chubu Hospital

Conflict of interest: None

A 48 year-old woman presented with 3 weeks duration of fatigue and fever. Epigastric and right flank pain associated with watery diarrhea and abdominal distention developed, and she could barely eat and sought

medical attention at our hospital. Physical examination was significant for right flank tenderness and anasarca. Laboratory test showed mild thrombocytopenia, renal dysfunction, elevated alkaline phosphatase (ALP) and inflammatory sign. Upper and lower endoscopies were unremarkable. Computed tomography (CT) of whole body without contrast material demonstrated swollen intraperitoneal lymph nodes, hepatosplenomegaly and pleural and abdominal effusion. Lactate dehydrogenase (LDH) and soluble IL-2 receptor were not elevated, and antinuclear antibody, anti SS-A antibody, MPO/PR3-ANCA antibody, tuberculin skin test, T spot and screening tests for viral serologies were all negative. Differential diagnosis included Castleman disease, TAFRO syndrome and POEMS syndrome. Bone marrow showed slightly myelofibrosis. Renal biopsy showed thrombotic microangiopathy following endothelial damage. This case illustrated TAFRO syndrome with predominant serositis and renal involvement.

P3-249

Canakinumab was effective for Atypical Familial Mediterranean fever : A case report and review of the literature

Mai Nakano, Masao Tamura, Rei Tadokoro, Kazuyuki Tsuboi, Chie Ogita, Tetsuya Furukawa, Takahiro Yoshikawa, Teppei Hashimoto, Mai Morimoto, Naoto Azuma, Masayasu Kitano, Kiyoshi Matsui
Division of Rheumatology, Hyogo College of Medicine

Conflict of interest: None

46 age female. She complained of fever of unknown origin and headache, heavy menstrual abdominal pain from 26 years old. When 44 year old, she was diagnosed with Atypical Mediterranean fever by gene mutation. She was treated with only colchicine 1.5 mg/day from that time. When 46 year old, She was admitted to the hospital for abdominal pain and headache, fever of unknown origin. Her attack of headache have a limited role in the treatment of colchicine. False menopause therapy had no effect on her abdominal pain. Therefor, we treated with canakinumab. The medication was effective for the fever, abdominal pain and endometrial thickening. We described the patient that canakinumab was effective for repetitive fever and abdominal pain of Atypical Familial Mediterranean fever, along with some literature review.

P3-250

Researching at evaluation of FM (fibromyalgia) in the method of SDS (self-rating Depression Scal by Dr.William Zung)

Sadahiko Kameda
Kameda Internal Medicine Clinic

Conflict of interest: None

FM is a disease well known to severe pain at the main complaint. At the same time, this disease is accompanying with psychosomatic complaint. The fact leads us to our interest of similarity of depression disease. This time, we searched the relationship between FM and depression condition in utilizing of SDS. The mean titer of SDS in 28 cases of FM was 45 points. That titer was definitely higher than 36 points of Japanese healthy person. This difference in statics aspects between the two above mean titers showed a definite gap, $\alpha=0.001$. The average titer of Japanese light depression is 45.3 points. And so, there is no gap between Japanese light depression cases and FM cases (28cases). The relative relation between ARA-2010 evaluation and SDS of FM 28 cases showed 0.65 at the relative relation index, $t=4.1$ $\alpha=0.001$. This result showed positive relative relation. The more, ten FM cases at the above IIIrd stage showed 54.5point in SDS evaluation. This result gave us no gap between the above IIIrd stage of FM and Japanese depression cases titer, 57.5 points, $t=0.75$ $\alpha=0.3$.

P3-251

A case of familial eosinophilia with deep vein thrombosis and intracardiac thrombosis

Yoshihisa Kobayashi, Kazuya Abe, Nozomi Nishimura, Kei Ikeda
Department of Internal Medicine, Chiba Aoba Municipal Hospital, Chiba, Japan

Conflict of interest: None

A 72-year-old-man was admitted to our hospital for the swelling in his left leg. Contrast-enhanced CT showed deep venous thrombosis and echocardiography detected intracardiac thrombosis. Blood test revealed eosinophilia (34%, 3,350/ μ l) and he was diagnosed with hypereosinophilic syndrome/Loffer's endocarditis. In addition to anticoagulant treatment, he received prednisolone 30 mg/day, which was later increased to 60 mg/day. However, his peripheral blood eosinophil counts did not decrease and the intracardiac thrombosis did not significantly improve, either. Therefore, treatment with hydroxyurea was started, while prednisolone was tapered and discontinued. However, hydroxyurea did not improve his eosinophil count, either. We found that he had had eosinophilia since his youth and that his father, brother and nephew also had eosinophilia. We diagnosed him with familial eosinophilia. Hydroxyurea was discontinued due to thrombocytopenia but he has been stable for months. Familial eosinophilia is a rare disease which has a benign clinical course as opposed to hypereosinophilic syndrome. However, when a life-threatening event occurs like in our case, it can be difficult to decide not to treat. Treatment indication of familial eosinophilia will be discussed with some literature review.

P3-252

Researching of serum histamine titer in fibromyalgia (FM)

Sadahiko Kameda
Kameda Internal Medicine Clinic

Conflict of interest: None

Among the initiating site of pain in FM cases, there is a notch-receptor. At this site, there are some relevant substances to exploit, ATP, histamine, bradykinin can be picked up. At the vicinity of notchireceptor, mast cell are excited. At the mediation of N-cadherin, mast cells will be degranuated into releasing histamine. The mean titer of histamine in healthy persson was said to be 0.43ng/ml. That mean titer of FM cases was 0.88ng/ml. Between those two showed gap at the point of those two mean titers, $t=5.3$, $\alpha=0.01$. The FM cases with alodenia (9cases) showed 0.98ng/ml at the mean titer. That titer didn't show gap between the mean titer of histamine in whole FM cases and the above 0.98ng/ml of FM cases with alodenia, $t=1.3$, $\alpha=0.1$. But the possibility of gap between the those two groups will be remained in the process at increasing of examined number. The relative relationship (RR) between histamine in serum and ARA points (2010), didn't show significance. The RR between SDS (self-rating depression scale) and histamine showed $\alpha=0.1$. and so the RR between FM cases with over 0.9ng/ml of histamine and ARA (2010) showed $\gamma=0.43$, $t=1.72$, $\alpha=0.1$. From the fact, there remains the possibility of significantRR at FM case with high histamine titer.

P3-253

A case of sarcoidosis successfully treated with Adalimumab

Rumi Minami, Kenji Tamagawa, Makiko Higuchi, Tomoaki Iwanaga, Motoko Ishida, Soichiro Takahama, Tomoya Miyamura, Masahiro Yamamoto, Eiichi Suematsu
Internal Medicine and Rheumatology, Clinical Resaerch Institute, National Hospital Organization Kyushu Medical Center

Conflict of interest: None

(Case) A 77-year-old-woman presented with a floater 8 years ago. The ophthalmologic examination revealed vitreous opacities compatible with sarcoidosis (SA) uveitis. Symptoms were stable in topical steroid and STTA. Six years ago, annular erythema appeared on her finger, which was diagnosed with cutaneous SA, but disappeared spontaneously. BHL enlargement was also observed at chest CT. BAL examination and TBLB showed compatible with pulmonary SA. No active lesions were observed in the lung field, then, she was followed up without any systemic medications. Three months ago, her uveitis relapsed with vitreous opacities. The topical steroid and oral prednisolone had no effects. Chest CT revealed nodules in both lung fields with the elevation of serum lysozyme. Adalimumab (ADA) treatment was then started. After 2 weeks, vitreous opacities were disappeared, and after 6 weeks, serous retinal detachment was improved with normalization of lysozyme. We continued

maintenance with ADA. (Conclusions) Since 2016, ADA has been available for non-infectious uveitis including SA uveitis. However, the ADA use for refractory SA is still limited in Japan. While TNF- α is the target of SA treatment, TNF- α inhibitor itself can cause SA. We need to carefully select the objects using ADA for SA.

P3-254

A case of idiopathic multicentric castlemans disease complicated with IgA nephropathy

Tomoya Nishida¹, Shoichiro Inokuchi¹, Tomofumi Tatsutani¹, Koji Mishima¹, Yojiro Arinobu¹, Masahiro Ayano¹, Hiroki Mitoma¹, Yasutaka Kimoto³, Mitsuteru Akahoshi¹, Koichi Akashi¹, Takahiko Horiuchi³, Hiroaki Niino²

¹Department of Clinical Immunology and Rheumatology/Infectious Disease, Kyushu University, Fukuoka, Japan, ²Department of Medical Education, Faculty of Medical Sciences, Kyushu University, Fukuoka, Japan, ³Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan

Conflict of interest: None

[Case] The patient was 66-year-old male. Two months before he visited our hospital, he presented low-grade fever and weight loss, and blood test showed elevated CRP, creatinine, and γ -globulin. A positive urine occult blood and cellular casts in urine sediment were observed. Computed tomography of whole body showed inguinal lymph node swelling. He was introduced to be admitted to our hospital. Lymph node biopsy showed the feature of plasma cell type of castlemans disease and kidney biopsy revealed IgA nephropathy (IgAN). As serum IL-6 was 118.6 pg/ml, we diagnosed the patients as idiopathic multicentric castlemans disease (iMCD) complicated with IgAN. Immunophenotyping examination was performed, and increased memory Th2 cells and CCR6-positive Tfh cells were identified in peripheral blood. Effector CD8-positive cells were increased and activated and a large number of plasmablasts in CD19-positive cells were observed. We treated the patient with a combination of corticosteroid and tocilizumab (TCZ) [Discussion] There have been a small number of reports which documented iMCD complicated with IgAN. Although efficacy of TCZ for primary IgAN have been unclarified, IgAN with iMCD may emerge through hypergammopathy of iMCD. TCZ may be effective for both iMCD and IgAN in our case.

P3-255

Four cases of TAFRO syndrome

Ayaka Kato, Hideki Tani, Motochika Asano, Koichiro Taguchi, Yoshihiko Kitada, Takahide Ikeda, Hiroyuki Morita
General Medicine, Gifu University Hospital

Conflict of interest: None

[Object] TAFRO syndrome has been described firstly by Takai in Japanese patients. It includes thrombocytopenia, anasarca, fever, reticulin fibrosis and organomegaly. [Methods] we present 4 cases of TAFRO syndrome. [Results] (CASE 1) A 70-year-old male patient referred to our hospital with thrombocytopenia and renal dysfunction. Methylprednisolone pulse therapy, IVIG, tocilizumab and cyclosporine resulted in improvement. (CASE 2) A man, who is 40 years old, referred to our hospital for fatigue and anasarca with thrombocytopenia and renal dysfunction. Prednisolone and cyclosporine resulted in improvement. (CASE 3) A 55-year-old man visited our hospital due to fatigue and anasarca. He underwent artificial dialysis for renal dysfunction. Methylprednisolone pulse therapy, followed oral prednisolone and azathioprine resulted in improvement. He could get off artificial dialysis. (CASE 4) A 39-year-old man had been diagnosed as having infectious endocarditis and treated with antibiotics. He visited our hospital due to right hypochondrium pain, fever and anasarca with thrombocytopenia and renal dysfunction. Methylprednisolone pulse therapy and followed prednisolone resulted in improvement. [Conclusions] We recommend cyclosporine if prednisolone is no effect.

P3-256

A patient with Necrotic myopathy who exhibited head down condition as the chief symptom

Kazuteru Noguchi, Chie Ogita, Teppei Hashimoto, Maki Shibamoto, Rei Tadokoro, Mai Nakano, Kazuyuki Tsuboi, Mei Tani, Masao Tamura, Takahiro Yoshikawa, Mai Morimoto, Naoto Azuma, Masayasu Kitano, Kiyoshi Matsui

Hyogo College Of Medicine Nishinomiya Hyogo Japan

Conflict of interest: None

[Case] 63 year-old woman [Chief complaints] head down [Current medical history] She had been healthy. On August X. Her sister came to her for the first time in a year. She made her go to the hospital when she saw her symptom. She was suspected and hospitalized myositis because of her serum CK value was high. [Clinical course] She was done a manual muscle test, so Head extension, iliopsoas muscle, Erector Spinae were poor. She had no eruption. MRI revealed Erector Spinae was atrophied. Electromyogram found biceps brachialis, iliopsoas muscle, trapezius muscle were abnormal. Biceps brachialis biopsies showed necrotic fibers scattered, and there were no infiltration of inflammatory cells. The antibody against signal recognition particle was detected by immunoprecipitation. The others were negative. Then we diagnosed her a necrotic myopathy. We administered steroid, tacrolimus, IVIG, and improved her serum value, however head down condition had been remained. [discussion] The anti-SRP antibody positive necrotizing myopathy is recognized symmetric proximal muscles weakness. In the neck, flexor muscle group are worse than extensor them. However in this case, the defective site was exchanged. There are few similar cases. We think it is important to treat of an inflammatory myopathy.

P3-257

A case of relapsing polychondritis only presenting airway symptoms

Taiga Kuga¹, Takayuki Kon², Shinya Kawano¹, Kurisu Tada¹, Ken Yamaji¹, Naoto Tamura¹

¹Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan, ²Juntendo University Nerima Hospital, Tokyo, Japan

Conflict of interest: None

A 49 year-old woman presented with dyspnea and hoarseness accompanied with 3 weeks of fever and upper airway symptoms admitted to our hospital. White blood cell count was 11200/ μ L and C reactive protein (CRP) was 6.6mg/dL. Fiber laryngoscopes revealed swollen subglottic larynx and CT scan showed bronchial wall thickening and stenosis of peripheral bronchi. Though she had no auricular pain, we performed auricular biopsy suspecting relapsing polychondritis (RP) and administered Hydrocortisone 500mg/day with antibiotic therapy targeting acute subglottic laryngitis. As her symptoms and CRP elevation were improved, we tapered steroid rapidly and switched to prednisolone (PSL) 50mg but recur after tapering to PSL10mg/day. Subglottic larynx was not swollen, but bronchoscopes revealed redness and swelling of tracheal mucosa, obscuration of cricoid cartilage and stenosis of peripheral bronchi. As the anti-type II collagen antibody was positive and other diseases were unlikely, we diagnosed her as RP. PSL50mg/day with methotrexate 6mg/week were initiated. Her symptoms improved and inflammatory responses normalized within a week. CT scan showed almost normal bronchi without bronchial wall thickening. We report this case as it is rare to diagnose RP presenting only airway symptoms.

P3-258

A case of relapsing polychondritis with central nerve system involvement

Shotaro Yamamoto, Katsuya Nagatani, Takeo Sato, Keisuke Saito, Yoichiro Akiyama, Masahiro Iwamoto, Seiji Minota

Division of Rheumatology and Clinical Immunology, Department of Medicine, Jichi Medical University

Conflict of interest: None

A 71-year-old man with ulcerative colitis had been diagnosed as re-

lapsing polycondritis (RP) based on sensory neural hearing loss, scleritis, and bronchial cartilage inflammation and treated with glucocorticoid, methotrexate, and infliximab. One year later, he developed diplopia, dizziness, paresthesia in the areas of trigeminal nerve, and ocular motility disorder. Brain MRI showed contrast enhancement on the cervicomedullary junction, the cerebellar peduncle, and the pontine tegmentum. *Candida parapsilosis* was cultured from cerebrospinal fluid (CSF) without pleocytosis. Although he was treated with antifungal agents, the treatment response was incomplete. Follow-up CSF study showed pleocytosis, the elevated level of protein and IL-6, and no cultured pathogens. Brain MRI showed contrast enhancement on the surface of the brainstem in addition to the known findings. Therefore, we considered *C. parapsilosis* cultured from the first CSF as contamination, and he was suspected as having RP with central nerve system (CNS) involvement, and his neurological and MRI findings improved with high dose glucocorticoid and intravenous cyclophosphamide. The involvement of CNS in RP is rare. In this case, treatment failure to antifungal agents and repeated brain MRI led to the final diagnosis.

P3-259

A case of sarcoidosis presenting acute renal failure

Michiko Ohashi¹, Akihiko Nakabayashi¹, Taro Akira¹, Hiroshi Shimagami¹, Masashi Okamoto¹, Takehiro Hirayama¹, Akira Mega², Yoshinobu Matsuura¹, Yoshinori Katada¹

¹Division of Rheumatology and Clinical Immunology, Sakai City Medical Center, ²Nephrology, Diabetology and Rheumatology, Sakai City Medical Center

Conflict of interest: None

[Case] A 24-year-old woman was referred to our hospital, because of arthralgia, high fever and exertional dyspnea. On admission, she had neither abnormal chest sound, swollen or tender joint, nor rash. Labo data include WBC 9900 / μ L, CRP 12.99 mg/dL, Cr 1.24 mg/dL, and ANA <40times, Both RF and ACPA were negative. Chest CT showed diffuse particulate opacity. On the 6th hospital day, serum Cr elevated to 2.35 mg/dL. Urine protein /creatinine 0.32 g/gCr, urine RBC count <1/HF, granular cast 1+, urine β 2MG 6599 μ g/L, NAG 15.8 IU/L. Renal pathology showed granulomatous interstitial nephritis with multinucleated giant cells, and interstitial fibrosis was 0-5%. ACE 31.6 U/L, sIL-2R 7645 U/mL, lysozyme 40.4 μ g/mL. With a diagnosis of sarcoidosis, 50mg (0.8mg/kg) of PSL was started. 1 month later, serum Cr was 0.94 mg/dL (PSL 50mg) and 5 months later, 0.97 (PSL 10mg). [Discussion] Acute onset sarcoidosis is rare. As our case, patients with milder interstitial fibrosis are likely to recover renal function sufficiently. Data from other 4 cases of renal sarcoidosis in our hospital support this finding.

P3-260

Tocilizumab (TCZ) treatment in the young female patient of Castleman's disease

Takashi Ogasawara, Manabu Tanabe, Makiko Kimura, Sayuri Yamashita, Atsuko Murota, Yuki Takahashi, Hidenaga Kawasumi, Mutsuto Tateishi
Department of Rheumatology, Tokyo Metropolitan Ohtsuka Hospital

Conflict of interest: None

[Castleman disease (CD) is a rare disease of lymph nodes and related tissues, recognized as a lymphoproliferative disorder, and similar in many ways to lymphomas. It was first described by Dr. Benjamin Castleman in the 1950s. It is also known as Castleman's disease, including angiofollicular lymph node hyperplasia (AFH). Even though CD is not logically a cancer, one form of multicentric Castleman disease acts very much like lymphoma. So CD is often treated with chemotherapy or radiation therapy. CD affects multiple organs and high value of IL-6 in serum. Our patients had one of CD at 27 years old with severe fatigue, polyarthralgia, and sub fever. Her Bood test indicates critical inflammation and anemia. There were almost no improvement of disease by NSAIDs and small amount of prednisolone (PSL). It speeded almost one year till the diagnosis of CD was diagnosed. The level of serum IL-6 was over 450 pg/ml, then we started her treatment with high dose of PSL and Tocilizumab. After almost 4years, the disease activity got completely in subjective symptoms and blood tests the we checked her serum level of IL-6, how-

ever, it still exists in the high level. Now we have to investigate the management of her CD, because she got married and is having the wish of having childs.

P3-261

A very severe and refractory case of TAFRO syndrome treated with Tacrolimus and Rituximab subsequent to Tocilizumab adding to glucocorticoids

Hidenori Takahashi, Naoto Umeda

Division of Rheumatology, Tsuchiura Kyodo General Hospital, Tsuchiura, Japan

Conflict of interest: None

A 53-year-old man developed fever, fatigue, anasarca, pleural effusion, ascites, thrombocytopenia, anemia, and renal failure. Diagnosis of TAFRO syndrome was made according to the 2015 diagnostic criteria. We administered methyl-prednisolone pulse therapy, high-dose glucocorticoids and cyclosporine A (CsA), however they were ineffective. Renal function worsened and hemodialysis has been administered. After administration of tocilizumab (TCZ) weekly, CRP has decreased. Due to a complication of sepsis, TCZ was discontinued. CsA was discontinued due to no effect. Then he had gradual improvement in renal function. Not only persistence of thrombocytopenia, but also fever and slight elevation of CRP appeared. We added tacrolimus (TAC) resulting in improvements of them. Approximately 5 months later, he developed the recurrence. Re-administration of TCZ was ineffective. He received rituximab (RTX) and increase in dosage of TAC and PSL, which resulted in remission again. The 2015 treatment strategy suggests CsA, TCZ or RTX in refractory cases. In this case adding TCZ, TAC and RTX to glucocorticoids was effective. The reports of very severe case treated successfully including recurrence are very rare. We suggest the possibility of efficacy of TAC and/or RTX for refractory TAFRO syndrome.

P3-262

Successful treatment of multicentric reticulohistiocytosis with enthesitis by Secukinumab: a case report

Kei Kobayashi^{1,2}, Daiki Nakagomi^{1,2}, Shunichiro Hanai^{1,2}, Yoshihiro Takayama^{2,3}, Kensuke Koyama^{2,3}, Hirotaka Haro^{2,3}, Kenichiro Kitamura^{1,2}

¹Third Department of Internal Medicine, University of Yamanashi Hospital, ²Center for Clinical Immunology and Rheumatology, University of Yamanashi Hospital, ³Department of Orthopaedic Surgery, University of Yamanashi Hospital

Conflict of interest: None

A 55-year-old woman was referred to our hospital complaining of papules without itching or pain on her forearms and polyarthrits for one year. Physical examination revealed pain and tenderness in shoulder, elbow, knee and distal interphalangeal joints, and also found dark red papules on her hands, forearms and elbows. Musculoskeletal ultrasound examination showed enthesitis in insertion of the triceps brachialis and quadriceps muscle tendon. Skin biopsy of papules revealed diffuse and nodular multinucleated giant cells infiltrating in the dermis. Finally, we diagnosed multicentric reticulohistiocytosis (MRH). Her symptoms deteriorated although we treated her with methotrexate, tacrolimus and denosumab. Next, we treated the patient with subcutaneous injection of anti-IL-17A antibody (secukinumab) and all the clinical features were significantly improved. MRH is a rare disease characterized by multiple nodular lesions of the skin and destructive arthritis. To our knowledge, anti-IL-17 biological agent therapy has never been applied for MRH. Secukinumab could be useful for the treatment of MRH.

P3-263

Elderly Onset Chronic Recurrent Multifocal Osteomyelitis

Kanako Kojima¹, Toshiyuki Aramaki¹, Shota Kurushima¹, Yoshika Tsuji¹, Natsumi Kawachi¹, Kaoru Terada¹, Katsumi Eguchi¹, Yukitaka Ueki¹, Atsushi Kawakami²

¹Rheumatic Collagen Disease Center, Sasebo Chuo Hospital, Sasebo, Nagasaki, Japan, ²Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: None

Introduction: Chronic recurrent multifocal osteomyelitis (CRMO) is an autoinflammatory bone disorder mostly affecting children and adolescents. We recently encountered a patient with elderly onset CRMO. **Case Report:** A 71-year-old man developed ankle pain and skin pigmentation changes bilaterally three years ago. Blood test showed positive rheumatoid factor and negative anti CCP antibody. Skin biopsy was normal. He was diagnosed with rheumatoid arthritis in his previous hospital. Treatments with methotrexate 6mg/week and salazosulfapyridine 1g/day were started. He had persisted symptoms and elevation of ESR and CRP. The patient was referred to our hospital for further examination. There was no evidence of palmoplantar pustulosis and chest pain. Ankle CT showed multifocal lytic areas and surrounding sclerosis. Ankle MRI showed marrow edema. Technetium 99m bone scintigraphy showed increased uptake in both legs. Left leg bone biopsy showed osteomyelitis and no malignancy. The findings led to a diagnosis of CRMO. **Discussion:** CRMO is currently seen as a closely related disorder with SAPHO syndrome. He had no findings suggestive of SAPHO syndrome. There is no consensus about treatment. The patient will need careful follow-up.

P3-264

A case of TAFRO syndrome with a multifocal cerebral infarction

Daisuke Kanai

Department of Nephrology, Kobe City Hospital Organization Kobe City Medical Center West Hospital

Conflict of interest: None

<Case> Sixty nine-years-old man who has been hospitalized because recognized edema, fever and proteinuria. After hospitalization, he had persistent fever, severe generalized edema, pleural effusions and ascites, thrombopenia, elevated serum level of ALP, kidney dysfunction. Histopathology of kidney revealed hyper cellular in tubule and swelling of endothelial cells. Bone marrow biopsy showed to fibrosis surrounding trabecular bone. The levels of IL-6 in serum / pleural Effusions are 11.4/1100pg/mL, serum level of VEGF was 190pg/mL. We diagnosed as TAFRO syndrome base on the criteria of 2015. We started medical treatment with steroid and cyclosporine. The fever, the level of CRP, kidney dysfunction ameliorated by treatment, but pleural effusions and ascites had sustained. On the 42th hospital day, he led to impaired consciousness. Brain diffusion-weighted MRI and T2WI/FLAIR showed scattered a high-intensity signal the white matter and he was diagnosed as multifocal cerebral infarction. We thought cerebral infarction was due to the TAFRO syndrome. <Discussion> Although it has been not clear, it was possible that an intravascular volume depletion with increased vascular permeability and vascular endothelial damage are the etiology of a multifocal cerebral infarction.

P3-265

Adalimumab was effective for uveitis-associated heart sarcoidosis

Takeshi Shoda¹, Yumiko Wada¹, Junichi Konma¹, Natsuko Fukuda^{1,2}

¹Clinical Immunology and Rheumatology, Yodogawa Christian Hospital, ²Ophthalmology, Yodogawa Christian Hospital

Conflict of interest: None

[Case] A 57-year old female. In 20XX-3, Health examination pointed out BHL on chest X-ray, and scattered micro nodule shadows in the lung area on HRCT, BAL showed CD 4/8 ratio of 12.3, TBLB showed granulomas, serum ACE 56.4U/L, sIL-2R 2220U/mL, lysozyme 18.2µg/mL increase was observed. Sarcoidosis uveitis and skin sarcoidosis were pointed out at the same time, and it was diagnosed as sarcoidosis. Afterwards, it was followed up with local treatment, but uveitis was refractory. In 20XX, retinal uveitis also complicated and repeating injection into Tenon capsule did not improve, so ADA administration was examined, and it was admitted to our hospital in 20XX August. There was appeal of palpitations, delayed enhancement MRI was performed, enhancement was observed in the ventricular septal base and posterior wall, and FDG accumulation was also observed in PET-CT and diagnosed as Heart sarcoidosis. ADA 40mgq2w started in September, improved uveitis, ACE 44→16U/L promptly decreased, BHL shranked, skin symptoms im-

proved. Combined with CsA 100mg from January 20XX+1, and in March the delayed enhancement MRI and PET-CT confirmed the loss of heart lesions. [Clinical Significance] ADA was effective in early stage Heart sarcoidosis.

P3-266

A case of sarcoidosis with large vessel vasculitis

Kimie Harama

Yamanashi Prefectural Central Hospital, Yamanashi, Japan

Conflict of interest: None

[Case] The patient was 79-year-old man. He was admitted our hospital presenting anemia for 8 weeks and general malaise, neck chest pain, shortness of breath and wobble for 4 weeks. Although he had slight fever and showed elevated CRP level, the following week he got a high fever, difficult to walk and his CRP increased to 19 mg/dL. Blurred vision and uveitis appeared 5 days after admission, which suggested sarcoidosis. The FDG-PET/CT showed higher FDG uptake in mediastinal lymph nodes, infiltration on both lungs, and wall thickening from the left common carotid to thoracic aorta. While ACE level was within the normal range, soluble IL-2R and CD4/8 ratio in his bronchoalveolar lavage fluid were high. Finally, he was diagnosed as sarcoidosis with eyes, lungs and large vessels. When corticosteroid therapy was started, general symptoms including ocular and pulmonary status were improved. Next, we plan to evaluate blood vessel thickening. [Discussion] Sarcoidosis is idiopathic disease that forms non-caseating epithelioid cell granuloma and exhibits various clinical symptoms. Although it is said that large-scale vasculitis is rare, it may have been overlooked because of lacking FDG-PET studies.

P3-267

Polymyalgia rheumatica and RS3PE syndrome occurring after immune checkpoint inhibitor treatment

Yonsu Son^{1,2}, Akihiro Tanaka^{1,2}, Saki Tsujimoto^{1,2}, Kai Imai^{1,2}, Minoru Shigesaka^{1,2}, Keiko Shimamoto^{1,2}, Yoshio Ozaki^{1,2}, Shosaku Nomura²

¹Department of Rheumatology and Clinical Immunology, Kansai Medical University Hospital, ²First Department of Internal Medicine, Kansai Medical University Hospital

Conflict of interest: None

[Case 1] A 76-year-old, man [Clinical course] In January 2016, he was diagnosed as NSCLC. He started treatment with chemotherapy but had no effect, then Nivolumab started. He presented with muscle pain of the lower thighs after 6 courses, and the pain gradually getting worse throughout the course after 9 courses. Grasping pain on the upper arm and femoral region. Ultrasound examination found active bursitis affecting biceps tendon. He was diagnosed of polymyalgia rheumatica. Oral corticosteroid (PSL 20mg) were effective. [Case 2] A 70-year-old, man [Clinical course] In January 2017, he was diagnosed as NSCLC. Since PD-L1 was 50%, Pembrolizumab was started as the first line. He presented with inflammatory arthralgia, synovitis of proximal interphalangeal, wrist and ankle joint, and edema of both hand and forearms. He was diagnosed of RS3PE syndrome. Oral corticosteroid (PSL 10mg) were effective. While immunecheckpoint inhibitors (ICIs) have been reported to be effective in cancer treatment, they are recognized as irAE due to concern that autoimmune diseases may be caused by their mechanism of action. We report patients with PMR and RS3PE syndrome, secondary to ICIs.

P3-268

Utilization of imaging procedures for giant cell arteritis according to distribution of affected vascular lesion

Kazutoshi Yukawa, Kei Araki, Hiroki Kohno, Katsuhiko Ohi, Tatsuomi Kuranobu, Tadahiro Tokunaga, Yusuke Yoshida, Tomohiro Sugimoto, Sho Mokuda, Keisuke Oda, Shintaro Hirata, Takaki Nojima, Eiji Sugiyama

Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital

Conflict of interest: None

<Introduction> Giant cell arteritis (GCA) is characterized with granulomatous vasculitis in elderly patients. Temporal artery is often involved, however only aortic involvements are identified in some cases. <Purpose> To investigate the frequency of large vessel lesion affected by GCA and the usefulness of imaging. <Method> We defined GCA according to the ACR 1990 classification criteria for GCA, or cases with a large vessel lesion similar to Takayasu arteritis with onset at ≥ 50 years old. The lesion only the temporal artery was classified as a cranial type, only the aorta as a large vessel type, and in the case of both lesions as a mixed type. During the period from January 2014 to March 2018, 15 GCA patients who required treatment were included retrospectively. <Results > There are 6 cases with cranial type (40%), 5 with large vessels (33%), and 4 with mixed type (27%). Temporal artery biopsy was performed in nine patients with positive for halo sign on ultrasonography in all cases. In the large vessel type, significant finding of CT and FDG uptake was confirmed. <Conclusion> Temporal artery ultrasonography was useful for diagnosis of cranial type. CT and PET-CT examinations were useful for diagnosis of large vessel type.

P3-269

Characteristics of patients with polymyalgia rheumatica; an experience in a general hospital in Japan

Akiko Aoki, Hiroshi Kobayashi, Hiroshi Oka

Department of Rheumatology, Tokyo Medical University Hachioji Medical Center

Conflict of interest: None

[Object] Clinical symptoms of polymyalgia rheumatica (PMR) are improved by low-dose glucocorticoids (GCs), but most patients require long-term GC therapy. We report the clinical characteristics and therapeutic response of PMR patients. [Methods] This was a retrospective study in a single general hospital in Japan. We reviewed the medical records of 87 PMR patients between April 2011 and September 2018. Diagnosis of PMR was based on Bird's criteria or 2012 provisional classification criteria. Relapse was defined as the reappearance of symptoms associated with elevated C-reactive protein (CRP) levels in patients receiving GCs. Remission was defined as the absence of clinical symptoms and normal CRP with discontinuation of GC. [Results] The Remission was achieved in 13% (8/61) after one-year GC therapy. At two-year follow-up, the remission rate was 57% (28/49). Patients were divided into 2 groups; those who achieved remission within 2 years ($n=28$) and those who required GC therapy for more than 2 years ($n=21$). No differences were observed in sex, age, and or clinical features at diagnosis. Body-mass index was significantly lower and CRP at diagnosis was higher in the early remission group. [Conclusions] According to the guidelines the remission rate in our hospital is not low.

P3-270

A case of a 48-year-old man of multicentric Castleman's disease (MCD) who developed SLE-like symptoms such as arthralgia, lymphopenia, hypocomplementemia

Takehiro Hirayama¹, Yoshinori Katada¹, Taro Akira², Michiko Ohashi², Masashi Okamoto², Hiroshi Shimagami², Akira Mega², Yoshinobu Matsuura¹, Akihiko Nakabayashi¹

¹Division of Rheumatology and Clinical Immunology, Sakai City Medical Center, Sakai, Japan, ²Nephrology, Diabetology and Rheumatology, Sakai City Medical Center, Sakai, Japan

Conflict of interest: None

We report a case of a 48-year-old man of multicentric Castleman's disease (MCD) who developed SLE-like symptoms such as arthralgia, lymphopenia, hypocomplementemia. Some patients with MCD might develop various symptoms and signs, including positive autoantibodies, thrombocytosis, elevation of ESR, hypoalbuminemia, proteinuria plus hypergammaglobulinemia. In this case, ANA $\times 40$ (Speckled, Cytoplasmic), UI-RNP Ab, TPO Ab and dsDNA Ab are positive. Interestingly, hypocomplementemia is also present, suggesting activation of classical pathway. Plasma cell type MCD can satisfy classification criteria of

SLE. In the Japanese criteria currently need patients who meet the lupus criteria are excluded from diagnosis of MCD. However, like this case, some patients seem to have both disease simultaneously.

P3-271

A 14-year-old girl who developed polyarthritis 13 years after umbilical cord blood bone marrow transplantation for infantile leukemia

Yoshiyasu Ogata¹, Tomoko Mera², Yukari Mizoguchi¹

¹Department of Pediatrics, Saga University Faculty of Medicine, ²Department of Pediatrics, Saiseikai Yahata General Hospital

Conflict of interest: None

[Case] 14-year-old girl [HPI] She developed leukemia at 8 months, remitted with umbilical cord blood bone marrow transplantation, and was on a outpatient follow-up. At the age of 14, because of the pain and swelling of the joints of the fingers, wrist joints, ankle joints and knee joints, she was introduced to our outpatients. [Progress] Physical findings confirmed swelling and pain in her joint. In the blood test, white blood cell count was 2800/mm³, RF was negative, CRP was 1.13 mg/dl, and MMP-3 was 64.2 mg/dl. Synovitis were confirmed by MRI. NSAID and MTX was started, but improvement was poor, and MMP-3 increased to 103.8 mg/dl. Tac was added, and MMP-3 became negative. Because the joint symptoms had been calm for 5 years, MTX was discontinued, then recurrence of arthralgia was recognized, and the symptoms improved with resumption of MTX. [Summary] She had no apparent chronic graft-versus-host disease (GVHD) until the onset of arthritis. Despite of polyarthritis, the findings of the declined leukocyte count, the relatively mild MMP-3 elevation and the effectiveness of Tac, were considered that this polyarthritis may be a pathological condition as chronic GVHD. In addition, it was thought that the use of MTX is useful in the chronic GVHD mainly comprising arthritis.

P3-272

A case of hypertrophic pachymeningitis accompanying ulcerative colitis

Hiroki Tanaka, Mizuho Muramatsu, Takayoshi Soga

Division of Rheumatology, Japanese Red Cross Shizuoka Hospital

Conflict of interest: None

A 34-year-old-male with a history of ulcerative colitis (UC) for 7 years was treated with mesalazine and his symptoms were improved. In mid-March 2018, he had the right temporal headache. In April, the laboratory results showed that the inflammatory responses were increased. He was referred to our hospital. Vascular ultrasound in the temporal artery revealed normal findings. Brain magnetic resonance imaging (MRI) revealed thick dura matter with abnormal enhancement in the right cerebral hemisphere. Colonoscopic findings revealed relapse of UC. Based on these findings, he was diagnosed with hypertrophic pachymeningitis (HP) as a complication of UC. His headache rapidly improved after the administration of oral prednisolone at 10mg/day. The dose of prednisolone was gradually tapered. Prednisolone was discontinued three months later. His headache disappeared at present. As a cause of HP, there are underlying diseases such as infection, malignancy and autoimmune disease. There were few reports HP associated with UC. We herein describe a case with reference to the literature.

P3-273

Adult-onset Still's disease presenting with high anti-streptolysin O and arthritis at onset

Kosuke Ota¹, Takato Nakadoi¹, Takahisa Takeyama²

¹Department of Nephrology, NHO Okayama Medical Center, ²Department of General Medicine, NHO Okayama Medical Center

Conflict of interest: None

[Case] forties male [Chief complaint] joint pain [Clinical course] In two months before admission, he manifested knee joints pain and fever of 38 degree. He visited local clinic to be prescribed levofloxacin. After several days he came to our hospital and was diagnosed as viral infection.

Even after visiting his fever continued and joint pain moved to elbows and shoulders. In a month before admission, erythema in upper limb arose, when laboratory data indicated as CRP 8.93mg/dL, ASO 225U/mL, ASK x10240, ferritin 1773.8ng/mL. Although he received 1g/day of ampicillin, his condition did not improve. Moreover, his right wrist swelled painfully. After he admitted our hospital, we clarified no obvious infection or malignancy, negative value of RF and ANA. His MRI of right wrist joint revealed synovitis, with worsening its clinical symptom. After synovectomy his wrist improved with normalizing ferritin value and decreasing of CRP around 3mg/dL. At this time, a diagnosis of AOSD was evoked. Three month later MTX was started, then up to 8mg. His joint swelling disappeared with the normalization of CRP, ASO, ASK. [Discussion] In this case even diagnosis can be PSRA or RA, we diagnosed as AOSD with the elevated ferritin value and its reactivity to MTX. This is rare case of high ASO with AOSD.

P3-274

Erdheim-Chester disease, a rare cause of secondary retroperitoneal fibrosis

Shogo Matsuda, Youhei Fujiki, Takaaki Ishida, Hidehiko Makino, Koji Nagai, Kenichiro Hata, Tohru Takeuchi, Shigeki Arawaka
Department of Internal Medicine IV, Osaka Medical College

Conflict of interest: None

Case: A 46-year-old woman presented to the rheumatology department with gradually worsening swollen lower limbs in September 2017. She had elevated serum creatinine levels (1.78 mg/dL). A contrast-enhanced CT scan revealed a soft-tissue abnormality that surrounds the circumference of the aorta and kidneys, which showed severe hydronephrosis. Serum IgG4 levels were normal. Retroperitoneal biopsy showed diffuse fibrotic change in the tissue. IgG4 was negative in immunohistochemistry. Also, there were no cancer in biopsy. The etiology of retroperitoneal fibrosis (RPF) was unknown, and we diagnosed her as idiopathic RPF. She was treated with glucocorticoid therapy, but she had a partial response. To elucidate the etiology, we further performed radiological examinations. MRI showed osteosclerotic changes in the thoracolumbar vertebral bodies. Technetium-99m methylene diphosphate bone scintigraphy revealed abnormal tracer uptake in the proximal tibias and distal femurs. These findings raised a possibility of Erdheim-Chester disease (ECD). When we re-evaluated biopsy, the infiltration of foamy histiocytes was found in the tissue on hematoxylin and eosin staining. The cells were immunohistochemically positive for CD68 and CD163, but negative for CD1a, confirming a diagnosis of ECD.

P3-275

A case of non-classified immunodeficiency syndrome (CVID) with systemic lupus erythematosus (SLE) like symptoms

Miyu Matsubara, Kae Takagi, Tetsuya Ogawa
Department of Internal Medicine, Tokyo Women's Medical University Medical Center East, Tokyo, Japan

Conflict of interest: None

(Case) A fifty years old male was diagnosed SLE with butterfly rash, arthritis, anti-nuclear antibody positive, and leukocytopenia, and was started PSL thirty nine years ago. He became nephrotic syndrome and was diagnosed with lupus nephritis by renal biopsy and was started PSL 60 mg/day thirty six years ago. But he was added to CPA 50 mg/day because of the relapse of PSL 25 mg alternate oral re-infection thirty years ago. He was suspended from CPA 24 years ago and transference to our hospital eleven years ago. Serum IgG level decreased to 800 mg/dL from seven years ago and not improved after the immunoglobulin have been administered. I asked other laboratories to analyze the lymphocyte subsets in the flow cytometry. The results which is remarkable reduction of B lymphocytes, increase of immature B lymphocytes with CD10+ CD24+, reversal of the CD4/8 ratio, loss of iNKT cell, effect memory T cells, central memory cells and central memory T cells were diagnosed as CVID. The serum IgG level has maintained a more than 700 mg/dL by the administration of IgG every month. (Clinical Significance) We experienced immune deficiency disease exhibiting symptoms of SLE-like condition. It is thought that investigating such a case is also useful for eluci-

ation of the pathology of SLE.

P3-276

Pathological features of lymph node in Adult-onset Still's disease (AOSD)

Masahiro Iida, Yoshiaki Nagai, Naoki Tanomogi, Shuhei Sano, Yusuke Nakamichi, Tatsuo Mori, Nanase Honda, Michiru Kina, Eisuke Takamasu, Kae Onishi, Takayasu Kise, Yuji Miyoshi, Masako Utsunomiya, Naoto Yokogawa, Kota Shimada, Shoji Sugii
Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan

Conflict of interest: None

[Objectives] To examine pathological features of lymph node (LN) in Adult-onset Still's disease (AOSD) and their usefulness in diagnosis in Japan. [Methods] From April 2010 to July 2018, 115 patients visited our department and received LN biopsy. Of these, 12 patients, in whom AOSD was suspected by clinicians, were analyzed retrospectively. [Results] The median age of the 12 (2 males, 10 females) was 60.5 (18-81). Paracortical hyperplasia was shown in 7, follicular hyperplasia in 1, histiocytic necrotizing lymphadenitis (HNL) in 3, and diffuse large B cell lymphoma (DLBCL) in 1. Of 9 who fulfilled Yamaguchi's criteria (except the item "excluding malignant lymphoma"), TAFRO syndrome was diagnosed in one. As for the other 8, diagnosis of AOSD was made and treated as AOSD. Although 1 of the 8 had pathological features of HNL, we treated her as AOSD because her clinical feature and laboratory data were not compatible with HNL. As for the 3 who did not meet the criteria, the diagnosis was HNL in 2 and DLBCL in 1. [Conclusions] In patient who fulfilled the criteria, many cases showed paracortical hyperplasia in LN as previously reported from outside Japan and no cases had malignant lymphoma. However, in diagnosing AOSD, LN biopsy is needed to exclude AOSD-mimicking malignant lymphoma.

P3-277

A case of pachydermoperiostosis in an elderly patient

Tomoe Kaieda, Hideo Ohtsubo, Satoru Nakashima, Sanae Shigemizu, Takemasa Matsuda
Department of Rheumatology, Japanese Red Cross Society Kagoshima Hospital

Conflict of interest: None

The patient was a 74-year-old man who was diagnosed with rheumatoid arthritis at around the age of 24. He had been treated with methotrexate and iguratimod since March 2012, but later developed refractory ulcers, anemia, and multiple erosions in the small intestine. Since these symptoms were suspected to have been drug-induced, the medications were discontinued and the patient was referred to our hospital in July 2017. The patient presented with periosteal formation, which was mainly noted around the long bones, as well as deep wrinkles and clubbed fingers. These observations suggested the diagnosis of pachydermoperiostosis, which was confirmed by skin biopsy and genetic testing for SLCO2A1 mutations. Gastrointestinal symptoms were likely attributable to chronic enteropathy associated with the SLCO2A1 gene (CEAS). Secondary hypertrophic osteoarthropathy causes clubbing of the fingers, periosteal formation of the long bones, and arthritis. Since the patient had a history of basal cell carcinoma, skin biopsy and genetic testing were required to confirm the diagnosis of pachydermoperiostosis. We report the rare case of pachydermoperiostosis in an elderly patient and discuss the literature.

P3-278

A rare case of glycogen storage disease type 5 (McArdle disease) associated with HLA B39 positive spondyloarthritis

Eri Amano, Taro Horino, Satoshi Inotani, Tatsuki Matsumoto, Yoshiko Shimamura, Kosuke Inoue, Yoshio Terada
Department of Endocrinology, Metabolism and Nephrology, Kochi Medical School, Kochi University

Conflict of interest: None

A 76-year-old woman with myalgia and arthralgia was admitted to our hospital. Physical examination revealed myalgia in upper arm and thigh and polyarthralgia in the shoulder and hip joints. Laboratory examination revealed the elevated levels of CRP (0.64mg/dL), MMP3 (78.3ng/mL) and CPK (1294 U/L). Serological testings were all negative. FDG-PET-CT revealed FDG accumulation in the tendon attachments around shoulder and hip joints. Although myositis could not be confirmed by muscle biopsy specimen, initial treatment with PSL 20 mg/day and Tac 1 mg/day was started. Myalgia and arthralgia improved, but CPK level did not normalize. As a result of retest of muscle biopsy specimen, glycogen storage disease type 5 (McArdle disease) was diagnosed, and PSL was tapered. However, myalgia and arthralgia relapsed. Based on clinical course, findings of FDG-PET-CT and HLA B39 positive, spondyloarthritis (SpA) was diagnosed. Treatment with PSL 10 mg/day was restarted and her symptoms improved. We herein a rare case of McArdle disease with HLA B39 positive SpA. Originally, polymyositis was suspected, and it was diagnosed as McArdle disease, so after discontinuation of steroid, recurrence of tendon adhesion flame was confirmed. We report this rare case because similar cases had never reported so far.

P3-279

Clinical presentation, organ involvement and outcomes of 10 cases with relapsing polychondritis

Hiroki Kohno, Kei Araki, Kazutoshi Yukawa, Tadahiro Tokunaga, Tatsuomi Kuranobu, Katsuhiko Ohi, Yusuke Yoshida, Tomohiro Sugimoto, Sho Mokuda, Keisuke Oda, Takaki Nojima, Shintaro Hirata, Eiji Sugiyama

Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan

Conflict of interest: None

[Object] Relapsing polychondritis (RP) is a rare disease characterized by systemic inflammation of cartilage. In this study, we report 10 cases with RP. [Methods] We retrospectively assessed clinical manifestations of 10 RP patients who attended our department from January 2009 to September 2018. [Results] Patient background was; age (mean \pm SD) 53.9 \pm 16.7 years; female 80%; mean time from initial symptom to diagnosis was 4.1 months. As for involved organs / symptoms, auricular chondritis was observed in 9 cases, arthritis in 6, skin lesions in 4, ocular involvement in 3 cases, tracheal involvement in 2, saddled nose, hearing impairment, cardiovascular involvement, and neurological symptoms in 1, respectively. At diagnosis, auricular biopsy was performed in 7 cases, while cartilage inflammation was identified in 5 cases. Ga-scintigraphy was performed in 6 cases. Initial therapy was PSL in 8 cases, and MTX or NSAIDs in one for each. Death and tracheotomy were not identified during observation period. [Conclusions] Female patients was dominant, and tracheal involvement was identified in 20% of the cases. In addition, skin lesions was relatively common.

P3-280

Clinical evaluation of patients with polymyalgia rheumatica in Ogawa Red Cross Hospital

Tatsuya Ito¹, Takashi Maruyama², Yuji Akiyama^{1,2}

¹Division of Rheumatology, Department of Internal Medicine, Ogawa Red Cross Hospital, ²Department of Rheumatology and Applied Immunology, Saitama Medical University

Conflict of interest: None

(Object) We investigated and examined patients of polymyalgia rheumatica (PMR) during treatment at the Division of Rheumatology, Department of Internal Medicine. (Methods) Examples of PMR patients, it was confirmed that the bird's standards were met at the start of the treatment. 25 Example (male 12 Cases, women 13 Example). Average Age of onset 74 year (61-89). After commencement of prednisolone (PSL) by medical records 52. We investigated the presence of clinical symptoms, test findings, and adverse events up to the week. Disease activity was determined by CRP. Rheumatoid arthritis (RA) was excluded by the presence of the manual arthritis of classification standards by ACR/eular. (Results) PSL at the beginning of treatment Using all cases. Average dosage 11.25mg (5 to 15). The term PSL treatment is good reac-

tivity all Example, 5 cases of flare-up during weight loss and 2 cases of PSL resistance. MTX was used in 2 cases. (Conclusions) PMR Although reactivity was good in a small amount of steroids when it comes to treatment, the cases that cause a flare-up at the time of gradual decrease are difficult to treatment, many cases of steroid withdrawal difficulties have been demanded that treatment method.

P3-281

Long-term treatment course of elderly-onset adult-onset Still's disease

Akihito Maruyama, Mariko Sakai, Yoshinobu Nakao, Yuri Sadanaga, Nobuyuki Ono, Syuichi Koarada, Yoshifumi Tada
Department of Rheumatology, Faculty of Medicine, Saga University

Conflict of interest: None

[Object] Adult onset Still's disease (AOSD) is a systemic inflammatory disease characterized by fever, rash, and joint pain. On the other hand, elderly-onset AOSD has been increasing in recent years and reported its atypical clinical features. In this study, we evaluated the long-term treatment outcome in elderly-onset AOSD. [Methods] For 49 patients diagnosed with AOSD in our department from February 1994 to June 2018, we investigated continuation / discontinuation of treatment by retrospective survey using electronic medical record. [Results] Twenty-nine of 49 patients (45.9%) had discontinued treatment during the observation period. Among them, fifteen cases (30.6%) of 49 patients with advanced age over 65 years of age and 5 cases (33.3%) of 15 patients with discontinued treatment were admitted. Comparative examination was made between clinical symptoms, examination values, treatment contents, recurrence rate, etc. Only the sex (P=0.0220) and the splenomegaly (P=0.0170) showed a significant difference between the treatment continuation group and the treatment discontinuation group with onset of over 65 years old. [Conclusions] In the elderly-onset AOSD, prediction of the withdrawal of treatment discontinuation before the start of treatment was difficult.

P3-282

Analysis of SAPHO syndrome

Eri Hayashi¹, Kurisu Tada¹, Shigeto Kobayashi², Hisashi Inoue³, Ken Yamaji¹, Naoto Tamura¹

¹Internal Medicine and Rheumatology, Juntendo University School of Medicine, ²Internal Medicine, Juntendo Koshigaya Hospital, ³Department of Orthopaedic Surgery, Juntendo University School of Medicine

Conflict of interest: None

[Object] The aim of this study is to evaluate the radiographic progression of patients with SAPHO syndrome by mSASSS (modified Stoke Ankylosing Spondylitis Spinal Score) and analyze the association between mSASSS progression and clinical characteristics. [Methods] There were 25 patients with SAPHO syndrome and we collect data of clinical symptoms, blood examinations, image findings, treatment. [Results] As skin symptoms, palmoplantar pustulosis was found in 14 cases, acne in 3 cases. As musculoskeletal symptoms, swelling and/or pain of the sternoclavicular joint was found in 21 cases, low back pain in 22, peripheral arthritis in 8. As image findings, sternocostoclavicular hyperostosis was found in 14 cases, sacroiliitis in 7 cases osteitis in 13 cases. The spinal ankylosis was observed in 17 cases, 11 of which were followed by X-rays and evaluated by mSASSS. The overall change in mSASSS was 1.9/2 years, and if the progression of mSASSS was more than 2 /2 years, the progress cases were 5.1 /2 years in 3 cases. Between progressive and non-progressive cases, no significant difference was observed. [Conclusions] We analyzed the association between mSASSS progression and clinical symptoms, inflammation and disease activity, but no significant difference was found between them.

P3-283

A case of hydroxychloroquine-induced generalized pustular psoriasis in systemic lupus erythematosus

Mayu Sugiyama, Masao Katayama, Nobuyoshi Minemura, Eiji Nagasawa, Kyoko Takano, Michita Suzuki, Kumiko Umemura, Syunsuke Yokoi, Takakazu Hasegawa, Kahori Oshima

Conflict of interest: None

[Case] A 51-year-old woman who was taking 7.5mg of prednisolone (PSL) daily for years with past medical history of systemic lupus erythematosus (SLE) complained of fever and rash lasted for a week. She started to take hydroxychloroquine (HCQ) a month ago. Erythema and pustula were located in her extremities, face, scalp and torso with fever and general fatigue. No mucosal lesions were identified. The skin feature indicated acute generalized exanthematous pustulosis (AGEP) or generalized pustular psoriasis (GPP) and we started PSL 1mg/kg/day. Though fever and rash resolved in a couple of days, the rash returned in steroid tapering process. The clinical course was atypical for AGEP and started sekukinumab for GPP induced by HCQ. Sekukinumab improved Psoriasis Area and Severity Index score rapidly and helped steroids tapered steadily. [Discussion] AGEP closely mimics GPP clinically and both would cause similar manifestations consisted of acute non-follicular pustular lesions, fever, leukocytosis and general inflammation. AGEP is mostly induced by drugs as type 4 allergic reaction and usually resolved spontaneously after the drugs withdrawn. Although it is difficult to distinguish each other visually and pathologically, it is important for clinicians since their treatments are different.

P3-284

Influence of the bone metabolism on relapsing polycondritis

Kumiko Tonooka, Seido Ooka, Tomofumi Kiyokawa, Yukiko Takakuwa, Hiromi Matsushita, Keiichi Sakurai, Yusa Asari, Takayasu Ando, Harunobu Iida, Marina Uchida, Kana Ishimori, Hisae Fujimoto, Kanako Suzuki, Yutaka Goto, Mitsuru Imamura, Takeshi Suzuki, Yoshioki Yamasaki, Kimito Kawahata

Influence of the Bone Metabolism on Relapsing Polycondritis, St Marianna University School of Medicine, Kanagawa, Japan

Conflict of interest: None

[Object] RP (Relapsing Polycondritis is a rare disease which causes inflammation to the cartilage tissue. Patients of RP are often complicated with osteoporosis. Although destruction of a cartilage decreases cytokine, such as IL-11 from a cartilage cell, and has a possibility of having controlled specialization and maturity of a bone blast cell, we investigated effect on bone cartilage metabolism of RP. [Methods] Eighteen RP patients from January, 2010 to May, 2018 were retrospectively evaluated with bone metabolism marker (1 type pro collagen Npeptide:P1NP, osteocalcin:OC, Tartrate-resistant acid phosphatase5b:TRAcP-5b, type 1 collagen cross-linked N-telopeptide:NTX) They satisfied classification of Damiani and Michet or MacAdams. As a control, we investigated 243 cases rheumatoid arthritis (RA) and 169 cases systemic lupus erythematosus (SLE). All these cases were treating the osteoporosis. [Results] P1NP which reflected bone matrix formation ability among osteoplasty and NTX which is formed the resolution of the type 1 collagen among bone destruction compared in the RP cases significantly decreased against RA and SLE group. [Conclusions] The decrease in bone metabolism marker are observed in RP patients. The osteoporosis is important in RP patient.

P3-285

HBV related cryoglobulinemia: A case report

Ayako Kitada, Masato Okada

St Luke's International Hospital, Tokyo, Japan

Conflict of interest: None

[Case] A 37 year-old-women who is HBV carrier presented with one week history of fever, epigastric pain and cervical lymphadenopathy. She was admitted and treated with ceftriaxone and azithromycin for five days. She developed conjunctivitis, erythema on the palms and around ankles, auricular inflammation and polyarthritis. She was transferred to our hospital. On the admission day we suspected viral infection because of her fever, liver function abnormality, thrombocytopenia and arthralgia and atypical lymphocyte. She also had hypocomplementemia and cryoglobulin

was positive. We started etodolac. Her skin symptom and arthralgia were getting better. She also had pulmonary edema and ECG showed diffuse negative T wave. It showed atrial ventricular dissociation and accelerated ventricular rhythm. We treated her with IVIG for myocarditis. She also has high P-AMY and suspected as having viral pancreatitis. Her liver function abnormality continued in outpatient clinic and her HBV-DNA titer was high which was 5.2 logIU/mL. We decided to treat her with entecavir. After that her liver function test turned to normal limit and arthralgia almost disappeared. [Conclusions] We report a 37 year-old-women with HBV related cryoglobulinemia which was treated by entecavir.

P3-286

Treatment as seronegative negative rheumatoid arthritis, a case diagnosed as recurrent polycondritis later

Keisuke Kamiya, Junichiro Hagita, Kiyomi Koike, Katsushi Koyama
Kariya Toyota General Hospital, Kariya, Japan

Conflict of interest: None

[Clinical significance] We reported to have difficulty diagnosing and treating recurrent polycondritis. [Case] 57-year-old man [Chief complaint] Respiratory distress [Current medical history] From X-1 July, He feels conscious pain of some joints. CRP was rising to 16 mg/dl, but RF and ACPA were negative. He was diagnosed seronegative RA, in August prednisolone (PSL) 15mg/day, then methotrexate (MTX), tocilizumab (TCZ) were sequentially started. But he was introduced to our hospital without improvement. Steroid pulse was started, but the arthritis didn't improve. In December, left knee resection was performed. He was introduced to the nearby doctor in February X. In July, diagnosed as uveitis. In August, breathing difficulty and wheezing appeared, urgent tracheotomy was performed. He managed with a mechanical ventilator. We diagnosed recurrent polycondritis (RP). Respiratory condition improved with steroid pulse, but tracheal lesions and arthritis findings remained. We treated with biologics and JAK inhibitors. [Consideration] Originally diagnosed as RA, poor therapeutic reactivity, later turned out to be RP. If the response is poor even if strong immunosuppressive treatment is performed in seronegative RA, it is necessary to suspect other diseases including RP.

P3-287

A patient with fever, pleural effusion, ascites, regarded as TAFRO syndrome

Kosuke Ota¹, Takato Nakadoi¹, Takahisa Takeyama²

¹Department of Nephrology, NHO Okayama Medical Center, ²Department of General Medicine, NHO Okayama Medical Center

Conflict of interest: None

[Case] seventies male [chief complaint] fever, edema [Clinical course] For forty years he was treated of type 1 diabetes mellitus without nephropathy. In a month before admission, he manifested cough and fever of 38 degree. Although he received antibiotics (MEPM, CAM) diagnosed as pneumonia, his symptom was not improved. Complicated with refractory edema, pleural effusion and ascites to diuretics and with renal impairment, he admitted to our hospital. He showed temperature was 37 degree and general edema. Laboratory data indicated as; Hgb 7.9g/dL, Plt 106,000/ μ L, Cre 2.7mg/dL, CRP 8.9mg/dL. CT scan revealed ascites, pleural effusion and lymph nodes swelling of mediastinum. Bone marrow aspiration indicated hypoplasia without reticulum fiber hypertrophy. Endothelial injury of glomeruli and arterioles was shown in renal biopsy specimen. As serum IL-6 and VEGF values elevated, a diagnosis of TAFRO syndrome could be made. Treated with corticosteroid normalized fever, RBC and Plt, also improved edema and renal impairment. [Discussion] In this case we regarded as TAFRO syndrome from his clinical course and the exclusion of other diseases. Endothelial injury of arterioles in TAFRO syndrome is considered not to be common.

P3-288

Change of thermal disparity among fingers in connective disease patients

Yoshimasa Goto, Shigeko Inokuma, Satoshi Miike, Tadamichi Kasuya

Conflict of interest: None

[Object] In connective tissue diseases (CTDs), blood flow disorder is frequently observed. When seeing it in the periphery of the fingers, not only low temperatures but temperature differences among fingers evaluated by thermographic inspection before and after cold stimulus. [Methods] CTD patients with suspected peripheral circulation disturbance were included. From baseline to 30' after hands immersion in 10°C water for 10", nailfold temperatures were measured by Thermo. Coefficient of variation (CV: SD/mean) was adopted as the indicator of the disparity. [Results] 47 CTD patients were included. The changing pattern of nailfold temperature was classified into normal, rebound, delayed recovery, persistently low/decline patterns. CV promptly recovered in normal pattern, did relatively soon in rebound pattern, did slowly and finally in delayed recovery, and sustained high in persistently low/decline pattern. [Conclusions] In CTD patients with peripheral circulation disturbance, the nailfold temperature disparity among fingers evaluated adopting CV tended to be high and sustained high after cold stimulus. The remaining disparity seemed to relate to severity of vascular involvement. The temperature disparity would be a characteristic feature of peripheral circulation disturbance in CTD.

P3-289

Clinical analysis of mutations in 22 genes related to autoinflammatory syndromes in patients with fever of unknown origin

Kyoko Fujimoto¹, Yukiko Hidaka¹, Yumi Yoshida¹, Makiko Hayashi¹, Takuma Koga¹, Shinjiro Kaieda¹, Satoshi Yamasaki², Tomoaki Hoshino¹, Hiroaki Ida¹

¹Division of Respiratory, Neurology and Rheumatology, Department of Medicine, Kurume University School of Medicine, ²Center for Rheumatic Diseases, Kurume University Medical Center

Conflict of interest: None

[Background] Autoinflammatory syndromes, cause systemic inflammation mainly by innate immunity abnormality and should be distinguished with fever of unknown origin. Examining gene mutations is valuable for the diagnosis of autoinflammatory syndromes; however, the frequency of genetic mutations in patients with fever of unknown origin is not reported in Japan. We comprehensively analyzed genetic mutations related to autoinflammatory syndromes. [Methods] We analyzed mutations of 22 genes related to autoinflammatory syndromes as follows; *TNFRSF1A*, *MEFV*, *NLRP3*, *MVK*, *NOD2*, *IL1RN*, *NLRP12*, *PSTPIP1*, *PSMB8*, *PSMB9*, *PSMA3*, *PSMB4*, *POMP*, *NLR4*, *PLCG2*, *HMOX1*, *CECRI*, *COPA*, *TNFAIP3*, *FAM105B*, *RNF31*, *RBCK1* in 75 patients with fever of unknown origin from May 2017 to June 2018. Genetic analysis was performed by the next generation sequencer. [Results] 15 genes were identified as having novel or rare variants. The most frequent variants was determined in *NLRP12* (8 cases, 6 sites), followed by *NLRP3* (7 cases, 4 sites). In addition, missense mutations including genetic polymorphisms were observed in *MEFV* (69.3%). [Conclusions] Novel or rare variants in *NLRP12* and *NLRP3* were noted in patients with autoinflammatory diseases of fever of unknown origin in our hospital.

P3-290

Ultrasound and biopsy findings of arthritis accompanied by Familial Mediterranean Fever

Yutaro Yamada^{1,2}, Kentaro Inui¹, Tadashi Okano¹, Koji Mandai^{1,3}, Kenji Mamoto¹, Yuko Sugioka⁴, Tatsuya Koike⁴, Daisuke Tsuruta⁵, Hiroaki Nakamura¹

¹Department of Orthopedics, Osaka City University Graduate School of Medicine, ²Department of Orthopedics, Yodogawa Christian Hospital, ³Department of Orthopedics, Osaka Social Care Center, ⁴Center for Senile Degenerative Disorders (CSDD), Osaka City University Graduate School of Medicine, ⁵Department of Dermatology, Osaka City University Graduate School of Medicine

Conflict of interest: None

[Introduction] Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disease characterized by recurrent fever and serositis. Among patients with FMF in Japan (estimated 300), 31% show arthritis. We report one case with arthritis in which we assessed presence of amyloidosis, known as poor prognostic factor, by ultrasound (US) and biopsy. [Case report] 70 year-old male was consulted because of recurrent fever and diffuse rash with tenderness mostly located at lower leg. He was diagnosed as FMF since MEFV gene examination revealed abnormality (not the typical one). The laboratory data for CRP was 3.34mg/dl, ESR 50mm/1h, MMP3 190.7ng/ml, Amyloid-A 251.2ug/ml. Colchicine therapy had been started but intolerable. Glucocorticoids and cyclosporine were added, but in vain. All symptoms had disappeared after IL-1 inhibitor canakinumab initiation. US showed positive Grey-Scale and negative Power-Doppler at 3 months later. We did biopsy of intraarticular tissue because it was unclear whether it reflects previous arthritis or amyloid deposition. However it showed only collagen proliferation. As arthritis accompanied by FMF typically heals without sequelae, intraarticular tissue with previous inflammation by US did not present amyloid deposition.

P3-291

A case of familial Mediterranean fever complicated with renal amyloidosis successfully treated with canakinumab accompanied by the changes in proportion of peripheral CD4+ T cell subsets

Yusuke Miyazaki¹, Shingo Nakayamada¹, Yoshiya Tanaka¹, Tadashi Nakamura²

¹The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, ²Sakurajyuji Hospital

Conflict of interest: None

Familial Mediterranean fever (FMF) caused by a mediterranean fever gene (MEFV) gene mutation is characterized by IL-1 β activation. However, immune cell subsets involved in the pathogenesis of FMF remain unclear. Here, we document a case of 57-year-old male with FMF complicated by renal amyloidosis, who is analyzed the phenotype of immune cell subsets by 8-color flow cytometry (FCM) before and after treatment with canakinumab. The patient had periodic fever, abdominal pain, diarrhea and proteinuria. After 6 months of treatment with canakinumab, those symptoms almost disappeared and the levels of CRP and serum amyloid A was markedly decreased. Phenotype of immune cells in the patient was compared with 12 healthy controls (HC). The proportion of Th1 cells was lower in the patient than in HCs, whereas that of Th17 and activated Th17 cells were higher. The proportion of Treg and Tfh cells was not different between the patient and HCs. At six months after treatment, the proportion of Th1 cells was increased and that of Th17 and activated Th17 cells were decreased. The data suggested that canakinumab could alter the proportion of CD4+ T cell subset and improved disease activity, indicating that activation of Th17 cells induced by IL-1 β may be involved in the pathogenesis of FMF.

P3-292

Clinical features of patients that has MEFV gene mutation in our hospital

Miharu Izumikawa^{1,2}, Tomohiro Kameda¹, Shusaku Nakashima¹, Hiromi Shimada¹, Risa Wakiya¹, Mikiya Kato¹, Taichi Miyagi¹, Noriyuki Kurata², Hiroaki Dobashi¹

¹Department of Internal Medicine, Hematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University, ²Tamamo Clinic

Conflict of interest: None

[Object] Familial Mediterranean Fever (FMF) is an autosomal recessive condition due to mutations in MEFV. FMF is characterized by relapsing and remitting 1-3 day episodes of fever, peritonitis, pleuritic, and arthritis. Genotype phenotype correlations studied in Japan suggest that mutations within MEFV exon 10 are associated with a typical FMF phenotype, whereas mutations within exons 2 or 3 are associated with an incomplete FMF phenotype. We investigate genotype-phenotype correlations of patients with MEFV gene mutations. [Methods] We collected the

data of 9 patients with MEFV gene mutations: genotype, the clinical records of them, CRP level, serum amyloid value and efficacy of colchicine. [Results] A genetic investigation of Mediterranean fever (MEFV) detected heterozygosity for the compound mutations E148Q, L110P/E148Q, R202Q, E148Q/P369S/R406Q, E148Q/G304R/P369S/R406Q, and E148Q/M694I. The average of onset age is 18.3±14.9 years old, the average of duration of attack is 3.9±2.7 day, the average CRP is 9.0±8.6mg/dl and the average SAA is 565±470µg/ml. 3 patients with an MEFV exon 3 mutation presented with incomplete phenotype. [Conclusions] All patients have mutations within exons 2. MEFV exon 3 mutation may relate incomplete phenotype.

P3-293

A Case of Familial Mediterranean fever with Difficulties in Diagnosis

Kaita Sugiyama, Marina Hamaguchi, Yutaka Tanikawa, Shoei Yoshizawa, Masashi Oshima, Hiroshi Tsuzuki, Yosuke Nagasawa, Atsuma Nishiwaki, Natsumi Ikumi, Takamasa Nozaki, Hidetaka Shiraiwa, Hiromi Karasawa, Noboru Kitamura, Mitsuhiro Iwata, Kumiko Akiya, Hitomi Haraoka, Yoshihiro Matsukawa, Masami Takei
Nihon University Itabashi Hospital

Conflict of interest: None

[Case] A 27-year-old female. February 2018 during pregnancy, fever, sore throat and cervical lymphadenopathy were observed. She was admitted to our hospital for further examination due to skin rash, thrombocytopenia, hepatic dysfunction and high serum ferritin. After cesarean section at 34 weeks 3 days, there was a complication of respiratory and heart failure. Steroid pulse therapy was performed with symptomatic clinical findings suspected to be diagnosed as hemophagocytic syndrome (HPS). Lymph node and random skin biopsy were performed, but we didn't have a diagnosis and the therapeutic effect was also poor as HPS. MEFV genetic tests submitted during hospitalization suggested mutations were found in S503C of exon 5, which may be atypical of Familial Mediterranean fever (FMF). We started colchicine and showed improvement. [Discussion] This example didn't satisfy the diagnostic criteria of typical cases of FMF, and confirmed by therapeutic diagnosis with gene mutation and colchicine. Atypical FMF in which mutation was observed in S503C of exon 5 is one case in the past and only a few reports in the world. Complications related to life prognosis such as amyloidosis may occur, so early diagnosis and treatment may be desired.

P3-294

A case of familial mediterranean fever (FMF) complicated with IgA deficiency (IgAD) and spondyloarthritis (SpA)

Tamao Nakashita¹, Akira Yoshida¹, Akira Jibatake¹, Takako Miyamae², Shinji Motojima¹

¹Rheumatology and Allergy, Kameda Medical Center, Kamogawa, Japan, ²Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

Conflict of interest: None

Immunodeficiency frequently accompany with autoimmune or auto-inflammatory diseases. We report a case of FMF complicated with IgAD and SpA. Case is a 39-years-old female. She noticed periodic fever of unknown origin from childhood. Fever subsided spontaneously without treatment but complicated by polyarthralgia and chest pain. Afterwards, joint pain and lumber pain developed and persisted without fever. She was referred to our department from orthopedics During the course, polyarthrits, dactylitis, and enthesitis were noticed and sacroiliitis was recognized on XR and CT images resulting in the diagnosis of SpA according to the CASPAR criteria. HLA-B27 was negative but B61 was positive that is one of disease susceptible gene for SpA in japan. FMF was diagnosed according to the Tel-Hashomer criteria and the autoinflammatory disease guideline in Japan that include search for the MEFV related gene mutations. Specifically, 3 mutations were found. IgA levels were less than 1.0 mg/dl. Drugs that induce IgAD were not used and the genetics of IgAD have not been known at present. SpA is thought to be related to IgAD. Colchicine and SASP were administrated and symptoms are getting better.

P3-295

Case report: Familial Mediterranean fever (FMF) complicated by diagnosis due to cytomegalovirus infection

Takuya Nemoto, Takashi Watanabe, Yusuke Ishibe, Nagachika Sugisaki, Makio Kusaoi, Michihiro Ogasawara, Ken Yamaji, Naoto Tamura
Department of Rheumatology and Internal Medicine, Juntendo University School of Medicine, Tokyo, Japan

Conflict of interest: None

A 45-year-old woman presented on November X-1 with fever and cervical lymph node swelling. She was admitted to another hospital because of Leukocytopenia and thrombocytopenia. The serum ferritin value increased, fever and skin rash, adult still's disease was suspected. She was treated with Prednisolone 60 mg/day, fever and cytopenia relapsed when PSL was reduced to 30 mg / day. PSL increased to 60 mg / day, but it was no response. She was transferred to our hospital for plasma exchange in February X because cytomegalovirus (CMV) was positive. We diagnosed hemophagocytic syndrome (HPS) and started ganciclovir (GCV) and plasma exchange. She was improved, and discharged in May X after PSL was stopped. But she was admitted again due to high fever in July X. Familial Mediterranean fever (FMF) was suspected, she was treated with colchicine 1 mg / day. pyrexia was quickly resolved. Although MEFV gene analysis was performed and mutations were not observed in exon 10 and 3, we diagnosed FMF. [Clinical Significance] Because of CMV infection, it was valuable case that it was reactive to both antiviral drugs and steroid treatments, and was confused by confirmed diagnosis.

P3-296

Two cases with TNF-receptor associated periodic syndrome treated by canakinumab with extended dose intervals

Junko Yasumura
Department of Pediatrics, Hiroshima University Graduate School of Biomedical & Health Sciences, Hiroshima, Japan

Conflict of interest: None

[Introduction] Although treatment of patient with TNF-receptor associated periodic syndrome (TRAPS) by canakinumab (CAN) is recommended at 4-week dose intervals, it may be able to extend according to the difference of disease severity and it's blood concentration. I will present two cases with TRAPS treated by CAN with extended dose intervals. [Case1] 36 years old man. He had been diagnosed with systemic-juvenile idiopathic arthritis, but his daughter was diagnosed with TRAPS (mutation of T50M in *TNFRSF1A*) when he was 32 years old. Same mutation was also identified in him. He was treated with etanercept, but it was not effective enough, so it was switched to CAN. It was very effective. After he had been started CAN every 4 weeks, the dose intervals were gradually extended until 9 weeks without attacks. [Case2] 4 years old girl. She was consulted our hospital because of fever unknown origin from 1 year old. Her grandfather, mother and aunt had been diagnosed with TRAPS (mutation of C43R in *TNFRSF1A*). Same mutation was also identified in her. Because she gradually developed resistance to steroid treatment, CAN was started every 4 weeks. The dose intervals were gradually extended until 6 weeks without attacks. [Conclusions] Dose intervals of CAN for TRAPS may be able to extend.

P3-297

A case of Cryopyrin-Associated Periodic Fever Syndrome that diagnosed at the age of 35

Yuichiro Taguchi¹, Ryuhei Ishihara², Tatsuo Inoue², Kenji Yamazaki², Toshiaki Miyamoto²

¹Japanese Red Cross Nagoya Daini Hospital, ²Seirei Hamamatsu General Hospital

Conflict of interest: None

A 35-year-old man who suffered from joint pain and skin rash. So even if it is scrutinized at many general hospitals, it does not reach diagnosis and has symptoms for about 30 years. He visited our hospital on February 23, X year. From detailed medical history listening, from No-

vember every year to the beginning of March every year, urticaria without fever, multijoint pain, pruritus Of skin eruption was admitted. In addition, he accepted mild hearing loss since childhood, and similar symptoms were recognized by mother as family history. We suspected cryopyrine-related cyclic fever syndrome from progress, symptoms, family history, etc. I searched for genes and found an NLRP3 gene mutation, which led to the diagnosis of clioperine related periodic fever syndrome. Next year, similar symptom appeared from the beginning of November, and it interferes with everyday life, so symptoms were markedly improved after administration of Canakinumab. After that, we use Canakinumab only in winter. Most of the symptoms of Cryopyrine related periodic fever syndrome develop in early childhood, but I experienced a case diagnosed after adult as in this case. Today, genetic tests have developed, since it has become possible to reach diagnosis from symptoms, medical history, etc., we report here.

P3-298

Four cases of adult-onset Still's disease (AOSD), in which severe flare accompanying liver dysfunction and/or disseminated intravascular coagulation (DIC) occurred, and diagnosis of macrophage activation syndrome (MAS) was made, during treatment with tocilizumab (TCZ)

Toru Yamabe, Taio Naniwa, Shin-ichiro Omura, Shinya Tamechika, Shinji Maeda, Koji Uehara
Nagoya City University Hospital

Conflict of interest: None

[Cases] Case 1: a 21 year-old female patient was started on TCZ. On day 5 she experienced disease flare with liver dysfunction and disseminated intravascular coagulation (DIC). TCZ was switched to etanercept (ETN), and her condition resolved. Case 2: a 42 year-old female patient was started on TCZ. On day 7, she experienced flare with liver dysfunction and DIC. TCZ was switched to certolizumab pegol (CZP), and her condition resolved. Case 3: A 79 year-old female patient was started on TCZ and achieved remission. In week 20 she experienced flare with DIC. With steroid pulse, her condition resolved. TCZ was withdrawn. Case 4: A 56 year-old female patient was started on TCZ and achieved remission. In week 64 she experienced flare with DIC. With steroid pulse, her condition resolved. TCZ was withdrawn. [Conclusion] We have instituted TCZ for 19 AOSD cases, and experienced four cases of severe flare. Two fulfilled the hemophagocytic lymphohistiocytosis (HLH) 2004 criteria. In maintenance-phase cases, there were no clear clinical signs of flare, and blood test abnormalities led to timely diagnosis. In induction-phase cases, switch of biologics was effective. MAS can develop during TCZ treatment for AOSD, and patient's condition should be closely monitored.

P3-299

PYCARD/ASC variant lacking exon2 expressed in Japanese patients with palindromic rheumatism increases IL-1beta secretion

Yumi Suganuma¹, Atsuko Yabuuchi¹, Fumi Otani¹, Koji Inoue², Shunichi Shiozawa³, Koichiro Komai¹

¹Department of Biophysics, Graduate School of Health Sciences, Kobe University, Kobe, Japan, ²Shichikawa Arthritis Center, Osaka Rehabilitation Hospital, Hannan, Japan, ³Institute for Rheumatic Diseases, Co., Ltd, Ashiya, Japan

Conflict of interest: None

[Object] Palindromic rheumatism (PR) is a rare periodicity arthritis characterized by relapsing short episodes. Although the pathogenesis of PR is not elucidated, the pathology is similar to that of autoinflammatory diseases *via* modulation of the inflammasome. Here, we analyzed the function of *PYCARD/ASC* lacking exon2 (Δ exon2) found in Japanese patients with PR. [Methods] Serum levels of IL-1 β were measured in three Japanese patients with PR. THP-1 cells overexpressing *PYCARD/ASC* variants were stimulated by PMA and MSU, and secreted IL-1 β was measured. Also, protein fractions of recombinant THP-1 cells were subjected to Western blotting and co-immunoprecipitation to determine expression levels of NLRP3 or Caspase-1 and their binding capacity with *PYCARD/ASC*. [Results] Serum IL-1 β level in patients with PR was higher as compared with controls (23.4 \pm 13.3 vs 3.5 \pm 1.8pg/mL). IL-1 β

secretion was significantly increased in THP-1 cells expressing Δ exon2 as compared with wild-type (44.3 \pm 4.1 vs 20.6 \pm 4.4pg/mL) (P <0.05). The amount of NLRP3 bound with Δ exon2 was increased as compared with wild-type, whereas Caspase-1 had no differences. [Conclusions] Our results suggest that Δ exon2 *PYCARD/ASC* increases IL-1 β secretion *via* enhanced binding capacity with NLRP3 as compared with wild-type.

P3-300

Risk factors associated with complication during pregnancy and delivery in patients with RA

Yoshino Inoue, Kazuhisa Nakano, Shingo Nakayamada, Shigeru Iwata, Kentaro Hanami, Shunsuke Fukuyo, Satoshi Kubo, Ipppei Miyagawa, Yusuke Miyazaki, Akio Kawabe, Yoshiya Tanaka
The First Department of Internal Medicine, University of Occupational & Environmental Health, Japan

Conflict of interest: None

[Object] To examine the relationship with perinatal background and pregnancy outcomes in RA female patients who were pregnant during treatment of RA in our hospital. [Methods] We retrospectively analysed pregnancy outcome data from subjects who were pregnant during treatment of RA in our department. The primary endpoint was the rate of full-term birth, and secondary outcomes were patient background, disease activity of RA (CDAI), maternal and neonatal complication. [Results] There were total 23 pregnancies in 16 subjects, 32.0 years of age. The rate of full-term birth was 74%. There were 1 induced abortion and 2 miscarriages in the first trimester, 2 preterm births and 1 stillbirth in the third trimester. Non full-term birth occurred in young women who had unexpected pregnancies and older women who had first pregnancies. Neonatal complications occurred in 5 cases, frequently occurred in mothers who exposed glucocorticoid (GC), in contract hardly occurred in mothers who had drug free. RA relapsed after childbirth in 9 pregnancies, frequently relapsed in patients who exposed GC and were pregnant over 35. [Conclusions] For full-term birth and prevention of neonatal complications, it is important to aim for drug free after achievement and maintain remission of RA without GC.

P3-301

Study on pregnancy and joint destruction in patients with rheumatoid arthritis

Eri Narita^{1,2}, Kentaro Inui³, Yuko Sugioka⁴, Kenji Mamoto³, Tadashi Okano³, Masahiro Tada⁵, Shuhei Ueno^{1,2}, Tatsuya Koike^{1,2,4}

¹Shirahama Hamayu Hospital, ²Search Institute for Bone and Arthritis Disease (SINBAD), ³Department of Orthopedic Surgery, Osaka City University Medical School of Medicine, ⁴Center for Senile Degenerative Disorders (CSDD), Osaka City University Medical School of Medicine, ⁵Osaka City General Hospital

Conflict of interest: None

[Object] We investigated the progress of joint destruction of RA patients who experienced pregnancy activities. [Methods] We examined the age, disease duration and medication of 16 patients. And joint destructive change was evaluated using Sharp/van der Heijde (SvdH) score. [Results] The average of age was 32.4 \pm 3.6 years, the disease duration was 8.1 \pm 4.8 years, and 9 patients got babies. There was no significant difference in age and duration of illness between a bearing baby group and a non-bearing baby group. In a bearing baby group, 6 used prednisolone only, 2 were drug free, 1 was contingent pregnancies using methotrexate and tocilizumab. In a non-bearing baby group, 5 used both of prednisolone and etanercept, and each one had prednisolone alone and drug free. Total SvdH score significantly deteriorated during the mean follow-up period of 38.5 months, but there was no significant difference between two groups. [Conclusions] Although there was no statistically significant difference, joint destruction did not progress in a non-bearing baby group in which majority was biologics user. Pregnancy activity under using biologics might be desirable.

P3-302

Treatment elapse of 31 examples of pregnancy, birth child's gross result and problem during joint rheumatism treatment

Tomohiko Yoshida^{1,2}, Naooki Katsuyama^{1,2}, Yoichiro Akiyama^{1,2}

¹Department of Rheumatology, Setagaya Rheumatology Clinic, ²Department of Rheumatology, Toshin Yoshida Internal Medicine Rheumatology

Conflict of interest: None

[Object] We analyzed the condition of pregnancy, pregnancy, postpartum babies and babies who gave birth in 31 patients who gave birth to pregnancy during rheumatoid arthritis (RA) treatment at our hospital. [Methods] From April 2013 to August 2018, we analyzed the disease activity and treatment method of pregnancy, pregnancy, and childbirth for cases of RA patients who attended our hospital. [Results] The number of cases was 31, the age at pregnancy was 34.8 years, and the mean disease duration was 8.52 years. Before pregnancy treatment, 24 biological products alone, 3 biologics + PSL, 2 SASP + PSL, 1 PSL mono, 1 no med. All cases were low disease activity at birth at pre-pregnancy DAS 28 (median) 1.74, delivery at delivery DAS 28 (median) 2.45. Treatment after childbirth was untreated 10 cases, PSL alone 3 cases, PSL + SASP 2 cases, PSL + biological preparation 12 cases, unknown 4 cases. [Conclusions] Advancement of biological products increases fertility, and safety to pregnant women and fetuses is also increasing. In this study, we reported that we can give birth safely by controlling the disease activity before and after pregnancy to below the low disease.

P3-303

A mutual influence of pregnancy birth on disease flares in patients with systemic lupus erythematosus

Motoko Ishida, Tomoya Miyamura, Makiko Higuchi, Kenji Tamagawa, Tomoaki Iwanaga, Soichiro Takahama, Rumi Minami, Masahiro Yamamoto, Eiichi Suematsu

Department of Internal Medicine and Rheumatology, National Hospital Organization, Kyushu Medical Center

Conflict of interest: None

[Object] Systemic lupus erythematosus (SLE) usually develops in young women at reproductive ages. Previous researches revealed that about 20%-60% of women with SLE experienced a flare during pregnancy. In contrast, others reported that there were no differences between disease activity and pregnancy. The purpose of this study is to investigate the mutual influence of pregnancy birth on disease flares in patients with SLE, retrospectively. [Method] Twenty-nine patients (44 pregnancies) who have been treated since April 2009 till January 2018 in our center were enrolled. [Results] The average age at pregnancy was 35.4 years old. Forty-one patients were treated with prednisolone (PSL); average 5.6mg/day, 10 patients with immunosuppressive drugs. The average SLEDAI was 6, BILAG was 1. Twenty-four babies were birth in full term, 6 were in premature, 5 were miscarry and 4 were born dead. The group of patients who had babies in full term birth were treated with lesser doses of PSL (5.0mg/day) than the group in non-full term birth (PSL 7.8mg/day). Four patients had moderate flare and recovered by increased PSL. [Conclusion] The disease activity of SLE should be controlled lower and the lower doses of PSL as much as possible is desirable during pregnancy.

P3-304

Study of pregnancy in patients with Sjogren's Syndrome (SjS)

Kumiko Shimoyama, Shogo Furukawa, Daisuke Suzuki, Noriyoshi Ogawa

Division of Immunology and Rheumatology, Department of Internal Medicine 3, Hamamatsu University School of Medicine

Conflict of interest: None

[Object] We reported the management of pregnancy in rheumatic disease in JCR 2017, 2018. Here, we report the study of pregnancy in Sjogren's syndrome (SjS). [Methods] Pregnancy was planned in 25 cases (32.1±7.0 y/o) of SjS patients from 2008 to 2018. Information concerning study subjects was retrospectively collected and analyzed. [Results]

There were 8 cases of primary SjS (pSjS 35.1±5.4y/o, duration 1.3±1.8y/o, ESSDAI 5.75±7.1), 17 cases of secondary SjS (sSjS 30.7±7.3y/o, duration 6.7±6.0y/o, ESSDAI 0.53±1.1). sSjS consisted of 16 cases of SLE and a case of RA. There was 24.0% (6 cases) of live birth (pSjS 12.5% (1 case), sSjS 29.4% (5 cases)). There were no significant difference between normal delivery group (NDG) and abnormal delivery group (ADG) at age, duration, ESSDAI and autoantibody. In ADG SLEDAI (5.18±2.79) is higher than in NDG (1.60±0.89) in sSjS with SLE. Neonatal lupus was not seen. 2 miscarriages, 1 artificial abortion, 1 neonatal death and 1 congenital heart block were noted. The level of anti SS-A antibody was higher than ×256 in a case of neonatal death and congenital heart block. [Conclusions] Further studies are needed in order to management of pregnancy in patients with SjS.

P3-305

Survey of the awareness of transitional Juvenile idiopathic arthritis (JIA) patients and their parents regarding transitional care

Takumi Matsumoto^{1,2}, Mariko Mouri³, Fumio Hirano^{1,2}, Masaaki Mori²

¹Department of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, ²Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, ³Department of Pediatrics and Developmental Biology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan

Conflict of interest: None

[Object] To understand the awareness of transitional JIA patients and their parents concerning transitional care. [Methods] We conducted a questionnaire survey of transitional care targeted for transitional JIA patients of Tokyo Medical and Dental University hospital and for members of JIA patient's association. [Results] 80% of transitional patients and 40% of parents did not know the term of transitional care. 50 to 60% did not have the opportunity to talk about transition. 55% of the transitional patients and 80% of the parents had anxiety about transition and transfer, and the biggest anxiety was to establish a relationship of trust with the new physician. Approximately half of the transitional patients wished to continue visiting pediatric rheumatology. Ideally, about half of parents wanted a shift to an adult rheumatology department after establishing a consultation period, but in fact 85% of transferred patients were directly transferred pediatric to adult rheumatology. They wanted to consider transfer timing based on consultation with their doctor, not age. As information that they want to know, data on the course and prognosis of the disease itself, adult medical system, pregnancy and childbirth was required. [Conclusions] Enhancement of transitional medical care is required.

P3-306

Investigation of rheumatoid arthritis cases whose pregnancies were established during treatment using biologics

Masao Sato¹, Masao Takemura², Noriko Iwata¹, Tomohisa Tani¹, Toshiro Ohashi¹

¹Ohashi-Tani Orthopedics, Gifu, Japan, ²Advanced Diagnostic System Laboratory, Fujita Health University

Conflict of interest: Yes

[Objectives] Rheumatoid arthritis (RA) cases in which pregnancy was established during biologic (BIO) therapy were examined. [Methods] We examined the type of BIO, the course of pregnancy, delivery, etc. for RA cases in which pregnancy was established during treatment using BIO. [Results] A total of 5 pregnancies were established in 4 women. The age at the time of confirmed pregnancy was 25 to 35 years old, average 31.4 years old. The breakdown of pregnancy was 2 cases of first pregnancy, 3 cases of second pregnancy. Tocilizumab (TCZ) was 3 times and Etanercept (ETN) was 2 times as BIO used when pregnancy was established. Three pregnancies that were established during TCZ administration were births with normal childbirth, and there was no problem with both mothers and children. Two cases in which pregnancy was established during ETN administration are currently under observation. Pregnancy cases during ETN administration were planned pregnancies under

patient acknowledgment. One case of pregnancy during ETN administration experienced miscarriage once in the past. [Discussion] Although there are many subjects such as selection of drugs used during pregnancy, control of RA disease activity, securing patient's mental stability, accumulation of established evidence is desired.

P3-307

Safety of tacrolimus treatment during pregnancy in inflammatory rheumatic disease: Report of three cases

Ran Matsudaira^{1,2}, Toshiyuki Kaneko², Ken Yamaji¹, Naoto Tamura¹

¹Internal Medicine and Rheumatology, Juntendo University, School of Medicine, ²Tokyo Skytree Station Medical Clinic

Conflict of interest: None

[Objectives] To study of safety during pregnancy in inflammatory rheumatic disease (IRD) patients treated with tacrolimus (TAC). [Cases] The cases were two rheumatoid arthritis (RA) and one dermatomyositis (DM) and we gave approval pregnancy because of their disease activity (DA) was controlled. One of the RA patients (case-1: 30 years old) were treated with TAC (3mg/day) and tocilizumab (TCZ) and stopped TCZ when she turned out to be pregnancy. We added prednisolone (4mg/day) because her DA got worse through the course of gestation. At 39 weeks, she gave birth to son (2781g) naturally without any complications. Another RA patient (case-2: 31 year old) was treated with TAC (3mg/day) and certizumab-pegol (CZP) and stopped CZP when she turned out to be pregnancy. Her DA was not worse and fetus growing was no problem. At 39 weeks, she gave birth to son (3258g) naturally without any complications. DM patient (case-3: 36 years old) was treated with TAC (2mg/day) and betamethasone (0.5mg/day) because of insufficient of PSL. She continued both drugs and her DA was not worse. At 37 weeks, she delivered daughter by Caesarean section (2100g). [Conclusion] We experienced three IRD patients treated with TAC during pregnancy. It was suggested that TAC treatment during pregnancy was safety.

P3-308

Generalized Pustular Psoriasis (GPP) was developed during administration of Hydroxychloroquine (HCQ) and improved by Infliximab (IFX) : A case of pregnancy in a patient with Systemic Lupus Erythematosus (SLE)

Shuko Mishima¹, Kayoko Kaneko¹, Chie Kohno¹, Chinatsu Takai², Mikako Goto², Misato Kawakami², Atsuko Murashima^{1,2}

¹Division of Maternal Medicine, Center of Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development, ²Japan Drug Information Institute in Pregnancy, National Center for Child Health and Development

Conflict of interest: None

[Background] GPP is a serious skin disease. It may appear due to pregnancy, and it is poor prognosis for both of mother and fetus. On the other way, there are some reports of GPP by HCQ. [Case] 31 y, first pregnancy, SLE at 23y. She was taking 10mg of PSL before pregnancy. She was presented with hair loss, low complement, thrombocytopenia at the first visit. We started HCQ from the 20 gestational weeks (GW). At 24 GW, erythema appeared in her trunk. We first suspected skin lesion of SLE and increased PSL to 30mg. However, the skin rash further expanded with increasing pustules and erosion. Skin biopsy revealed GPP. We stopped HCQ immediately and administered IFX at 28 GW. The skin lesion remarkably improved the following day, so we tried to reduce PSL. She complained of empyema at 30 GW and could not be treated with IFX. However, there was no recurrence of the eruption. She gave birth to 2,048 grams of baby at 36 GW. [Discussion] This case was thought that HCQ induced GPP because dermatitis was improved dramatically by withdrawing HCQ and once administration of IFX, and rash did not recur during pregnancy. If skin rash develops or worsens during HCQ administration, it should be carefully observed and considered in drug-induced skin lesions.

P3-309

Measurements of tocilizumab concentrations in maternal and umbilical cord blood at the time of delivery and in breast milk of a lactating mother: A case report of Takayasu arteritis

Mayuko Moriyama, Manabu Honda, Masahiro Kondo, Yohko Murakawa
Department of Rheumatology, Faculty of Medicine, Shimane University

Conflict of interest: None

[Case] A 32-year-old woman, who developed Takayasu arteritis (TA) in September 2005, was commenced treatment with 162 mg of tocilizumab (TCZ) s.c. every 2 weeks in April 2016. She attained remission with TCZ, azathioprine, and prednisolone 8 mg/day. In March 2017, azathioprine was discontinued. She became pregnant in December 2017. Although safety of TCZ for pregnancy has not been established yet, the patient and we decided to continue TCZ treatment throughout pregnancy. She had no problems and a girl weighing 3188 g was born at 39 weeks and 4 days by spontaneous delivery. Apgar scores at 1 and 5 minutes were 8 and 9, respectively. No abnormalities except neonatal jaundice were observed. TCZ concentrations in the maternal serum and in umbilical cord blood were 14,146 ng/ml and 1,967 ng/ml, respectively. The concentrations in her breast milk at several points were lower values but still detectable. [Conclusions] A small number of cases have been reported in which patients received TCZ continuously throughout the entire course of pregnancy and lactation. Especially in TA, no case has as yet been reported. TA occurs frequently among younger women whose future pregnancies and births can be a major problem, indicating that our study is extremely significant.

P3-310

A case of lupus nephritis that caused acute kidney injury (AKI) after parturition

Takahiro Oonishi¹, Satoshi Hosoi²

¹Department of Rheumatology, Ise Red Cross Hospital, ²Orthopedic Surgery, Ise Red Cross Hospital

Conflict of interest: None

Case 30 year old woman In December X-5 she diagnosed SLE with lupus nephritis IV - S (A) and underwent treatment. X-2 December eGFR 90 ml / min / 1.73 m², urine protein 0.8 - 1.3 g / g Cr, with hope of birth, X-1 September pregnancy was established. With control of prednisolone 10 mg, hydroxychloroquine 200 mg, takurorimus 1 mg, aspirin 100 mg, nifedipine CR 20 mg, blood pressure 160 units eGFR 58 ml / min / 1.73 m² urine protein 5.98 g / gCr, and hypertension and renal function decrease were observed at 30 weeks of pregnancy, caesarean section I gave birth to a girl (weight of 998 g). On the next day, a feeling of abdominal fullness appeared, CT showed a remarkable pancreatic swelling and ascitic fluid, and I suspected acute pancreatitis. It resulted in oliguria, acute renal injury occurred, strengthened steroid treatment and slow blood filtration dialysis was performed from 3 days after parturition. On the 11th day, diuresis accompanied, withdrawal from dialysis, discharge from hospital on day 45 of birth. Discussion: Pancreatic swelling which appeared the next day after parturition did not show abdominal symptoms or pancreatic enzyme elevation, and it was due to serositis because it responded to steroid therapy

P3-311

A case of severe relapsing polychondritis in a pregnant woman

Mayu Yagita, Masayuki Nishide, Yusuke Manabe, Yumiko Mizuno, Yuta Yamaguchi, Takayoshi Morita, Yuichi Maeda, Hyota Takamatsu, Toru Hirano, Masashi Narazaki, Atsushi Kumanogoh

Department of Respiratory Medicine and Clinical Immunology, Osaka University

Conflict of interest: None

(Case) A 39-year-old Japanese pregnant woman at 37 weeks of gestation was referred to our hospital with acute respiratory failure. She required intubation due to subglottic edema. The patient had experienced nose pain, cough, and wheezing for 3 months and noticed swelling of her left ear for 3 weeks before hospitalization. Upon admission, she presented

with swelling of both ears and saddle nose deformity. Computed tomography (CT) scan showed severe subglottic edema. Biopsy of auricular cartilage revealed the infiltration of T cells. Based on these findings, she was diagnosed as relapsing polychondritis. Fetal growth was normal at the time. Pulse methylprednisolone therapy was performed, followed by oral prednisolone at 60 mg/day. Etanercept 50 mg/week was added on 14th day. As the dose of oral prednisolone carefully tapered, she was started on Azathioprine (50 mg/day). Under these intensive treatments, the disease activity did not get worse and the patient then vaginally delivered a female infant at 36 weeks of gestation. (Discussion) We experienced a case of severe relapsing polychondritis in a pregnant woman. Treatment strategies and clinical courses of acute worsening of relapsing polychondritis during pregnancy were rarely reported, therefore this case may be of interest.

English Poster Session

EP1-01

Real-world sensitivity analysis of the 2017 classification criteria of systemic lupus erythematosus

Masei Suda

Immuno-Rheumatology Center, St. Luke's International Hospital, Japan

Conflict of interest: None

[Object] Two major classification criteria have been used in the clinical trials of systemic lupus erythematosus (SLE). One is the American College of Rheumatology (ACR) criteria first developed in 1982 and revised in 1997 (1997 criteria), and the other is Systemic Lupus International Collaborating Clinics (SLICC) criteria developed in 2012 (2012 criteria). Currently, the new classification criteria of SLE (2017 criteria) have been proposed by steering committee from ACR and the European League Against Rheumatism (EULAR), aiming for better sensitivity and specificity. They were made based on the agreement of expert panel¹, and have not been validated in the real-world practice. [Methods] We retrospectively reviewed the electronic medical record of the consecutive 100 patients who visited St. Luke's International Hospital, a tertiary care center in Tokyo, Japan, searching back from November 13, 2017. Patients were included if they are clinically diagnosed as having SLE with board-certified doctors, and excluded if they complicated with other autoimmune disease or if they are under 18-year-old. The patients were evaluated for fulfillment of the 1997, 2012, or 2017 criteria. [Results] Among the 100 cases, the sensitivity of 1997, 2012, 2017 criteria are, 97%, 99%, 92% respectively. The total score that the patients got with the 2017 criteria ranged from 12 to 44 (mean: 27.3). All the cases who were classified as non-SLE with the 2017 criteria had anti-nuclear antibody (ANA) <80. [Conclusions] 2017 criteria for SLE accomplished modestly high sensitivity in the real-world practice, but not as high as 1997 and 2012 criteria. They possibly miss-classify the real SLE cases as non-SLE, especially if patients have low titer (<80) of ANA.

EP1-02

A prospective cohort study of the predictive factors for the development of glucocorticoid-induced diabetes mellitus in patients with rheumatic disease (DIMERD study)

Yosuke Asano, Yoshinori Matsumoto, Ken-ei Sada, Keigo Hayashi, Yuriko Yamamura, Sumie Asano Hiramatsu, Michiko Morishita, Keiji Ohashi, Haruki Watanabe, Mariko Narazaki, Tomoko Kawabata, Jun Wada

Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Department of Medicine and Clinical Science., Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Conflict of interest: None

[Object] Osteocalcin (OC) is a protein in the bone matrix which is produced by osteoblasts. Previous studies reported that OC reduced insulin resistance and stimulated pancreatic beta cell proliferation and production of insulin in mice, and undercarboxylated OC (ucOC) regulated glucose metabolism. Additionally, the previous report showed that glucocorticoid (GC) affected serum OC levels. In this clinical study, we prospectively investigate the association between ucOC, lipid and glucose metabolism among inpatients with GC treatment for rheumatic diseases. [Method] We prospectively enrolled inpatients at rheumatology unit of Okayama University Hospital from October 2017 to July 2018. In this interim analysis, we evaluated the association between ucOC levels, a complication of diabetes mellitus (DM) and GC usage at enrollment. Statistical analyses were performed by applying student's t-test, Spearman rank correlation coefficients or chi-square test. [Result] Of 77 patients enrolled in this study, the mean age was 60 years old and 46 (60%) were female. Although the complication of DM was comparable between patients with and without GC (10/33 [30%] vs. 13/44 [30%], $p = 0.94$), ucOC levels of patients treated with GC were significantly lower than without GC (1.09 vs. 3.32 ng/ml, $p < 0.001$). Mean daily dose of prednisolone in patients treated with GC was 13.3 mg. Among patients treated with GC, a daily dose of prednisolone was higher in patients with undetectable ucOC levels (<0.38 ng/ml) than those with detectable ucOC levels (19.2 ± 2.1 vs.

8.7 ± 1.8, $p = 0.0005$). [Conclusion] In spite of the same frequency of DM among patient with and without GC, GC usage is associated with ucOC levels, that is consistent with the previous studies. Because the research is cross-sectional, we could not conclude the causal relationship yet.

EP1-03

Serum tenascin-C levels in patients with idiopathic inflammatory myopathy as a possible biomarker of myocardial injury

Aya Nishiwaki, Toshihiko Komai, Yasuo Nagafuchi, Hirofumi Shoda, Keishi Fujio

Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Conflict of interest: None

[Object] Tenascin-C (TNC) is an extracellular matrix glycoprotein which contributes to tissue remodeling. Serum TNC levels are elevated in patients with cardiac diseases, interstitial pneumonia, and connective tissue diseases such as rheumatoid arthritis (RA) and systemic sclerosis (SSc). The aim of this study is to investigate the relationship between serum TNC levels and clinical disease status of idiopathic inflammatory myopathy (IIM). [Methods] Fourteen IIM patients and 6 healthy controls (HC) were recruited. As disease control groups, blood samples from patients with RA ($n=5$), and SSc ($n=5$) were also analyzed. Serum TNC levels were quantified by ELISA. Clinical characteristics of IIM patients were retrospectively collected from medical records to assess whether they could be associated with serum TNC levels. [Results] Serum TNC levels were significantly elevated in IIM patients compared to HC (mean, 91.1 ng/ml [95% CI, 71.3-111.0] versus 45.9 ng/ml [15.6-76.2], $p=0.0159$). The mean serum TNC levels of RA and SSc patient were 66.4 ng/ml [33.2-99.6], and 95.6 ng/ml [62.4-128.8], respectively. TNC was positively correlated with cardiac biomarkers such as troponin I ($r=0.725$, $p=0.0033$) and CK-MB ($r=0.596$, $p=0.0246$), but not with total CPK, KL-6, SP-A, SP-D, and CRP. Among clinical disease status of IIM, the presence of anti-Mi-2 autoantibody was associated with higher serum TNC levels. [Conclusions] Our findings indicate that serum TNC levels are high and specifically correlated with cardiac enzymes in IIM patients especially with anti-Mi-2 antibody. TNC could be a useful cardiac-specific biomarker in IIM.

EP1-04

Five cases of IgG4-related disease in nasal mucosa and sinus lesion

Masanobu Ueno, Kazuhisa Nakano, Ippei Miyagawa, Shingo Nakayamada, Shigeru Iwata, Shunsuke Fukuyo, Satoshi Kubo, Akio Kawabe, Yusuke Miyazaki, Yoshiya Tanaka

The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: None

IgG4-related disease (IgG4-RD) is frequently associated with allergic diseases. Recently, chronic sinusitis with IgG4-RD has also been reported. In such cases, characteristic pathological findings of IgG4-RD can be observed from nasal mucosa biopsy. We report five cases of IgG4-RD with nasal mucosa and sinus lesions. Five cases were all female and the mean age was 56.4 ± 15.1 years old. All cases presented with nasal obstructions. Of them, four had bilateral eyelid swelling and three had oral dryness. Two had been diagnosed as allergic rhinitis and two as chronic sinusitis. The allergic rhinitis and chronic sinusitis were refractory. The mean serum IgG value was 2091.2 ± 561.1 mg/dL and IgG4 value was 791.4 ± 489.5 mg/dL. In the CT images, sinusitis and bilateral eyelid swelling were observed in all cases and in four cases, respectively. We performed lip biopsy in four cases and nasal mucosal biopsy in all cases. Two cases had histopathological findings that met the IgG4-RD comprehensive diagnostic criteria in both lip and nasal mucosa biopsy. There was one case each satisfying the criteria by lip biopsy or mucosa biopsy. One case without having done a lip biopsy had histopathological finding in nasal mucosa biopsy. We started treatment with medium dose of oral glucocorticoid (GC) therapy (PSL 0.5-0.6 mg/kg/day) in four cases and their nasal obstruction was improved promptly. We confirmed improvement of sinusitis and bilateral eyelid swelling in two cases from CT im-

ages after treatment. In one case who had advanced obesity, mild sinusitis findings on CT images and no other organ involvement, corticosteroid nasal drops were used and nasal obstruction improved without oral GC. We suggested that nasal mucosal biopsy may be useful for diagnosis as IgG4-RD with nasal and paranasal lesions. In refractory allergic rhinitis and chronic sinusitis, the possibility of nasal and paranasal lesions as an organ disorder of IgG4-RD should be considered.

EP1-05

The efficacy of Classical Indian Yoga in the treatment of Fibromyalgia: A Randomized Controlled Trial

Vikas Trivedi, Panna Mishra

Era's Lucknow Medical College, Era University, Lucknow, India

Conflict of interest: None

Purpose: Ø Fibromyalgia (FM) is a complex musculoskeletal disorder treated with multidisciplinary therapies. Ø Classical Indian Yoga is an ancient life style healing technique which has an integrated mind-body approach to enhance both physical and mental health. **Methods:** Ø 6 months, single-blind, randomized trial of Classical Indian Yoga (50 patients) versus attention control group (stretching and wellness education) of 50 patients for Fibromyalgia. Ø The classical Indian Yoga involved 60-minute group sessions thrice-weekly. Ø The primary outcome measure was change in the FM Impact Questionnaire (FIQ) score at 1 year. Ø Secondary outcome measures were tender point count, patient and physician global assessments, sleep quality (PSQI), 10-minute walk, timed chair stand, grip strength, depression and quality of life. Ø These outcome measures were repeated at 1 year to test durability of response. Both groups were compared using an intent-to-treat analysis. **Results:** Ø Mean age of 100 patients was 55 years (SD 11), disease duration 10 years (SD 7) and BMI 30 kg/m² (SD 8). Ø 80 patients were females. Ø Patients baseline expectations of benefit from an exercise intervention were similar: Classical Yoga =4.1 and the controls=4.3. Ø After 6 months patients in the classical Yoga group had a significantly greater improvement in FIQ score: between-group change -20, 95% CI (-24.0 to -8.8); $P=0.0005$. Ø The Yoga group patients also had significant improvement in secondary outcome measures: reduction in pain scale (VAS), improved patient global assessment, physical function, depression, and health status. Ø After 1 year patients compliant with the classical Yoga had sustained and durable benefits in FIQ score quality of sleep and quality of life. Ø The two groups did not differ in medication usage. No adverse events were noted. **Conclusion:** Classical Indian Yoga appears to be highly effective in the management of FM having a positive impact on physical, psychological and social aspects

EP1-06

Perinatal exposures and risks for coronary artery lesion formation and IVIG resistance in Kawasaki disease

Kuo Ho-chang

Kaohsiung Chang Gung Memorial Hospital, Taiwan

Conflict of interest: Yes

[Object] Kawasaki disease (KD) is featured by acute febrile systemic vasculitis and most affect children less than five years old. Nowadays the mean maternal age of giving birth is increasing in most countries in recent three decades. The effect of maternal age in KD has been reported before. This study was conducted to survey patients' potential perinatal exposures and clinical outcome of KD. [Methods] A total of 185 KD patient-caregiver dyads were enrolled in this study through questionnaires in Kaohsiung Chang Gung Memorial Hospital. Questionnaire content included two categories: (1) children's characteristics: age at disease onset (years), gender, gestational age at delivery, birth body weight, delivery methods (vaginal/cesarean), and breast-feeding; (2) caregivers' characteristics: caregiver (parents/non-parents), education levels (senior high school/university), maternal age of giving birth to the KD patient, total number of offspring born to each patient's mother, and family income. CAL formation and IVIG treatment response of KD were analyzed with these factors retrospectively. [Results] KD with CAL formation had higher maternal age than non-CAL patients (32.49 ± 3.42 vs. 31.01 ± 3.92 years, $p = 0.016$). We also found that group of maternal age ≥ 32 years

had higher rate to have KD patients with CAL (39/81 vs. 24/74, $p = 0.047$) when compared with group of maternal age < 32 years. KD patients with male gender had higher incidence of CAL formation than female (56/112 vs. 19/73, $p = 0.001$). Group of maternal age ≥ 35 years had higher rate to have KD patients with IVIG resistance (6/31 vs. 6/116, $p = 0.01$). [Conclusions] The present study first reported that increasing maternal age is significant associated with CAL formation and IVIG resistance in KD. We suggested that maternal age less than 32 and 35 years will be benefit for coronary artery status and IVIG response in KD offspring, respectively.

EP1-07

Serum Aldolase as a Diagnostic Marker and Indicator of Disease Activity in Patients with Adult-onset Still's Disease

Shinji Izuka, Hiroyuki Yamashita, Sotaro Nakajima, Toshiaki Kobayashi, Kyoko Motomura, Nanami Mino, Shunta Kaneko, Yuko Takahashi, Hiroshi Kaneko

National Center for Global Health and Medicine, Shinjuku, Tokyo, Japan

Conflict of interest: None

[Object] Adult-onset Still's disease (AOSD) is an acute systemic inflammatory disorder that is commonly diagnosed using Yamaguchi's criteria. AOSD is difficult to diagnose, and it is hard to determine whether it is active or inactive. A few studies have reported that serum aldolase (ALD) increases in AOSD patients. However, the specific relationship between AOSD and serum ALD has not been clarified. The aim of this study was to address the possible role of serum ALD as a biomarker for differential diagnosis and disease activity in patients with AOSD. [Methods] Blood samples and symptom data were collected from 8 patients with AOSD, 28 patients with rheumatic arthritis (RA) who have active arthritis with positive C-reactive protein, 34 patients with Sjogren's syndrome (SjS) who did not take glucocorticoids or immunosuppressants, 19 patients with systemic lupus erythematosus (SLE) whose SLE Disease Activity Index was higher than 8, and 12 patients with systemic sclerosis (SSc) who did not take glucocorticoids or immunosuppressants. Follow-up samples of all patients with AOSD were collected after resolution of disease activity. Correlations were performed between serum ALD and Pouchot's score, ferritin, and other enzymes in patients with AOSD. [Results] Serum levels of ALD in AOSD patients were higher than in the control groups (RA, SjS, SLE, and SSc patients; all p -values were < 0.001). The sensitivities and specificities for the diagnosis of AOSD were 87.5%/100%, 88%/95%, 87.5%/100%, and 87.5%/100%, respectively. All cutoff values were 8.9 U/L. Serum ALD was found to be decreased after disease activity was resolved in the follow-up of AOSD patients ($p=0.02$). In addition, serum ALD was correlated with Pouchot's score and ferritin levels among AOSD patients ($r = 0.71$, $p=0.003$ and $r = 0.6$, $p=0.02$). [Conclusions] The data suggest that serum ALD may be a useful biomarker for diagnosis and evaluating disease activity in patients with AOSD.

EP1-08

Can cancer trigger autoimmunity disease? Features of autoimmune disorder of patients with cancer

Sayaka Tsuzuki, Hideyuki Takahashi, Fangyi Chin, Keigo Setoguchi
Systemic Immunological Disease, Tokyo Metropolitan Cancer and Infectious Disease Center Komagome Hospital, Japan

Conflict of interest: None

[Object] Association between cancer and autoimmune diseases are reconsidered by frequent use of immune checkpoint inhibitor. In previous research, the childhood cancer patients have the higher possibility of developing autoimmune disease than general population. In this study, we examine the autoimmune diseases that appear after the cancer onset. [Methods] Date on clinical characteristics, laboratory features, and treatment from 107 patients with autoimmune disease in our hospital retrospective survey were analyzed. [Results] 107 patients were included; their median duration of follow-up was 39 months. The period of diagnosing cancer from autoimmune disease was 17 months, and age of the patients with autoimmune diseases at diagnosis was 68 years. Baseline manifestations included rheumatoid arthritis (RA) 43%, polymyalgia

rheumatica (PMR) 20%, systemic sclerosis (SSc) 9%, Sjogren syndrome (SjS) 8%, IgG4-related disease 7%, vasculitis 6%, interstitial pneumonia 4%, polymyositis and dermatomyositis 3%. In patients with RA, 53% were positive for both rheumatoid factor (RF) and anti-CCP antibody (median RF 155IU/mL, CCP antibody 380U/mL). The median age of diagnosis was 68 years, and 51% were female. The average serum C-reactive protein (CRP) was 1.7mg/dL. Treatments used were MTX in 34%, SASP in 29%, PSL alone in 8%. The response to therapy was 70% overall. In PMR, all cases were seronegative. The median age of diagnosis was 71 years, and 63% were female. The average CRP was 5.4mg/dL. All case started treatment using PSL 15mg and responded to treatment. They all tapered PSL. In SSc, 77% had centromere antibody and the median titer of the antibody were 1280. Interestingly, even in SjS patients, the same antibody was positive in 50%. Seeing from cancer side, 19% had colon cancer, 16% had breast cancer, 11% had lung cancer, 9% had gastric cancer. [Conclusions] Patients with cancer developed autoimmune diseases, and had different characteristics from primary autoimmune disease.

EP1-09

Preliminary report on genetic analysis for an immune-related adverse event caused by immune checkpoint inhibitors

Naoki Hamada¹, Yohei Kirino¹, Ryusuke Yoshimi¹, Yukie Yamaguchi², Michiko Aihara², Hideaki Nakajima¹

¹Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Japan, ²Department of Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine, Japan

Conflict of interest: None

[Background] Immune checkpoint inhibitors (ICI) have shown marked efficacy in multiple cancers. However, an immune-related adverse event (irAE) may occur in any organ at any time point. Search for biomarkers to predict irAE is highly needed. [Object] To identify susceptibility gene polymorphisms of onset of specific irAE. [Methods] ICI monitoring committee including rheumatologist was established in our hospital. Since Sep 2014, cancer patients who received approval of ICI treatment (nivolumab, pembrolizumab, atezolizumab, ipilimumab) participated in our study. Clinical information was obtained from the electronic medical record. Genotypes of genetic polymorphisms associated with autoimmune diseases such as HLA and CTLA-4 were determined by next-generation sequencer using genomic DNA extracted from the saliva or whole blood. We analyzed the association between the onset of irAE and their genetic polymorphism. [Results] 100 patients who underwent ICI therapy (malignant melanoma; $n=19$, non-small cell lung cancer; $n=22$, head and neck cancer; $n=24$, renal cell carcinoma; $n=21$) participated in the study. As an adverse event, diarrhea, thyroid dysfunction, and a rash appeared in about 20% of all patients, respectively. Interstitial pneumonia and arthralgia were found in 10% of cases. Genetic analysis is currently underway. [Conclusions] Genetic factors may be involved in the onset of irAE. Further study of the large cohort in Japan can lead to elucidation of the genetic risk of irAE and appropriate use of ICI.

EP1-10

Association of Serum MMP-3 Concentrations with Disease Progression after the Onset of Rapidly Destructive Coxopathy

Tadashi Yasuda
Department of Orthopaedic Surgery, Kobe City General Hospital Medical Center, Kobe, Japan

Conflict of interest: None

[Object] Rapidly destructive coxopathy (RDC) is an unusual subset of osteoarthritis. It is characterized by rapid joint space loss, chondrolysis, and sometimes marked femoral head and acetabular destruction as a late finding. Although the exact pathogenetic mechanism is unknown, potential causes of RDC include high serum levels of matrix metalloproteinase (MMP)-3 as biological factors. No previous study has investigated MMP-3 in association with the disease progression of RDC. This study was aimed to elucidate association of MMP-3 with the time course after the onset of RDC. [Methods] Of female patients who visited our

hospital with hip pain from 2012 through 2018, this study enrolled female patients with the clinical records including the onset of hip pain, a series of radiographs during the period of ≥ 12 months from the onset of hip pain, and hematological data of MMP-3. We found the hip joints of 30 patients meet the diagnostic criteria of RDC; chondrolysis >2 mm with subsequent femoral head destruction in one year. Serum MMP-3 was measured with blood samples within one year after the onset. This study excluded male patients because RDC occurs mainly in elderly females and the reference intervals (RIs) of MMP-3 are different between males and females. [Results] When the approximate curve obtained from the scatter diagram of serum MMP-3 concentrations obtained from 30 patients with RDC were plotted in association with the duration between the onset of hip pain and MMP-3 determination, we found a significant exponential decrease in MMP-3 with time ($R^2=0.304$, $P=0.002$). MMP-3 kept higher levels over >59.7 ng/ml, the upper limit of RI, within 10 months after the onset in every patient with RDC. [Conclusions] In female patients with RDC, serum MMP-3 may stay at increased levels during the period of chondrolysis after the onset of hip pain and thereafter decrease with time.

EP1-12

Effectiveness of tocilizumab and impact of cancer for large-vessel giant cell arteritis developing recurrent ischemic stroke: a case report

Masashi Watanabe

Department of Neurology, Ehime Prefectural Central Hospital, Matsuyama, Japan

Conflict of interest: None

[Object] Here we report a rare case of large-vessel GCA (LV-GCA) refractory to antithrombotic drugs and corticosteroid (CS) with adrenal cancer. [Methods] We analyzed its clinical course retrospectively. [Results] A 76-years-old woman has had recurrent cerebral embolisms 6 times for 2 years despite optimal antithrombotic treatments. She presented with right-side dominant tetraparesis with frontal releasing signs. Cardiovascular tests detected neither atrial fibrillation nor arterial stenosis. Brain MRI showed multiple cortical and subcortical high intensity lesions in both anterior and posterior circulations. Blood investigations indicated only elevated erythrocyte sedimentation rate and d-dimer without abnormal findings associated with cerebral embolisms. Contrast CT and FDG-PET/CT showed abnormal enhancement in the thoracic aorta with its branches suggesting vasculitis and left adrenal tumor without hormonal abnormality. Urologists and Radiologists diagnosed it as benign adenoma then. Biopsy of left temporal artery showed no findings of vasculitis. We diagnosed her as LV-GCA with recurrent ischemic stroke based on scan findings. Treatment with CS, aspirin, and apixaban temporarily prevented ischemic attacks for only 2 months. Combination of tocilizumab (TCZ) with CS completely resolved recurrence for several months. However, serial CT showed increase in the adrenal tumor with invasion to surrounding tissues and systemic metastases. Carcinoma was detected from gingival biopsy. After that, she suffered from frequent ischemic attacks due to Trousseau's syndrome and died of sepsis due to duodenal perforation caused by tumor invasion. [Conclusions] CS treatment alone was reported to be insufficient to prevent ischemic stroke related to LV-GCA. Combination of TCZ with CS might be effective for preventing recurrent ischemic stroke of LV-GCA. It should be kept in mind to make adequate surveillance as much as possible for coexistence of cancer in patient with LV-GCA.

EP1-13

Cervical lymphadenopathy uncovered: Kikuchi-Fujimoto Disease as initial presentation of mixed connective tissue disease

Maeflor Q Ofilas, Maria Roselle E Guzman, Joseph Patrick N Patricio Ilocos Training and Regional Medical Center, San Fernando City, La Union, Philippines

Conflict of interest: None

Kikuchi-Fujimoto Disease is a rare, benign, self-limiting systemic lymphadenitis with unknown etiology presenting with lymphadenopathy, fever and leukopenia. It can be associated with Systemic Lupus Erythematosus and Mixed Connective Tissue Disease (MCTD). We report a 36-

year old female, initially presenting with posterior neck lymphadenopathy, fever, arthralgia, leukocytosis managed with series of antibiotics. There was no decrease in lymph node size which warranted ruling out tuberculosis and lymphoma with negative Tuberculin skin test and IGRA. Lymph node biopsy revealed lymphoid tissue fragments with interfollicular histiocytic necrotizing lymphadenitis characteristic of KFD. Immunohistochemical stain results were positive for CD20, CD3, Ki67, and CD68; CD30 and EBER were negative. Ruling in connective tissue disease, Immunologic profile showed ANA 1:5120 (speckled pattern), elevated Anti-U1RNP antibodies, normal complement 3. She was managed as case of MCTD with Methylprednisolone and Hydroxychloroquine rendering resolution of symptoms. This case supports the idea that KFD and MCTD may share common pathogenesis.

EP2-01

Comparison of clinical efficacy and safety of tofacitinib and baricitinib in patients with rheumatoid arthritis in our department

Shunta Kaneko, Hiroyuki Yamashita, Shinji Izuka, Sotaro Nakajima, Toshiaki Kobayashi, Kyoko Motomura, Nanami Mino, Yuko Takahashi, Hiroshi Kaneko

Division of Rheumatic Disease, National Center for Global Health and Medicine, Japan

Conflict of interest: None

[Object] Few studies have directly compared the Janus kinase (JAK) inhibitors tofacitinib and baricitinib in terms of their effects in, and safety for, patients with rheumatoid arthritis (RA); we retrospectively report our departmental experience with this topic. [Methods] We evaluated the therapeutic effects and safety of tofacitinib and baricitinib in 17 and 9 patients, respectively, after 4 and 12 weeks of treatment. [Results] The characteristics of the two treatment groups such as swollen and tender joints and C-reactive protein (CRP) levels did not differ. Improvements in joint symptoms and significant decreases in CRP levels were observed at 4 weeks (tofacitinib: -3.36 ± 3.35 mg/dL, $p<0.01$, baricitinib: -3.44 ± 3.23 mg/dL, $p<0.01$) and 12 weeks (tofacitinib: -3.18 ± 3.10 mg/dL, $p<0.01$, baricitinib: -3.77 ± 3.28 mg/dL, $p<0.01$). In patients taking tofacitinib, the higher the anti-cyclic citrullinated peptide (CCP) antibody titer, the less the change in CRP level after 4 weeks ($p=0.83$, $p<0.05$). On the other hand, in patients given baricitinib, effects were evident regardless of the anti-CCP antibody titer. No patient discontinued baricitinib within 3 months, but six discontinued tofacitinib because of infection or lymphocytopenia; the difference was significant ($p<0.05$). [Conclusions] The anti-inflammatory effects of the two JAK inhibitors in RA patients varied by the anti-CCP antibody titer.

EP2-02

The role of methotrexate monotherapy along with high dose vitamin D in newly diagnosed rheumatoid arthritis

Vikas Trivedi, Yashasvi Bansal

Era's Lucknow Medical College, Era University, Lucknow, India

Conflict of interest: None

Introduction: Rheumatoid arthritis is a very common chronic inflammatory and autoimmune disease affecting approximately 1-2% of Indian population. The subsequent inflammatory changes lead to cartilage and bone destruction and the corresponding systemic inflammation may result in disorders of multiple organ systems. AIM: To study the role of methotrexate monotherapy along with high dose vitamin D in newly diagnosed cases of rheumatoid arthritis. Materials and Methods: This is a prospective randomized controlled study. It comprised of two groups each having 50 patients of RA each. One group only methotrexate subcutaneously was given and in another group along with methotrexate, Vitamin D in a high loading dose was given. The dosage of Methotrexate was 25mg/week and 0.6 million IU Vitamin D was given. The maximum follow up was of about 3 years which was done by clinical evaluation, ACR and DAS28 scoring. RESULTS: On the basis of this study it was found that patients who were given vitamin D along with subcutaneous methotrexate injection therapy, the relief to the symptoms was early, significant ($P<0.05$) and more dramatic as compared to patients receiving only subcutaneous methotrexate. A significant association between vitamin D levels

and ACR scores, CRP levels and ESR was observed. Lower vitamin D levels were associated with higher ACR scores, CRP levels and ESR. Conclusions: 1. Vitamin D deficiency was quite common in patients with rheumatoid arthritis and vitamin D deficiency was significantly associated with disease activity. 2. Vitamin D supplementation helped to improve the outcome of methotrexate therapy among early cases of rheumatoid arthritis and also helped to eradicate the vitamin D deficiency in the targeted group. 3. These findings suggest subcutaneous Injection Methotrexate monotherapy along with high dose Vitamin D is an excellent and highly cost effective treatment regime for adult patients diagnosed with early RA.

EP2-03

Comparison between Denosumab and Teriparatide treatments for osteoporosis in patients with Japanese rheumatoid arthritis; 18 months of follow-up

Tokutaro Okawa¹, Shuhei Ueno², Eri Narita², Tatsuya Koike^{2,3}

¹Okawa Orthopedic Surgery Hospital, Japan, ²Search Institute for Bone and Arthritis Disease, Shirahama Foundation for Health and Welfare, Japan, ³Center for Senile Degenerative Disorders, Osaka City University Medical School, Japan

Conflict of interest: None

[Background] DMB and TPTD are well known as a great useful treatment medication in OP. Comparison between these medications for OP in RA patients is not well addressed previously. [Object] In this retrospective study, we compared BMD changes with DMB and TPTD treatment for OP in Japanese RA patients for 18 months of follow-up. [Methods] Patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria. All patients were postmenopausal women with OP who were OP treatment naïve. The DMB dose was 60mg at once every six months with daily native vitamin D. The TPTD included 20µg daily or 56.5µg weekly by subcutaneous injection. BMD was measured with DXA for lumbar spine (LS), femoral neck (FN) and total hip (TH) at baseline and months 6, 12, 18 during treatment. We assessed the TBS (trabecular bone score) at the same regions used for LS DXA scans, using TBS iNsight Software v2.2 at baseline and months 12 and 18. [Results] DMB (n=30) and TPTD (n=13) were enrolled. Patients' characteristics of DMB and TPTD. The Mean age 72.0 and 70.6 years old. The body mass index 19.7 and 20.4. Baseline LS-BMD 0.647 and 0.655. The LS-BMD change from baseline to 6, 12 and 18 months were each 0.671 vs 0.649 (p<0.05) at 6 month, 0.686 vs 0.650 (p<0.01) at 12 month and 0.694 vs 0.655 (p<0.05) at 18 month. Baseline FN-BMD 0.435 and 0.449. The FN-BMD from baseline to 6, 12 and 18 months were each 0.441 vs 0.435 (N.S.;no significant) at 6 month, 0.443 vs 0.434 (p<0.05) at 12 month and 0.444 vs 0.436 (N.S.) at 18 month. Baseline TH-BMD 0.566 and 0.561. The change of TH-BMD from baseline to 6, 12 and 18 months were each 0.579 vs 0.548 (p<0.05) at 6 month, 0.586 vs 0.549 (p<0.01) at 12 month and 0.586 vs 0.557 (p<0.05) at 18 month. Baseline TBS 1.266 and 1.273. The change of TBS from baseline to 12 and 18 months were each 1.267 vs 1.274 (N.S.) at 12 months and 1.268 vs 1.269 (N.S.) at 18 months. [Conclusions] This study shows that DMB was more useful to increase BMD than TPTD in OP of RA patients.

EP2-04

The relationship between the precise region of ultrasound joint synovitis and joint examination findings in the wrist joints of patients with rheumatoid arthritis

Norihide Hayashi^{1,2}, Takehisa Ogura¹, Ayako Hirata¹, Rie Kujime¹, Hideki Ito¹, Sayaka Takenaka¹, Munetsugu Imamura¹, Yuki Inoue¹, Chihiro Imaizumi¹, Yuto Takakura¹, Hideto Kameda¹

¹Division of Rheumatology, Department of Internal Medicine Toho University Ohashi Medical Center, Tokyo, Japan, ²Medical Corporation Syurinkai Yoshimi Hospital, Japan

Conflict of interest: None

[Object] Joint examination is the core assessment of the clinical evaluation of rheumatoid arthritis (RA). We have previously demonstrated a limited concordance between ultrasound (US) joint synovitis and joint examination by swelling and tenderness in various joints of patients with

RA. The aim of this study was to elucidate the precise localization of US joint synovitis in wrist joints which are the most frequently involved in RA and anatomically complex, and its importance in the concordance with joint examination. [Methods] We enrolled 208 RA patients who were examined for the presence of arthritis in wrist joints by physical examination and US in this study. Clinical joint assessment determined the presence of tenderness alone (T), swelling alone (S), both (TS) or none (N) of them. US evaluation was performed in radial, median and ulnar regions of the dorsal side by longitudinal and transverse scans. US synovitis was defined as gray-scale (GS) imaging score ≥ 2 (graded 0-3) or a synovial power Doppler (PD) signal score ≥ 1 (graded 0-3) for each region of wrist joints. Binominal data were examined by Fisher's exact test. [Results] Among total wrist joints assessed, US synovitis was observed in 95 of 285 N joints (33%), 11 of 20 T joints (55%, p=0.056 versus N joints), 37 of 52 S joints (71%, p<0.001 versus N joints) and 51 of 59 TS joints (86%, p<0.001 versus N joints), respectively. US synovitis was observed in 28% of radial, 38% of median, and 30% of ulnar regions, respectively. When US synovitis was confined to only one of three regions, clinical examination was positive (other than N joint) only in 33% (26 of 79 joints), while it was positive in 69% (61 of 89 joints) when US synovitis was found in all the three regions of the wrist. [Conclusion] The detection rate of arthritis by joint examination is decreased when RA synovitis is confined to a particular region of the wrist joint.

EP2-05

The Clinical Features and Outcome of Native Vertebral Osteomyelitis in Patients with Rheumatoid Arthritis

Ming-li Hung¹, Chang-youh Tsai²

¹Kuanshan Tzu Chi Hospital, Taitung, Taiwan, ²Division of Allergy, Immunology, & Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taiwan

Conflict of interest: None

Objective: The clinical features and outcomes of native vertebral osteomyelitis diseases in patients with rheumatoid arthritis are unknown. We analyzed such the relevant data in from a medical center in Taiwan. Methods: We retrospectively reviewed the medical records of patients with RA diagnosed with NVO between 2006 and 2016 in Taipei Veterans General Hospital, Taiwan. Clinical presentations, laboratory parameters, and treatment outcomes were analyzed. Results: Twelve eligible patients with 26 NVO episodes were enrolled and separated into groups of primary episodes (12) and recurrent episodes (14). The median age of the cohort was 70 years, and 8 (67 percentage) were female. The spinal pain was the most common presenting symptom (100 percentage). The lumbar to sacral spine was the most common site of NVO (85 percentage), followed by the thoracic spine (19 percentage) and cervical spine (8 percentage). The most common organisms organism was methicillin-sensitive Staphylococcus aureus (19 percentage of bacteremia), followed by methicillin-resistant Staphylococcus S. aureus (8 percentage of bacteremia and 8 percentage of biopsy specimens). The median duration of the parenteral antibiotic course was 53 days (interquartile range, 30 to 67 days). Recurrence developed in 75 percent of patients developed recurrence, and the median time to recurrence after completing treatment was 37 days (interquartile range, 14 to 418 days). Vertebral osteomyelitis developed in 58 percentage of patients developed vertebral osteomyelitis after an invasive spinal procedure, and six patients experienced the recurrence. Conclusions: The recurrence of native vertebral osteomyelitis in patients with rheumatoid arthritis is relatively high. Back pain is the most common presentation and the can provide a hint for diagnosis.

EP2-06

Cartilage oligomeric matrix protein, a biomarker of arthritis, could be useful for predicting the response to biologic therapy in Rheumatoid Arthritis?

Claudia S Cioflu, Macovei Liviu, Victor Stoica, Ioan Ancuta, Mihai Bojinca, Bogdan I Gavrilă

Department of Internal Medicine and Rheumatology "Dr. I. Cantacuzino" Clinical Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Conflict of interest: None

[Object] evaluating the predictive role for the response to anti-TNF α of cartilage oligomeric matrix protein (COMP), a biomarker which evaluates the articular cartilage degradation and its turnover. [Methods] prospective/observational study including 64 patients followed 12 months with active RA, uncontrolled by csDMARDs. Clinical assessment was performed at 0,6,12 months according to ACR criteria approved by OMERACT and evaluation of treatment response according to EULAR criteria (good/moderate /nonresponder). [Results] 64 patients included,59 (92.2%) were women and 5 (7.9%) men, mean age 57.55 \pm 9.42 years. After 6 months,7 patients were declared nonresponders,38 achieved a moderate response and 19 good response. Following baseline COMP titres and the EULAR response at 6 months, general tests identified significant differences between groups. Lower baseline titres had predictive value for achieving a good response (746.04 \pm 130.095 ng/ml) comparing with moderate responders (1032.8 \pm 188.671ng/ml) and nonresponders (1042.2 \pm 181.717 ng/ml, $p=0.000$). After 12 months,11 patients achieved moderate response,44 a good response and just 1 patient was declared nonresponder. At this visit, even if we didn't find significant differences between baseline COMP titres and the EULAR response ($p=0.1430$), we observed lower baseline titres for good responders (917.8 \pm 219.943 ng/ml) vs moderate responders (1042.7 \pm 193.117 ng/ml). Grouping patients in 2 categories (responders/nonresponders) there were no differences between groups at 6 months ($p=0.227$) or 12 months ($p=0.9753$). Following the status pretreatment of COMP and EULAR response at 6 months, we identified differences between groups ($p=0.0001$), all 7 patients declared nonresponders were COMP positive and only 13/19 (68.4%) of good responders were tested positive. At 12 months there were no differences between groups ($p=0.2805$). [Conclusions] COMP could be one of the biomarkers for identifying pretreatment the patients who will respond to anti-TNF therapy in RA.

EP2-07

Bone mineral density and microarchitecture among Chinese patients with rheumatoid arthritis

Shangyi Jin¹, Evelyn Hsieh², Mengtao Li¹, Weibo Xia³, Qian Wang¹, Xiaofeng Zeng¹

¹Department of Rheumatology, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Key Laboratory of Rheumatology and Clinical Immunology, Beijing, China, ²Section of Rheumatology, Yale School of Medicine, USA, ³Department of Endocrinology, Key Laboratory of Endocrinology, Ministry of Health, Peking Union Medical College Hospital, Chinese Academy of Medical Science, Beijing, China

Conflict of interest: None

[Object] To evaluate risk factors associated with alterations in bone mineral density and microarchitecture in patients with rheumatoid arthritis. [Methods] In this case-control study, patients with RA were recruited from the Chinese Registry of rheumatoid arthritis (CREDIT). The primary outcomes were HRpQCT at distal radius and tibia (Scanco XtremeCT II), and data from age- and sex-matched healthy controls were included for comparison. In the RA group, data was also collected regarding demographic and clinical characteristics, OP risk factors, RA history, thoracolumbar X-ray, and central DXA. Correlation between HRpQCT and covariates were analyzed using linear regression models. [Results] A total of 81 RA patients (69 women, aged 57.9 \pm 8.7y, duration 5.7 (IQR 1.4-11.2)y) and 81 healthy controls were included. Compared with controls, patients had larger bone area and lower vBMD at the distal radius and tibia. HRpQCT at the distal tibia also showed lower cortical bone thickness in patients. Among those with RA, aBMD at lumbar spine and total hip positively correlated with vBMD, trabecular bone volume fraction, trabecular number and cortical thickness, and negatively correlated with trabecular separation and inhomogeneity. vBMD correlated positively with BMI, grip strength, HCQ and correlated negatively with age, RA duration and DAS28. Parameters reflecting impairment of microstructure negatively correlated with BMI and grip strength, and positively correlated with age, disease duration and activity. Current GCs was related to lower vBMD, trabecular number and impaired microstructure. Patients with fragility fractures had lower vBMD in both trabecular and cortical bone, thinner cortical bone and impaired trabecular bone microstructure. [Conclusions] Patients with RA have BMD and microstructural alterations compared to healthy individuals, which may lead to higher

fracture risk. Both traditional and RA-related factors should be considered in bone quality assessment in RA.

EP2-08

The role of low socio-economic status, education and occupation in patients with Rheumatoid arthritis

Panna Mishra, Vikas Trivedi

Era's Lucknow Medical College, Era University, Lucknow, India

Conflict of interest: None

Background: There are few studies evaluating community poverty association with RA especially in an emerging economy like India. In other chronic diseases, the poverty rate of one's community was found to be associated with disease prevalence and health status outcomes independent of a person's education level. Purpose: The aim of this study is to critically evaluate associations between education, occupation, and community poverty with rheumatoid knee symptoms and radiographic knee RA parameters. Method: A cross-sectional analysis was conducted on 500 patients with RA who resided in a district setting comprising of low income and high income groups. Education (less than High School) and occupation (physically demanding or not) were used as individual measures. The annual income of 1000 USD is used as defining criteria for community poverty with about 250 patients selected with < 1000 USD annual income and rest 250 above it. Covariates included age, gender, number of dependents and current smoking. Three outcomes were assigned as a finding in one or both knee joints: r RA defined as Larsen grade 2 and rheumatoid knee symptoms (pain, swelling and stiffness). Multivariate analyses were also performed adjusting for the covariates. Results: In bivariate analyses with education and the covariates, less than High School was significantly associated with r RA (OR equal to 1.3, CI 1.3, 1.5), symptoms (OR equal to 1.6, CI 1.5,1.9), and symp RA (OR equal to 1.6, CI 1.3,2.0). In an urban group with >20% poverty was significantly associated with r RA (OR equal to 1.8, CI 1.3,2.5) and symp RA (OR equal to 1.5 CI 1.1, 2.1) in bivariate analyses. Conclusion: The community and individual Socio-economic status (SES) measures were independently associated with knee RA in this population-based study of individuals from a urban community.

EP2-09

Importance of the sites of affected joint in clinical assessment of rheumatoid arthritis

Hideki Ito, Takehisa Ogura, Chihiro Imaizumi, Yuki Inoue, Sayaka Takenaka, Norihide Hayashi, Ayako Hirata, Hideto Kameda
Division of Rheumatology, Department of Internal Medicine Toho University Ohashi Medical Center, Japan

Conflict of interest: None

[Object] Current assessment of rheumatoid arthritis (RA) is primarily based on the evaluation of affected joint counts. The aim of this study was to examine the importance of the sites of affected joint in clinical assessment of patients with RA. [Methods] A total of 305 patients with RA were enrolled in this cross-sectional study. All the patients met 1987 American College of Rheumatology (ACR) and/or 2010 ACR/European League Against Rheumatism classification criteria, and visited our center between May 2014 and March 2015. Their medical records were reviewed for tender, swollen, and/or subjectively painful joint sites, as well as patient's and physician's global assessments (PtGA and PhGA, respectively), health assessment questionnaire-disability index (HAQ-DI), serum level of C-reactive protein (CRP) and RA treatments received. A stepwise regression analysis was performed for a multivariate analysis of factors determining each clinical assessment. [Results] Simplified disease activity index (SDAI) remission rate was 49.8% in our patients. Tender joint count (TJC) and swollen joint count (SJC) mainly depended on the small joints, as expectedly, while HAQ-DI and CRP depended on the large joints (Figure 1). Interestingly, the determinant factors of HAQ-DI and PtGA did not overlap with those of SJC and CRP, both of which have been demonstrated to be closely associated with the radiographic progression evaluated by hand and foot X-rays. In addition, patients with large joint predominance (large swollen joint count > small swollen joint count) showed a higher rate of receiving biological agents than the other

patients (55.2% vs. 34.1 %, respectively, $p=0.03$) despite smaller number of total swollen joints in patients with large joint predominance than others (median 1 vs. 2, respectively, $p=0.002$). [Conclusions] Consideration of the sites of diseased joint is important in clinical evaluation of patients with RA.

EP2-10

The Study of Predictors of Osteoporotic Fracture in Rheumatoid Arthritis

Panna Mishra, Vikas Trivedi

Era's Lucknow Medical College, Era University, Lucknow, India

Conflict of interest: None

Purpose: Osteoporosis and osteoporotic fractures are commonly associated with Rheumatoid Arthritis (RA). We assessed the association between osteoporotic fractures and RA clinical features, other organ damage and the impact of treatment, especially corticosteroids. **Method:** This is a large prospective cohort study of 500 RA patients, there were 200 osteoporotic fractures. Variables evaluated were sociodemographic data, disease variables, clinical features, Uveitis, the use of corticosteroids and other complications. Clinical associates of fractures were determined by univariate and multivariate analyses. **Results:** In the best multivariable model, More than 3 major joint involvement, smoking ever, uveitis, prednisone ever, pulse steroid ever and obesity remained significant. (Detailed results will be presented in the JCR meeting) **Conclusion:** This study identified multiple risk factors for osteoporotic fracture in RA. Corticosteroid use (ever, current, pulse) was a strong risk factor. This new study also identifies smoking, uveitis and polyarticular involvement as additional risk factors.

EP2-11

Prescriber Attitudes and Beliefs about Triple Therapy for Patients with Rheumatoid Arthritis: Knowledge Exchange in Internet Forums and Social Media

Maria A Lopez-olivo, Jude K Des Bordes, Gregory Pratt, Maria E Suarez-almazor

The University of Texas, MD Anderson Cancer Center, USA

Conflict of interest: None

[Objective] Several forums on the internet serve as repositories of personal experiences and exchange of health information. Online discussions among healthcare providers about management of patients with rheumatoid arthritis occur on a regular basis. Therefore, we explored and characterized the discussions about the use of triple therapy (methotrexate, sulfasalazine, hydroxychloroquine) on Internet forums, as differences in utilization among countries have been reported. [Methods] Online discussions were collected from three "leading edge" forums (ResearchGate, Medscape, and Twitter). Threads of discussion were systematically examined and interpreted to reveal recurring topics and patterns. Each post was coded and arranged into broader categories, which were combined into overarching themes. [Results] Twelve threads with 96 posts were identified. Seventy-nine of the posts were categorized. Seventeen were discarded because they were questions or comments unrelated to the topic discussed in the original thread. Four themes emerged during the analysis: (i) effectiveness, (ii) costs, (iii) safety, and (iv) adherence. The first theme dealt primarily with the effectiveness of triple therapy compared with tumor necrosis factor inhibitors. The second theme focused on the costs. Although the majority agreed that it is a cost-saving alternative, especially in developing countries, some believed that biosimilars will be as cost-saving and more effective. The third theme involved a multitude of safety and tolerance concerns. The last theme covered the use of multiple drugs, which minimizes adherence. [Conclusions] The discussions in online forums showed extensive and cumulative discussions on attitudes and beliefs exchanged about triple therapy. Main concerns included radiographic progression, safety, and adherence which could partially explain low utilization of triple therapy in some countries.

EP2-12

Short to mid-term outcomes of Golimumab for rheumatoid arthritis in our hospital

Junichi Fujisawa¹, Naoki Kondo², Takehiro Murai², Naoko Kudo², Naoto Endo²

¹Carrier Support Center for Resident, Niigata University Medical and Dental Hospital, Niigata, Japan, ²Division of Orthopedic Surgery, Department of Regenerative and Transplant Medicine, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

Conflict of interest: None

[Object] To investigate short to mid-term outcomes of Golimumab for rheumatoid arthritis in our hospital [Methods] fifty-eight cases of rheumatoid arthritis who introduced Golimumab between February 2012 and August 2018 in our hospital were included in this study. The average age at the start of administration was 66-year-old. The average observation period was 1.2 year. The examination items consist of 1) Changes in DAS28 from the start up to 12 months after the administration 2) Cumulative survival rate of Kaplan-Meier method 3) Combined use rate and dose of MTX at the start of administration 4) DAS28 and survival rate in combined with or without MTX 5) DAS28 and survival rate of each bio-naïve and switch cases. [Results] DAS28 was 4.4 at the start, 3.4 at 3 months, 3.3 at 6 months, 2.8 at 9 months and 2.7 at 12 months after the administration. The cumulative survival rate was 60% for 1 year and 46% for 2 years. The case of concomitant use of MTX at the start of administration was 44 cases (76%) and the average dose was 7.4 mg/week. There was no significant difference in the transition of DAS28 with or without MTX combination and survival rate was 63% for 1 year, 52% for 2 year in combination cases, 51% for 1 year, 25% for 2 year in non-combination cases. By comparing the bio-naïve and switch cases, the DAS28 declining rate from the start, the naïve case was significantly higher. The survival rate was 71% for 1 year, 56% for 2 year in bio-naïve cases, and 33% for 1 year in bio-switch cases. [Conclusions] Administering Golimumab for rheumatoid arthritis at our hospital showed a trend towards gradual improvement over the course of 12 months for disease activity. Although there was no significant difference in the transition of disease activity with or without MTX combination, survival rate was significantly higher in MTX combination cases. The rate of decline in disease activity and the survival rate were also significantly higher in the bio-naïve cases.

EP2-13

The clinical outcome of tofacitinib in patients with rheumatoid arthritis

Naoki Kondo¹, Naoko Kudo², Junichi Fujisawa¹, Naoto Endo¹

¹Division of Orthopedic Surgery, Department of Regenerative and Transplant Medicine, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan, ²Katsumi Orthopedic Clinic, Japan

Conflict of interest: None

[Object] To evaluate the efficacy and safety of tofacitinib (TOF) in patients with rheumatoid arthritis (RA). [Methods] Twenty-four RA patients (23 females and 1 male) who were administered with TOF and could be followed more than 3 months were recruited. Of 24 patients, 19 cases (79%) had been treated with biological DMARDs more than 1 agent. The mean age was 66±9.9 years old (43 to 85) and the average RA disease duration was 16.3±13.3 years. The mean dose of methotrexate was 3.0±4.0 mg/week (0 to 12) at TOF administration. The mean follow up duration was 7.9± 10 months. Disease activity score 28 (DAS28) and clinical disease activity index (CDAI) were evaluated and the retention rate was examined. The cessation cases were examined. The statistical analysis was performed with Student-t test and p-values less than 0.05 were defined as significant difference. [Results] The average DAS28 was 4.02 at the administration of TOF, and significantly decreased to 3.43, 3.24, and 2.77 at 1, 3, and 6 months after TOF administration. The average CDAI was 20 at the administration of TOF, and significantly decreased to 15, 11, and 6.3 at 1, 3, and 6 months after TOF administration. The retention rate was 79 % at 1-year. Five case were ceased with TOF because of 3 cases of no efficacy and 2 cases of adverse events such as herpes zoster and dysphoria. [Conclusions] Although the almost subjects were refractory RA, TOF demonstrated good efficacy.

EP2-14

Our experience of administering Sarilumab for rheumatoid arthritis: Three cases report

Junichi Fujisawa¹, Naoki Kondo², Takehiro Murai², Naoko Kudo², Naoto Endo²

¹Carrier Support Center for Resident, Niigata University Medical and Dental Hospital, Niigata, Japan, ²Division of Orthopedic Surgery, Department of Regenerative and Transplant Medicine, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

Conflict of interest: None

[Object] To report three cases of administering Sarilumab for rheumatoid arthritis in our department. [Case 1] A 54-year-old female. After Abatacept became secondary ineffective, changing to Tocilizumab, but caused sepsis from UTI and Tocilizumab had to be discontinued. After a while the disease activity of rheumatoid arthritis was gradually increased. Patient global assessment was 8.0, CRP was 4.42 mg/dl, RF was <5 IU/ml, MMP-3 was 115.9 ng/ml, DAS28 (4)-ESR was 5.88, SDAI was 40.4 and CDAI was 36.0. Then changing to Sarilumab, four weeks later, patient general assessment was 3.0, CRP 0.01, RF <5, MMP-3 80.9, DAS28 (4)-ESR 0.91, SDAI 6.01, CDAI 6.00. [Case 2] A 64-year-old female. Tocilizumab started at the age of 55. Although low disease activity was obtained, RF and MMP-3 gradually increased. Thereafter, disease activity scores also increased, and at the age of 64, even when changing to Golimumab, it was primary ineffective. Patient global assessment was 10.0, CRP 7.48, RF 533.4, MMP-3 712.1, DAS28 (4)-ESR 6.08, SDAI 35.48, CDAI 28.0. Then changing to Sarilumab, seven weeks later, patient global assessment was 2.0, CRP 0.45, RF 353.1, MMP-3 534.2, DAS28 (4)-ESR 3.14, SDAI 8.45, CDAI 8.0. [Case 3] A 65-year-old man. At the age of 54, Etanercept was started. But it became secondary ineffective, changed to Tocilizumab at the age of 57. At the age of 64, the disease activity of rheumatoid arthritis was increased and it changed to Golimumab, but it became secondary ineffective. Patient global assessment was 6.0, CRP 3.01, RF 222.7, MMP-3 199.0, DAS28 (4)-ESR 5.28, SDAI 31.01, CDAI 28.0. Then changing to Sarilumab, five weeks later, patient global assessment was 2.5, CRP 0.03, RF 221.0, MMP-3 55.5 DAS28 (4)-ESR 2.32, SDAI 13.03, CDAI 13.0. [Conclusions] We reported three cases of administering Sarilumab for rheumatoid arthritis in our department. All cases were bio-switch cases, but both patient global assessment and disease activity were improved from a relatively early stage.

EP3-01

The autophagy receptor optineurin negatively regulates RANKL expression in synovial fibroblasts derived from patients with rheumatoid arthritis

Wen Shi Lee, Masaru Kato, Eri Sugawara, Michihiro Kono, Ryo Hisada, Yuki Kudo, Michihito Kono, Yuichiro Fujieda, Toshiyuki Bohgaki, Olga Amengual, Kenji Oku, Shinsuke Yasuda, Tatsuya Atsumi
Department of Rheumatology, Endocrinology, and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Conflict of interest: None

[Object] Autophagy has recently been shown to play an important role in the pathogenesis of rheumatoid arthritis (RA). Autophagy receptors help to shuttle misfolded, polyubiquitinated proteins to autophagosome through their ubiquitin-binding domains. In this study, we aimed to explore the role of optineurin, one of the TNF- α inducible autophagy receptors, in the joint destruction in RA. [Methods] The expression of optineurin was analyzed in RA synovial fibroblasts (RASFs) 6 and 24 hours after treatment with inflammatory cytokines, including TNF- α and IFN- γ by real-time PCR and western blotting. Optineurin was downregulated in RASFs using siRNA. The expression of receptor activator for nuclear factor- κ B ligand (RANKL) on optineurin-downregulated RASFs and control RASFs was analyzed by flow cytometry 72 hours after treatment with inflammatory cytokines, mRNA levels were analyzed 6 hours after treatment. Cellular levels of I κ B α were determined by western blotting 1 and 2 hours after treatment with TNF- α to evaluate NF- κ B activity. [Results] The expression of optineurin was significantly increased following treatment with TNF- α or that with IFN- γ at both mRNA ($n=3$, $p<0.05$) and protein levels ($n=3$, $p<0.05$). After siRNA mediated knockdown of

optineurin, compared to control siRNA transfection, the expression of cell surface RANKL following treatment with TNF- α ($n=3$, $p<0.01$), that with IFN- γ ($n=3$, $p<0.001$), or that with both ($n=3$, $p<0.05$) was significantly increased on RASFs. The mRNA levels of RANKL was also increased on optineurin-downregulated RASFs compared to control RASFs ($n=3$, $p<0.05$). The degradation of I κ B α following TNF- α treatment was more pronounced in optineurin-downregulated RASFs compared to control RASFs. [Conclusions] We newly identified the autophagy receptor optineurin as a negative regulator of RANKL expression on RASFs, via NF- κ B pathway. Our data suggests the novel role of autophagy and autophagy receptors in the pathogenesis of RA.

EP3-02

A culture engineering strategy to enhance mesenchymal stromal cells for treatment of osteoarthritis

Kevin P Robb^{1,2}, Alejandro Gómez-aristizábal^{1,2}, Shashank Bhatt¹, Rajiv Gandhi^{1,3}, Sowmya Viswanathan^{1,2,4}

¹The Arthritis Program, University Health Network, Canada, ²Institute of Biomaterials and Biomedical Engineering, University of Toronto, Canada, ³Division of Orthopaedic Surgery, Toronto Western Hospital, University of Toronto, Canada, ⁴Cell Therapy Program, University Health Network, Canada

Conflict of interest: None

Osteoarthritis (OA) is a progressive joint disease linked to chronic inflammation for which mesenchymal stromal cells (MSCs) have been investigated as a promising therapy. We hypothesize that enhanced MSCs (eMSCs; by 3D culture using a proprietary method (US62/397,572) and hypoxic stimulation) will augment their ability to reduce inflammation, fibrosis, and cartilage degradation relative to naïve MSC (nMSC) controls within *ex vivo* and animal OA models. In 24 h licensing experiments with the pro-inflammatory cytokine TNF α , eMSCs displayed a 5-fold increase in transcript levels of the anti-inflammatory MSC potency marker TSG-6 versus nMSCs as measured by qPCR. After stimulation with the pro-inflammatory cytokine IFN γ , eMSCs also showed reduced gene expression of the pro-inflammatory markers CXCL8 and COX2, as well as the fibrotic marker TGF- β relative to nMSCs suggesting that eMSCs could help to mitigate the inflammatory and fibrotic microenvironment in OA. Co-culture studies with human monocytes or CD4⁺ T cells revealed that the eMSCs caused a modest increase in the expression of the homeostatic monocyte/macrophage marker CD163 after 48 h with a reduction in the pro-inflammatory phenotypic marker CD86 observed in parallel by flow cytometry. In terms of suppressing CFSE-labeled CD4⁺ T helper cell proliferation, preliminary results show that eMSCs are equivalent to nMSCs under fresh conditions, but that after cryopreservation and thawing, eMSCs are much more effective than nMSCs. In conclusion, eMSCs have improved immunomodulatory characteristics relative to nMSCs and may therefore be more clinically effective in OA. In ongoing work, we are investigating mechanism of action of eMSCs through mRNA profiling with RNA-sequencing and by examining cartilage gene expression changes as well as glycosaminoglycan content after co-culture of the eMSCs with human osteoarthritic cartilage and synovium.

EP3-03

Interleukin-6 Receptor Blocker Increases Revascularization and New Bone Formation in a Murine Model of Ischemic Osteonecrosis

Gen Kuroyanagi^{1,2,5}, Yuko Nagaya³, Ryosuke Yamaguchi^{4,5}, Harry Kim^{5,6}

¹Department of Orthopaedic Surgery, Nagoya City University Graduate School of Medical Sciences, Japan, ²Department of Rehabilitation Medicine, Nagoya City University Graduate School of Medical Sciences, Japan, ³Department of Joint Surgery for Rheumatic Diseases, Nagoya City University Graduate School of Medical Sciences, Japan, ⁴Department of Orthopaedic Surgery, Kyushu University, Japan, ⁵Center for Excellence in Hip Disorders, Texas Scottish Rite Hospital for Children, Dallas, USA, ⁶Department of Orthopaedic Surgery, University of Texas Southwestern Medical Center, USA

Conflict of interest: Yes

[Background] Ischemic osteonecrosis of femoral head includes chronic synovitis, increased bone resorption and decreased bone formation.

Recently, patients with juvenile ischemic femoral head osteonecrosis shows significant elevation of the pro-inflammatory cytokine interleukin-6 (IL-6) in the synovial fluid. Thus, IL-6 is implicated in playing important pathologic roles in increasing bone formation and decreasing bone resorption following ischemic osteonecrosis. [Object] The purpose of this study was to investigate whether IL-6 receptor inhibition prevents bones loss and healing process in a mouse model of ischemic osteonecrosis. [Methods] Ischemic osteonecrosis was surgically induced in the distal femoral epiphysis by vessels cauterization. Anti-mouse IL-6 receptor antibody (MR16-1) or saline was administrated after the surgery. MR16-1 effects on bone formation, bone resorption, and healing response were assessed at 2 weeks and 4 weeks after the surgery using histologic, histomorphometric and micro-CT methods. [Results] IL-6 immunohistochemistry showed increased IL-6 immunostaining in the distal femoral epiphysis after ischemic osteonecrosis induction. Histologic assessment showed significantly increased revascularization and restoration of the necrotic marrow with new hematopoietic marrow in the MR16-1 group at 2 and 4 weeks after the surgery. Micro-CT assessment showed significantly increased bone volume in the osteonecrosis side of the MR16-1 group at 4 weeks following ischemic osteonecrosis compared to the saline group. Histomorphometric assessment showed significantly increased osteoblast number/bone surface, bone formation rate, and mineral apposition rate in the MR16-1-group. However, the number of osteoclast/bone surface was also increased in the MR16-1 group. [Conclusions] IL-6 receptor inhibition increases revascularization and restoration of the hematopoietic bone marrow, and stimulates new bone formation following ischemic osteonecrosis.

EP3-05

4-Phenylbutyric Acid Mediates Therapeutic Effect in Systemic Lupus Erythematosus: Observations in an Experimental Murine Lupus Model

Yunjung Choi¹, Eunhyeong Lee², Ji-hyeon Jeong², Wan-hee Yoo^{1,2}

¹Department of Internal Medicine, Chonbuk National University Hospital, Jeonju, Korea, ²Research Institute of Clinical Medicine of Chonbuk National University-Biomedical Research Institute of Chonbuk National University Hospital, Jeonju, Korea

Conflict of interest: None

[Object] Recently, several studies have revealed the pathological role of endoplasmic reticulum (ER) stress in the autoimmune and inflammatory diseases. The purpose of the present study was to investigate whether ER stress inhibition by 4-phenylbutyric acid (4-PBA) ameliorates arthritis in an experimental model and the effect of ER stress inhibition by 4-PBA on interleukin-1 β -induced proliferation and inflammatory response of rheumatoid synovial fibroblasts (RASFs). [Methods] The proliferation of RASFs was evaluated in the presence of IL-1 β with/without 4-PBA. The expression of ER stress markers and matrix metalloproteinases were examined. The in vivo effects of 4-PBA were investigated using DBA/1 mice with collagen-induced arthritis (CIA). [Results] 4-PBA markedly attenuated the severity of arthritis in CIA mice, such as ameliorated joint swelling and reduced bone erosion and destruction. Furthermore, the level of proinflammatory cytokines including IL-1 β , IL-6 and TNF- α in joint extracts were suppressed in the CIA model treated with 4-PBA. In vitro, the elevated level of GRP78 was detected in IL-1 β -stimulated RASFs. 4-PBA treatment suppressed the IL-1 β -induced proliferation, production of proinflammatory cytokines and metalloproteinase (MMP-1, MMP-3) in IL-1 β -stimulated RASFs [Conclusions] These findings suggest that 4-PBA ameliorates experimental arthritis by inhibition of ER stress in RASFs. 4-PBA could be a therapeutic option for the treatment of RA.

EP3-06

The accumulation of microdamage is the most related factor than biopsy-proven severely suppressed bone turnover (SSBT) in bisphosphonate-associated atypical femoral fractures

Naoki Kondo¹, Hiroe Sato², Naoto Endo¹

¹Division of Orthopedic Surgery, Department of Regenerative and Transplant Medicine, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan, ²Health Center, Niigata University, Niigata, Japan

Conflict of interest: None

[Objective] The pathogenesis of atypical femoral fractures (AFF) remains unknown. The accumulation of microdamage, SSBT, and the bone metabolism decreases are supposed to be the critical factors for the incidence of bisphosphonate (BP)-related AFFs. In this study, we determined which factors was the most related for the incidence of AFFs. [Methods] Twenty-five patients of BP-associated atypical femoral fractures were registered. Most patients were primary osteoporosis (n=15). The others were SLE (4 cases), RA (3 cases), angitis (2 cases), and PMR (1 case). BP duration was 6.2 years on average. Age was 72 years old (range; 49-93) on average, and 1 male and 24 females. The site of fractures was subtrochanteric in 14 and diaphysic in 11 cases. Iliac bones were harvested and subjected bone histomorphometric findings. Fracture sites were harvested and the cortex was stained with bulk or Villaneuva bone staining. When bone histomorphometric findings demonstrate that bone formation (osteoid) parameters were low and bone resorption parameters were low, the situation was defined as SSBT. The former specimens were the quantitative analysis of microcracks. The crack density (Cr. Dn: N/mm²) and the crack surface density (Cr.S. Dn: μ m/mm²) were measured. The latter ones were the quantitative analysis of the densities of empty lacunae and osteocytes. Then in the case of the empty lacunae density was superior to the osteocyte density, the situation was defined as "the decreased state of bone metabolism". The incidences were calculated. [Results] SSBT was detected in 3 cases (16%). Microcracks were detected in the all 17 cases (100%), and the average Cr. Dn was 1.56 and the average Cr.S. Dn was 154, respectively. Empty lacuna density was more elevated than osteocyte density in 14 cases (64%). [Conclusions] Microdamage was the most related factor in the incidence of atypical femoral fractures, followed by the bone metabolism decreases and SSBT in order.

EP3-07

Biomarker discovery in early knee osteoarthritis using microRNA-sequencing

Shabana A Ali, Konstantin Shestopaloff, Rajiv Gandhi, Mohit Kapoor
Krembil Research Institute, University Health Network, Toronto, Canada

Conflict of interest: None

Objectives: Despite extensive research, there is still a lack of specific OA biomarkers that can be used in a therapeutic, prognostic, or diagnostic manner. Since microRNAs are promising biomarkers for several diseases, we previously used microRNA PCR-arrays and identified a panel of microRNAs in the synovial fluid that differentiate between early- and late-stage radiographic knee OA. We also performed microRNA microarrays and identified 2 microRNAs as mediators of cartilage degeneration. However, the gold standard approach to identifying biomarkers is next generation sequencing (NGS) because it offers the sensitivity and specificity to detect novel and low abundance microRNAs that are unique to early versus late OA. Here, we use NGS to identify signatures of circulating microRNAs as biomarkers for knee OA. **Methods:** Patient cohorts include healthy donors with no history of musculoskeletal disease (N=100), Kellgren-Lawrence grade-I for early OA (N=100), and Kellgren-Lawrence grade-III/IV for late OA (N=750). In a pilot experiment, 5 plasma samples from each group with a particular age, sex, body mass index, ethnicity, and comorbidity status were subjected to NGS using Illumina NextSeq500. Bioinformatic and statistical analyses were performed to filter and interpret the results. **Results:** The most differentially expressed microRNAs were identified based on false discovery rate less than 0.05, log counts per million greater than 2, and log fold change greater than 1.5. Hierarchical clustering of these microRNAs revealed a distinct pattern where 60 microRNAs were upregulated only in early OA samples. Among these are 4 novel putative microRNAs that have not previously been identified. We are currently repeating sequencing experiments in each group to validate and establish a clear microRNA signature for early knee OA. **Conclusion:** Our pilot data suggest that NGS is a powerful approach for identifying differentially expressed circulating microRNAs as biomarkers for knee OA.

EP3-08

Inhibitor of DNA binding 1 protein is expressed in rheumatoid arthritis

Takeo Isozaki, Masahiro Hosonuma, Airi Nishimi, Shinichiro Nishimi, Sho Ishii, Takahiro Tokunaga, Yuzo Ikari, Hidekazu Furuya, Kuninobu Wakabayashi, Tsuyoshi Kasama
Division of Rheumatology, Showa University School of Medicine, Japan

Conflict of interest: None

[Object] Angiogenesis is one of the important reaction in rheumatoid arthritis (RA) pathology. Inhibitor of DNA Binding 1 (Id1) is a transcription factor unique to endothelial progenitor cells (EPCs) that influences cell maturation. In this study, we showed Id1 expression in RA. [Methods] The levels of Id1 in RA and healthy controls serum were measured with enzyme-linked immunosorbent assays (ELISA). In order to investigate the relationship of disease activity, we measured correlations between Id1 and DAS28 (ESR) or MMP-3. In addition, to examine the differences of Id1 in RA serum with infliximab treatment, ELISA was used. Finally, to clarify the Id1 expression in RA synovium, immunohistochemistry was performed. [Results] Id1 in RA was significantly higher compared with that in healthy controls (mean \pm SE; 102 ± 20 pg/ml and 40 ± 15 pg/ml, $p < 0.05$, respectively). Id1 in RA was also positively correlated with DAS28 (ESR) and MMP-3. The levels of Id1 decreased after treatment with infliximab (pre: 102 ± 20 pg/ml and post: 58 ± 9 pg/ml, $p < 0.05$, respectively). Finally, we found that Id1 was expressed in RA synovial tissues. [Conclusions] Id1 is expressed on RA synovium and is correlated with disease activity.

EP3-09

Beclin-1 activator induces severe synovial fibrosis and does not protect cartilage from degeneration in a mouse model of OA

Jason S Rockel¹, Brian Wu¹, Sayaka Nakamura¹, Mohit Kapoor^{1,2,3}

¹Krembil Research Institute, University Health Network, Toronto, Ontario, Canada, ²Department of Surgery, University of Toronto, Ontario, Canada, ³Department of Laboratory Medicine and Pathobiology, University of Toronto, Ontario, Canada

Conflict of interest: None

Object: Beclin-1 is a component of the autophagy pathway necessary for formation of autophagosomes, contributing to autophagy-mediated cellular homeostasis. Enhancing autophagy through inhibition of mTOR activity, either via genetic deletion in chondrocytes or intra-articular injection of rapamycin, attenuates progression of surgically-induced models of osteoarthritis (OA). For this study, we sought to determine if a potent, soluble activator of Beclin-1 could also attenuate OA in a mouse model. **Methods:** Nine-week old C57BL/6 mice underwent destabilization of the medial meniscus (DMM) surgery to induce OA, or sham surgery as a control. Mice were injected intra-articularly with retro-inverso TAT-Beclin-1 (2mg/kg in 5 μ l) twice weekly for 9 weeks. Mice were sacrificed at 10-weeks post-surgery. Knee joints were stained with safranin-O/fast green to evaluate cartilage degeneration and Masson's trichrome to determine degree of synovitis using OARSI scoring for mice. Sections were stained for α -SMA (myofibroblast) and CD45 (hematopoietic-origin cell). **Results:** TAT-Beclin-1-treated mice showed no difference in the degree of articular cartilage degeneration in the tibia or femur of DMM surgical mice as compared to PBS-injected DMM mice. Surprisingly, in both sham and DMM mice, TAT-Beclin-1 treatment induced a pronounced thickening of the synovium with increased cell numbers and collagen deposition compared to PBS-treated mice. The increased number of synovial cells did not show substantial expression of α -SMA⁺ or CD45⁺ cells. **Conclusions:** Contradictory to our expected results, TAT-Beclin-1 did not attenuate cartilage degeneration. Rather, it exacerbated synovial thickening likely through cell proliferation and collagen deposition, resulting in a severe fibrotic phenotype independent of myofibroblast differentiation or inflammation. We are evaluating alternate injection and dosing strategies to determine if OA may be modified by TAT-Beclin-1 treatment.

AUTHORS' INDEX

- PL** **Presidential Lecture**
- PS** **Presidential Symposium**
- SS** **Special Symposium**
- S** **Symposium**
- EL** **Educational Lecture**
- MTE** **Meet the Expert**
- LS** **Luncheon Seminar**
- ES** **Evening Seminar**
- ACL-LS** **Annual Course Lecture Luncheon Seminar**
- W** **Workshop**
- ICW** **International Concurrent Workshop**
- P** **Poster Session**
- EP** **English Poster Session**

Bold Abstract No. Presenting Author

A			
Abe, Asami	S11-3, W25-4, W65-3, ICW2-2, P1-085, P1-088, P1-144, P1-170, P2-019, P2-155	Akebo, Hiroyuki	W42-6, W53-1, P3-030, P3-109, P3-147
Abe, Chizuru	P3-062	Akihiro, Nakamura	ICW13-2
Abe, Fumito	P2-066	Akioka, Shinji	W7-4
Abe, Hidekazu	S3-3, W24-2, P1-003, P1-086, P2-171	Akira, Taro	P2-097, P2-126 , P3-246, P3-259, P3-270
Abe, Kazuya	P3-251	Akita, Asami	W69-5, P3-203
Abe, Koki	EL24-1	Akita, Shosuke	W28-5, W50-6, W73-1, P1-149
Abe, Kyosuke	P3-050	Akiya, Kumiko	W10-5, W59-3, P2-249 , P3-293
Abe, Mai	W36-1, W37-4, W70-1 , W70-7, P1-001	Akiyama, Haruhiko	P1-148
Abe, Masanori	W40-2	Akiyama, Yoichiro	W28-6, P2-198, P3-150, P3-154, P3-177, P3-258, P3-302
Abe, Naoki	P2-250	Akiyama, Yuji	W45-5, W55-3, P1-082 , P3-280
Abe, Nobuya	W31-2-5, ICW4-3, ICW8-5, ICW10-2	Akizuki, Shuji	W9-5, W32-1, W78-6, P3-012, P3-091, P3-239
Abe, Saori	EL7, W1-2, W20-3, W43-3, W76-2, W76-5, ICW12-4, ICW14-4 , P2-111, P2-239, P2-240, P2-242	Akutsu, Yuko	W7-3
Abe, Takeo	P2-020	Alase, Adewonuola A	ICW17-5
Abe, Yoshiyuki	W70-5 , P1-097, P1-196, P2-223, P2-272 , P3-069, P3-103, P3-234	Ali, Shabana A	EP3-07
Adachi, Nobuo	S3-4	Alten, Rieke	ICW6-3
Adachi, Soichiro	P3-228	Amano, Eri	P3-278
Agarwal, Vikas	ICW20-6	Amano, Hirofumi	W26-3, P2-004, P2-187, P2-194, P2-199, P2-246
Agematsu, Kazunaga	W63-1, W63-5, ICW15-1	Amano, Kanzo	P2-159
Aggarwal, Amita	ICW8-2, ICW20-6	Amano, Koichi	W2-5, W3-3, W30-4, W35-4, W39-4, W60-3, W60-4, ICW6-2, ICW6-6, ICW7-3, ICW17-3, ICW20-5, P2-119
Ahmed, Sakir	ICW20-6	Amano, Norihiko	W3-5, W51-1, W77-4, P2-247 , P3-121
Aihara, Michiko	W69-5, P3-203, EP1-09	Amano, Tatsuaki	P3-183
Aita, Tetsushi	W31-1-1, W31-2-4, W36-5, W73-5, P1-064 , P2-060	Amano, Yuichiro	P2-137
Aizaki, Yoshimi	W17-5, ICW2-5, P2-006	Amasaki, Yoshiharu	W35-3, W47-4, P1-096, P3-228
Aizawa, Ayako	W34-3, P1-235, P2-219, P3-115	Amengual, Olga	W62-4, ICW3-5, ICW4-3, ICW4-4, ICW8-5, ICW10-2, ICW16-6, ICW19-4, P2-215, EP3-01
Aizawa, Toshiaki	S3-3, W24-2, P1-003, P1-086, P2-094 , P2-115, P2-171	Amin, Shreyasee	ICW17-4
Ajima, Chisaki	W35-2, P2-073 , P3-175	Amuro, Hideki	W18-4, W36-6, W51-5, W55-2, W55-6, W75-2, ICW6-1, ICW7-4, P1-231 , P2-052, P3-007, P3-048, P3-060, P3-116
Ajiro, Junya	P2-117, P3-066	An, Di	ICW6-3
Akagawa, Manabu	S3-3	Ancuta, Ioan	ICW5-6, EP2-06
Akagi, Midori	P2-206 , P3-062	Ando, Fumihiko	W29-6, P1-128
Akagi, Takahiko	W73-2, P1-063, P2-202 , P2-225	Ando, Kiichiro	P1-080
Akahoshi, Mitsuteru	W26-4, W33-2, W34-5, W65-1, ICW11-4, ICW14-6, P1-203, P2-037, P2-072, P2-221, P2-241, P3-052, P3-152, P3-202, P3-217, P3-254	Ando, Seiichiro	P2-194, P2-246
Akai, Yasuhiro	P2-052, P3-222	Ando, Takayasu	W39-3, W59-4, W64-6, W65-5, P2-105, P3-090 , P3-126, P3-284
Akamine, Keiji	P2-251 , P2-311	Anno, Shohei	W16-6, W23-6 , P2-062
Akao, Satoshi	P3-248	Antonova, Jenya	ICW7-6
Akasaki, Yukio	W26-2, ICW19-5, P1-065, P2-172	Aochi, Satsuki	W42-2, P2-300 , P3-037 , P3-176
Akashi, Kengo	W75-2, ICW6-1, ICW7-4, P1-107, P1-231, P2-052, P2-278 , P2-299, P3-077, P3-114, P3-181	Aoi, Hiroshi	P1-247
Akashi, Koichi	W26-4, W33-2, W34-5, W65-1, ICW11-4, ICW14-6, P1-203, P2-037, P2-072, P2-221, P3-052, P3-063, P3-152, P3-202, P3-217, P3-254	Aoki, Akiko	P3-269
Akashi, Yoshihiro	P1-100	Aoki, Kazutoshi	W14-1
Akazawa, Hiroki	W20-5, W22-6 , W28-2, P1-208, P2-212, P3-143, P3-178	Aoki, Naoko	W10-2, W55-4
		Aoki, Sadao	S21-3
		Aoki, Yasuaki	P1-006
		Aoki, Yuko	P1-014, P1-048, P1-057
		Aono, Hiroyuki	P2-001
		Aonuma, Hiroshi	S3-3, W24-2, P1-003, P1-086,

Blanco, Ricardo	W38-2	Ciofu, Claudia S	EP2-06
Bohgaki, Miyuki	W10-3	Clancy, Robert M	ICW17-4
Bohgaki, Toshiyuki	W62-4, ICW3-5, ICW4-3, ICW4-4, ICW8-5, ICW10-2, ICW16-6, ICW19-4, P2-215, EP3-01	Clark, Ken	W76-3
Bojinca, Mihai	ICW5-6, EP2-06	Claudia, Ciofu S	ICW5-6
Bono, Stephanie	W38-6	Cohen, Stanley	W38-3
Borada, Kaushik H	ICW22-5	Cseuz, Regina	ICW6-3
Brockett, Robert	ICW5-1	Curiel, Rodolfo V	ICW8-4
Bruce, Ian	W31-1-7	D	
Burmester, Gerd R	PS-1, SS2-1, S6-5, ES17-2, W30-3	Dan, Hidekazu	P1-006
Burns, Ariel	ICW4-6	Date, Hideki	P2-153
Buyon, Jill P	ICW17-4	Datta, Poulami	ICW21-3, ICW22-5
Byers, Nicole	W38-6	David, Harris	ICW14-3
C		De Vlam, Kurt	ICW6-2
Cai, Zhihong	P1-104	Deane, Kevin D	PS-2, ICW16-2
Camp, Heidi S	W38-3	Deguchi, Hitoshi	P2-226, P3-123
Cardiel, Mario	W31-1-7	Demoruelle, Kristen M	PS-2, ICW16-2
Carlier, Hilde	W44-2	Des Bordes, Jude K	EP2-11
Chae, Jin-nyeong	ICW13-1	Dickson, Chris	W39-1
Chan, Mable Wing Yan	ICW22-3	Ding, Feng	ICW3-1
Chang, Song Ho	P1-173	Dobashi, Hiroaki	S14-2, LS12-2, LS31, W10-4, W13-3, W20-4, W30-4, W70-5, W72-6, W78-2, W78-4, P3-226, P3-292
Chen, Hua	ICW14-2	Dobashi, Naofumi	P1-040, P1-193, P2-178
Chen, Jen-hao	ICW4-2	Doe, Kentaro	P1-129
Chen, Lei	W38-6	Doi, Hiroshi	W32-1, W78-6
Chen, Ming-han	ICW13-3	Doi, Kentaro	ICW10-1
Chen, Su	W38-2	Doi, Kohei	W26-1, W51-3
Chen, Weijia	W6-6, W22-5, P1-005	Doi, Takanobu	P1-172
Chen, Yi-Hsing	W38-4	Dore, Robin K	ICW7-6
Chen, Zhilei	ICW14-2	Dörner, Thomas	W31-1-7
Chen, Zhu	ICW8-6	Dorschner, Jessica M	ICW17-4
Cheng, Sue	W72-6	Dudek, Anna	ICW6-3
Chia, Jean-san	ICW4-2	E	
Chiba, Asako	W26-3, W79-3, W79-5, P1-020	Ebe, Hiroshi	P2-005
Chiba, Junji	P1-073, P1-115	Ebina, Kosuke	S3-2, S11-5, LS28-1, W36-6, W49-1, W51-5, W55-2, W55-6, W75-2, ICW2-1, ICW6-1, P1-149, P1-231, P2-052, P3-007
Chiba, Ko	W48-5, W48-6, P1-070	Ebisuno, Yukihiko	W8-1
Chiba, Noriyuki	W10-5, W34-1	Eguchi, Katsumi	W34-2, W37-2, W62-1, ICW15-1, ICW15-4, P2-122, P3-263
Chien-chih, Lai	ICW9-6	Eguchi, Kouhei	W31-1-2
Chifu, Yutaka	W59-5, P2-305	Eldred, Ann	W22-2
Chijiwa, Tatsumi	W6-1, W6-2, P1-009, P1-038, P1-133, P2-028, P2-065, P2-168	Elewaut, Dirk	LS1-2
Chikuda, Hirotaka	S11-6, MTE1, W8-5	Emery, Paul	S13-3, LS21, W38-3, W38-6, ICW17-5
Chin, Fangyi	W43-5, P2-228, P3-235, EP1-08	Endisha, Helal	ICW22-5
Chinen, Naofumi	P2-296, P3-106	Endo, Akiko	W41-1
Chino, Kentaro	W2-5, W3-3, W35-4, W39-4, W60-3, W60-4, ICW20-5, P2-119	Endo, Hirahito	W58-1, P2-038, P2-211
Chinone, Ori	W31-1-4	Endo, Naoto	ICW2-2, ICW2-3, ICW13-4, ICW22-2, EP2-12, EP2-13, EP2-14, EP3-06
Cho Hee, Bang	ICW22-4	Endo, Toshio	ICW10-1
Cho, Soo-kyung	ICW7-5	Endo, Yushiro	S2-3, W9-4, W11-5, W31-1-6, W32-2, W32-6, W33-5, W48-5,
Choe, Hyonmin	W50-2, W75-6, P2-166		
Choi, Seongmi	ICW7-5		
Choi, Sung Jae	ICW22-4		
Choi, Yunjung	EP3-05		
Chosa, Etsuo	P2-151, P2-169		
Chowdhary, Vaidehi R	ICW17-4		
Chriswell, Meagan	PS-2		
Chu, Hui	ICW14-1, ICW18-6		

	W62-5, ICW10-3 , ICW15-1, P1-037, P1-069, P3-171	Fujisawa, Junichi	ICW13-4, ICW22-2, P3-038, EP2-12 , EP2-13, EP2-14
Ernste, Floranne C	ICW17-4	Fujisawa, Yuhei	W61-5, P3-009
Eshiro, Hisako	P2-047	Fujishiro, Daisuke	W31-1-2
Etani, Yuki	ICW2-1	Fujita, Hideki	P3-033
Etori, Keishi	P3-166	Fujita, Kazuyuki	W60-2
Ezawa, Kazuhiko	S1-3, W66-5, P1-079	Fujita, Masaaki	P2-235, P3-132
		Fujita, Shinichiro	S1-3 , W66-5
F		Fujita, Shunichi	W73-2 , ICW1-6, P1-063, P2-202, P2-225
Favio, Enriquez-sosa	ICW6-3	Fujita, Takayuki	W40-2
Feser, Marie	PS-2	Fujita, Yoko	W20-6, W72-5
Friedman, Alan	W38-2, W38-3	Fujita, Yoshimasa	P3-225
Fujibayashi, Takayoshi	W28-1, W71-7, P2-051	Fujita, Yoshiro	W13-1, P1-054, P1-226 , P2-229, P2-276, P2-297, P3-107
Fujieda, Yuichiro	W35-3 , W47-4 , W54-5, W62-4, ICW3-5, ICW4-3, ICW4-4, ICW8-5, ICW10-2, ICW16-6, ICW19-4, P2-215, EP3-01	Fujita, Yukihiko	P2-253
Fujii, Asami	S2-4	Fujita, Yuya	W29-2, W43-2, W43-4, W55-1, W63-5 , ICW3-4, ICW15-4 , P1-021, P1-183, P1-204, P2-237
Fujii, Hiroshi	W20-6, W27-2, W72-5, ICW20-4	Fujiwara, Hiroshi	W46-4, W47-3, P2-049, P2-181, P3-156, P3-189
Fujii, Hiroshi	W42-1, W43-6, W56-6, W61-5, P3-009 , P3-067, P3-102, P3-192	Fujiwara, Hiroyoshi	W25-1, W25-2
Fujii, Ryoji	P2-001	Fujiwara, Kazuo	P1-068
Fujii, Takao	MTE15 , ES8-2 , W30-1, P2-018, P2-041, P2-128	Fujiwara, Michio	W31-1-4
Fujikawa, Keita	W9-4 , W32-2, W33-5, P1-053	Fujiwara, Toshifumi	W26-2, ICW19-5 , P1-041, P1-065, P2-172
Fujikawa, Satoshi	W7-2	Fujiwara, Yuko	P1-131, P1-222
Fujikawa, Yoshikazu	ICW7-4, P1-098, P1-107, P2-278, P3-114	Fukae, Jun	P1-014, P1-048, P1-057
Fujiki, Youhei	W1-6, W2-1, W13-4, W58-6, P2-058, P2-116, P2-196 , P2-216, P3-073, P3-108, P3-122, P3-125, P3-157, P3-274	Fukasawa, Chikako	W58-2
Fujimaki, Hiroshi	W74-2	Fukaya, Naoki	P1-066
Fujimori, Misuzu	S1-3, W66-5, P1-079	Fukaya, Shinji	W11-7 , W35-3
Fujimoto, Hisae	W12-4, W39-3, W59-4, W64-6, W65-5, P1-046, P2-105, P3-090, P3-126 , P3-284	Fukaya, Shusaku	W2-2, W12-6, W77-6, P2-236, P3-113
Fujimoto, Kyoko	W54-1, P3-096, P3-186, P3-289	Fuke, Yoshinobu	W40-2
Fujimoto, Manabu	S7-4, W58-1	Fukuda, Koji	W8-6, W15-1, W51-4, P1-029 , P1-035, P1-090, P2-042, P2-089 , P3-014
Fujimoto, Minoru	W2-4	Fukuda, Masashi	P1-050, P1-205
Fujimoto, Shino	S21-2, S21-3, P2-292 , P3-225	Fukuda, Michio	P3-080, P3-224
Fujimoto, Sho	P3-233	Fukuda, Natsuko	P3-265
Fujimoto, Takashi	P1-247, P2-052, P3-222	Fukuda, Takaaki	W37-2
Fujimura, Kenjiro	P1-150, P1-151, P1-165, P2-161 , P2-167, P2-185	Fukuda, Wataru	W34-4 , W44-5, W73-3, P1-236 , P2-077, P3-089
Fujimura, Takanori	W9-2, P1-247	Fukue, Ryosuke	W8-2
Fujinaga, Hiroshi	W19-4, P1-141	Fukuhara, Shunichi	S17-1
Fujio, Keishi	S5-2, ES15-1 , ES7-2 , W1-5, W9-6, W30-1, W52-1, W52-5, W64-3, W72-1, W78-5, ICW1-2, ICW1-4, ICW6-4, ICW7-3, ICW11-3, ICW18-1, ICW18-4, ICW21-1, P1-201, P1-234, P3-022, EP1-03	Fukui, Akihiro	P3-029
Fujioka, Kazuki	W18-2, W27-6, W33-3, W60-6 , W77-1, P2-087, P2-210, P2-301, P2-303, P3-042, P3-046, P3-128, P3-170, P3-212, P3-243	Fukui, Jun	W46-4, W47-3, P2-049 , P2-181, P3-156, P3-189
Fujioka, Kei	W63-3, P1-077 , P3-071	Fukui, Naoshi	W26-6, P2-011
		Fukui, Sho	P2-227, P3-196, P3-213
		Fukumi, Sachiko	P3-065
		Fukuoka, Kazuhito	W40-5, W41-1, W60-1, P1-125
		Fukushi, Junichi	W26-2, ICW19-5, P1-065, P2-172
		Fukushima, Mayuko	W73-2, P1-063 , P2-202, P2-225
		Fukushima, Toshihiro	P2-292
		Fukuyo, Shunsuke	W4-1, W13-2, W51-2, W55-1, ICW6-5 , ICW7-1, ICW8-1, ICW9-4, ICW12-1, ICW12-2, ICW12-6,

	ICW13-5, ICW14-5, ICW17-2, ICW17-6, ICW19-2, ICW21-5, P3-300, EP1-04	Gomez, Elisa	W31-1-7
Funabiki, Masahide	P3-040	Gómez-aristizábal, Alejandro	ICW22-3, EP3-02
Funada, Masashi	ICW3-4	Gómez-reino Carnota, Juan José	W30-3
Funahashi, Keiko	S1-2 , W8-6, W51-4, P1-010 , P1-011 , P1-035, P1-090, P2-089, P2-123, P3-014	Gono, Takahisa	EL18 , LS10 , W1-1 , W3-1, W21-4, W23-2, W54-6, W67-3, W69-1, W69-2, P1-229, P3-230
Funahashi, Koji	W49-6, P1-066 , P2-021	Goodman, Brent P	ICW19-1
Funahashi, Shinji	P2-096, P2-114	Goronzy, Jorg	ICW5-1
Funaki, Masamoto	W2-6, P2-147	Goshima, Atsushi	P1-127, P2-310
Funaki, Yoshihiro	W11-4, P1-012, P2-259	Goto, Daisuke	W58-1
Funakoshi, Kenji	W46-4, W47-3 , P2-049, P2-181, P3-156 , P3-189	Goto, Hisatsugu	P2-142
Funakoshi, Noboru	W74-6	Goto, Hitoshi	P3-195, P3-244
Funakubo, Yu	W28-3, W55-3, P1-008, P1-082, P2-201, P3-138	Goto, Manaka	P1-224
Funamura, Kei	P1-216	Goto, Mikako	S9-5 , W13-1, W13-6, P3-308
Funauchi, Masanori	S20-4 , W20-5, W22-6, W28-2, W35-6, W46-2, W65-4, W75-1, P1-095, P1-207, P1-208, P2-054, P2-090, P2-212, P3-143, P3-178	Goto, Tomohiro	P1-062
Furie, Richard	W31-1-7	Goto, Yoshimasa	P3-288
Furu, Moritoshi	P1-058	Goto, Yutaka	W39-3, W59-4 , W64-6, W65-5, P1-046, P2-105, P3-090, P3-126, P3-284
Furuichi, Kengo	P2-068, P3-051	Gottenberg, Jacques-eric	ICW6-2
Furukawa, Hiroshi	W41-6, ICW15-4, P2-011	Graham, Neil	W30-2
Furukawa, Masaaki	W35-2, P2-073	Green, Peter J	ICW4-6
Furukawa, Shin	W35-3, W47-4, P3-083	Greenstein, Andrew	ICW5-1
Furukawa, Shogo	W4-4 , P1-199, P3-304	Greenwald, Maria	ICW6-3
Furukawa, Tetsuya	W51-6, P2-139, P2-213 , P3-082, P3-094, P3-173, P3-249	Greer, Joy	ICW6-3
Furumitsu, Yutaka	W53-6	Grill, Marie	ICW19-1
Furusaki, Akira	P1-096 , P2-043	Grundeken, Vincent	W48-2
Furuta, Rie	P2-063	Gu, Jieruo	ICW3-1
Furuta, Shunsuke	W4-3, W12-5, W40-6, P1-050, P1-205, P3-104	Guo, Ying	ICW6-2
Furuya, Hidekazu	W17-2, P1-024, P1-032 , P2-002, P2-034, EP3-08	Gupta, Latika	ICW8-2 , ICW20-6
Furuya, Hiroki	P1-050, P3-104	Gushiken, Kikuko	P2-030, P2-131
Furuya, Kazuhiro	W64-1	Guzman, Maria Roselle E	EP1-13
Furuya Yashiro, Makiko	W43-2, W63-5, ICW15-4, P1-021, P1-183, P1-204, P2-237		
Furuyama, Kotona	W17-3 , P2-009	H —————	
Furuyama, Masako	W47-1, P2-207	Haemmerle, Sibylle	W44-1
Fusama, Mie	LS4	Haga, Hironori	W26-1
Futami, Hidekazu	W33-1, ICW18-2, P1-039 , P1-233	Haga, Nobuhiko	W49-6
Fuwa, Tatsunari	P1-245	Hagimori, Kohei	W22-3
		Hagino, Hiroshi	P1-146, P1-247, P2-100, P2-174
		Hagino, Noboru	EL9 , P1-102, P1-232
		Hagino, Owen	W30-2, P1-099
		Haginoya, Toshiko	P2-070
		Hagio, Tomonobu	P1-171
		Hagita, Junichiro	P1-066, P1-220 , P3-286
		Hagiwara, Kiyofumi	P2-274
		Hagiwara, Shigeo	W50-1, P2-262
		Hagiwara, Takafumi	W36-2 , P1-101, P1-123
		Hagiyama, Hiroyuki	W34-4, P1-236, P3-120
		Haji, Yoichiro	P2-229 , P3-160
		Hajime, Maiko	ICW11-2, ICW11-5 , ICW11-6, ICW17-1
		Hamada, Akihiko	P1-239 , P1-241
		Hamada, Daisuke	P1-062
		Hamada, Hiroaki	P2-149 , P2-151, P2-169
		Hamada, Hiroshi	P3-098 , P3-205
G —————			
Gallant, Christopher	ICW4-6		
Gamo, Kanae	W8-1		
Gandhi, Rajiv	ICW22-3, ICW22-5, EP3-02, EP3-07		
Gao, Jie	ICW6-2		
Gavrila, Bogdan I	ICW5-6 , EP2-06		
Gellett, Amanda M	W22-1		
Genovese, Mark C	W30-3, W39-1, ICW6-2, ICW6-3		
Gill, Navjeet	ICW3-3		
Glowacka-kulesz, Maria	ICW6-3		

Hamada, Kazuya	P2-254	Harigae, Hideo	W20-6, W27-2, W72-5, ICW20-4
Hamada, Naoki	W31-2-2, ICW3-2, ICW12-3, P1-034, P1-179, P2-188, P2-277, P2-281, EP1-09	Harigai, Masayoshi	S7-3, S13-2, EL24-2, LS9-1 , W21-1, W31-2-3, W32-5, W37-5, W38-6, W39-1 , W41-5, W41-6, W68-4, W70-4, W70-5, P2-071, P2-128, P3-167
Hamada, Riku	P2-251	Harigane, Kengo	W75-6
Hamaguchi, Marina	W59-3, ICW10-4, ICW10-5, P1-211, P3-210, P3-293	Haro, Hirota	P1-155, P3-262
Hamano, Ryoko	W43-6	Harvey, Nicholas C	S8-5
Hamano, Yoshimasa	P2-226, P3-123	Hase, Kayoko	W27-3
Hamamoto, Kazuhiro	P2-134, P2-205	Hasegawa, Eiko	W21-6, W53-4, P1-055
Hamatani, Hiroko	W32-4, P2-012	Hasegawa, Eriko	W25-4, W65-3, ICW2-2, P1-085 , P1-088, P1-144, P2-019, P2-155
Hammer, Anne	W76-3	Hasegawa, Hitoshi	W21-3, W41-2, W47-6, P1-052
Hanabayashi, Masahiro	W71-7	Hasegawa, Ken	W57-5 , P2-030, P2-131
Hanai, Shunichiro	W4-3, P3-175 , P3-262	Hasegawa, Kiminori	P1-096, P1-119
Hanami, Kentaro	W13-2, W51-2, W55-1, ICW6-5, ICW7-1, ICW8-1, ICW12-1, ICW12-2, ICW12-6, ICW13-5, ICW14-5, ICW17-2, ICW17-6, ICW21-5, P3-300	Hasegawa, Masahiro	P2-074, P2-163
Hanaoka, Hideki	W29-6, P1-128	Hasegawa, Minoru	W58-1
Hanaoka, Hironari	W11-3, W20-2, W31-2-1, W31-2-6 , W33-6, P1-135	Hasegawa, Takakazu	P2-197 , P3-098, P3-164, P3-205, P3-221, P3-283
Hanaoka, Masanori	W79-4, P1-186, P1-206 , P2-071, P2-220, P2-232, P3-070, P3-167, P3-219	Hasegawa, Yasuhiro	W31-1-3 , P2-189, P3-092, P3-190
Hanaoka, Ryosuke	P2-070	Hashiba, Yayoi	W29-4, W34-3, W57-6
Hanata, Norio	W1-5, W52-5, ICW11-3	Hashiguchi, Tomomitsu	W5-6
Handa, Tomohiro	P3-091	Hashimoto, Atsushi	W10-5, W16-2, W34-1 , W55-5, W71-1 , P1-008, P1-043, P2-011
Handa, Yuichi	W33-4, W34-4, P1-236, P3-149, P3-216	Hashimoto, Hiroo	P3-018
Hanioka, Yusuke	P3-195, P3-244	Hashimoto, Hiroshi	W41-6
Hanly, John G	S4-1 , ICW4-6	Hashimoto, Jun	S3-2, S11-5, MTE2 , W28-5, W49-1, W49-6, W50-6, W61-3, W73-1, ICW9-1, ICW9-2, P1-061, P1-149, P2-036, P2-067, P3-036, P3-078
Hanyu, Tadamasa	W34-4, ICW22-2, P1-162, P1-236	Hashimoto, Keisuke	P1-010, P1-011
Hara, Akinori	P2-068	Hashimoto, Kotaro	P3-167
Hara, Kazusato	P3-220	Hashimoto, Marowa	W8-6 , W51-4, P1-035, P1-090, P2-089, P3-014
Hara, Ryoki	W3-4, W57-1, P2-244, P2-265	Hashimoto, Masahiro	ICW10-1
Hara, Ryosuke	P1-215 , P3-088	Hashimoto, Motomu	LS27, ES10-2 , W7-4, W9-5, W32-1, W36-6, W50-5, W51-3, W51-5, W55-2, W55-6, W75-2, W78-6, ICW6-1, ICW7-4, ICW16-1, P1-058, P1-231, P1-240, P2-052, P3-007, P3-012, P3-091, P3-239
Hara, Ryota	S3-5 , W9-2, W36-6, W51-5, W55-2, W55-6, W75-2, ICW6-1, ICW7-4, P1-231, P1-247, P2-052 , P3-007	Hashimoto, Naoaki	W54-3
Hara, Satoshi	W42-1, W43-6, W56-6, P3-009, P3-067, P3-102, P3-192	Hashimoto, Takako	W2-2, W12-6, W77-6, P2-236, P3-113
Harada, Hiroaki	W1-5	Hashimoto, Takenori	W54-3
Harada, Koji	P3-017	Hashimoto, Teppei	W41-3 , W47-5, W51-6, P2-107, P2-139, P3-015, P3-082, P3-094, P3-173, P3-185, P3-249, P3-256
Harada, Mariko	P3-234	Hashimoto, Yoshinori	P2-145
Harada, Ryozo	S1-3, S11-2, W66-5 , P1-079	Hashiramoto, Akira	W17-6, W37-6, W41-3, P1-030, P1-033
Harada, Tomoya	W11-4 , P1-012, P2-259	Hasui, Keisuke	W12-1, P2-108 , P2-193
Harada, Toshihiko	P1-153	Hata, Kenichiro	W1-6, W23-4, W51-5, W52-6, W58-6, W61-4, W75-2, P2-058, P2-116, P2-196, P2-216 , P3-073, P3-108, P3-122, P3-125, P3-157, P3-274
Harada, Yoshinori	W28-5, W61-3, W73-1, ICW9-1, ICW9-2, P1-061, P2-036, P2-067, P3-078 , P3-118		
Haraguchi, Akihisa	W26-2, P1-041		
Haraguchi, Kazushi	P2-263		
Harai, Hiroaki	LS17		
Harama, Kimie	W4-3, P3-175, P3-266		
Haraoka, Hitomi	W54-5, W59-3, ICW6-6, ICW10-4, ICW10-5, P1-211, P3-033, P3-047, P3-210, P3-293		

Hatachi, Saori	W3-5, W51-1, W77-4, ICW1-1, P2-247, P3-121	Higuchi, Toshie	P3-303 W62-3
Hatakeyama, Akira	P3-247	Higuchi, Yoko	W36-1, W37-4, W70-1, W70-7, P1-001
Hatano, Hiroaki	W46-3, W52-1, W64-3, W72-1, ICW1-2 , ICW1-4, ICW11-3	Hikiami, Hiroaki	P1-141
Hatano, Mika	W65-6, P1-105, P1-191 , P2-280, P3-144	Himuro, Naoko	P1-171
Hataya, Hiroshi	P2-251	Hinamoto, Norikazu	P3-172
Hatta, Kazuhiro	W30-4, W42-6 , W53-1, P3-030 , P3-091, P3-109, P3-147	Hino, Shoichi	W22-6
Hattori, Koto	W31-1-4	Hinz, Boris	ICW21-3
Hattori, Kyosuke	W24-5	Hioki, Shigeru	W74-3, P1-142
Hattori, Seira	W3-4, W57-1, P2-244 , P2-265	Hira, Kayo	P2-283
Hattori, Shuhei	P1-102, P1-232	Hirabayashi, Hiromi	P2-208, P2-234
Hattori, Toshiyuki	P1-014, P1-048, P1-057	Hirabayashi, Yasuhiko	W20-6, P1-091
Hattori, Yosuke	W28-1, W65-2 , W71-5, W71-7, P1-154, P2-035, P2-083, P2-136	Hiraga, Hiroto	W12-1, P2-108, P2-193
Hayakawa, Kazue	P2-153	Hiraga, Kenichi	W57-2, P2-200, P3-211
Hayami, Noriko	W53-4, P1-055	Hiraguri, Masaki	W42-4, P2-290
Hayashi, Ayano	ES4, W74-1 , P1-152	Hirahara, Lisa	P1-102, P1-232
Hayashi, Daiki	P2-068	Hirahara, Shinya	W31-2-3, W79-4 , P1-206, P2-071, P2-232, P3-070, P3-167, P3-219
Hayashi, Eri	W44-3, P3-234, P3-282	Hirai, Takayuki	P3-199
Hayashi, Haeru	W78-5, P1-016, P1-017, P2-291, P2-295, P2-307	Hiraiwa, Toshihito	W19-4
Hayashi, Hiroaki	W73-2	Hiramatsu, Rikako	P1-055
Hayashi, Junji	W5-2	Hiramatsu, Yuri	W13-1, W13-4 , P2-116
Hayashi, Keigo	W40-1, P2-024 , EP1-02	Hiramoto, Kazuoto	W31-2-6, ICW10-1
Hayashi, Makiko	W54-1, W69-3, P3-096, P3-186 , P3-289	Hirano, Aiko	W27-6, P3-046 , P3-128, P3-170, P3-212, P3-243
Hayashi, Masatoshi	W28-1, W34-4, W71-7, P1-236	Hirano, Daisuke	W2-2, W12-6, W77-6, P2-236, P3-113
Hayashi, Nobuhide	W68-6	Hirano, Fuminori	W10-5, W34-1
Hayashi, Norihide	W9-1, W36-4, W45-2, P1-188, P2-218, EP2-04 , EP2-09	Hirano, Fumio	S9-7, W37-5, W41-6, P3-305
Hayashi, Noriyuki	W53-6	Hirano, Hiroyasu	W73-2, ICW4-5, ICW15-2, P2-202, P2-225
Hayashi, Reika	W3-2, W32-3, P1-056	Hirano, Kazuki	P1-180, P2-306, P3-084, P3-087 , P3-184
Hayashi, Seigaku	W68-5	Hirano, Motoharu	W74-2
Hayashi, Shinya	W8-6, W51-4, P1-029, P1-035, P1-090 , P2-089, P3-014	Hirano, Toru	W31-2-5, W36-6, W45-4, W48-3 , W51-5, W55-2, W55-6, W75-2, ICW7-4, P1-231, P3-049, P3-311
Hayashi, Taichi	W70-5, P2-191	Hirano, Yuji	LS13-1 , W19-3 , W28-1, W71-7, W75-4, P1-049, P1-075, P2-051, P2-102 , P2-118, P2-175
Hayashi, Tomoki	W65-6, P1-105, P1-182, P1-192, P2-280 , P3-144	Hirao, Makoto	S3-2 , S11-5 , W49-1 , W55-2, W55-6, ICW2-1, P1-149
Hayashibara, Masako	P1-146, P2-100 , P2-174	Hiraoka, Daisuke	P2-183, P2-230, P2-302
Hazama, Momoko	P1-197	Hirase, Nobuhisa	P1-218 , P3-059
Hazue, Ryo	W10-1, P3-044	Hirata, Ayako	W9-1, W36-4 , W45-2, P1-188, P2-218, EP2-04, EP2-09
Heap, Graham	W22-2	Hirata, Manami	W4-6, W60-2, W71-4 , P3-162
Hemmi, Seiichiro	W40-2	Hirata, Shintaro	MTE21 , W4-5, W30-4, W57-4 , ICW6-6, ICW7-3, P1-036, P2-010, P2-217, P3-072, P3-091, P3-131, P3-268, P3-279
Henmi, Mihoko	P1-014, P1-048 , P1-057	Hirata, Shinya	P2-063
Hibi, Arata	P3-061	Hirayama, Takehiro	P2-097, P2-126, P3-204, P3-246, P3-259, P3-270
Hidaka, Noriaki	ICW22-6, P3-001, P3-003, P3-004, P3-005, P3-006	Hirohata, Shunsei	S14-2, P1-202, P3-229
Hidaka, Toshihiko	W29-4 , W34-3, W37-2, W57-6	Hiromura, Keiju	W32-4, P2-012
Hidaka, Yukiko	P3-096, P3-186, P3-289	Hirooka, Yasuaki	W20-5, W22-6, W35-6 , P1-095,
Hidekawa, Chiharu	W31-2-2, ICW3-2, ICW12-3, P1-034, P1-179, P2-188, P2-277, P2-281 , P3-198		
Higashioka, Kazuhiko	ICW14-6 , P2-241		
Higashiyama, Mari	P3-036		
Higuchi, Makiko	P1-212, P2-025, P3-161 , P3-253,		

	P1-207	Hoshino, Junichi	W21-6, W53-4, P1-055
Hirose, Hikaru	P3-219	Hoshino, Keisuke	P2-096, P2-114
Hirose, Jun	W9-6, ICW22-1, P1-173, P3-022	Hoshino, Tomoaki	W69-3, P3-096, P3-186, P3-289
Hirose, Kei	W4-6, W60-2 , W71-4, P3-162	Hoshiyama, Takayuki	W31-1-3, P2-189, P3-092, P3-190
Hirose, Sachiko	P2-004	Hosoi, Satoshi	P3-310
Hirose, Tatsuo	P2-143	Hosokawa, Takashi	W46-4 , W47-3, P2-049, P2-181, P3-156, P3-189
Hiroshima, Ryo	P1-002		
Hirota, Keiji	S12-4	Hosokawa, Yohei	W2-6, P2-039, P2-112
Hirota, Takuo	P3-099	Hosono, Yuji	P3-091
Hiroumi, Shiori	P1-112, P3-043	Hosonuma, Masahiro	W17-2, P1-024, P1-105, P1-192 , P2-002, P2-034, EP3-08
Hisada, Ryo	W47-4, EP3-01		
Hisada, Yukimasa	P3-051	Hosoya, Tadashi	P1-022
Hisatome, Ichiro	S14-1	Hounoki, Hiroyuki	P1-023, P2-285, P3-064, P3-076, P3-086, P3-180, P3-182, P3-207
Hiura, Junki	P1-122		
Ho-chang, Kuo	ICW20-2, EP1-06	Howarth, Peter	LS2-2
Hoffman, Robert	W31-1-7	Hsieh, Evelyn	EP2-07
Hojo, Tatsuya	W74-6	Hsieh, Song-chou	ICW4-2
Holers, Michael V	PS-2 , ICW16-2	Huizinga, Tom WJ	S13-5, LS14
Honda, Fumika	EL7, W1-2, W20-3, W43-3, W54-5 , W76-2, W76-5, ICW12-4, ICW14-4, P2-111, P2-239, P2-240, P2-242	Hung, Ming-li	EP2-05
		Hyodo, Chinatsu	P1-125
Honda, Manabu	P1-121, P3-093 , P3-309	Hyodo, Yuka	P1-112, P3-043
Honda, Nanase	W66-2, P1-184, P1-224, P2-224, P2-264, P2-282, P2-287, P2-296, P2-311, P3-031, P3-074, P3-081 , P3-276	I	
		Iagnocco, Annamaria	SS2-2
Honda, Saho	W42-2, P2-300, P3-037	Ibayashi, Yuta	P3-063
Honda, Seiyo	P3-111	Ichihara, Shie	P3-187
Honda, Suguru	W32-5 , W68-4, W70-4	Ichikawa, Kenji	W10-5, W34-1
Honda, Zenichiro	P2-195, P3-232	Ichikawa, Naomi	W66-3, P2-309
Honma, Ryusuke	P2-013 , P2-016	Ichikawa, Norihiro	P1-138, P2-180
Honma, Sakae	W41-6	Ichikawa, Shinya	P3-050
Horai, Yoshiro	W32-2, W37-2, P2-206, P3-062	Ichikawa, Takanori	W46-1, P2-288, P3-054 , P3-168, P3-208
Hori, Hiroshi	P1-087		
Horie, Koichiro	W16-2, P1-043	Ichikawa, Tetsuya	W49-5, P1-044
Horii, Takeshi	P2-150	Ichimura, Yuki	W58-2
Horii, Yuka	P1-248	Ichinohe, Kazue	P2-027
Horikawa, Yukio	P3-099	Ichinose, Kunihiro	W31-1-6 , W31-2-2, W32-2, W32-6, W33-5 , W34-2, W37-2, W43-4, W47-1, W48-5, W62-5, ICW3-2, ICW10-3, ICW15-1, P1-037, P1-069, P1-179, P1-182, P1-187, P1-191, P2-188, P2-277, P2-281, P3-171
Horikoshi, Hideyuki	W67-2 , W67-6		
Horikoshi, Masanobu	W33-4 , P3-149, P3-216	Ichise, Yoshihide	W9-2, ICW7-4, P1-107, P2-278, P3-114
Horino, Taro	W40-3, W58-3, P1-185 , P3-032, P3-134, P3-278		
		Ida, Hiroaki	W54-1, W63-2, W69-3, P3-096, P3-186, P3-289
Horita, Masahiro	P1-251		
Horita, Shigeto	P1-210, P3-009	Iemura, Fumika	P2-291
Horita, Tetsuya	W4-2, W35-3	Iesaka, Hiroshi	W4-2
Horiuchi, Hiroshi	W66-6	Igarashi, Hiroko	W58-5
Horiuchi, Takahiko	EL25 , W26-4, W33-2, W34-5, W59-5, W60-5, W65-1, W79-6, ICW11-4, ICW14-6, ICW15-2, P1-203, P2-037, P2-072, P2-221, P2-241, P3-052, P3-063, P3-152, P3-202, P3-217, P3-254	Igarashi, Toru	W7-2
		Igarashi, Toshihisa	W72-4
Horiuchi, Tomonari	P2-056	Igawa, Takashi	W31-1-6, W32-6 , W33-5, W43-4, W48-5, W62-5, P1-037, P1-069, P3-171
Hosaka, Michio	W65-6		
Hosen, Naoki	EL1	Iguchi, Mikiko	W53-2
Hoshi, Tetsuya	P3-176	Ihara, Koji	P2-146
Hoshi, Yousuke	W72-5	Ihata, Atsushi	W10-5, W13-1, W72-4
Hoshida, Yoshihiko	W10-5 , P3-118	Ihn, Hironobu	S7-5 , W58-1, P2-214, P2-222
		Iida, Harunobu	W11-3 , W39-3, W59-4, W64-6,

	W65-5, P2-105, P3-090, P3-126, P3-284	Imamura, Mitsuru	W39-3, W59-4, W64-6, W65-5, P2-105, P3-090, P3-126, P3-284
Iida, Kazuma	W42-4	Imamura, Munetsugu	W36-4, P1-188, P2-218, EP2-04
Iida, Mami	P2-204	Imoto, Kazuhiko	P1-225, P2-289
Iida, Masahiro	W66-2, P1-184, P1-224, P2-224, P2-264, P2-282, P2-287, P2-296, P2-311, P3-031, P3-074, P3-081, P3-276	Imoto, Seiya	S16-2
Iida, Satoshi	P2-176, P2-182	Imura, Haruki	P2-294
Iimura, Yukiya	P3-194	Imura, Yoshitaka	P2-235, P3-091, P3-132
Iizuka, Yuki	W31-2-2, W72-4, ICW3-2, ICW12-3, P1-034, P2-188, P2-277, P2-281, P3-198	Inaba, Masaaki	W53-6
Ikai, Hiroki	P1-054 , P1-226, P2-276, P2-297, P3-107	Inaba, Yutaka	W50-2, W74-2, W75-6, P2-166
Ikari, Katsunori	S3-6, MTE19 , LS20-1 , W7-2, W36-1, W37-4, W49-4, W70-1, W70-7, ICW16-1, P1-001, P1-002, P1-115, P1-163, P1-169	Inagaki, Katsunori	P1-024, P1-170
Ikari, Yuzo	W17-2, P1-024, P1-032, P2-002 , P2-034, EP3-08	Inamo, Jun	ICW1-5 , ICW10-1, ICW20-3
Ikechi, Yuta	W31-1-2	Inamo, Yasuji	P2-253
Ikeda, Fusayo	W20-5, W22-6, W28-2, P1-208 , P2-212, P3-143, P3-178	Ino, Kazuma	W31-1-3, P2-189, P3-092 , P3-190
Ikeda, Kei	S2-6 , EL20 , W12-5, W29-6, W40-6, W47-2, P1-050 , P1-205, P2-022, P3-104, P3-251	Inokuchi, Shoichiro	W34-5, ICW11-4 , P2-241, P3-052, P3-254
Ikeda, Keigo	P3-095, P3-129, P3-193	Inokuma, Shigeko	W34-4, W57-2, P1-236, P3-288
Ikeda, Nobuaki	W69-5, P3-203	Inoo, Masayuki	W30-4, ICW6-6, P1-100
Ikeda, Takahide	W35-5 , W63-3, W78-1, P2-190, P2-261, P3-255	Inotani, Satoshi	W40-3, W58-3, P1-185, P3-032, P3-134, P3-278
Ikeda, Wataru	P1-027	Inoue, Akira	W15-5 , W39-5, P1-174 , P2-138, P2-141
Ikeda, Yukihiko	P2-227, P3-196 , P3-213	Inoue, Asuka	W20-5, W22-6, W28-2, W35-6, W65-4, P1-095, P1-207, P1-208, P2-090, P2-212, P3-143, P3-178
Ikegaya, Noriko	W40-5, W41-1	Inoue, Ayaka	P1-118, P1-230, P1-237 , P2-098, P2-130, P2-279, P3-238
Ikemura, Satoshi	W26-2, ICW19-5, P1-065 , P2-172	Inoue, Eisuke	MTE16 , W7-2, W36-1, W37-4, W70-1, W70-7, P1-001
Ikenaka, Tatsuoh	P1-043	Inoue, Hironori	P3-046, P3-128 , P3-170, P3-212, P3-243
Ikeno, Yoshihiko	W34-4, P1-236	Inoue, Hisako	W59-5, W60-5
Ikeuchi, Hidekazu	W32-4, P2-012	Inoue, Hisashi	S18-6 , W44-3, P3-282
Ikeuchi, Hiroko	P2-183, P2-230, P2-302	Inoue, Hisayoshi	P3-247
Ikezawa, Taiga	P2-134, P2-205	Inoue, Junpei	P2-096 , P2-114
Ikka, Tsunakuni	EL14	Inoue, Kenshi	P1-040, P1-193 , P2-178
Ikuma, Daisuke	W53-4, P1-055	Inoue, Kie	S1-3, W66-5
Ikumi, Natsumi	W59-3, ICW10-4, ICW10-5, P1-211, P3-033 , P3-047, P3-210, P3-293	Inoue, Koji	P3-299
Ikuta, Ken	P1-066	Inoue, Kosuke	W40-3, W58-3, P1-185, P3-032, P3-134, P3-278
Ikuta, Kenji	P1-209	Inoue, Mariko	ICW6-4 , ICW18-1, ICW18-4, P3-022
Ikuta, Yasunari	S3-4	Inoue, Megumi	P1-239, P1-241
Im, Seul Gi	ICW7-5	Inoue, Mitsuyo	LS29-1
Imada, Chiharu	W1-4	Inoue, Natsumi	W7-6
Imafuku, Aya	W21-6	Inoue, Ryo	W61-5
Imafuku, Shinichi	S6-4 , EL8	Inoue, Sanshiro	P3-233
Imagama, Takashi	P2-270	Inoue, Takuya	W18-2, W33-3, W60-6, W77-1, P2-210, P2-301 , P2-303
Imai, Atsuko	P1-010, P1-011	Inoue, Tatsuo	P3-297
Imai, Kai	P3-048, P3-267	Inoue, Yasuo	P1-073 , P1-115
Imai, Shunichi	P2-030 , P2-131	Inoue, Yasushi	W59-5, W60-5, P3-152
Imai, Toshio	W52-2, P1-027	Inoue, Yoshikazu	S10-6
Imaizumi, Chihiro	W9-1, W36-4, W45-2, P1-188 , P2-218, EP2-04, EP2-09	Inoue, Yoshino	ICW3-4, ICW8-1, ICW12-1, ICW12-2, ICW17-2 , P3-300
		Inoue, Yuki	W9-1, W36-4, W45-2, P1-188, P2-218 , EP2-04, EP2-09
		Inoue, Yuzaburo	S9-4 , P2-290
		Inui, Hiroshi	S5-2

Inui, Kentaro	S2-4, W5-1, W16-5, W16-6, W23-6, W36-3, W37-1, W44-6, W68-1, W70-6, P2-023, P2-062, P3-004, P3-005, P3-008, P3-019, P3-020, P3-021, P3-290, P3-301		
Inui, Saori	W63-3, P1-077, P3-071		
Irabu, Hitoshi	W7-6		
Irino, Kensuke	P2-241, P3-152		
Isaacs, John D	LS8		
Iseki, Masako	LS33-2		
Iseki, Masanori	ICW1-6, ICW15-2		
Ishibashi, Mika	P1-239, P1-241		
Ishibashi, Yasuyuki	P2-027, P3-002		
Ishibe, Yusuke	P3-295		
Ishida, Motoko	P1-212, P2-025, P3-161, P3-253, P3-303		
Ishida, Takaaki	W1-6, W2-4 , W13-4, W58-4, W58-6, P2-058, P2-116, P2-196, P3-122, P3-125, P3-157, P3-274		
Ishie, Shinichiro	W51-3		
Ishigaki, Kazuyoshi	S5-2		
Ishigaki, Sho	W10-1, P3-044		
Ishigaki, Yasuhito	S21-3		
Ishigatsubo, Yoshiaki	S14-2, W72-4		
Ishiguro, Naoki	LS37-2 , W5-3, W14-2, W24-5, W28-1, W49-6, W50-4, W71-7, W75-3, W75-4, ICW6-2, ICW7-2, P2-021, P2-026, P2-051, P2-118, P2-173		
Ishiguro, Yoh	W12-1		
Ishihara, Katsuhiko	ICW1-6		
Ishihara, Ryuhei	W19-6, W28-4, W71-2, P1-116, P1-137 , P2-046, P2-088, P3-297		
Ishihara, Yoshihiro	P1-176		
Ishii, Kayo	P2-291, P2-295		
Ishii, Koji	W1-4, W79-6, ICW5-2		
Ishii, Naoto	P1-027		
Ishii, Nobuyasu	P3-048, P3-060, P3-116		
Ishii, Sho	W17-2, W34-6, P1-024, P1-032, P2-002, P2-034 , EP3-08		
Ishii, Taeko	W31-1-7, W39-1, P2-128		
Ishii, Tomonori	S6-2 , W20-6, W27-2, W37-2, W47-2, W72-5, ICW20-4		
Ishii, Wataru	P1-215, P3-088		
Ishijima, Kazuyuki	W33-1, P1-039, P1-233		
Ishikawa, Eiji	P1-181		
Ishikawa, Hajime	S20-2, W10-6, W25-4, W49-6, W65-3, ICW2-2, P1-085, P1-088, P1-144, P1-170, P2-019, P2-144, P2-155		
Ishikawa, Hisato	W71-7		
Ishikawa, Junichi	W42-4 , P2-290		
Ishikawa, Osamu	W52-4, W58-1, ICW21-2		
Ishikawa, Yuichi	W31-1-4		
Ishikawa, Yuki	ICW16-1		
Ishimaru, Hiroyasu	W42-6, W53-1, P3-030, P3-109, P3-147		
Ishimori, Kana	W12-4, W33-6, W39-3, W59-4,		
		Ishimura, Kaori	W64-6, W65-5 , P1-046, P2-105, P3-090, P3-126, P3-284
			W20-5, W22-6, P1-208, P2-212, P3-143 , P3-178
		Ishioka Takei, Eriko	P2-245
		Ishitoku, Michinori	P2-147
		Ishizaka, Kosuke	P1-147
		Ishizaki, Jun	W21-3, W41-2 , W47-6, P1-052
		Ishizawa, Nobuhiro	P1-003, P2-115, P2-154
		Ishizu, Akihiro	MTE13 , P3-151
		Ishizuka, Tatsuo	W63-3 , P1-077, P3-071
		Isobe, Masato	P1-014 , P1-048, P1-057
		Isobe, Mitsuaki	LS9-2
		Isoda, Kentaro	W28-5, W50-6, W61-3, W73-1 , ICW9-1, ICW9-2, P1-061, P2-036, P2-067, P3-078, P3-118
			W27-6, P3-046, P3-128, P3-170, P3-212 , P3-243
		Isoda, Yu	W13-1, W65-6, P1-105, P1-182, P1-192
			P1-229
		Isojima, Sakiko	W17-2, P1-024, P1-032, P2-002, P2-034, EP3-08
			W38-6
		Issa, Maher	W1-5
		Isshiki, Rei	P3-191
		Itagane, Masaki	P3-120
		Itakura, Takuji	W20-5, W22-6, W28-2, W35-6, W65-4, W75-1, P1-208, P2-054 , P2-212, P3-143, P3-178
		Itami, Tetsu	P2-195, P3-232
		Itamiya, Takahiro	P2-152
		Ito, Eriko	P1-190
		Ito, Gen	P3-206
		Ito, Hanako	W14-1
		Ito, Haruko	W8-4
		Ito, Haruyasu	W9-1, W36-4, W45-2, P1-188, P2-218, EP2-04, EP2-09
		Ito, Hideki	S3-3, W24-2, P1-003, P1-086, P2-171
		Ito, Hiroki	W5-4 , W9-5, W26-1, W36-6, W49-3, W50-5, W51-3, ICW16-1, P1-058, P1-240, P3-007
		Ito, Hiromu	W20-2 , P1-135
			P2-160
		Ito, Hiroshi	W68-2, W75-5, P1-134
		Ito, Juji	W42-1, W43-6, W56-6, P3-009, P3-102, P3-140, P3-192
		Ito, Katsumi	W59-2, P2-192 , P2-209, P3-101, P3-206
		Ito, Kiyooki	LS26-1
		Ito, Mayumi	S20-2, W10-6, W25-4, W65-3 , ICW2-2, P1-085, P1-088, P1-144, P1-170, P2-019, P2-144, P2-155
			S14-2, MTE5 , W3-4, W7-5, W57-1, P2-244, P2-265
		Ito, Nobuaki	P2-229, P3-160
		Ito, Satoshi	P1-014, P1-048, P1-057
			P3-280
		Ito, Shuichi	
		Ito, Takanori	
		Ito, Takeya	
		Ito, Tatsuya	

Ito, Tomoki	W18-4, P3-116	Iwata, Yasunori	W31-2-5, P2-068
Ito, Tomoyuki	W42-3	Izaki, Teruaki	P1-171
Ito, Yasuhiko	W59-2, P1-238, P2-192, P2-209, P3-101, P3-206	Izawa, Kazushi	W63-2
Ito, Yasumasa	P2-158	Izawa, Naohiro	W68-2, W75-5, P1-134
Itoh, Hirotaka	P3-165	Izmirly, Peter	ICW17-4
Itoh, Kenji	W67-2, W67-6	Izubuchi, Yuya	P1-160
Itoh, Takashi	W40-6, P1-050	Izuka, Shinji	W46-3, W69-4, P1-178, EP1-07 , EP2-01
Itoi, Eiji	P3-034	Izuka, Yuki	P1-179
Itoi, Megumi	W74-6	Izumi, Keisuke	ICW10-1 , P2-249
Itotagawa, Eri	S5-3, P3-085	Izumi, Yasumori	P2-206, P3-062
Iwagaitsu, Shiho	W59-2, P2-192, P3-101, P3-206	Izumi, Yusuke	P2-076
Iwahashi, Mitsuhiro	W8-6, P1-089 , P2-121, P3-112	Izumi, Yuto	P1-180, P2-306, P3-084, P3-087, P3-184
Iwai, Hideyuki	W31-2-5, ICW7-3	Izumihara, Tomomaro	W8-6, P1-010, P1-011
Iwai, Yuki	ICW10-1	Izumikawa, Miharu	P3-292
Iwakura, Mikako	P2-063	Izumiyama, Takuya	P3-034
Iwamoto, Itsuo	W40-6	Izumiyama, Tomomasa	MTE22 , W37-2
Iwamoto, Masahiro	P2-198, P3-150, P3-154, P3-177, P3-258	Izutsu, Hiroyuki	W38-4, W38-5
Iwamoto, Naoki	W31-1-6, W32-2, W32-6, W33-5, W34-2, W37-2, W43-4, W47-1, W48-5 , W48-6, W62-5 , ICW7-3, ICW10-3, ICW15-1, P1-037, P1-069, P1-070, P2-170, P3-171	J —————	
Iwamoto, Rimi	P1-118, P2-279 , P3-238	Jain, Avinash	ICW20-6
Iwamoto, Taro	ICW17-4	Jang, Eun Jin	ICW7-5
Iwamoto, Yosuke	S3-3, P1-003, P1-086	Janssen, William J	ICW16-2
Iwanaga, Nozomi	W47-1, P2-206, P3-062	Jayne, David	W40-6
Iwanaga, Tomoaki	P1-212, P2-025, P3-161, P3-253, P3-303	Jensen, Mark A	ICW17-4
Iwanami, Keiichi	P2-298	Jeong, Hye-jin	ICW13-1
Iwao, Chihiro	W34-3, P2-219 , P3-115	Jeong, Ji-hyeon	EP3-05
Iwao, Haruka	P2-292	Ji, Beulah	W76-3
Iwao, Kosho	W34-3, P2-219, P3-115	Jibatake, Akira	W23-3, W76-4, P2-059, P2-061, P2-081, P2-091, P2-093, P3-041, P3-075, P3-294
Iwasaki, Megumi	W10-1, P3-044	Jin, Shangyi	EP2-07
Iwasaki, Norimasa	W35-3	Jinnin, Masatoshi	P2-214
Iwasaki, Takeshi	W32-1 , W78-6	Jinno, Sadao	W36-6, W51-5, W55-2, W55-6, ICW6-1 , ICW7-4, P2-278, P3-007
Iwasaki, Tsuyoshi	W54-3	Jotoku, Tsuyoshi	W19-5
Iwasaki, Yukiko	W1-5 , W52-1, W52-5, W64-3, W72-1, W78-5, ICW1-2, ICW1-4, ICW18-1, ICW18-4, ICW21-1, P1-201	Jouyama, Kazuo	W70-2, P1-018, P1-217 , P2-257, P2-293
Iwasawa, Mitsuyasu	W24-4, W26-6, W49-2, W71-6, ICW10-6	Joyo, Yuji	P1-124
Iwata, Arifumi	P1-205	Juji, Takuo	W68-2, W75-5, P1-134
Iwata, Kanako	W16-2, P1-043	Jung, Chiau-jing	ICW4-2
Iwata, Mitsuhiro	W59-3, ICW10-4, ICW10-5, P1-211, P3-047, P3-210, P3-293	Jung, Jae Hyun	ICW22-4
Iwata, Naomi	W7-1, W76-3, P2-250	Jung, Jae-hun	ICW13-1
Iwata, Noriko	W14-4 , P3-306	Jung, Lawrence	ICW15-5
Iwata, Shigeru	W4-1, W13-2, W51-2, W55-1, ICW6-5, ICW7-1, ICW8-1, ICW9-4, ICW11-2 , ICW11-5, ICW11-6, ICW12-1, ICW12-2, ICW12-6, ICW13-5, ICW14-5, ICW16-4, ICW17-1 , ICW17-2, ICW17-6, ICW19-2, ICW21-5, P3-300, EP1-04	Jung, Sun-young	ICW7-5
Iwata, Takahiro	P1-161	K —————	
		Kachi, Asako	W59-2, P2-209, P3-206
		Kadoba, Keiichiro	W31-1-5, W59-1, W61-2 , W73-4, P1-195
		Kadono, Yuho	S5-2, S18-3 , LS22-2 , ES9-2
		Kadota, Hiroko	W21-4, W69-1 , W69-2
		Kadoya, Masatoshi	W34-4, W44-5 , W73-3, P1-236, P2-077, P3-089
		Kaga, Nozomi	W24-2
		Kagami, Shin-ichiro	W16-1, W40-6, ICW9-5, P1-223, P2-022, P3-166

Kagawa, Hideo	W18-4	Kanbe, Katsuaki	P2-113
Kagawa, Hidetoshi	W3-2, W32-3, W79-6, P1-006 , P1-056	Kanda, Hiroko	W9-6, ICW6-4, P3-022
Kageyama, Goichi	P3-050	Kanda, Masatoshi	W62-4
Kageyama, Takahiro	P3-104	Kanda, Ryuichiro	W13-2, ICW3-4, ICW14-5
Kagitani, Maki	W1-6 , P3-122, P3-157	Kaneko, Atsushi	W10-5, W28-1, W34-1, W55-5, W65-2, W71-5 , W75-4, P1-008, P1-154, P2-035 , P2-051, P2-083 , P2-136
Kai, Motokazu	W6-4, W6-5, W16-4, W48-4, W67-1 , P1-047	Kaneko, Hiroshi	W46-3, W69-4, P1-178, EP1-07, EP2-01
Kai, Tatsuya	P2-183, P2-230 , P2-302	Kaneko, Kaichi	W74-4
Kaieda, Shinjiro	W54-1 , W69-3, P3-096, P3-186, P3-289	Kaneko, Kayoko	S9-5, S14-2, W13-1, W13-6, W31-2-5 , P3-308
Kaieda, Tomoe	P3-277	Kaneko, Shunta	W46-3, W69-4, P1-178, EP1-07, EP2-01
Kajihara, Ikko	P2-214	Kaneko, Takeshi	W46-4, W47-3, P2-049, P2-181, P3-156, P3-189
Kajio, Nobuhiko	ICW10-1	Kaneko, Tetsuya	W8-5
Kajiyama, Hiroshi	W55-3, P1-008 , P1-082, P2-201 , P3-138	Kaneko, Toshiyuki	P3-307
Kakuchi, Yasushi	W61-5	Kaneko, Utako	P3-038
Kakutani, Rika	P1-162	Kaneko, Yoriaki	W32-4, P2-012
Kakutani, Takuya	W16-2, P1-043	Kaneko, Yuichiro	W38-4, W38-5
Kalunian, Kenneth	W31-1-7, ICW6-2	Kaneko, Yuko	ES4, W30-1, W30-4, W31-2-1, W31-2-6, W47-2 , W54-5, ICW6-6, ICW7-3, ICW10-1, ICW15-3, ICW20-3, P1-104
Kamada, Kazuya	W36-2, P1-101, P1-123	Kanemitsu, Munekazu	S3-4
Kamata, Yasuyuki	P1-004 , P2-198	Kaneshiro, Kenta	W17-6, W37-6, P1-030, P1-033
Kamatani, Naoyuki	PS-3	Kaneshiro, Shoichi	P1-139 , P2-120
Kameda, Hideto	S19-3 , LS22-1 , ES17-1 , W9-1, W22-3 , W30-1, W30-2, W30-3, W36-4, W38-1 , W45-2, W47-2, P1-084 , P1-099 , P1-188, P2-218, EP2-04, EP2-09	Kaneshita, Shunya	W18-2, W33-3, W60-6, W77-1, P2-210, P2-303 , P3-042
Kameda, Sadahiko	P3-250 , P3-252	Kanno, Atsuko	S18-3
Kameda, Tomohiro	W10-4 , W13-3, W20-4, W78-2, W78-4, P3-226, P3-292	Kanno, Takashi	P1-197
Kamenaga, Tomoyuki	W51-4 , P1-035, P1-090, P2-089	Kano, Toshikazu	W57-2, P2-200, P3-211
Kameoka, Junichi	W27-2, W53-3, P2-086	Kanzaki, Takeyuki	W4-3
Kamikawa, Teppei	W33-4, P3-149 , P3-216	Kaplan, Mariana J	PS-2, ICW16-2
Kamino, Yoichi	P2-140	Kapoor, Mohit	ICW21-3, ICW22-5, EP3-07, EP3-09
Kamishima, Tamotsu	P1-057	Karasawa, Hiromi	ICW10-4, ICW10-5, P3-293
Kamiya, Keisuke	P1-220, P3-286	Karino, Kohei	ICW8-5 , ICW10-2
Kamiya, Mari	ICW8-3	Kariya, Yumi	W34-3, P1-028 , P1-235, P2-219, P3-115
Kamiyama, Reikou	W31-2-2, ICW3-2, ICW11-1, ICW12-3, P1-034, P1-179, P2-188, P2-277, P2-281, P3-198	Karube, Miho	W40-5 , W41-1
Kamo, Keiji	S3-3, W24-2, P1-003, P1-086, P2-171	Kasagi, Tomomichi	P2-209
Kamogawa, Yukiko	W72-5	Kasahara, Akiko	W18-2 , W33-3, W60-6, W77-1, P2-087, P2-210
Kamura, Satoshi	P1-150, P1-151, P1-165 , P2-161, P2-167, P2-185	Kasahara, Hideki	W10-3, W35-3, W47-4
Kanai, Daisuke	W48-1, P1-045, P2-260 , P3-035, P3-136, P3-264	Kasahara, Yuto	P3-061
Kaname, Shinya	W40-5, W41-1, W43-1, W60-1, W70-5, P1-125	Kasai, Taro	P1-173
Kanaoka, Miwa	W69-5 , P3-203	Kasama, Tsuyoshi	W17-2, W34-6, W65-6, P1-024, P1-032, P2-002, P2-034, EP3-08
Kanaya, Fuminori	P1-213, P2-267	Kashihara, Naoki	ICW1-6
Kanayama, Yasuhide	W9-2, W28-1 , W71-7, P1-051, P1-078 , P2-051, P2-118	Kashihara, Yuko	P1-112, P3-043
Kanayama, Yoshiro	W10-1, P3-044	Kashiwado, Yusuke	P2-221
Kanazawa, Hiroshi	W19-2	Kashiwagi, Satoshi	P2-294
Kanazawa, Ippei	S8-3	Kashiwagura, Takeshi	S3-3 , W24-2, P1-003, P1-086, P2-094, P2-115, P2-154, P2-171
Kanazawa, Satoshi	W17-1	Kashiwakuma, Daisuke	W40-6, ICW9-5, P1-223, P3-166
Kanazawa, Toshikatsu	P2-159	Kashiwaya, Satomi	P1-135

Kassai, Yoshiaki	W8-1, ICW1-5	ICW13-5, ICW14-5, ICW17-2,
Kasuya, Tadamichi	P1-050, P3-104, P3-288	ICW17-6, ICW21-5, P3-300, EP1-04
Katada, Yoshinori	W54-4, P2-097, P2-126, P3-204, P3-246, P3-259, P3-270	P2-250
Katagiri, Takaharu	W9-1, W36-4	W34-2, P2-122, P3-263
Kataoka, Hiroshi	W45-3 , W47-4	W21-6, P1-055
Kataoka, Yoichi	W24-2, P1-003, P2-115, P2-154	W14-1
Kataoka, Yuko	P3-196	P2-273
Katayama, Kou	W8-6, W35-3	P2-005 , P2-007
Katayama, Masaki	W34-4, W36-6, W51-5, W55-2, W55-6, W75-2, ICW6-1, ICW7-4, P1-231, P1-236, P2-052, P3-007, P3-091, P3-165	P2-258
Katayama, Masao	W10-5, W34-1, W71-5, P2-011, P2-083, P2-136, P2-197, P3-098, P3-164, P3-205, P3-221, P3-283	P1-120
Katayama, Michihito	P2-226, P3-123	P2-253
Katayama, Motoko	P2-278, P2-299 , P3-114, P3-181	W34-3, P1-028, P1-235, P2-219, P3-115
Katayama, Yoshio	S15-3	W31-2-3, W58-1, W58-2, W79-4, P1-186, P1-206, P2-220, P3-070
Katayama, Yu	P2-231	P1-124
Kato, Akari	W33-4, P3-149, P3-216	P3-028
Kato, Ayaka	W35-5, P2-190, P3-255	P2-206, P3-062
Kato, Daisuke	P2-081	ICW1-6, P1-019
Kato, Eri	P1-016, P1-017, P2-295	P1-135
Kato, Ichiro	P3-247	S9-2 , W11-3, W12-4, W17-4, W33-6, W39-3, W45-1, W59-4, W62-6, W64-6, W65-5, ICW8-3, P1-022, P1-046, P2-105, P3-090, P3-126, P3-284
Kato, Jiro	P1-172	W31-1-2
Kato, Manami	P1-050, P3-104	W15-4, W18-2, W25-1, W25-2, W25-3, W27-6, W33-3, W60-6, W77-1, P2-087, P2-210, P2-301, P2-303, P3-042, P3-046, P3-128, P3-170, P3-212, P3-243
Kato, Masaru	LS30 , ES6 , W35-3, W62-4, ICW3-5, ICW4-3, ICW4-4, ICW6-6 , ICW8-5, ICW10-2, ICW16-6, ICW19-4, P2-215, EP3-01	W52-2
Kato, Mikiya	W10-4, W13-3, W20-4 , W78-2, W78-4, P3-226, P3-292	S2-3, S21-2, S21-7, LS36-2 , ES16 , W9-4, W11-5, W31-1-6, W32-2, W32-6, W33-5, W34-2, W37-2, W38-4, W38-5, W43-4, W47-1, W48-2, W48-5, W48-6, W54-5, W62-1, W62-5, W63-1, W63-5, W71-3, ICW7-3, ICW10-3, ICW15-1, ICW15-4, P1-037, P1-053, P1-069, P1-070, P2-170, P2-206, P2-207, P2-243, P3-062, P3-146, P3-171, P3-220, P3-223, P3-263
Kato, Mizuki	P2-229, P3-160	W13-1, W13-6, P3-308
Kato, Shinichi	W15-3, W19-4	W40-5, W41-1
Kato, Takashi	W6-4, W6-5, W16-4, W48-4, W67-1, P1-047	W70-5, P3-151
Kato, Takefumi	W28-1, W71-7, P2-173	W58-2, P2-015, P2-220
Kato, Tomohiro	P2-017	P1-164, P2-176 , P2-182
Kato, Yasuhiro	S5-3, W72-2, P3-085	W3-6 , P2-199
Katsuda, Rinko	P1-126, P1-189	W1-5, W52-5
Katsumata, Kazuaki	W35-3, P3-176	P1-156
Katsumata, Yasuhiro	EL22 , W31-2-3, W68-4, W79-4, P1-186, P1-206, P2-071, P2-220, P2-232, P3-070, P3-167, P3-219	W5-6
Katsuno, Takayuki	W59-2, P2-192, P2-209, P3-101, P3-206	P1-156
Katsuragawa, Takao	P1-242, P3-117	P1-126, P1-189
Katsuyama, Naooki	W28-6, P1-190, P3-302	P2-292, P3-225
Kavanaugh, Arthur	ICW6-3	W40-1, P2-024, EP1-02
Kawa, Shigeyuki	S21-4	W4-1, W13-2, W51-2, W55-1, ICW6-5, ICW7-1 , ICW8-1, ICW9-4, ICW12-1, ICW12-2, ICW12-6,
Kawaai, Satoshi	W10-1, P3-044	
Kawabata, Hiroshi	S21-2 , S21-3, P2-292, P3-225	
Kawabata, Kensuke	P1-173	
Kawabata, Tomoko	W40-1, P2-024, EP1-02	
Kawabe, Akio	W4-1, W13-2, W51-2, W55-1, ICW6-5, ICW7-1 , ICW8-1, ICW9-4, ICW12-1, ICW12-2, ICW12-6,	
Kawabe, Shinji		
Kawachi, Natsumi		
Kawada, Masahiro		
Kawagoe, Mitsuhiro		
Kawaguchi, Atsushi		
Kawaguchi, Hoshimi		
Kawaguchi, Kouhei		
Kawaguchi, Mayumi		
Kawaguchi, Tadayasu		
Kawaguchi, Takeshi		
Kawaguchi, Yasushi		
Kawaguchi, Yohei		
Kawaguchi, Yoshiharu		
Kawahara, Chieko		
Kawahara, Kyoko		
Kawahara, Sanae		
Kawahata, Kimito		
Kawahata, Tomoki		
Kawahito, Yutaka		
Kawai, Shinichi		
Kawakami, Atsushi		
Kawakami, Misato		
Kawakami, Takahisa		
Kawakami, Tamihiro		
Kawamoto, Manabu		
Kawamoto, Taisei		
Kawamoto, Toshio		
Kawamura, Akito		
Kawamura, Daisuke		
Kawamura, Seiichi		
Kawamura, Sumito		
Kawamura, Tetsuji		
Kawanami, Takafumi		
Kawane, Takashi		
Kawano, Hiroshi		

Kawano, Mika	W36-1, W37-4, W70-1, W70-7, P1-001	Kimoto, Yasutaka	W26-4, W33-2, W34-5, W59-5, W60-5, W65-1 , ICW11-4, ICW14-6, P1-203, P2-037, P2-072, P2-221, P2-241, P3-052, P3-063, P3-152, P3-202, P3-217, P3-254
Kawano, Mitsuhiro	S21-6 , W38-1, W42-1, W43-6, W54-5, W56-6, W61-5, P1-210, P3-009, P3-067, P3-102, P3-110, P3-140, P3-192	Kimura, Fumihiko	W67-2, W67-6
Kawano, Shinya	P2-194, P3-257	Kimura, Junko	P1-094
Kawano, Shotaro	ICW11-4, P1-203, P2-241	Kimura, Makiko	P3-137, P3-260
Kawano, Tetsuya	S3-3, W24-2, P1-003, P1-086, P2-094, P2-115, P2-171	Kimura, Masatoshi	P2-219, P3-115
Kawano, Yutaka	W63-6, ICW3-6	Kimura, Naoki	W64-5
Kawarai, Yuya	W50-1, P2-262	Kimura, Tomoatsu	LS18, W19-4, W49-6, P3-028
Kawasaki, Aya	W41-6	Kimura, Yoshiaki	S3-3
Kawasaki, Makoto	P1-031	Kimura, Yoshitaka	W66-1 , P2-003, P2-195, P3-232
Kawasaki, Masashi	P2-051	Kimura, Yuko	P1-042, P1-250, P2-057 , P2-124 , P3-241
Kawasaki, Yoshiko	W17-6, W37-6, P1-030, P1-033	Kina, Michiru	W13-1, W66-2, P1-184, P2-224, P2-264, P2-282, P2-287, P2-296, P2-311, P3-031, P3-074, P3-081, P3-276
Kawashima, Hiromasa	P3-222	Kinjo, Mitsuyo	P1-007, P2-069, P3-145, P3-191, P3-248
Kawashima, Hirotoshi	W40-6, W42-4, P2-290	Kinjo, Noriko	P2-254
Kawashima, Soko	W40-5, W41-1, W43-1, W60-1	Kinoshita, Koji	W20-5, W22-6, W28-2, W35-6, W46-2, W65-4, P1-095, P1-207, P1-208, P2-054, P2-090, P2-212, P3-143, P3-178
Kawashiri, Shin-ya	S2-3 , W31-1-6, W32-2, W32-6, W33-5, W37-2, W43-4, W47-1, W48-5, W62-5, W71-3, ICW10-3, ICW15-1, P1-037, P1-069, P2-170, P3-171	Kinoshita, Masato	W32-4, P2-012
Kawasumi, Hidenaga	W79-4, P3-137, P3-260	Kira, Tsutomu	P2-052
Kawata, Daisuke	P3-120	Kirino, Yohei	S14-2, W31-2-2, W72-3, W72-4, ICW3-2, ICW11-1, ICW12-3, P1-034, P1-179, P2-188, P2-277, P2-281, P3-198, P3-203, P3-229, EP1-09
Kawata, Junko	P2-271	Kise, Takayasu	MTE12, W66-2 , P1-184, P2-224, P2-264, P2-282, P2-287, P2-296, P2-308, P2-311, P3-031, P3-074, P3-081, P3-276
Kawataka, Masatoshi	P2-285	Kishi, Jun	W27-3
Kawato, Rui	P3-196, P3-213	Kishi, Takayuki	W7-2 , W7-4, ICW8-4, P2-255
Kawazoe, Mai	W74-4, P3-133	Kishida, Aiko	W66-4, P1-175, P2-148
Keeling, Stephanie	ICW3-3	Kishida, Dai	W12-1, W46-1 , P1-026, P2-288, P3-054, P3-127, P3-208
Kelly, Colleen	ICW4-6	Kishimoto, Daiga	W31-2-2 , ICW3-2, ICW11-1, ICW12-3, P1-034, P1-179, P2-188, P2-277, P2-281, P3-198
Kerr, Lisa	W22-1	Kishimoto, Hiroki	P1-064
Kiboshi, Takao	W13-4, W52-6, W58-6 , P2-058, P2-116, P2-196, P2-216, P3-073, P3-122, P3-125, P3-157	Kishimoto, Kazuya	W20-5, W22-6, W28-2, W35-6, W46-2, W65-4 , P1-208, P2-054, P2-212, P3-143, P3-178
Kida, Daihei	W65-2, P1-154, P2-051	Kishimoto, Kenji	W24-5
Kida, Issei	W14-6	Kishimoto, Mitsumasa	ES1-1 , ES13-1 , W44-1 , W72-6, P2-227, P3-196, P3-213
Kida, Takashi	W18-2, W33-3, W60-6, W77-1, P2-087, P2-210 , P2-303	Kiso, Yohei	S11-2, ICW9-3 , P1-059, P1-168, P3-016
Kido, Akira	P2-052	Kita, Yasuhiko	W31-1-4
Kido, Toshiki	P3-076, P3-086 , P3-180, P3-182, P3-207	Kitada, Ayako	P2-227, P3-196, P3-213, P3-285
Kihira, Daisuke	W19-3, P1-049, P1-075 , P2-102, P2-175	Kitada, Yoshihiko	W35-5, W78-1, P2-190, P3-255
Kijima, Takeshi	P1-170	Kitade, Makoto	P1-160
Kikuchi, Eigo	W10-2, W55-4 , P1-147		
Kikuchi, Hirotoshi	S14-2, ES3-2 , P2-195, P3-229, P3-232		
Kikuchi, Jun	W31-2-1 , ICW10-1, P1-200		
Kikuchi, Tamami	P2-132		
Kikuta, Junichi	S12-5		
Kim, Harry	EP3-03		
Kim, Hyoungyoung	ICW7-5		
Kim, Ji-min	ICW13-1		
Kim, Jong-seo	ICW13-1		
Kim, Sang-hyon	ICW13-1		
Kim, Tae-hwan	ICW13-1		

Kitagawa, Akiko	P1-126, P1-189	Kobayashi, Takashi	ICW5-2
Kitagawa, Atsushi	P2-286	Kobayashi, Tatsuya	P1-164
Kitahara, Hideyuki	P1-141	Kobayashi, Tetsuo	S20-2, P2-144
Kitajima, Shinji	P2-068	Kobayashi, Toshiaki	W46-3, W69-4, P1-178 , EP1-07, EP2-01
Kitajima, Susumu	W43-6		
Kitakawa, Hirohiko	P3-083	Kobayashi, Yoshiaki	P3-175
Kitamura, Fumiya	P1-054, P1-226, P2-276 , P2-297, P3-107	Kobayashi, Yoshihisa	P3-251
		Kobayashi, Yuto	P3-008
Kitamura, Kenichiro	W4-3, P2-073, P3-175, P3-262	Koboyama, Tomohiko	P3-108
Kitamura, Noboru	S10-4, W40-2, W59-3 , ICW10-4, ICW10-5, P1-211, P3-033, P3-047, P3-210, P3-293	Kochi, Yuta	S5-2, S5-5 , W64-3, ICW1-2, P1-201
		Kodama, Kako	W16-2, P1-043
Kitamura, Susumu	W22-2, W38-1	Kodama, Satoru	W31-1-2
Kitani, Atsushi	ICW5-5	Kodama, Shogo	W1-4
Kitano, Akemi	P1-014, P1-048, P1-057	Kodera, Hitoshi	W76-1, P3-026
Kitano, Masayasu	W9-2, W47-5, W51-6, W54-3, W54-4, P2-107 , P2-139, P2-213, P3-082, P3-094, P3-173, P3-185, P3-249, P3-256	Kodera, Masanari	W62-2
		Kodera, Takao	W27-2, W37-2, P2-086
		Koenuma, Naoko	P1-163 , P1-169
Kitano, Sachie	W54-4	Koga, Keiko	W8-1
Kitaori, Toshiyuki	W19-4, W34-4, P1-108 , P1-110, P1-167, P1-236	Koga, Takuma	W54-1, W69-3, P3-096 , P3-186, P3-289
Kitawaki, Toshio	S21-2	Koga, Tomohiro	S21-2, S21-7 , W11-5, W30-4, W31-1-6, W32-2, W32-6, W33-5, W37-2, W43-4, W47-1, W48-5, W62-5, W63-1, W63-5, ICW10-3, ICW15-1 , ICW15-4, P1-037, P1-069, P3-171
Kitayama, Midori	P1-118 , P1-230, P1-237, P2-098, P2-125, P2-130, P2-279, P3-238		
Kiyokawa, Shigeto	P1-010, P1-011	Kogami, Masahiro	P3-103
Kiyokawa, Tomofumi	W39-3 , W59-4, W64-6, W65-5, P2-105, P3-090, P3-126, P3-284	Koh, Rei	P3-175
		Kohagura, Toaki	P2-250
Kizaki, Kazuha	W74-6	Kohno, Chie	W13-1 , W13-6, P3-308
Koarada, Syuichi	W18-3, W22-4 , W59-5, W60-5, P3-097, P3-142, P3-281	Kohno, Hiroki	W4-5, W57-4, P2-010, P2-217, P3-131, P3-268, P3-279
Kobashi, Yasuko	P1-251	Kohno, Masataka	W15-4, W18-2, W25-1, W25-2, W25-3, W27-6, W33-3, W60-6, W77-1, P2-087, P2-210, P2-301, P2-303, P3-042, P3-046, P3-128, P3-170, P3-212, P3-243
Kobashigawa, Tsuyoshi	P1-087, P2-015, P2-238, P3-231 , P3-240		
		Kohsaka, Hitoshi	W30-1, W62-6, W64-5, ICW8-3, P1-022
Kobayakawa, Tomonori	W71-7		
Kobayashi, Atsushi	W31-1-2	Koide, Yohei	W11-5
Kobayashi, Daisuke	W10-6 , W16-3, W21-5, W40-4, W65-3, W68-3, ICW2-2, ICW2-3, P1-013, P1-088, P1-144, P1-170, P1-177, P1-198	Koike, Kiyomi	P1-066, P1-220, P3-286
		Koike, Takao	W30-4, P1-014, P1-048, P1-057
Kobayashi, Hiroki	P3-055 , P3-112	Koike, Tatsuya	S2-4, S8-4 , W5-1, W9-2, W16-5, W16-6, W23-6, W36-3, W37-1, W44-6, W68-1, W70-6, P2-023, P2-062, P2-179, P3-003, P3-006, P3-008, P3-019, P3-020, P3-021, P3-290, P3-301, EP2-03
Kobayashi, Hiroko	W43-2, W63-5, ICW15-4, P1-021, P1-183, P1-204, P2-237		
		Koizumi, Sayaka	P2-070
Kobayashi, Hiroshi	P3-269	Koizumi, Yasuhiko	W31-1-4
Kobayashi, Ichiro	S14-5, EL2 , W7-4	Kojima, Kanako	W34-2, W62-1, P2-122, P3-263
Kobayashi, Kei	W4-3, P3-175, P3-262	Kojima, Kyoko	W27-3
Kobayashi, Kouji	W31-2-2, ICW3-2, P1-034, P1-179, P2-188, P2-277, P2-281, P3-188	Kojima, Masayo	W49-6, W70-3
		Kojima, Mina	P1-245
Kobayashi, Megumi	W14-5	Kojima, Sachiko	P1-135
Kobayashi, Moto	S3-3, W24-2, P1-003 , P1-086, P2-115, P2-154, P2-171	Kojima, Shotaro	P3-079, P3-135
		Kojima, Toshihisa	S11-1, MTE18 , W5-3, W14-2, W24-5, W28-1, W30-1, W49-6 ,
Kobayashi, Norimoto	W7-4		
Kobayashi, Satomi	W52-1, W52-5, W64-3, W72-1, ICW21-1		
Kobayashi, Seiji	W3-1, W21-4 , W23-2, W54-6, W69-1, W69-2, P1-229, P3-010		
Kobayashi, Shigeto	S18-1 , W14-6, W41-6, W44-1, W44-3, P3-282		

	W50-4, W71-7, W75-3, W75-4, ICW7-2, P2-021, P2-026, P2-051, P2-118, P2-173	Kono, Masanori Kono, Michihiro Kono, Michihito	ICW18-1 W62-4, ICW3-5, ICW8-5, EP3-01 W62-4, ICW3-5, ICW4-3, ICW4-4, ICW5-3 , ICW8-5, ICW10-2, ICW16-6, ICW19-4, P2-215, EP3-01 W31-1-7, W44-2 W74-4, P3-133 W59-2, P2-209, P3-206 W4-2 P1-087, P2-015, P2-238, P3-231, P3-240 W2-1, W2-4, W13-4, W23-4, W27-4, W36-6, W52-6 , W58-4, W58-6, W61-4, W75-2, ICW6-1, ICW7-4, P2-058, P2-116, P2-196, P2-216, P3-073, P3-108, P3-122, P3-125 P1-108, P1-110, P1-167 P3-171 W66-6 P3-018 P1-066, P1-220, P3-286 P1-157, P1-158 P1-155 , P3-262 P2-246 P1-248, P2-184 MTE26 W56-5, P1-180, P2-306 , P3-084, P3-087, P3-184 W34-4, W62-3 , P1-236, P2-037 W14-5 W28-3, W55-3, ICW2-5, P1-082 P1-228, P2-133, P2-308, P3-237 W1-5, P1-234 W29-4, W34-3, W57-6 P3-242 W4-1, W13-2, W51-2, W55-1, ICW6-5, ICW7-1, ICW8-1, ICW9-4, ICW12-1, ICW12-2, ICW12-6, ICW13-5, ICW14-5, ICW17-2, ICW17-6, ICW19-2, ICW21-5, P3-300, EP1-04 P3-091 W25-1, W25-2, W27-6, P2-087 P1-027 W14-6 W24-1 , W56-1 P1-093 W79-1 W7-1 P1-060 W58-6, P2-116, P2-196, P3-122, P3-125, P3-157 W43-3, ICW14-4, P2-239, P2-240 , P2-242 EP2-12, EP2-13, EP2-14 W62-4 , ICW16-6, ICW19-4, EP3-01 P2-246, P3-257 P2-081
Kokuryo, Waka	P1-054, P1-226, P2-276, P2-297, P3-107		
Kokuzawa, Ayako	P2-198, P3-150, P3-154, P3-177	Konomi, Ayako	
Kollias, George	S15-2	Koshihara, Keiko	
Komagamine, Masataka	P2-044	Koshino, Masako	
Komagata, Yoshinori	W40-5, W41-1, W43-1, W60-1, P1-125	Kosumi, Yui	
	P3-299	Kotake, Shigeru	
Komai, Koichiro	W1-5, ICW11-3, ICW18-1, ICW18-4 , P1-234, EP1-03	Kotani, Takuya	
Komai, Toshihiko	W66-4 , P1-071, P1-072, P1-175, P1-245, P2-148		
Komano, Yukiko	P2-001	Kotani, Tomoya	
Komatsu, Rie	P1-151, P1-165, P2-161, P2-167, P2-185	Koto, Serina	
Komatsu, Takashi	W18-1 , P2-066	Kotouda, Yoshiyuki	
	W22-4	Koumoto, Kiichi	
Komatsuda, Atsushi	W16-2, P1-043 , P2-011	Koyama, Katsushi	
Komine, Mitsunori	W31-2-2, ICW3-2, ICW11-1, ICW12-3 , P1-034, P1-179, P2-188, P2-277, P2-281	Koyama, Keita	
Komiya, Akiko	P2-223 , P2-246, P3-119, P3-257	Koyama, Kensuke	
Komiya, Takaaki	S5-3, W72-2 , P3-085	Koyama, Mayuko	
	W31-2-3 , W68-4	Koyama, Takeko	
Kon, Takayuki	W70-2, P1-018 , P1-217, P2-257, P2-293	Koyama, Tetsuo	
Konaka, Hachirou	P3-053	Koyama, Yasushi	
Kondo, Naoko	W31-1-3, P2-189 , P3-092, P3-190		
Kondo, Atsushi	W45-3	Koyama, Yoshinobu	
	P1-121 , P3-093, P3-309	Koyanagi, Ryoko	
	W26-2, P1-041	Kozu, Noritsune	
	P2-142	Kozuki, Tomohiro	
	ICW2-2, ICW2-3, ICW13-4 , ICW22-2 , P3-038, EP2-12, EP2-13 , EP2-14, EP3-06	Kubo, Kanae	
Kondo, Seiko	P3-040	Kubo, Kazuyoshi	
Kondo, Tsuneo	W2-5, W3-3, W35-4, W39-4 , W60-3, W60-4, ICW17-3, ICW20-5, P2-119	Kubo, Kenichirou	
	S10-1 , W1-3	Kubo, Satoshi	
Kondo, Yasuhiro	W8-1, W9-3 , W56-5, P1-180, P2-306, P3-084, P3-087, P3-184		
Kondo, Yasushi	EL7, W1-2, W17-3, W20-3, W26-5, W43-3, W76-2, W76-5, ICW12-4, ICW14-4, ICW16-3, P2-005, P2-007, P2-009 , P2-111, P2-239, P2-240, P2-242	Kubo, Takeshi	
	W42-1, W43-6, P3-009, P3-067, P3-102, P3-192	Kubo, Toshikazu	
	P2-249	Kuboi, Yoshikazu	
Konishi, Masahiro	S3-3, W24-2, P1-003, P1-086, P2-115, P2-154, P2-171	Kubono, Kyoko	
	W58-6, P2-099 , P3-265	Kubota, Ayako	
Konishi, Misako	P2-126	Kubota, Takao	
Konishi, Natsuo	W66-1, W72-6, P2-003, P2-195, P3-232	Kubota, Tetsuo	
		Kubota, Tomohiro	
Konma, Junichi		Kubota, Yasuhiro	
Konma, Kazushi		Kuboyama, Tomohiko	
Kono, Hajime			

Kuhn, Kristine A	PS-2	P3-113
Kujime, Rie	W36-4, P1-188, P2-218, EP2-04	W34-2, W62-1 , P2-122, P3-263
Kukimoto, Hikaru	W43-1	P1-140
Kumagai, Ken	W50-2, W75-6, P2-166	P3-177, P3-245
Kumagai, Shunichi	W3-5, W51-1, W77-4, ICW1-1, P2-247, P3-121	P3-157
Kumagai, Takashi	P1-050, P3-104	W67-2, W67-6
Kumakura, Shunichi	P3-093	P3-069 , P3-295
Kumano, Kotaro	W53-5	W74-2
Kumanogoh, Atsushi	S5-3, W45-4, W48-3, W51-5, W72-2, ICW16-5, ICW20-1, P2-008, P3-049, P3-085, P3-214, P3-311	P1-138
Kunder, Rebecca	ICW6-3	P1-203, P3-202
Kunishita, Yosuke	W31-2-2, ICW3-2, ICW11-1 , ICW12-3, P1-034, P1-179, P2-188, P2-277, P2-281	W52-2
Kunugiza, Yasuo	S3-2, S11-5, W18-4, W49-1, P2-031	P2-038, P2-211
Kuo, Yu-min	ICW4-2	P3-046, P3-128, P3-170, P3-212, P3-243
Kurabayashi, Takayoshi	W56-5, P1-180 , P2-306, P3-084, P3-087, P3-184	S21-5
Kuramoto, Nobuo	P2-018 , P2-041	S4-3 , S10-1, S14-2, EL19 , LS38 , ES18-1 , W1-1, W3-1, W8-2, W21-4, W23-2, W54-6, W58-1, W58-5 , W67-3, W69-1, W69-2, W77-2, W77-5, P1-229, P2-128, P3-124, P3-230
Kuranobu, Tatsuomi	W4-5, W57-4, P2-010, P2-217, P3-131, P3-268, P3-279	W28-5, W61-3 , W73-1, ICW9-1, ICW9-2, P1-061, P2-036, P2-067, P3-078, P3-118
Kurasawa, Kazuhiro	W2-3, W23-1, W23-5, W61-1, W64-4 , P2-050, P3-130, P3-215	ICW5-3
Kurasawa, Takahiko	W2-5, W3-3, W35-4, W39-4, W60-3 , W60-4 , ICW17-3, ICW20-5, P2-119	
Kurashina, Junichi	P3-194	L —————
Kurata, Izumi	W1-2, W20-3, W26-5, W76-2, ICW12-4, ICW14-4, ICW16-3 , P2-005, P2-007, P2-111, P2-240	Lagares, David ICW21-3
Kurata, Noriyuki	P1-100, P3-292	Lawrence, Able ICW8-2, ICW20-6
Kuratani, Ruriko	W12-2, W27-1, P1-074, P2-203 , P2-248	Lee, Eunkyeong EP3-05
Kurihara, Hidemi	P1-036, P3-072	Lee, Hyeryong W43-1
Kurihara, Shunjiro	W42-4, P2-290	Lee, Hyunho P1-144 , P1-170
Kurihara, Yuko	P3-058	Lee, Ji-hyun ICW13-1
Kurisu, Rina	W8-1, ICW1-5	Lee, Wen Shi W62-4, ICW16-6, ICW19-4, EP3-01
Kurita, Takashi	W35-3, W47-4	Li, Mengtao ICW3-1, ICW4-1, ICW19-3, ICW19-6, EP2-07
Kuroda, Hiroshi	W29-4, W57-6	Li, Xiangpei ICW8-6, ICW14-1, ICW14-3, ICW18-6
Kuroda, Ryosuke	W15-1, W51-4, P1-029, P1-035, P1-090, P2-042, P2-089	Li, Xiaomei ICW8-6, ICW14-1, ICW14-3, ICW18-6
Kuroda, Takeshi	W16-3, W21-5, W40-4, W68-3, ICW2-3, P1-013 , P1-177, P1-198, P2-132, P2-258	Li, Yang ICW3-1
Kuroe, Yuriko	S1-6	Lian, Chaofeng ICW14-2
Kurokawa, Hiroaki	S3-5	Lin, Yen-chun ICW4-2
Kurokawa, Manae	P2-017	Lin, Yong W30-3
Kuroki, Keiko	P1-245	Liu, Suying ICW14-2
Kurosaka, Daitaro	W8-4, W64-1, P1-025	Liu, Yang ICW15-5
Kurosaki, Nami	W73-2	Liu, Yi ICW3-1
Kurosawa, Michiko	W72-3, W72-4	Liu, Ziwei ICW19-6
Kurosawa, Yoichi	W25-4, W65-3, ICW2-2, P1-085, P1-088 , P1-144, P2-019, P2-155	Liviu, Macovei EP2-06
Kurose, Nozomu	S21-2, S21-3	Loomis, Cynthia A ICW17-4
Kurose, Rie	P2-027 , P3-002	Lopez-olivo, Maria A EP2-11
Kuroyanagi, Gen	P1-124, EP3-03	Lotz, Martin K ICW2-6
Kurumizawa, Megumi	W2-2, W12-6, W77-6, P2-236,	Ly, Thai Yen ICW4-6
Kurushima, Shota		M —————
Kusaba, Atsushi		Mabuchi, Mayuko S1-5
Kusaka, Hiroi		Machida, Akitoshi P1-042, P1-250, P2-124
Kusakabe, Masako		Machiyama, Tomoaki W72-5
Kusanagi, Yasuyoshi		
Kusaoui, Makio		
Kusayama, Yoshihiro		
Kushida, Taketoshi		
Kushimoto, Kazuo		
Kusunoki, Natsuko		
Kusunoki, Yoshie		
Kusuoka, Hiroaki		
Kuwabara, Satoshi		
Kuwana, Masataka		
Kuzuya, Kentaro		
Kyttaris, Vasileios C		

Macias, William	W38-6	Maruyama, Takashi	W55-3, P1-082, P3-138, P3-280
Macovei, Liviu	ICW5-6	Masaki, Yasufumi	S21-2, S21-3 , P2-292, P3-225
Maeda, Ayaka	W12-3, P3-120	Mashiba, Koichi	P3-233
Maeda, Hiroyuki	P3-055, P3-112	Masuda, Ikuko	MTE12, W66-2, W66-4, P1-071, P1-072, P1-175, P1-245, P2-148
Maeda, Junko	W52-1 , W64-3, W72-1		P3-151
Maeda, Kayaho	ICW5-3	Masuda, Sakiko	W57-2, P2-200 , P3-211
Maeda, Masataka	P1-216	Masui, Yoshinori	P2-205
Maeda, Shinji	P2-032 , P3-224, P3-298	Masujima, Kaori	W63-1, ICW15-1
Maeda, Takuro	P1-118, P1-230, P1-237, P2-098, P2-130, P2-279, P3-238	Masumoto, Junya	W74-4, P3-133
		Masuoka, Shotaro	W66-4, P1-175, P2-148
Maeda, Tomoyo	P2-032	Mata, Toshihiro	W70-2, P1-018, P1-217, P2-257, P2-293
Maeda, Toshihisa	ICW5-1, P1-029	Matoba, Kenichiro	P2-075, P2-085
Maeda, Yuichi	S20-5 , W45-4, W51-5 , W55-2, W55-6, ICW6-1, ICW7-4, ICW16-5, P2-052, P3-007, P3-049, P3-214, P3-311	Matsubara, Hiroyuki	P3-275
		Matsubara, Miyu	W8-6, W51-4, W75-1, ICW6-2, P1-010, P1-011, P1-035, P1-090, P2-089, P2-123, P3-014
Maeshima, Keisuke	W1-4, ICW5-2	Matsubara, Tsukasa	S18-4
Maeyama, Akira	P1-171		P1-247
Maezawa, Reika	W2-3, W23-1, W23-5, W61-1, W64-4, P2-050, P3-130, P3-215	Matsubara, Yuri	P3-168
		Matsuda, Akiko	W28-3 , W55-3, P2-201, P3-138
Maezawa, Yuko	P1-205	Matsuda, Masayuki	W34-3, P1-028, P1-235, P2-219, P3-115
Mahomed, Nizar N	ICW22-3, ICW22-5	Matsuda, Mayumi	P3-072
Majima, Masako	W37-5 , W68-4	Matsuda, Motohiro	W1-6, W52-6, W58-6, P2-058, P2-116, P2-196, P3-073, P3-122, P3-274
Majumder, Sanjukta	ICW8-2		LS33-1 , W5-4, W26-1, W49-3, W50-5, W51-3, P1-058, P3-007
Makabe, Kenta	W24-3, P1-145	Matsuda, Shinji	P2-095, P3-277
Makino, Hidehiko	W1-6, W2-1, W27-4, W58-4, W58-6, W61-4, P2-116, P2-196, P3-073, P3-122 , P3-125, P3-274	Matsuda, Shogo	P1-097, P3-307
			P1-120
Makino, Hirofumi	W41-5, W41-6	Matsuda, Shuichi	W31-1-3, W77-3, P1-202 , P2-189, P3-190
Makino, Katsunari	P2-214, P2-222		P1-014, P1-048, P1-057
Makino, Shigeki	W1-6, W2-1 , W2-4, W13-4, W23-4, W27-4 , W58-4 , W58-6, W61-4 , P2-116, P2-196, P2-216, P3-125	Matsuda, Takemasa	S11-2, ICW9-3, P1-059 , P1-168, P3-016
		Matsudaira, Ran	P3-180, P3-182
Makino, Takamitsu	P2-214	Matsueda, Megumi	W29-3
Makino, Yuichi	W31-1-2	Matsueda, Yu	W35-3, P1-096, P3-228
Makita, Sohei	P1-050		W41-3, W47-5, W51-6, W54-4, P1-008, P2-107, P2-139, P2-213, P3-082, P3-094, P3-173, P3-185, P3-249, P3-256
Makiyama, Ayako	W79-5 , P1-020	Matsueda, Megumi	P1-083
Makol, Ashima	ICW17-4	Matsueda, Yu	S9-1 , W8-3, W13-5 , W16-2, W26-6, W34-1, W55-5 , W71-1, W71-5, W71-6, P1-008, P1-015 , P1-016, P1-017, P1-043, P1-106, P2-011, P2-055, P2-083, P2-095, P2-136
Maldonado-cocco, José Antonio	W30-3		P2-227
		Matsui, Atsushi	P3-293
Mamoto, Kenji	W9-2, W16-5, W23-6, W37-1, W68-1, W70-6, P2-023, P2-062, P3-008, P3-019, P3-290, P3-301	Matsui, Eiji	P3-079, P3-135
		Matsui, Kazuo	W3-6
Mamyrova, Gulnara	ICW8-4	Matsui, Kiyoshi	P1-160
Manabe, Miho	W74-5		P2-018, P2-041
Manabe, Takehiko	P3-240	Matsui, Nobuo	
Manabe, Yusuke	W45-4, W51-5, P3-049, P3-214 , P3-311	Matsui, Toshihiro	
Mandai, Koji	S2-4, W16-5, W16-6 , W37-1, W44-6, W68-1, ICW22-6, P3-001, P3-003 , P3-004, P3-005, P3-006 , P3-019, P3-020, P3-021 , P3-290		
Mannami, Kenji	P1-114		
Mannami, Makoto	P1-114		
Marshall, Wayne	ICW22-3		
Maruno, Fumimasa	P2-286		
Maruyama, Akihito	W18-3, W22-4, W59-5, W60-5, P3-097, P3-142, P3-281		

Matsumoto, Akihiko	W1-5	Mawatari, Masaaki	P2-152
Matsumoto, Isao	EL7, LS25 , W1-2, W17-3, W20-3, W26-5, W43-3, W54-5, W76-2, W76-5, ICW12-4, ICW14-4, ICW16-3, P2-005, P2-007, P2-009, P2-111, P2-239, P2-240, P2-242	Mawatari, Noriko	S1-4
Matsumoto, Kazuko	W63-4, P3-023	Mayumi, Norihiro	P2-074
Matsumoto, Kazuya	W3-2, W32-3 , P1-056	Mazur, Minodora	ICW6-3
Matsumoto, Takumi	S3-1 , S9-7, EL12 , W68-2, W75-5, ICW10-6, ICW22-1, P1-134, P1-173, P1-242, P3-117, P3-305	McInnes, Iain	W38-6
Matsumoto, Takuya	W5-3, W14-2, W21-3, W24-5, W41-2, W47-6, W50-4 , W71-7, ICW7-2, P1-052, P2-021, P2-173	Md Yusof, Md Yuzaiful	ICW17-5
Matsumoto, Tatsuki	W40-3, W58-3, P1-185, P3-032, P3-134 , P3-278	Meerwein, Sebastian	W38-1
Matsumoto, Yoshifuji	W76-1, P3-026	Mega, Akira	P2-097, P2-126, P3-204, P3-246, P3-259, P3-270
Matsumoto, Yoshinori	W40-1, ICW2-4 , P2-024, P3-172, EP1-02	Memida, Takumi	P3-072
Matsumoto, Yuki	P1-050	Mera, Tomoko	P3-271
Matsumura, Itaru	W20-5, W22-6, W28-2, W35-6, W46-2, W65-4, W75-1, P1-095, P1-207, P1-208, P2-054, P2-090, P2-212, P3-143, P3-178	Meuleners, Luc	ICW6-3
Matsumura, Ryutaro	W33-1 , W34-1, ICW18-2, P1-039, P1-233, P2-022	Mezzano, Valeria	ICW17-4
Matsumura, Yoko	W23-4, W75-2, P2-058, P2-116	Mibe, Junya	P2-164
Matsunaga, Keiichiro	P3-065	Michitsuji, Tohru	P3-223
Matsunaga, Takahiro	P1-210, P3-009	Migita, Kiyoshi	W43-2, W63-1, W63-5, ICW15-1, ICW15-4, P1-021, P1-183, P1-197, P1-204, P2-011, P2-237
Matsuno, Hiroaki	LS13-2, ES14 , W8-6, P2-128	Miike, Satoshi	P3-288
Matsuo, Haruna	P3-223	Mikami, Hiroshi	P2-156
Matsuo, Takashi	W36-6, P1-231	Mikami, Yasuo	W15-4, W25-3
Matsuoka, Hidetoshi	W28-5, W61-3, W73-1, ICW9-1, ICW9-2, P1-061 , P2-036, P2-067, P3-078, P3-118	Mikami, Yukio	P2-182
Matsuoka, Naoki	W32-2, W43-2, W63-5, ICW15-4, P1-021, P1-183 , P1-204, P2-237	Miki, Kenji	ES9-3
Matsuoka, Naoya	W59-2, P3-101 , P3-206	Miller, Frederick W	ICW8-4
Matsuoka, Yuki	P3-129	Mimori, Tsuneyo	S21-2, W9-5, W30-4, W32-1, W36-6, W50-5, W51-3, W54-5, W78-6, ICW7-3, ICW16-1, P1-058, P1-094, P1-240, P3-007, P3-012, P3-091, P3-109, P3-239
Matsushima, Hideyuki	P3-199	Mimura, Norihiro	W42-4, P2-134, P2-205, P2-290
Matsushita, Hiromi	W12-4, W39-3, W59-4, W64-6, W65-5, P1-046, P2-105, P3-090, P3-126, P3-284	Mimura, Toshihide	W17-5, W28-3, W54-5, W55-3, ICW2-5, P1-008, P1-082, P2-006, P2-201, P3-138
Matsushita, Isao	LS18 , W19-4, P3-028	Minami, Rumi	P1-212, P2-025, P3-161, P3-253 , P3-303
Matsushita, Masakazu	W3-6, P2-223, P2-246	Minami, Runa	P1-111
Matsushita, Takashi	P3-110	Minami, Shota	P3-199
Matsushita, Takayuki	P1-025	Minamoto, Hiroko	P1-049
Matsuura, Isao	W18-6, P2-266, P3-148	Mine, Masanobu	W9-4
Matsuura, Mio	P1-081	Minemura, Nobuyoshi	P2-197, P3-098, P3-164, P3-205, P3-221, P3-283
Matsuura, Takanori	P1-031	Mino, Nanami	W46-3 , W69-4, P1-178, EP1-07, EP2-01
Matsuura, Yoshinobu	W9-2, P2-097, P2-126, P3-204 , P3-246, P3-259, P3-270	Minoda, Masahiro	P2-275, P3-045
Matsuyama, Tsuyoshi	W7-2	Minoda, Saki	W53-1 , P3-109, P3-147
Matsuyama, Yukihiro	W49-5, P1-044	Minota, Seiji	P1-004, P2-198, P3-150, P3-154, P3-177, P3-245, P3-258
Matsuzaki, Tomoko	P1-214	Minowa, Kentaro	P1-129, P2-187, P2-194 , P2-199, P3-234
Matsuzawa, Hiroki	P3-176	Misaki, Kenta	S2-1, MTE24, LS7-1, LS37-1 , ICW1-1, P1-040, P1-193, P2-178
Matsuzawa, Yasuo	W53-5	Misaki, Yoshikata	P3-242
Matzkies, Franziska	ICW6-2	Mishima, Koji	W34-5, P3-052 , P3-254
		Mishima, Shuko	W13-1, W13-6, P3-308
		Mishra, Panna	EP1-05, EP2-08, EP2-10
		Misra, Durga	ICW20-6
		Misra, Ramnath	ICW8-2, ICW20-6
		Mitoma, Hiroki	W26-4, W33-2, W34-5, W65-1,

Mitsugi, Naoto	ICW11-4, ICW14-6, P1-203, P2-037, P2-072, P2-221, P2-241, P3-052, P3-152, P3-202, P3-217, P3-254	Miyanaga, Akiko	P2-198, P3-154, P3-177
Mitsuhashi, Masaki	W75-6	Miyanaga, Tatsuhito	W43-6
Mitsuhashi, Takashi	W31-2-2, ICW3-2, ICW12-3, P1-034, P1-179 , P2-188, P2-277, P2-281, P3-198	Miyao, Tomoyuki	W2-3, W23-1, W23-5 , W61-1, W64-4, P2-050, P3-130, P3-215
Mitsuhashi, Takashi	P1-114	Miyara, Tadashi	P2-080
Mitsui, Hiroto	P1-124	Miyasaka, Nobuyuki	W30-4, ICW6-6, P1-022
Mitsuka, Takeshi	P1-010, P1-011	Miyasato, Hitoshi	P3-248
Mitsuo, Akiko	W10-5	Miyashima, Shigeo	W18-4
Mitsuzaki, Akio	P1-014, P1-048, P1-057	Miyashita, Taiichiro	W37-2, W47-1
Miura, Yasushi	S20-3 , W15-1 , P1-029, P2-042	Miyashita, Tomoko	P1-196
Miura, Yoko	W13-1, W17-1 , W21-2 , W31-2-5, W34-6, W65-6, P1-105, P1-182, P1-192	Miyata, Hiroko	ICW3-4, ICW11-2, ICW11-5, ICW19-2
Miwa, Yusuke	W65-6 , P1-105, P1-182	Miyata, Masayuki	W34-4, W57-3 , ICW6-6, P1-236
Miya, Masaaki	P2-033	Miyauchi, Shunichi	W34-3, P1-028, P1-235, P2-219, P3-115
Miya, Masahiko	P2-101	Miyawaki, Shoji	W31-1-1, W31-2-4 , W73-5, P1-064, P2-060
Miyabe, Yoshishige	ICW5-4	Miyawaki, Yoshia	P1-187
Miyachi, Kazusa	P2-134, P2-205	Miyazaki, Moemi	P1-040 , P1-193, P2-178
Miyagawa, Eiko	P2-063	Miyazaki, Yoichi	P2-084
Miyagawa, Ippei	W4-1, W13-2, W51-2, W55-1, ICW6-5, ICW7-1, ICW8-1, ICW12-1, ICW12-2 , ICW12-6, ICW13-5 , ICW14-5, ICW16-4, ICW17-2, ICW17-6, ICW19-2, P3-229, P3-300, EP1-04	Miyazaki, Yusuke	W4-1, W13-2, W51-2, W55-1, ICW6-5, ICW7-1, ICW8-1, ICW9-4, ICW12-1, ICW12-2, ICW12-6, ICW13-5, ICW14-5, ICW17-2, ICW17-6 , ICW21-5, P3-291 , P3-300, EP1-04
Miyagawa, Taro	P2-269	Miyoshi, Shuntaro	P1-089, P2-121, P3-112
Miyagawa-Hayashino, Aya	W26-1	Miyoshi, Yuji	MTE12, W66-2, P1-184, P1-228, P2-133, P2-224, P2-264, P2-282, P2-287, P2-308 , P2-311, P3-031, P3-074, P3-081, P3-237, P3-276
Miyagi, Rumiko	W12-2, W27-1 , P1-074, P2-203, P2-248	Mizoguchi, Fumitaka	W62-6, ICW8-3
Miyagi, Taichi	W10-4, W13-3, W20-4, W78-2, W78-4 , P3-226, P3-292	Mizoguchi, Yukari	P3-271
Miyaguchi, Yuki	P3-187	Mizokami, Akinari	W9-4, W33-5, W47-1, P1-053
Miyahara, Hisaaki	W49-6, P1-150, P1-151, P1-165, P1-222, P2-161, P2-167, P2-185	Mizunashi, Yumiko	P2-063
Miyake, Hirofumi	W42-6, W53-1, P3-030, P3-109, P3-147	Mizukawa, Kaoru	W31-1-5 , W59-1, W61-2, W73-4, P1-195
Miyake, Katsuhisa	W59-5, W60-5, P1-171	Mizuki, Nobuhisa	S14-2
Miyake, Kohei	P1-126, P1-189	Mizuki, Shinichi	W30-4, W34-4, P1-236, P2-183 , P2-230, P2-302
Miyake, Nobuaki	P1-010, P1-011	Mizuno, Hiroaki	W6-4, W6-5, W16-4, W48-4
Miyake, Okiko	SS1-1	Mizuno, Hiroki	W53-4 , P1-055
Miyake, Sachiko	EL5 , W26-3, W79-3, W79-5, P1-020	Mizuno, Masami	P3-099
Miyake, Yoshihiro	S20-1	Mizuno, Masashi	P3-080
Miyakoshi, Naohisa	S3-3, W24-2, P1-003, P1-086, P2-094, P2-115, P2-154, P2-171	Mizuno, Yumiko	W45-4, W51-5, P3-049 , P3-214, P3-311
Miyama, Akira	ICW2-1	Mizushima, Ichiro	W42-1 , W43-6, W56-6, P3-009, P3-067, P3-102, P3-192
Miyamae, Takako	W7-2, W31-2-5, P2-255, P3-294	Mizushima, Machiko	W64-6, P1-190
Miyamoto, Shigeki	P2-312	Mizushina, Kennosuke	W9-1, W36-4, P2-218
Miyamoto, Shigeyuki	W49-5, P1-044	Mizuta, Mao	W7-1, W7-6
Miyamoto, Toshiaki	W11-1, W11-2, W11-6, W19-6 , W28-4 , W71-2, ICW7-3, P1-116 , P1-137, P2-046 , P2-088 , P2-277, P3-297	Mizuta, Shuichi	P2-292
Miyamura, Tomoya	W10-5, W59-5, W60-5, P1-212, P2-025 , P3-161, P3-253, P3-303	Mizutani, Satoshi	W74-4, P3-133
		Mizutani, Yasuhiko	W66-6
		Mizutani, Yuki	W44-4, P1-181, P2-040, P3-100 , P3-124, P3-164 , P3-205
		Mizutomi, Kazuaki	W56-6, P3-140
		Mizuuchi, Takahiro	P1-016 , P2-291, P2-295

Mo, Shoin	P2-078	Morita, Yoshitaka	W73-2, ICW1-6, ICW4-5, ICW15-2,
Mochida, Yuichi	W75-6		P1-019, P1-063, P2-202, P2-225
Mochizuki, Takeshi	P1-002	Moriwaki, Kazuhiko	P3-018
Moder, Kevin	ICW17-4	Moriya, Atsushi	P1-067
Mogi, Shinsuke	P1-214	Moriyama, Masafumi	P2-239
Mohamed, Mohamed Eslam		Moriyama, Mayuko	P1-121, P3-093, P3-309
	W38-2	Moriyama, Rina	W31-2-3
Mohning, Michael P	ICW16-2	Morooka, Mizuho	P3-179
Mokuda, Sho	W4-5, W57-4, ICW2-6 , P2-010, P2-217, P3-131, P3-268, P3-279	Mosca, Marta	W31-1-7
Momohara, Mariko	W69-6	Moss, Laura K	PS-2
Momohara, Shigeki	P1-084, P2-128	Moss, Phillip	ICW4-6
Momoki, Noriya	W4-6, W60-2, W71-4, P3-162	Motegi, Sei-ichiro	W52-4, ICW21-2
Momose, Masashi	P1-007	Motohashi, Yutaka	P2-033
Momoyama, Gen	P3-010	Motojima, Shinji	W23-3 , W76-4, P2-059 , P2-061 , P2-081, P2-091, P2-093, P3-041, P3-075, P3-294
Monnier, Philippe P	ICW21-3		
Morand, Eric	S4-2, ES2-2	Motojima, Yasuhito	P1-031
Mori, Hiroaki	P1-016, P1-017, P2-291, P2-295	Motomura, Hiraku	LS18, W19-4 , P3-028
Mori, Hiroyoshi	P2-008	Motomura, Kyoko	W46-3, W69-4 , P1-178, EP1-07, EP2-01
Mori, Ichiro	W63-3, P1-077, P3-071		
Mori, Kei	EL24-1	Motonaga, Takuro	S1-5
Mori, Koichi	W65-2	Mototani, Hideyuki	W8-1
Mori, Masaaki	S7-4 , S9-3, S9-7, S14-5, EL13 , LS35-2 , W7-1, W7-3, W7-4, W31-2-5, W76-3, P1-015, P3-305	Mouri, Mariko	S9-7 , W7-3, P3-305
		Mozaffarian, Neelufar	ICW6-2
Mori, Mika	S1-5	Mozaffarian, Neely	ICW6-3
Mori, Shotaro	W65-2, W71-5, P1-154, P2-035, P2-083, P2-136	Mugii, Naoki	P3-110
		Mukae, Hiroshi	S19-1 , W11-5
Mori, Shunsuke	S19-2 , W10-5	Mukai, Akihiko	P1-120
Mori, Shunsuke	P1-106, P2-078	Mukai, Masaya	W45-3, W47-4
Mori, Tatsuo	W66-2, P1-184, P2-224, P2-264, P2-282, P2-287, P2-296, P2-311, P3-031 , P3-074, P3-081, P3-106, P3-276	Mukai, Tomoyuki	W73-2, ICW1-6, ICW4-5, ICW15-2, P1-019, P1-063, P2-202, P2-225
			P1-209
Mori, Yu	P3-034	Mukofujiwara, Yuka	W3-5, W51-1, W77-4, P2-247, P3-121
Morii, Kanta	W17-6, W37-6 , P1-030, P1-033	Mukohara, Saki	
Morimoto, Mai	W41-3, W47-5, W51-6, P2-107, P2-139 , P3-082, P3-094, P3-173, P3-185, P3-249, P3-256	Mukoyama, Hiroki	W31-1-5, W59-1 , W61-2, W73-4, P1-195
Morimoto, Norio	W19-5	Mukunoki, Daichi	P1-146 , P2-100, P2-174
Morimoto, Shinji	P3-095, P3-129, P3-193	Munenaga, Syuichi	P1-036
Morinobu, Akio	S6-1, ES7-1 , W31-1-1, W68-6, ICW1-1, ICW6-1, ICW7-4, P1-107, P2-278, P2-299, P3-077, P3-114, P3-181	Murai, Masayuki	P2-063
		Murai, Takehiro	EP2-12, EP2-14
Morio, Tomohiro	W7-3	Murai, Yasuhisa	W12-1, P2-108, P2-193
Morise, Hiroko	P1-108, P1-110, P1-167	Murai, Yukari	P1-054, P1-226, P2-276, P2-297, P3-107
Morishige, Masashi	P1-113		
Morishita, Michiko	W40-1, P2-024, EP1-02	Murakami, Akinori	P1-108, P1-110 , P1-167
Morishita, Shinobu	W18-4	Murakami, Daisuke	P2-273
Morita, Akimichi	W22-1, W22-2	Murakami, Isao	P3-012
Morita, Akira	W50-2	Murakami, Ken	P3-227
Morita, Hiromi	P1-003, P2-115, P2-154	Murakami, Kenya	P3-002
Morita, Hiroyuki	W35-5, W63-3, W78-1, P2-190, P2-261, P3-255	Murakami, Kosaku	W9-5, W30-4, W32-1, W36-6 , W47-2, W51-5, W54-5, W75-2, W78-6, ICW7-4, P1-058, P1-240, P3-007, P3-012, P3-091, P3-239
Morita, Kaoru	ICW18-4	Murakami, Miho	ICW7-3
Morita, Kazuo	P1-094	Murakami, Rieko	W42-2, P2-300, P3-037
Morita, Takayoshi	W45-4, P3-049, P3-311	Murakami, Tetsushin	W26-4, W65-1, P2-037, P2-072 , P3-063
		Murakawa, Yohko	S14-4 , ICW6-6, P1-121, P3-093, P3-309

Nakagawa, Natsuko	MTE20, ES19-1 , W54-2, P1-153, P3-141, P3-236	Nakamura, Shigeru	W71-6
Nakagawa, Shiori	P3-051	Nakamura, Shinichiro	W50-5
Nakagishi, Yasuo	W7-1	Nakamura, Shohei	W18-6 , P2-266, P3-148
Nakagome, Yoko	P1-180, P2-306, P3-084 , P3-087, P3-184	Nakamura, Tadashi	P3-111 , P3-291
Nakagomi, Daiki	W4-3 , W40-6, P2-073, P3-175, P3-262	Nakamura, Takashi	P1-158
Nakahara, Hideko	S1-1	Nakamura, Takayuki	ICW9-5, P1-223 , P3-166
Nakahara, Mami	W14-1, W14-6	Nakamura, Takeomi	W24-4, W49-2, ICW10-6
Nakahara, Ryuichi	S11-2, EL15 , W66-5, ICW9-3, P1-059, P1-168, P1-251, P3-016	Nakamura, Tomoko	P2-286
Nakajima, Arata	W5-5, W24-1, W56-1, W56-2 , P1-157, P1-158, P2-157	Nakamura, Tomoyuki	P3-195, P3-244
Nakajima, Ayako	W36-1, W37-4, W44-4, W70-1, W70-7, P1-001, P1-181, P2-040, P3-100, P3-124	Nakamura, Yoshihiro	P1-054, P1-226, P2-276, P3-107
Nakajima, Hideaki	W31-2-2, W72-4, ICW3-2, ICW11-1, ICW12-3, P1-034, P1-179, P2-188, P2-277, P2-281, P3-188, P3-198, EP1-09	Nakamura, Yoshikazu	S18-4
Nakajima, Hiroshi	W4-3, W12-5, W29-6, W40-6, ICW17-4, ICW18-2, P1-050, P1-205, P2-022, P3-104	Nakamura, Yoshiyuki	W66-6
Nakajima, Kazue	EL6	Nakamura, Yutaro	S10-5
Nakajima, Kyoichi	P2-233	Nakanishi, Kensuke	P3-169
Nakajima, Mikio	W19-5	Nakanishi, Koichi	P2-254
Nakajima, Sotaro	W41-4 , W46-3, W69-4, P1-178, EP1-07, EP2-01	Nakanishi, Yuichiro	P3-042
Nakajima, Tomoya	P1-098	Nakano, Hiroto	P1-034
Nakajima, Toshihiro	P2-001	Nakano, Kazuhisa	LS15-2 , W4-1, W13-2, W30-4, W51-2 , W54-5, W55-1, ICW3-4, ICW6-5, ICW7-1, ICW7-3, ICW8-1, ICW9-4, ICW12-1, ICW12-2, ICW12-6, ICW13-5, ICW14-5, ICW17-1, ICW17-2, ICW17-6, ICW19-2, ICW21-5, P3-300, EP1-04
Nakajima, Toshiki	P2-235 , P3-132	Nakano, Mai	W51-6, P2-107, P3-082, P3-173, P3-249 , P3-256
Nakajo, Ko	W22-1, W22-3, W44-2	Nakano, Masaaki	W16-3, W21-5, W40-4, W68-3, ICW2-3, P1-013, P1-177, P1-198
Nakakubo, Yuto	P3-132	Nakano, Masahiro	W52-1, P1-201
Nakamachi, Yuji	W68-6	Nakano, Miki	P1-203 , P3-202
Nakamichi, Yusuke	W66-2, P1-184, P2-224, P2-264 , P2-282, P2-287, P2-296, P2-311, P3-031, P3-074, P3-081, P3-276	Nakano, Naoko	W63-1
Nakamura, Akihiro	ICW21-3	Nakano, Shiho	W5-5, W56-2, P1-157, P1-158, P2-157
Nakamura, Eri	W13-4	Nakano, Shota	P3-209 , P3-218
Nakamura, Hideki	W31-1-6, W32-6, W33-5, W37-2, W43-4, W47-1, W48-5, W54-5, W62-5, ICW10-3, ICW15-1, P1-037, P1-069, P2-243 , P3-171	Nakano, Souichiro	W3-6, P1-129
Nakamura, Hiroaki	S2-4, W5-1, W16-5, W16-6, W23-6, W36-3, W37-1, W44-6, W68-1, W70-6, P2-062, P3-004, P3-005, P3-019, P3-020, P3-021, P3-290	Nakano, Yumiko	P2-235, P3-132
Nakamura, Hiroshi	P2-048	Nakao, Yoshinobu	W18-3, W22-4, W55-3, W59-5, W60-5, P3-097, P3-138, P3-142 , P3-281
Nakamura, Hiroyuki	W4-2, W47-4, ICW4-3, P2-215	Nakaoka, Yoshikazu	S4-5 , P2-008
Nakamura, Ichiro	W68-2 , W75-5, P1-134	Nakasa, Tomoyuki	S3-4
Nakamura, Junichi	W50-1, P2-262	Nakasatomi, Masao	W32-4, P2-012
Nakamura, Ryota	P3-195, P3-244	Nakaseko, Haruna	W7-4, P2-250
Nakamura, Satoko	W42-2, P1-096, P1-119	Nakashima, Akikatsu	P1-210
Nakamura, Satoshi	W5-2	Nakashima, Daisuke	P2-270
Nakamura, Sayaka	ICW21-3, ICW22-5, EP3-09	Nakashima, Hitoshi	W59-5, W60-5, P1-171
Nakamura, Seiji	P2-239	Nakashima, Munetoshi	W37-2, W47-1, P3-013
Nakamura, Shigeo	S21-3	Nakashima, Ran	W9-5, W32-1, W78-6, P3-012, P3-091, P3-109, P3-239
		Nakashima, Satoru	P3-277
		Nakashima, Shusaku	W10-4, W13-3, W20-4, W78-2, P3-226, P3-292
		Nakashima, Syusaku	W78-4
		Nakashima, Yasuharu	W26-2, ICW19-5, P1-041, P1-065, P2-172
		Nakashima, Yoshikazu	P1-069, P3-146, P3-220
		Nakashita, Tamao	W23-3, W76-4 , P2-059, P2-061, P2-081 , P2-091, P2-093, P3-041 ,

	P3-075, P3-294	Nawata, Takashi	W3-1, W67-3, W77-2
Nakata, Chiai	P3-201	Nawata, Yasushi	P2-022, P2-134, P2-135, P2-205
Nakata, Hitoshi	P2-294	Negishi-Hoshino, Kana	P1-027
Nakatani, Tomoya	P1-027	Negoro, Nobuo	P3-199
Nakatsubo, Daisuke	P2-226, P3-123	Nemoto, Takuya	W31-2-5, P3-069, P3-295
Nakatsue, Takeshi	W16-3, W21-5 , W40-4, W68-3, ICW2-3, P1-013, P1-177, P1-198	Nemoto, Tetsuya	P1-170
		Nemoto, Yoko	W14-1
Nakatsuka, Keisuke	W13-2, ICW3-4	Nezu, Takahiro	P1-162
Nakaya, Hiroyuki	W49-1, P1-225, P2-289	Niewold, Timothy B	ICW17-4
Nakaya, Izaya	P3-179	Nigil, Haroon	ICW13-2
Nakayama, Kaori	EL24-1	Nii, Takuro	ICW16-5
Nakayama, Takeo	ES4	Niuro, Hiroaki	W26-4, W33-2, W34-5, W59-5, W60-5, W65-1, ICW11-4, ICW14-6, P1-203, P2-037, P2-072, P2-221, P2-241, P3-052, P3-063, P3-152, P3-202, P3-217, P3-254
Nakayama, Yoichi	W53-1, P3-109 , P3-147		P2-001
Nakayamada, Shingo	S5-4, W4-1 , W13-2, W51-2, W55-1, ICW3-4, ICW6-5, ICW7-1, ICW8-1, ICW9-4, ICW11-2, ICW11-5, ICW11-6, ICW12-1, ICW12-2, ICW12-6, ICW13-5, ICW14-5, ICW16-4, ICW17-1, ICW17-2, ICW17-6, ICW19-2, ICW21-5, P3-291, P3-300, EP1-04	Niki, Hisateru	W49-6
		Niki, Yasuo	ICW6-3
Nakazaki, Satoshi	W15-3 , W19-4, P3-009	Nikulenkova, Natalya	ICW3-5, ICW4-3, P2-215
Nakazawa, Akihiro	W74-2	Ninagawa, Keita	W76-3
Nakazawa, Daigo	P3-151	Nino, Antonio	W7-5
Nakazawa, Takashi	W54-3, ICW1-1, P1-098	Nishi, Kentaro	P3-095, P3-129 , P3-193
Nakazawa, Takuya	W33-1, ICW18-2, P1-039, P1-233	Nishi, Takuya	P3-151
Nakazono, Kiyoshi	W10-6, W25-4, W65-3, ICW2-2, P1-085, P1-088, P1-144, P1-170, P2-019, P2-155	Nishibata, Yuka	P2-250
		Nishida, Daisuke	S1-3, S11-2, ES19-2, ES8-1 , W49-6, W66-5, ICW9-3, P1-059, P1-079, P1-084, P1-168, P1-251, P3-016
Nameki, Shinichiro	W46-4, W47-3, P2-049, P2-181, P3-156, P3-189	Nishida, Keiichiro	W3-5, W51-1 , W77-4, ICW1-1, P2-247, P3-121
Namura, Noriyuki	W36-2, P1-101 , P1-123		S2-5
Nangaku, Masaomi	W1-5	Nishida, Mutsumi	P3-254
Naniwa, Taio	W11-1, W11-2, W11-6, P2-032, P3-080, P3-224, P3-298	Nishida, Tomoya	W7-4
		Nishida, Yutaka	W45-4, W48-3, ICW20-1 , P3-049, P3-311
Nanke, Yuki	P2-015	Nishide, Masayuki	P2-180
Nanki, Toshihiro	W52-2, W74-4, P1-084, P3-133		P1-111
Nara, Mizuho	P2-066	Nishihara, Ayumu	W39-1, P2-128
Narazaki, Mariko	W40-1, P2-024, EP1-02	Nishijima, Naoki	P3-134
Narazaki, Masashi	W45-4, ICW16-5, P3-049, P3-214, P3-311	Nishikawa, Atsushi	S12-3
		Nishikawa, Hirofumi	P1-127 , P2-310
Narazaki, Shinji	P1-068	Nishikawa, Hiroyoshi	W24-3, P1-145, P2-055
Narii, Nobuhiro	P2-128	Nishikawa, Masataka	S7-1 , W63-2, ICW15-2
Narita, Akihiro	P1-014, P1-048, P1-057	Nishikawa, Takuji	W17-2, P1-024, P1-032, P2-002, P2-034, EP3-08
Narita, Eri	P2-179 , P3-008, P3-301 , EP2-03	Nishikawa, Ryuta	W17-2 , P1-024, P1-032, P2-002, P2-034, EP3-08
Narita, Ichiei	W10-6, W16-3, W21-5, W40-4, W42-3, W65-3, W68-3, ICW2-2, ICW2-3, P1-013, P1-085, P1-088, P1-177, P1-198, P2-132	Nishimi, Airi	ICW7-3, P1-010, P1-011
			P1-031
Nasu, Yoshihisa	S11-2 , W66-5, ICW9-3, P1-059, P1-168, P1-251, P3-016	Nishimura, Haruki	P2-004
		Nishimura, Hiroyuki	MTE7
Natsume, Tadahiro	P1-066	Nishimura, Katsuji	W31-1-5, W59-1, W61-2, W73-4, ICW1-1, P1-195
Natsumeda, Masamitsu	P1-079, P1-246, P2-268	Nishimura, Keisuke	W3-4 , W7-1, W7-4, W57-1, P2-244, P2-265
Natsumoto, Bunki	W1-5		W12-5, P3-251
Nawachi, Shoichi	W3-2, W32-3, P1-056	Nishimura, Kenichi	W21-1 , W79-4, P1-186, P1-206, P2-071, P2-232, P3-070, P3-167,
Nawata, Aya	ICW3-4 , ICW14-5	Nishimura, Nozomi	
Nawata, Kento	W50-1, P2-262	Nishina, Hirokazu	
Nawata, Masao	W13-2, W29-2 , W55-1, ICW3-4		

Nishina, Naoshi	P3-219 W1-1, W31-2-1, W31-2-5, W56-3 , P2-245	Norris, Jill M	PS-2, ICW16-2
Nishino, Akira	W31-2-3, W79-4, P1-206, P2-071 , P2-232, P3-070, P3-167, P3-219	Nose, Yoko	P2-278, P2-299, P3-077, P3-114, P3-181
Nishino, Jinju	W68-2, W75-5, P1-134, P2-055	Nozaka, Koji	S3-3
Nishino, Jo	W2-2, W12-6, W77-6, P2-236, P3-113	Nozaki, Takamasa	W40-2, W59-3, ICW10-4, ICW10-5, P1-211, P3-033, P3-047 , P3-210, P3-293
Nishio, Kenji	P3-222	Nozaki, Yuji	W20-5, W22-6, W28-2, W35-6, W46-2, W65-4, W75-1, P1-095 , P1-207, P1-208, P2-054, P2-090 , P2-212, P3-143, P3-178
Nishioka, Aki	W54-4, P3-185	Nozato, Satoko	W12-2
Nishioka, Kusuki	P2-001	Nozawa, Daisuke	W74-3 , P1-142
Nishioka, Yasuhiko	P2-142	Nozawa, Kazuhisa	P1-129, P3-069, P3-119
Nishioka, Yosuke	P1-010, P1-011	Nozawa, Yukiko	W16-3, W40-4, W68-3, P1-177
Nishisaka, Kazuma	P3-050	Nuka, Hiromi	P3-009, P3-024
Nishitani, Kohei	W9-5, W26-1, W36-6, W50-5 , W51-3, P1-058, P1-240	Nunokawa, Takahiro	W16-2, P1-043
Nishiume, Tsuyoshi	W5-3, W14-2, W24-5, W50-4, W71-7, ICW7-2, P2-021, P2-173	O	
Nishiura, Satoko	P1-247	Ochi, Takahiro	P3-002
Nishiwaki, Atsuma	W59-3, ICW10-4, ICW10-5 , P1-211, P3-047, P3-210, P3-293	Ochiai, Moeko	W36-1, W37-4, W70-1, W70-7, P1-001
Nishiwaki, Aya	W1-5, ICW9-5, EP1-03	Oda, Hiromi	S18-3, W49-6, ICW2-5
Nishiyama, Susumu	LS34-1 , W31-1-1, W31-2-4, W36-5 , W54-5, W73-5, P1-016, P1-017, P1-064, P2-060	Oda, Katsuhiko	P1-239, P1-241, P3-105
Nishiyama, Taihei	W1-2, W20-3, W76-2 , W76-5, ICW12-4, P2-111	Oda, Keisuke	W4-5, W57-4, P2-217, P3-131, P3-268, P3-279
Nishizawa, Tohru	W18-4, P3-048 , P3-060, P3-116	Oda, Kosaku	P1-136
Niwano, Tomoko	W64-2	Oda, Ryo	W15-4, W25-1 , W25-2, W25-3, W27-6, P2-087
Nobata, Hironobu	W59-2 , P1-238, P2-192, P2-209, P3-101, P3-206	Ofilas, Maeflor Q	EP1-13
Nobuhara, Yumiko	ICW1-1, P1-098	Oga, Kenya	W15-1
Noda, Kentaro	W8-4, W44-4 , W64-1, P1-025, P1-181, P2-040, P3-100, P3-124 W16-2 , P1-043	Ogane, Kunihiro	P3-024, P3-102
Nogi, Shinichi	W47-4, P1-096, P3-228	Ogasawara, Masami	P3-032
Noguchi, Atsushi	P1-136	Ogasawara, Michihiro	S2-2 , MTE9 , W3-6, P1-097, P2-223, P2-272, P3-069, P3-295
Noguchi, Ikuyo	W51-6, P3-082, P3-094, P3-173, P3-256	Ogasawara, Takashi	P3-137, P3-260
Noguchi, Kazuteru	S3-2, S11-5, W28-5, W49-1, W50-6, W73-1, P1-149	Ogata, Yoshiyasu	P3-271
Noguchi, Takaaki	W3-5 , W51-1, W77-4, P2-247, P3-121	Ogawa, Eisuke	P2-137
Nohda, Yasuhiro	W4-5, W57-4, P2-217, P3-091, P3-131, P3-268, P3-279	Ogawa, Hiroaki	P3-247
Nojima, Takaki	P2-012	Ogawa, Kunikazu	W6-4, W6-5, W16-4, W48-4, W67-1, P1-047
Nojima, Yoshihisa	P2-153	Ogawa, Mika	P1-135
Nojiri, Sho	S17-2 , MTE25 , P1-008	Ogawa, Noriyoshi	W4-4, P1-199 , P3-304
Noma, Hisashi	W74-1, P1-152	Ogawa, Tetsuya	P3-275
Nomoto, So	W79-3	Ogihara, Hideki	W16-2, P1-043
Nomura, Atsushi	P1-242, P3-117	Ogino, Hirokazu	P2-142
Nomura, Hitoha	W46-4, W47-3, P2-049, P2-181	Ogino, Masaaki	P1-003, P2-115
Nomura, Koji	W18-4, P1-231, P3-048, P3-060, P3-116, P3-267	Ogita, Chie	W51-6, P2-139, P3-082 , P3-094, P3-173, P3-185, P3-249, P3-256
Nomura, Shosaku	P1-215, P3-088	Oguchi, Hiroko	P3-232
Nomura, Shun	W10-4	Oguchi, Takeshi	W75-4, P1-166 , P2-051
Nomura, Yumi	W32-2, ICW15-1	Oguni, Hidetomo	P2-191
Nonaka, Fumiaki	W35-2, P2-073	Ogura, Masao	W7-5
Norimoto, Ayako		Ogura, Takashi	S10-4
		Ogura, Takehisa	W9-1 , W36-4, W45-2, P1-188, P2-218, EP2-04, EP2-09
		Oguri, Yusuke	P1-124
		Oguro, Eri	W28-5, W61-3, W73-1, ICW9-1 ,

	ICW9-2, P1-061, P2-036, P2-067, P3-078, P3-118	Oishi, Yukiyoshi	P1-075, P2-102, P2-118
Ohguro, Masahiko	W53-4	Oishi, Yuko	W32-4, P2-012
Ohguro, Nao	W65-6, P1-105, P1-182, P1-192, P2-280, P3-144	Oiwa, Hiroshi	W2-6, P2-039 , P2-112
Oh, Koei	S3-6, P1-115	Ojima, Tomohiro	W68-5
Ohara, Masato	W25-1, W25-2	Oka, Hiroshi	P3-269
Ohara, Yuri	P3-196	Oka, Shomi	P2-011
Ohashi, Hideki	S11-2, ICW9-3, P1-168, P1-251, P3-016	Oka, Yumiko	P2-086
Ohashi, Hiroyuki	P3-159	Okabayashi, Ryo	P1-044
Ohashi, Keiji	W40-1 , P2-024, P3-172, EP1-02	Okabayashi, Ryou	W49-5
Ohashi, Michiko	P2-097, P2-126, P3-246, P3-259 , P3-270	Okada, Akinori	W20-5, W22-6, P1-095, P1-207
Ohashi, Satoru	W24-4, W26-6, W49-2, ICW10-6	Okada, Akitomo	W34-4, W37-2, P1-236, P3-146, P3-220
Ohashi, Toshiro	W14-4, W37-3, P1-221, P2-103, P2-106, P3-306	Okada, Hideyuki	P2-204
Ohi, Katsuhiko	W4-5, W57-4, P2-010, P2-217, P3-131, P3-268, P3-279	Okada, Hiroyuki	ICW22-1
Ohki, Hisashi	P1-160	Okada, Masato	S9-6, LS11, LS28-2, W22-1, W22-2 , P2-227, P3-196, P3-213, P3-285
Ohkubo, Naoaki	W13-2, ICW3-4, ICW8-1, ICW11-2, ICW11-6, ICW12-6 , ICW17-1	Okada, Norihiro	W58-5
Ohkura, Toshiaki	P2-051	Okada, Ryoko	P1-249
Ohmagari, Norio	EL23	Okada, Yukinori	S12-1, ICW1-3
Ohmura, Koichiro	LS35-1 , W9-5, W32-1, W36-6, W66-4, W78-6, ICW16-1, P1-071, P1-072, P1-175, P1-245, P2-148, P3-012, P3-091, P3-239	Okada, Yusuke	W2-5, W3-3 , W35-4, W39-4, W60-3, W60-4, ICW20-5, P2-119
Ohnari, Shimpei	P3-058	Okahata, Akinori	W26-1
Ohnishi, Ai	W3-4, W57-1 , P2-244, P2-265	Okai, Takahiro	W10-2 , W55-4, P1-147, P2-045
Ohnishi, Ako	W14-3, W15-6	Okamoto, Akira	W10-5, W34-1, W73-5, P1-126 , P1-189
Ohnishi, Hideo	P1-031	Okamoto, Hideyuki	P1-006
Ohnishi, Naoki	ICW4-3, ICW4-4	Okamoto, Kazuo	S15-4
Ohnishi, Yasutaka	P1-126, P1-189	Okamoto, Keiji	P1-219
Ohno, Shigeru	W31-1-6, W31-2-2, W32-6, W72-4, ICW3-2, ICW12-3, P1-034, P1-179, P1-182, P1-187, P1-191, P2-188, P2-277, P2-281, P3-188	Okamoto, Keita	W55-3
Ohsaki, Hirofumi	P3-039	Okamoto, Kensaku	W31-1-2
Ohsawa, Suguru	P2-082	Okamoto, Masaki	P3-096
Ohsawa, Yoshikiyo	P2-294	Okamoto, Masashi	P2-097, P2-126, P3-246, P3-259, P3-270
Ohshige, Tatsuhiko	W31-2-6	Okamoto, Momoko	W31-1-6, W32-2 , W32-6, W33-5, W48-5, W62-5, P1-037, P1-069
Ohshima, Miho	P1-228 , P2-133, P2-308, P3-237	Okamoto, Nami	W7-1, W13-4, P2-252
Ohshima, Shiro	W10-5, W28-5 , W50-6, W54-5, W61-3, W67-5, W73-1, ICW9-1, ICW9-2, P1-061, P2-036, P2-067, P3-078, P3-118	Okamoto, Shota	W1-2, W20-3 , W76-2, W76-5, ICW12-4, P2-111
Ohson, Yasuo	W10-1, P3-044	Okamoto, Yuko	PS-2, W31-2-3, ICW16-2
Ohta, Fumie	P1-214	Okamura, Koichi	W8-5
Ohta, Shun-ichiro	W59-5, W60-5	Okamura, Tomohisa	W52-1, W64-3, W72-1, ICW1-2, ICW1-4, ICW11-3, ICW18-1, ICW18-4, ICW21-1, P1-201
Ohtori, Seiji	W50-1	Okano, Tadashi	S2-4 , W5-1, W9-2 , W16-5, W16-6, W23-6, W36-3, W37-1, W44-6 , W68-1, W70-6, P2-023, P2-062, P3-003, P3-006, P3-008, P3-019, P3-020, P3-021, P3-290, P3-301
Ohtsubo, Hideo	P2-095 , P3-277	Okano, Takaichi	W9-2, ICW7-4, P1-107, P2-278, P2-299, P3-077, P3-114, P3-181
Ohtsuji, Mareki	P2-004	Okano, Yutaka	W10-1, P3-044
Ohya, Naoko	P1-190	Okari, Takuro	W15-5, W39-5, P1-174, P2-138, P2-141
Ohyama, Ayako	W1-2, W20-3, W26-5, W76-2, W76-5, ICW12-4, ICW16-3, P2-007 , P2-111	Okawa, Tadashi	P2-165
Oikawa, Emiko	EL24-1	Okawa, Tokutaro	EP2-03
		Okayama, Akihiko	W34-3, P1-028, P1-235, P2-219, P3-115
		Okazaki, Ayana	P3-073

Okazaki, Hideki	P2-004	Ono, Nobuyuki	W18-3, W22-4, W59-5, W60-5,
Okazaki, Kazuichi	S7-6	Ono, Seiichi	P3-097 , P3-142, P3-152, P3-281
Okazaki, Ken	S3-6, EL11 , W49-4, P1-002, P1-115, P1-163, P1-169	Ono, Yuko	P3-194 EL7, W43-3, ICW14-4, P2-239 , P2-240, P2-242
Okazaki, Ryota	W11-4, P1-012, P2-259	Onobori, Makoto	W11-7
Okazaki, Yuka	W8-2, W69-1, W69-2	Onose, Takafumi	P3-076 , P3-086, P3-180, P3-182, P3-207
Oketani, Yuto	W17-6, W37-6, P1-030, P1-033	Oohara, Asami	W7-4 , P2-250
Oki, Hiroharu	W18-5, ICW18-3, P2-016, P2-079, P2-110, P2-160, P2-256	Ooka, Seido	W12-4 , W39-3, W59-4, W64-6, W65-5, P1-046, P2-105, P3-090, P3-126, P3-284
Oki, Nozomi	W48-2, W48-5, W48-6, P1-069, P1-070	Oonishi, Takahiro	P3-310
Okita, Rina	W12-2, W27-1, P1-074, P2-203, P2-248	Oribe, Motohiro	W8-6, W38-1, W79-6, P1-010, P1-011
Okita, Shunji	S11-2, ICW9-3, P1-059, P1-168 , P3-016	Origuchi, Tomoki	W31-1-6, W32-2, W32-6, W33-5, W37-2, W43-4, W47-1 , W48-5, W62-5, ICW10-3, ICW15-1, P1-037, P1-069, P2-170, P2-207, P3-171
Okita, Yasutaka	W28-5, W61-3, W73-1, ICW9-1, ICW9-2, P1-061, P2-036, P2-067, P3-078, P3-118	Orita, Kazuki	W36-3 , P2-179
Oku, Kenji	W31-2-5, W35-3, W62-4, ICW3-5, ICW4-3, ICW4-4, ICW8-5, ICW10-2, ICW16-6, ICW19-4, P2-215, EP3-01	Oroku, Masato	P3-201
Okubo, Mai	W52-1, W64-3, W72-1 , ICW21-1	Orui, Hiroshi	W18-5, ICW18-3, P2-079, P2-110, P2-256
Okuda, Kosuke	W8-6, W75-1, P2-123, P3-014	Oryoji, Daisuke	W26-4, W65-1, P2-037, P2-072, P3-063
Okuda, Toshiharu	W25-5	Oryoji, Kensuke	LS7-2 , W59-5, W60-5, P2-183, P2-230, P2-302
Okuda, Yasuaki	W14-3, W15-2, W70-2 , P1-018, P1-217, P2-257, P2-258, P2-293	Osada, Atsumu	W1-2, W20-3, W26-5 , W76-2, W76-5, ICW12-4, ICW16-3, P2-005, P2-007, P2-111
Okumura, Ikumi	W17-6, W37-6, P1-030 , P1-033	Osaki, Makoto	W48-5, W48-6, P1-070
Okumura, Maiko	P1-023 , P2-285	Osborn, Thomas	ICW17-4
Okuno, Hiroshi	W37-2, P3-247	Oshikawa, Hideto	W20-1
Okura, Chisa	W8-5	Oshima, Akira	P2-265
Okura, Yuka	W7-1	Oshima, Hisaji	W6-4, W6-5, W16-4, W48-4, P1-047
Okuyama, Ayumi	W35-4, ICW20-5	Oshima, Kahori	P2-197, P3-098, P3-164, P3-205, P3-221 , P3-283
Okuyama, Shin	P2-066	Oshima, Masashi	W59-3, ICW10-4, ICW10-5, P1-211, P3-047, P3-210, P3-293
Okuzono, Yuumi	W8-1, ICW1-5	Oshimura, Aya	P1-248 , P2-184
Olmer, Merissa	ICW2-6	Oshiro, Takuya	P3-057, P3-201
Olsen, Bjorn R	S15-1	Östör, Andrew	ES5-2
Omata, Yasunori	ICW18-5 , ICW22-1	Ota, Kosuke	P3-273 , P3-287
Omoteyama, Kazuki	P2-017	Ota, Mineto	S5-2, W52-1, W64-3, W72-1, ICW1-2, ICW1-4, ICW21-1, P1-201
Omoto, Atsushi	W34-4, W44-5, W73-3 , P1-236, P2-077, P3-089	Ota, Muneo	P3-247
Omura, Satoshi	W44-5, W73-3, P2-077, P3-089	Ota, Shinji	P2-193
Omura, Shin-ichiro	W11-1 , W11-2 , W11-6 , P3-224, P3-298	Ota, Shusuke	P1-172
Omura, Yuichi	W1-4	Ota, Toshiyuki	W54-2, P1-122
Onishi, Akira	W36-6, W51-1, W51-5, W55-2, W55-6, W75-2, ICW1-1 , ICW6-1, ICW7-4 , P1-107, P1-231, P2-052, P2-278, P2-299, P3-007, P3-077, P3-114, P3-181	Ota, Tsuguhito	W31-1-2
Onishi, Ikuko	P1-100	Ota, Yuichiro	ICW10-1, ICW20-3
Onishi, Kae	W31-2-5, W66-2, P1-184, P2-224 , P2-264, P2-282, P2-287, P2-296, P2-311, P3-031, P3-074, P3-081, P3-276	Ota, Yuki	S3-4
Onishi, Makoto	W14-3, W15-2, W15-6, W70-2, P1-018, P1-217, P2-257, P2-293	Ota, Yuko	ICW5-5
Ono, Kumiko	W9-6, P3-022	Otaki, Yasuhiro	W28-6
		Otani, Fumi	P3-299
		Otani, Hiroshi	W25-4, W65-3, P1-085, P1-088, P1-144, P1-170, P2-019, P2-155
		Otani, Kazuhiro	W8-4, P1-025

Othman, Ahmed A	W38-1, W38-3		P3-178
Oto, Yohsuke	W8-4, P1-025	Rider, Lisa G	ICW8-4
Otomo, Kotaro	W31-2-1	Rigby, William	W38-3
Ototake, Yasushi	W69-5, P3-203	Rikitake, Mao	W34-3, P2-219, P3-115
Otsu, Makoto	P2-242	Rikitake, Yuki	P2-219, P3-115
Otsuka, Fumio	P3-018	Rischmueller, Maureen	W38-2
Otsuka, Kyoko	W59-5, W60-5, P3-152	Riyadh, Asrafuzzaman	ICW21-3
Otsuka, Mizuna	W31-1-6, W32-6, W33-5, W48-5, W62-5, P1-037 , P1-069	Robb, Kevin P	EP3-02
Otsuka, Yukimi	P2-037	Rockel, Jason S	ICW22-5, EP3-09
Ouhara, Kazuhisa	P1-036 , P3-072	Rogai, Veronica	W38-6
Owada, Takayoshi	W2-3, W23-1, W23-5, W61-1, W64-4, P2-050 , P3-130, P3-215	Rokutanda, Ryo	P2-227, P3-196, P3-213
Owaki, Hajime	P1-127, P2-310	Rooney, Terence	W38-6, W39-1
Oya, Yoshihiro	W33-1, ICW18-2 , P1-039, P1-233	Rossomacha, Evgeny	ICW21-3, ICW22-5
Oyabu, Hideaki	W74-6	Roth, David	W76-3
Oyakawa, Tomo	P1-213, P2-267	S _____	
Oyama, Junji	P3-179	Sada, Eiji	W21-3, W41-2, W47-6, P1-052
Ozaki, Hiroki	P3-226	Sada, Ken-ei	LS2-1 , W31-1-6, W31-2-2, W32-6, W40-1, W41-5, W41-6, ICW2-4, ICW3-2, P1-179, P1-182, P1-187, P1-191, P2-024, P2-188, P2-277, P2-281, P3-172, EP1-02
Ozaki, Kyoko	P3-165	Sada, Ryuichi	W42-6, W53-1, P3-030, P3-109, P3-147
Ozaki, Shoichi	W17-4, W41-6	Sadanaga, Yuri	W18-3, W22-4, W59-5 , W60-5, P3-097, P3-142, P3-281
Ozaki, Takashi	W1-4, ICW5-2	Saegusa, Jun	W68-6, ICW6-1, ICW7-4, P1-107, P2-278, P2-299, P3-077, P3-114, P3-181
Ozaki, Takuro	P3-029	Saeki, Takako	W42-3
Ozaki, Toshifumi	S11-2, ICW9-3, P1-059, P1-168, P1-251, P3-016	Saeki, Yukihiko	W10-5, W28-5, W34-1, W50-6, W61-3, W67-5, W73-1, ICW9-1, ICW9-2, P1-061, P2-036, P2-067, P3-078, P3-118
Ozaki, Yoshio	W18-4 , P1-138, P1-231, P3-048, P3-116, P3-267	Sagawa, Akira	W8-6, W35-3, P1-010, P1-011, P1-096, P2-043
Ozawa, Yuko	W40-5	Sagawa, Risa	W18-2, W77-1, P2-087 , P3-046, P3-128, P3-170, P3-212, P3-243
P _____		Sagawa, Tomoya	W18-2, W33-3, W60-6, W77-1 , P2-087, P2-210, P2-303
Paccaly, Anne	P1-099	Sagisaka, Tamaki	P3-159
Pangan, Aileen L	W38-1, W38-2, W38-3	Sahara, Kagayaki	W75-6
Paris, Maria	W72-6	Saiga, Kenta	P1-251
Park, Jeong Hoon	S5-3, W72-2, P3-085	Saiki, Osamu	W19-1
Parsons, Angela	ICW19-1	Saio, Yukie	P1-132, P2-029
Pasternak, Sylvia	ICW4-6	Sairyo, Koichi	P1-062
Patricio, Joseph Patrick N	EP1-13	Saisho, Koichiro	W34-1, P1-008, P2-011, P2-169
Peng, Liying	ICW19-3	Saito, Atsushi	P2-294, P3-185
Perry, Kim	ICW22-5	Saito, Kazuyoshi	S14-2, LS24 , W13-2, W29-2, W30-1, W51-2, W55-1 , ICW6-5, ICW8-1, ICW9-4, ICW19-2
Petri, Michelle	W31-1-7	Saito, Keisuke	P2-198, P3-177 , P3-258
Polinski, Kristen J	PS-2	Saito, Keitaro	P3-046, P3-128, P3-170 , P3-212, P3-243
Ponce, Lucia	ICW6-3	Saito, Kuniaki	W67-4
Porter, Brian	W44-1	Saito, Masaya	P2-066
Pratt, Gregory	EP2-11	Saito, Mayu	W65-6, P1-105, P1-182, P1-192
Psarras, Antonios	ICW17-5	Saito, Mitsuru	P1-161
Purdy, Kerri	ICW4-6		
Q _____			
Qi, Wufang	ICW3-1		
Qian, Junyan	ICW3-1		
Qiu, Huizhong	ICW8-6		
R _____			
Rathmann, Suchitrita	W22-3		
Rhee, Jin-seol	ICW13-1		
Ri, Shinkai	W20-5, W22-6, W28-2 , W35-6, W65-4, P1-208, P2-212, P3-143,		

Saito, Shigeru	S14-4	Sanada, Hajime	W42-1, W43-6, P3-009, P3-067 , P3-102, P3-192
Saito, Shu	P1-144	Sanayama, Yoshie	W35-2, P2-022, P2-073
Saito, Shuntaro	W31-2-1, W31-2-6, ICW20-5 , P1-200	Sano, Hajime	W54-4, W54-5, P2-011, P2-107, P3-185
Saito, Takanori	P1-138	Sano, Shuhei	W66-2, P1-184, P2-224, P2-264, P2-282, P2-287 , P2-311, P3-031, P3-074, P3-081, P3-276
Saito, Tetsuya	W62-6, P1-022	Sano, Shunsuke	P2-056
Saito, Yukie	P1-045	Sasaki, Akiko	W18-5, ICW18-3, P2-079 , P2-110, P2-160, P2-256
Saitou, Moe	W8-4	Sasaki, Kan	ICW18-3, P2-160
Saka, Kumiko	W36-1 , W37-4, W70-1, W70-7, P1-001	Sasaki, Kaneshige	P3-174
Sakaguchi, Noriko	W46-1, P2-288 , P3-054, P3-208	Sasaki, Noriko	W6-3 , W46-6, P2-306
Sakai, Hiroaki	P1-080	Sasaki, Oh	W1-5
Sakai, Kenji	W20-5, W22-6, W28-2, W35-6, W65-4, P1-208, P2-212 , P3-143, P3-178	Sasaki, Rie	P1-089, P2-121, P3-112
Sakai, Mariko	W18-3, W22-4, W59-5, W60-5, P3-097, P3-142, P3-281	Sasaki, Sho	W56-5 , P1-180, P2-306, P3-084, P3-087, P3-184
Sakai, Norihiko	P2-068	Sasaki, Takeshi	W53-3
Sakai, Ryoko	W21-1, W32-5, W37-5, W70-4	Sasaki, Tomohiro	W67-4
Sakai, Ryota	ICW17-3 , ICW20-5	Sasaki, Yoshiko	P2-044
Sakai, Shunsuke	W16-3, W21-5, W68-3, ICW2-3, P1-013, P1-177 , P1-198	Sato, Hiroe	W16-3, W21-5, W40-4, W68-3, ICW2-2, ICW2-3 , P1-013, P1-177, P1-198, EP3-06
Sakai, Tomoyuki	P2-292	Sato, Hiroko	W72-5
Sakai, Yoshie	S1-5	Sato, Hiroshi	W52-2, W74-4, P3-133
Sakai, Yoshitada	W17-6, W37-6, P1-030, P1-033, P2-089	Sato, Katsumi	P3-247
Sakairi, Toru	W32-4, P2-012	Sato, Kojiro	W17-5, W28-3, W55-3, ICW2-5, P1-008, P1-082, P2-006, P2-201, P3-138
Sakakibara, Akira	S16-1	Sato, Masaaki	P2-017
Sakamoto, Fumihiko	P1-014, P1-048, P1-057	Sato, Masao	W14-4, W37-3 , W67-4, P1-221 , P2-103 , P2-106 , P3-306
Sakamoto, Satoshi	P3-096	Sato, Masayo	P1-104
Sakamoto, Takero	P2-151	Sato, Minako	W39-1, P1-104
Sakamoto, Tomonori	W25-4, P1-144, P2-019	Sato, Motohiko	P3-120
Sakane, Hideo	W8-5	Sato, Narumi	P1-242
Sakashita, Aki	W27-6 , P3-046, P3-128, P3-170, P3-212, P3-243	Sato, Ryo	P1-244
Sakata, Kei	ICW11-5	Sato, Ryo	P2-075 , P2-085
Sakata, Komei	ICW10-1	Sato, Ryosuke	W27-3
Sakaue, Saori	ICW1-3	Sato, Satoshi	W7-4, W63-6, ICW3-6
Saku, Aiko	P1-050	Sato, Seidai	P2-142
Sakuma, Shota	P3-069, P3-095, P3-193	Sato, Shinichi	W9-6, W58-1, P3-022
Sakuma, Yu	S3-6, P1-163, P1-169	Sato, Shinji	S10-2 , W1-1, W9-3, W14-3, W15-2, W15-6, W56-5, P1-180, P2-306, P3-084, P3-087, P3-184
Sakumura, Naoto	W7-6	Sato, Shuzo	W43-2, W63-5, ICW15-4, P1-021, P1-183, P1-204 , P2-237
Sakuraba, Hirotake	W12-1, P2-108, P2-193	Sato, Taiki	ICW3-5, ICW4-3 , P2-215
Sakuraba, Koji	P1-165	Sato, Takeo	P3-154, P3-177, P3-245, P3-258
Sakuraba, Mita	W69-2	Sato, Tomoo	P2-001
Sakuraba, Tsutomu	S3-3, W24-2, P1-003, P1-086, P2-115 , P2-171	Sato, Tomotaro	W65-2, W71-5, P1-154, P2-083, P2-136
Sakuragi, Takahide	W26-2 , P1-041	Sato, Toshiyuki	P2-017
Sakurai, Keiichi	W39-3, W59-4, W64-6 , W65-5, W79-6, P2-105, P3-090, P3-126, P3-284	Sato, Yukihiko	W5-2
Sakurai, Kosuke	W65-6, P1-105 , P1-182	Sato, Yurie	ICW3-4, ICW21-5
Sakurai, Natsuki	W31-2-2, ICW3-2 , ICW12-3, P1-034, P1-179, P2-188, P2-277, P2-281, P3-198	Satoh, Minoru	ICW8-1, ICW21-5
Sakurai, Ryuta	P1-151 , P1-165, P2-161	Sawa, Naoki	W21-6, W53-4, P1-055
Salazar-buitrago, Juan Carlos	W30-3		

Sawabe, Kazuma	P1-111	Shibata, Akiko	W2-5 , W3-3, W35-4, W39-4, W60-3, W60-4, ICW20-5, P2-119
Sawabe, Takuya	W59-5, W60-5, P3-202, P3-209, P3-218	Shibata, Hirofumi	W63-2
Sawachika, Hiroshi	W73-2, P1-063, P2-202, P2-225	Shibata, Hirotaka	W1-4, ICW5-2
Sawada, Haruki	P2-227, P3-196, P3-213	Shibata, Sadamu	P2-165
Sawada, Naoya	W6-1, W6-2, W14-3, W15-2, W15-6 , W70-2, P1-009, P1-018, P1-038, P1-133, P1-217, P2-028, P2-065, P2-168, P2-257, P2-293	Shibata, Terufumi	P1-171
Sawada, Tetsuji	S14-2, W36-5, W78-5 , P1-016, P1-017, P2-291, P2-295, P2-307, P3-229	Shibata, Tomohiko	P1-190
Sawai, Takashi	P3-002	Shibata, Toshiko	P1-190
Sawamukai, Norifumi	P1-014, P1-048, P1-057	Shibata, Yuhei	W62-4
Schett, Georg	ICW18-5	Shibuto, Nobuyuki	P2-231
Schlichting, Douglas	W38-6	Shibuya, Hitoshi	S2-5
Segawa, Seiji	P2-242	Shibuya, Takaaki	P2-082
Seida, Yuka	P1-249	Shichi, Daisuke	W11-1, W11-2, W11-6
Seifert, Jennifer	PS-2	Shiga, Toshihiko	W20-5, W22-6, W28-2, W35-6, W46-2 , W65-4, P1-208, P2-212, P3-143, P3-178
Seki, Iwao	P2-001	Shigemizu, Sanae	P3-277
Seki, Kaori	W12-2, P3-195, P3-244	Shigesaka, Minoru	P3-048, P3-267
Seki, Kazushige	P2-270	Shiigi, Eiichi	P1-067
Seki, Masanori	P2-304	Shikano, Kotaro	W74-4 , P3-133
Seki, Shinya	P3-158	Shima, Natsuki	P2-198, P3-150
Sekiguchi, Akiko	W72-4	Shima, Yoshihito	W58-5
Sekiguchi, Masahiro	W42-5 , W54-4, P3-185	Shimada, Hiromi	W10-4, W13-3 , W20-4, W78-2, W78-4, P3-226, P3-292
Sekiguchi, Masayuki	W24-1	Shimada, Kota	W66-2, P1-184, P1-224, P2-011, P2-224, P2-251, P2-264, P2-282, P2-287, P2-296, P2-311, P3-031, P3-074, P3-081, P3-276
Sekiguchi, Yukio	W53-3	Shimada, Yoichi	S3-3, W24-2, P1-003, P1-086, P2-094, P2-115, P2-154, P2-171
Sekijima, Yoshiki	W46-1, P1-026, P2-288, P3-054, P3-127, P3-208	Shimada, Yosuke	P2-272
Sekimoto, Tomohisa	P2-151	Shimada, Yuki	W45-5
Sekine, Akinari	W21-6, W53-4, P1-055	Shimagami, Hiroshi	P2-097 , P2-126, P3-246, P3-259, P3-270
Sekine, Kazuomi	P2-252	Shimahara, Noriyoshi	W14-3, W15-2 , W15-6
Selvaraj, Shanmugapriya	ICW17-4	Shimamoto, Keiko	W18-4, P3-048, P3-116, P3-267
Sendo, Sho	W9-2, ICW7-4, P1-107 , P2-278, P2-299, P3-077, P3-114, P3-181	Shimamura, Yoshiko	W40-3, W58-3, P1-185, P3-032, P3-134, P3-278
Seno, Takahiro	P3-042	Shimane, Kenichi	W24-3, P1-145, P2-055
Seo, Kenichi	W5-6	Shimaoka, Erina	P1-239, P1-241
Seri, Yu	W45-6	Shimizu, Hideaki	P2-229
Seto, Nickie	PS-2, ICW16-2	Shimizu, Hideki	P3-153
Seto, Yohei	W18-6, W66-3 , P2-266, P2-309, P3-148	Shimizu, Hisanori	P3-196, P3-213
Setoguchi, Keigo	W43-5 , P2-228, P3-235, EP1-08	Shimizu, Jun	W45-1
Shabana, Kosuke	W7-1 , W13-4, P1-015, P2-252	Shimizu, Masaki	MTE6 , W7-1, W7-6
Shao, Tihong	ICW14-2	Shimizu, Masaru	W1-2, W17-3, W20-3, W76-2, W76-5, ICW12-4 , P2-009, P2-111
Shestopaloff, Konstantin	EP3-07	Shimizu, Masato	P1-014, P1-048, P1-057
Shevach, Ethan	ICW18-2	Shimizu, Miho	P2-068
Shiba, Hideyuki	P1-239, P1-241, P2-058 , P2-116, P3-105	Shimizu, Takako	ICW10-4
Shiba, Takeshi	W63-2	Shimizu, Toshimasa	W31-1-6, W32-2, W32-6, W33-5, W43-4, W48-5, W62-5, ICW15-4, P1-037, P1-069, P2-243, P3-171
Shibahara, Nobuhisa	P1-042, P1-250, P2-057, P2-124, P3-241	Shimizu, Yuka	W47-4, ICW3-5
Shibamoto, Maki	W51-6, P3-082, P3-094 , P3-173, P3-256	Shimmyo, Naoki	P2-052
Shibanuma, Nao	W17-6, W37-6, P1-030, P1-033, P2-042	Shimogori, Kei	P1-102, P1-232
		Shimojima, Yasuhiro	W46-1, P1-026 , P2-288, P3-054, P3-127, P3-208

Shimomura, Kota	W24-4, W49-2 , ICW10-6	W55-6, W75-2, ICW6-1, ICW7-4,
Shimomura, Shuji	P3-051	P1-138, P1-231, P2-052, P3-007,
Shimoyama, Kumiko	W4-4, P1-199, P3-304	P3-048, P3-116, P3-267
Shimura, Kanako	P1-132 , P2-029	ICW22-4
Shinagawa, Shoshi	W64-6, P1-190 , P3-090	W38-4
Shindo, Keisuke	P2-252	Sonobe, Masato
Shindo, Yasufumi	P2-233	W5-5, W24-1, W56-1, W56-2,
Shinoda, Koichi	P2-261	P1-157, P1-158 , P2-157
Shinoda, Koichiro	W19-4, P1-023, P2-285, P3-064 ,	Sonohata, Motoki
	P3-076, P3-086, P3-180, P3-182,	Sorachi, Ken-ichi
	P3-207	Spindler, Alberto
	P2-011	St John, Gregory
Shinohara, Satoshi	P3-193	Stanislavchuk, Mykola
Shinoura, Marina	P3-057, P3-201	Stoica, Victor
Shiohira, Yoshiki	W28-1, W71-7	Strand, Vibeke
Shioura, Tomone	W54-2 , W79-6, P3-141, P3-236	Strober, Warren
Shiozawa, Kazuko	W52-3, W54-2, W79-6 , P3-299	Suarez-almazor, Maria E
Shiozawa, Shunichi	W9-6, W52-1, W64-3, W72-1, W78-5	EP2-11
Shirai, Harumi	W20-6 , W27-2, W72-5, ICW20-4	Suárez-fueyo, Abel
Shirai, Tsuyoshi	W3-1, W21-4, W23-2, W54-6,	Suda, Akiko
Shirai, Yuichiro	W67-3, W69-1, W69-2, W77-2,	Suda, Masei
	W77-5 , P1-229	Suda, Takafumi
Shiraishi, Chizuru	P2-140	Sudo, Akihiro
Shiraishi, Naoki	P3-111	Sudo, Ko
Shiraiwa, Hidetaka	P1-211, P3-033, P3-293	Sudo, Masanori
Shirota, Yuko	W27-2 , P2-086	Sueda, Yuriko
Shishido, Eri	P3-194	Suematsu, Eiichi
Shoda, Hirofumi	S5-2, W1-5, W52-1, W52-5, W64-3,	Suematsu, Rie
	W72-1, ICW1-2, ICW1-4, ICW11-3,	Suemori, Koichiro
	ICW18-1, ICW18-4, ICW21-1,	Suenaga, Yasuo
	P1-234, EP1-03	Suga, Kensuke
Shoda, Takeshi	W2-1, W23-4 , W27-4, W58-4,	Suga, Norihiro
	W58-6, W61-4, P2-058, P2-099,	Sugano, Eri
	P2-216, P3-265	Sugano, Masahiko
	P2-038, P2-211	Suganuma, Eisuke
Shoji, Aki	P1-003, P2-115	Suganuma, Yumi
Shoji, Kazuhiro	W47-1	Sugawara, Eri
Shomura, Fumiko	W8-6, P1-010, P1-011	Sugi, Suzuna
Shono, Eisuke	P2-012	Sugihara, Makoto
Shrestha, Shreya	P3-027	Sugihara, Takahiko
Shuto, Toshihide	W31-1-7	Sugii, Shoji
Silk, Maria	ES15-2	Sugimori, Yusuke
Singh, Gurkirpal	S13-1, ES11-1 , W38-3, W39-1	Sugimoto, Hideyasu
Smolen, Josef S	W5-3, W14-2, W24-5, W50-4,	Sugimoto, Naoki
Sobue, Yasumori	W71-7, W75-3, ICW7-2, P2-021 ,	Sugimoto, Tomohiro
	P2-173	Sugimoto, Toshitsugu
Soda, Daijirou	W31-1-1	Sugimoto, Toyohiko
Soejima, Yutaro	W31-2-2, W72-3, W72-4 , ICW3-2,	Sugimura, Atsuhō
	ICW12-3, P1-034, P2-188, P2-277,	Sugimura, Yusuke
	P2-281	
Soezima, Yutaro	P1-179	
Sofue, Hideaki	P3-227	
Soga, Takayoshi	P3-272	
Sogabe, Ayuko	W70-2, P1-018, P1-217, P2-257 ,	
	P2-293	
Someya, Kazuki	W29-2	
Son, Chang-nam	ICW13-1	
Son, Yonsu	W18-4, W36-6, W51-5, W55-2,	

	P2-115, P2-154, P2-171	Susaki, Kentaro	P1-100
Sugino, Masakazu	P1-239, P1-241, P2-058, P3-105	Suto, Akira	P1-205, P3-104
Sugioka, Yuko	S2-4, W5-1, W9-2, W16-5, W16-6, W23-6, W36-3, W37-1, W44-6, W68-1, W70-6, P2-023, P2-062, P3-008, P3-019, P3-020, P3-021, P3-290, P3-301	Suto, Takahito	W8-5
		Suwa, Junya	W32-4, P2-012
Sugisaki, Nagachika	P1-097 , P3-295	Suwabe, Tatsuya	W53-4, P1-055
Sugishita, Naonori	P3-076, P3-086, P3-180 , P3-182, P3-207	Suyama, Yasuhiro	P2-274
		Suzue, Ai	P3-025
Sugita, Ryo	W5-4	Suzuka, Takayasu	W52-6, W58-6, W61-4, P2-116, P2-216, P3-125
Sugita, Yuko	P2-252		W41-6
Sugitani, Naohiro	W36-1, W37-4, W44-4, W70-1, W70-7, P1-001, P1-181, P2-040 , P3-100, P3-124	Suzuki, Aika	S5-2
		Suzuki, Akari	W45-6, P2-045 , P2-064
Sugiura, Tomoko	W29-1 , P1-121	Suzuki, Akitake	W42-2
Sugiyama, Eiji	MTE21, W4-5, W57-4, ICW2-6, ICW6-2, P1-036, P2-010, P2-039, P2-217, P3-072, P3-091, P3-131, P3-268, P3-279	Suzuki, Chisako	W4-4, P1-199, P3-304
		Suzuki, Daisuke	W39-2, P2-129
Sugiyama, Hirokazu	W59-2, P2-209, P3-206	Suzuki, Daisuke	ICW15-4, P1-021, P1-197
Sugiyama, Kaita	W59-3, ICW10-4, ICW10-5, P1-211, P3-047, P3-210, P3-293	Suzuki, Eiji	W56-6
		Suzuki, Fae	P3-053
Sugiyama, Mai	P1-180, P2-306, P3-084, P3-087	Suzuki, Fumihito	P1-031
Sugiyama, Masafumi	W35-6, P1-207 , P2-273	Suzuki, Hitoshi	P3-079 , P3-135
Sugiyama, Mayu	P2-197, P3-098, P3-164, P3-205, P3-221, P3-283	Suzuki, Junya	W12-4, W39-3, W59-4, W64-6, W65-5, P1-046, P3-090, P3-126, P3-284
		Suzuki, Kanako	ICW10-1
Sugiyama, Takahiro	W12-5 , P1-050	Suzuki, Kanata	S5-1 , W8-1, W9-3, W31-2-1, ICW1-5, ICW17-3, P1-200, P2-245
Sugiyama, Takao	W4-3, W10-5, W12-5, W13-5, W34-1, W35-2 , W40-6, P2-022, P2-073	Suzuki, Katsuya	P1-050, P1-205
		Suzuki, Kazumasa	W42-1, W43-6, P3-009, P3-067, P3-102 , P3-140, P3-192
Sugiyama, Yumiko	W31-2-2, ICW3-2, ICW11-1, P1-034, P1-179, P2-188 , P2-277, P2-281, P3-188	Suzuki, Kazuyuki	P1-033
		Suzuki, Kohjin	P1-156
Suguro, Toru	W6-6, W22-5, W24-1, W56-1, P1-005, P1-158	Suzuki, Koji	P1-205, P3-104
		Suzuki, Kotaro	P2-256
Suh, Min-ho	ICW13-1	Suzuki, Mao	W50-1
Suh, Seong-il	ICW13-1	Suzuki, Masahiko	W2-2, W12-6 , W77-6, P2-236, P3-113
Suhara, Mai	P3-184	Suzuki, Masashi	P2-197, P3-098, P3-164, P3-205, P3-221, P3-283
Suma, Harumichi	P3-209, P3-218	Suzuki, Michita	W54-6
Sumida, Takayuki	S7-4, EL7, W1-2, W17-3, W20-3, W26-5, W41-6, W43-3, W54-5, W76-2, W76-5, ICW7-3, ICW12-4, ICW14-4, ICW16-3, P2-005, P2-007, P2-009, P2-111, P2-239, P2-240, P2-242	Suzuki, Mikito	W5-3, W14-2, W24-5, W50-4, W71-7, ICW7-2 , P2-021, P2-173
		Suzuki, Mochihito	W49-5 , P1-044
Sumita, Yoshiko	P3-093	Suzuki, Motohiro	W45-1
Sumitomo, Shuji	S5-2, W1-5, W9-6 , W52-1, W64-3, W72-1, ICW1-4, ICW18-1, ICW18-4, ICW21-1, P1-201	Suzuki, Noboru	P3-009
		Suzuki, Nobuhiro	P3-010
Sumiyoshi, Remi	S21-7, W31-1-6, W32-2, W32-6, W33-5, W37-2 , W43-4, W48-5, W62-5, ICW15-1, P1-037, P1-069, P3-171	Suzuki, Nobuyuki	S3-3, W24-2, P1-003, P1-086, P2-171 W67-2, W67-6
		Suzuki, Norio	P2-137, P3-194
Sun, Jinlei	ICW14-2	Suzuki, Rika	P3-095 , P3-129, P3-193
Sunaga, Naomi	P1-094	Suzuki, Sadahiro	W32-5, W70-4
Sundy, John S	ICW6-2	Suzuki, Satoshi	P1-102, P1-232
Sung, Yoon-kyoung	ICW7-5	Suzuki, Sho	W29-6, P1-128, P3-058
		Suzuki, Shotaro	P3-146 , P3-220, P3-223
		Suzuki, Takahiro	W34-4, W45-6 , P1-236
		Suzuki, Takahisa	W39-3, W59-4, W64-6, W65-5, P2-105 , P3-090, P3-126, P3-284
		Suzuki, Takeshi	P2-013, P2-016
		Suzuki, Takeshi	W54-5, W56-6, P3-009, P3-140
		Suzuki, Tomoto	
		Suzuki, Yasunori	

Suzuki, Yasuo	ACL-LS , W6-3, W44-4, W46-6, P1-181 , P2-040, P2-306, P3-100, P3-124	Takahashi, Hiroyuki	P1-157, P1-158, P2-157 EL7, W1-2, W20-3, W43-3, W76-5, ICW12-4, ICW14-4, P2-111, P2-239, P2-240, P2-242
Suzuki, Yukari	P1-250	Takahashi, Kentaro	P3-079, P3-135
Suzuki, Yuta	W18-5, ICW18-3, P2-079, P2-110 , P2-160, P2-256	Takahashi, Kozo	P1-141
Szombati, Istvan	ICW6-3	Takahashi, Naomi	W14-3
		Takahashi, Naoyuki	EL17
T		Takahashi, Nobunori	W5-3, W14-2, W24-5, W28-1, W50-4, W56-4 , W71-7, W75-3, W75-4, ICW7-2, P2-021, P2-051, P2-118, P2-173
Tabata, Kayoko	P2-018, P2-041	Takahashi, Ryo	W65-6, P1-105, P1-182, P1-192, P2-280, P3-144
Tabuchi, Yuya	W9-5 , W32-1, W78-6	Takahashi, Sari	P2-044
Tachibana, Masahiro	W8-5	Takahashi, Shigekazu	P2-134 , P2-135, P2-205
Tachihara, Miho	P1-132, P2-029	Takahashi, Shunsuke	W32-4
Tada, Hitoshi	P1-131 , P1-222	Takahashi, Soshi	W3-5, W51-1, W77-4, P2-247, P3-121
Tada, Kurisu	S18-2 , W44-3 , P1-097, P2-246, P2-272, P3-103, P3-119, P3-234, P3-257, P3-282	Takahashi, Takayuki	W43-1
Tada, Masahiro	W5-1, W9-2, W16-5, W16-6, W23-6, W36-3, W68-1, W70-6, ICW22-6 , P2-023, P2-062, P3-001 , P3-003, P3-004, P3-005, P3-006, P3-008, P3-021, P3-301	Takahashi, Yoshinori	W30-2, P3-009
Tada, Tomomi	W46-4, W47-3, P2-049, P2-181, P3-156, P3-189	Takahashi, Yuichi	W37-2, P2-092
Tada, Yoshifumi	W18-3 , W22-4, W59-5, W60-5, P3-097, P3-142, P3-281	Takahashi, Yuki	P3-260
Tadokoro, Rei	W51-6, P3-082, P3-094, P3-173 , P3-249, P3-256	Takahashi, Yuko	W46-3, W69-4, P1-178, P2-128, EP1-07, EP2-01
Tagawa, Yasuhiro	P1-022	Takahei, Tamio	P2-081
Tago, Mayu	P1-016, P1-017, P2-295	Takahi, Koichiro	S3-2, S11-5, W10-5, W49-1, P1-225 , P2-289
Taguchi, Hiroaki	W10-1, P3-044	Takai, Chinatsu	W13-1, W13-6 , ICW2-2 , P1-144, P1-170, P3-308
Taguchi, Koichiro	W35-5, W63-3, W78-1 , P2-190, P3-255	Takai, Kazue	S21-3
Taguchi, Yoshio	P3-091	Takai, Osamu	W37-2
Taguchi, Yuichiro	P3-297	Takaichi, Kenmei	W21-6, W53-4, P1-055
Tahara, Koichiro	W78-5, P1-016, P1-017, P2-291, P2-295, P2-307	Takajo, Ichiro	W34-3, P1-028, P1-235, P2-219, P3-115
Tai, Yoshiaki	P3-222	Takajo, Katoko	W34-3, P2-219, P3-115
Tajima, Setsuko	P1-132, P2-029	Takakubo, Yuya	S11-4 , W18-5 , ICW18-3 , P2-013, P2-016, P2-079, P2-110, P2-160, P2-256
Takabayashi, Katsuhiko	LS20-2 , W29-6 , P1-128	Takakura, Yuto	W9-1, W10-1, W45-2, P2-218, P3-044, EP2-04
Takada, Hideto	W68-4 , P2-071	Takakuwa, Maiko	W7-6
Takagi, Haruki	W19-4, P1-108, P1-110, P1-167	Takakuwa, Yukiko	W11-3, W12-4, W33-6, W39-3, W59-4, W64-6, W65-5, P2-105, P3-090, P3-126, P3-284
Takagi, Hideki	P1-076 , P1-227	Takamasu, Eisuke	W66-2, P1-184 , P1-224, P2-224, P2-264, P2-282, P2-287, P2-296, P2-311, P3-031, P3-074, P3-081, P3-276
Takagi, Ikuyo	W3-1	Takamatsu, Hisanori	P1-014
Takagi, Kae	W58-2 , P1-073, P1-115, P2-220, P3-275	Takamatsu, Hyota	S5-3 , W45-4, W47-2, W72-2, P3-049, P3-085, P3-311
Takagi, Kasumi	W3-1	Takamatsu, Ko	W67-2, W67-6
Takagi, Michiaki	S11-4, W18-5, ICW18-3, P2-013, P2-016, P2-079, P2-110, P2-128, P2-160, P2-256	Takamatsu, Ryota	P3-168
Takahama, Soichiro	P1-212, P2-025, P3-161, P3-253, P3-303	Takamatsu Sakamoto, Mayuko	P1-082
Takahashi, Chihiro	ICW10-1	Takami, Kenji	ICW2-1
Takahashi, Haruka	W1-5	Takami, Yuichiro	P1-081
Takahashi, Hidenori	P3-261		
Takahashi, Hideyuki	W43-5, P2-228 , P3-235, EP1-08		
Takahashi, Hiroki	W42-2, W58-1		
Takahashi, Hiroshi	W5-5 , W24-1, W56-1, W56-2,		

Takamura, Akito	W12-3		
Takamura, Sayuri	W16-3, W21-5, W68-3 , ICW2-3, P1-013, P1-177, P1-198	Takemura, Tamiko	P2-106, P2-261, P3-306
Takamura, Yoshiko	P1-243	Takenaka, Katsuto	S19-4
Takamura, Yuta	W2-3, W23-1 , W23-5, W61-1, W64-4, P2-050, P3-130, P3-215	Takenaka, Sayaka	W21-3, W41-2, W47-6, P1-052
Takamure, Hiroshi	ICW10-6	Takeno, Mitsuhiro	W9-1, W36-4, W45-2 , P1-188, P2-218, EP2-04, EP2-09
Takanashi, Satoshi	ICW10-1		S14-2 , MTE8 , ES3-1 , W3-1, W21-4, W23-2, W54-6, W67-3, W69-1, W69-2, W72-3 , W72-4, W72-6, P1-229, P3-229, P3-230
Takanashi, Tetsuo	W35-1	Takenouchi, Seiji	P1-102, P1-232
Takano, Kyoko	P2-197, P3-098, P3-164, P3-205 , P3-221, P3-283	Takeshima, Yusuke	W52-1, W64-3, W72-1, ICW1-2, ICW1-4, ICW18-1, ICW21-1, P1-201
Takao, Ken	P3-099		W8-1 , ICW1-5
Takaori-Kondo, Akifumi	S21-2	Takehita, Masaru	P2-086
Takasaki, Minoru	P1-218	Takehita, Miki	S5-2
Takasaki, Yoshinari	W54-5	Taketomi, Shuji	P2-195, P3-232
Takasawa, Naruhiko	W53-3	Takeuchi, Akiteru	W35-3
Takashima, Yoshinori	W51-4, P1-035 , P1-090, P2-089	Takeuchi, Kaoru	S7-2 , S14-2
Takasu, Hiroshi	P1-150 , P1-165, P2-161	Takeuchi, Masaki	W1-6, W2-1, W2-4, W13-4, W23-4, W27-4, W36-6, W51-5, W52-6, W55-2, W55-6, W58-4, W58-6, W61-4, W75-2, ICW6-1, ICW7-4, P1-231, P2-052, P2-058, P2-116, P2-196, P2-216, P3-007, P3-073, P3-108, P3-122, P3-125, P3-157, P3-274
Takasugi, Kiyoshi	W15-6, W70-2, P1-018, P1-217, P2-257, P2-293	Takeuchi, Tohru	S5-1, LS23 , ES11-2 , ES1-2 , W8-1, W9-3, W30-4, W31-2-1, W31-2-5, W31-2-6, W38-1, W38-2 , W38-4, W38-5 , W38-6, W39-1, W47-2, W54-5, W56-3, ICW1-5, ICW6-2 , ICW6-6, ICW7-3, ICW10-1, ICW15-3, ICW17-3, ICW20-3, ICW21-4, P1-094, P1-200, P2-245
Takasugi, Koji	S1-3, W66-5, P1-079		P2-208 , P2-234
Takasugi, Koji	P1-054, P1-226, P2-276, P2-297, P3-107	Takeuchi, Tsutomu	P3-273, P3-287
Takata, Kokoro	P1-248, P2-184		W59-5, W60-5 , P2-305
Takata, Miki	W11-4, P1-012 , P2-259		W7-4
Takatani, Ayuko	W31-1-6, W32-2, W32-6, W33-5, W43-4, W48-5, W62-5, P1-037, P1-069 , P2-243, P3-171	Takeuchi, Yohei	W19-4, P1-023, P2-285, P3-064, P3-076, P3-086, P3-180, P3-182, P3-207
Takatori, Kyohei	W31-1-2	Takeyama, Takahisa	P2-047
Takatori, Sayaka	W31-1-2	Takeyama, Yukiko	W8-1, ICW1-5
Takatsuka, Kazutaka	P1-108, P1-110, P1-167	Takezaki, Shunichiro	P1-239, P1-241
Takayama, Hirokuni	P2-180	Taki, Hirofumi	W31-1-7, W38-6, W39-1
Takayama, Yoshihiro	P1-155, P3-262		P1-054, P1-226, P2-229, P2-276, P2-297, P3-107
Takebe, Ken	P1-248, P2-125, P2-184, P3-015		W66-6
Takeda, Chikako	P1-146, P2-100, P2-174	Takigawa, Naohide	P3-010
Takeda, Ryutaro	P1-173	Takiguchi, Maiko	P1-205, P3-104
Takeda, Setsuko	S2-4	Takiguchi, Mitsuko	P1-212 , P2-025, P3-161, P3-253, P3-303
Takeda, Tomofumi	W63-3, P1-077, P3-071	Takita, Yasushi	P1-164
Takeda, Tomoki	P2-086	Takizawa, Naoho	ICW10-1, ICW15-3
Takeda, Tsuyoshi	W35-3		MTE23
Takehara, Kazuhiko	W58-1, W58-5, P3-110	Takizawa, Tsutomu	W31-1-6, W32-2, W32-6, W33-5, W37-2, W47-1, W48-2 , W48-5, W62-5, W71-3 , ICW10-3, ICW15-1,
Takehisa, Tomoko	P1-244	Takizawa, Yasunobu	
Takei, Hirofumi	W2-5, W3-3, W35-4 , W39-4, W60-3, W60-4, ICW20-5, P2-119	Tamachi, Tomohiro	
Takei, Hiroshi	W10-1, W31-2-6, ICW10-1, ICW21-4 , P3-044	Tamagawa, Kenji	
Takei, Masami	W40-2, W54-5, W59-3, ICW10-4, ICW10-5, P1-211, P3-033, P3-047, P3-210, P3-293		
Takei, Reoto	W1-3		
Takei, Syuji	S14-5, W76-3 , P2-128		
Takei, Yoshinori	W32-4		
Takeji, Akari	W42-1, W43-6, P3-009, P3-192		
Takemori, Hiromitsu	W19-2		
Takemoto, Miyuki	P1-246 , P2-268		
Takemoto, Toki	W71-7, W75-4 , P1-166, P2-051		
Takemura, Masao	W37-3, W67-4 , P1-221, P2-103,		

Tamaki, Hiromichi	P1-037, P1-069, P2-170	Tanaka, Shigeru	P1-205, P2-022
Tamaki, Masashi	P2-227 , P3-196, P3-213	Tanaka, Shin	ICW8-1
Tamaki, Shigenori	P1-006	Tanaka, Shinya	ICW2-5
Tamechika, Shinya	EL16, W6-4, W6-5, W16-4 , W48-4, W67-1, P1-047	Tanaka, Sumiaki	W31-1-3, W58-1, W77-3 , P1-202, P2-189, P3-092, P3-190
Tamimoto, Yasuhiro	P2-032, P3-224, P3-298	Tanaka, Takayuki	W63-2
Tamura, Hiroaki	P2-259	Tanaka, Tomoki	P2-137, P3-194
Tamura, Maasa	P1-242, P3-117	Tanaka, Yasuhito	S3-5, P1-247, P2-052, P3-222
Tamura, Masao	W42-3	Tanaka, Yasushi	W54-2, P3-141, P3-236
	W9-2, W47-5 , W51-6, P2-139, P3-082, P3-094, P3-173, P3-185, P3-249, P3-256	Tanaka, Yoshihito	W62-2
Tamura, Naoto	LS1-1 , W3-6, W26-3, W30-1, W31-2-5, W44-3, W54-5, W70-5, W79-5, P1-020, P1-097, P1-129, P1-176, P1-196, P2-128, P2-187, P2-194, P2-199, P2-223, P2-246, P2-272, P3-069, P3-095, P3-103, P3-119, P3-129, P3-193, P3-234, P3-257, P3-282, P3-295, P3-307	Tanaka, Yoshiya	S5-4, S7-4, S13-4 , S14-2, ES18-2 , W4-1, W13-2, W29-2, W30-1 , W30-2 , W30-3 , W30-4 , W31-1-7 , W38-1, W38-3 , W38-4 , W38-5, W38-6 , W39-1, W47-2, W51-2, W54-5, W55-1, W58-5, W72-6, ICW3-4, ICW6-2, ICW6-3 , ICW6-5, ICW6-6, ICW7-1, ICW7-3, ICW8-1, ICW9-4, ICW11-2, ICW11-5, ICW11-6, ICW12-1, ICW12-2, ICW12-6, ICW13-5, ICW14-5, ICW16-4, ICW17-1, ICW17-2, ICW17-6, ICW19-2, ICW21-5, P1-094 , P1-099, P1-194, P3-229, P3-291, P3-300, EP1-04
Tan, Zhen	ICW14-1		W14-3 , W15-2
Tanabe, Manabu	P3-137, P3-260	Tanaka, Yuki	W35-5, W78-1, P2-190, P3-255
Tanaka, Akihiro	W18-4, P3-048, P3-116 , P3-267	Tani, Hideki	W51-6, P3-082, P3-094, P3-173, P3-185, P3-256
Tanaka, Atsushi	P3-209, P3-218	Tani, Mei	S3-3, W24-2, P1-086, P2-171
Tanaka, Ayae	W23-1, W23-5, W61-1 , W64-4, P2-050, P3-130, P3-215	Tani, Takayuki	W14-4, W37-3, P1-221, P2-103, P2-106, P3-306
Tanaka, Chihiro	P1-118, P1-230, P1-237, P2-098, P2-130, P2-279, P3-238	Tani, Tomohisa	P1-067
Tanaka, Eiichi	MTE17 , LS3 , LS15-1 , W7-2, W21-1, W30-1, W30-4, W36-1, W37-4, W70-1, W70-7 , ICW6-6, P1-001, P2-255	Tani, Yasuhiro	W7-2, P2-255
Tanaka, Eriko	W67-5	Tani, Yumi	W74-1, P1-152
Tanaka, Genichi	P3-233	Tanigawa, Hidenori	S3-5
Tanaka, Hidekazu	P3-010	Taniguchi, Akira	S18-5 , W7-2, W36-1, W37-4, W44-1, W66-3, W70-1, W70-7, ICW16-1, P1-001, P2-309
Tanaka, Hiroaki	ICW3-4, ICW9-4	Taniguchi, Atsuo	W25-1, W25-2, W34-4, P1-236
Tanaka, Hiroki	P3-272		W20-1
Tanaka, Hiroshi	P1-067	Taniguchi, Daigo	W25-4 , W56-2, W65-3, ICW2-2, P1-085, P1-088, P1-144, P1-157, P1-158, P2-019, P2-155
Tanaka, Hiroya	P3-206	Taniguchi, Mana	P2-070
Tanaka, Ikuko	EL16 , W6-4 , W6-5 , W16-4, W48-4, W67-1, P1-047	Taniguchi, Shinji	P3-056
Tanaka, Katsunori	P2-018, P2-041	Tanikawa, Akiko	W59-3, ICW10-4, ICW10-5, P1-211, P3-047, P3-210 , P3-293
Tanaka, Kitaru	W31-1-2	Tanikawa, Yutaka	P3-055, P3-112
Tanaka, Masao	W9-5, W32-1, W36-6, W50-5, W51-3, W78-6, ICW16-1, P1-058, P1-240, P3-007, P3-012, P3-091, P3-239	Tanimoto, Takuya	W35-3, ICW7-3, P1-014, P1-048, P1-057
Tanaka, Masaru	W38-6	Tanimura, Kazuhide	P3-091
Tanaka, Nahoko	W12-1, P2-108, P2-193	Tanizawa, Kiminobu	W66-2, P1-184, P2-224, P2-264, P2-282, P2-296 , P2-311, P3-031, P3-074, P3-081, P3-276
Tanaka, Nobuho	W26-6	Tanomogi, Naoki	ICW8-4
Tanaka, Nozomi	P3-239		W47-4
Tanaka, Rikiai	P2-140	Targoff, Ira N	ES12
Tanaka, Ryo	P1-148 , P3-056	Tarumi, Masato	
Tanaka, Sakae	S5-2, MTE23, W9-6, W38-4, W38-5, W49-6, W68-2, W71-6, W75-5, ICW22-1, P1-134, P1-159, P1-173, P2-055, P3-022	Tasaka, Sadatomo	
Tanaka, Seiji	W78-3		

Tasaka, Yuji	P2-143	Tokunaga, Kenichiro	W20-1
Tashiro, Yuka	P1-135	Tokunaga, Tadahiro	W4-5, W57-4, P2-010 , P2-217, P3-131, P3-268, P3-279
Tasset, Chantal	ICW6-2	Tokunaga, Takahiro	W17-2, W34-6 , P1-024, P1-032, P2-002, P2-034, EP3-08
Tateishi, Chiharu	P3-019, P3-020, P3-021	Tokura, Masami	W64-2
Tateishi, Koji	P1-030, P1-033, P1-248, P2-125, P2-184, P3-015	Tokushige, Atsunori	P2-270
Tateishi, Mutsuto	P3-137, P3-260	Toma, Tomoko	W63-3
Tateishi, Shoko	W9-6, ICW6-4, P3-022	Tomaru, Utano	P3-151
Tatsumi, Emiko	P3-222	Tomiita, Minako	S14-5
Tatsuno, Yurika	P3-175	Tominaga, Akito	W16-2, P1-043
Tatsutani, Tomofumi	W34-5 , P3-052, P3-254	Tominaga, Masaki	P3-096
Tawada, Kaneaki	P2-096, P2-114	Tomita, Daisuke	W20-5, W22-6, W75-1 , P1-095, P2-123
Temmoku, Jumpei	W43-2, W63-5, ICW15-4, P1-021 , P1-183, P1-204, P2-237	Tomita, Tetsuya	S18-4 , W44-2 , P3-036
Ten Brinck, Robin	W48-2	Tomita, Tomoko	W45-3
Terabe, Kenya	W65-2, P1-154	Tomizawa, Takuya	W5-4, W49-3 , W51-3
Terada, Kaoru	W34-2, W62-1, P2-122, P3-263	Tomizuka, Takafumi	P2-195, P3-232
Terada, Makoto	P1-112, P3-043	Tomozawa, Sho	W46-5
Terada, Yoshio	W40-3, W58-3, P1-185, P3-032, P3-134, P3-278	Tono, Midori	P1-143
Terai, Chihiro	W69-1, W69-2, P1-087, P2-238	Tono, Toshihiro	S14-2, W31-1-3, P2-189, P3-092, P3-190, P3-229
Teranishi, Tsuyoshi	W18-4	Tonooka, Kumiko	W12-4, W39-3, W59-4, W64-6, W65-5, P2-105, P3-090, P3-126, P3-284
Terao, Chikashi	EL21 , ICW16-1	Tonozuka, Norihiko	P2-038, P2-211
Terashima, Yasuhiro	P1-030, P1-033, P1-118, P1-248, P2-125 , P2-184, P3-015	Topp, Andrew	W22-2
Terui, Tadashi	LS19-2	Torigoe, Masataka	W1-4, ICW11-5
Teruya, Hiroyuki	P3-145	Torikai, Eiji	W39-2 , W49-5, P1-044, P2-129
Teshigawara, Satoru	W28-5, W61-3, W73-1, ICW9-1, ICW9-2, P1-061, P2-036, P2-067, P3-078, P3-118	Torisu-Itakura, Hitoe	W22-1
Teshima, Takanori	S2-5	Totoribe, Koji	P2-151
Thomas, Stacey M	ICW16-2	Toujima, Akihiro	P3-025
Tian, Lu	ICW5-1	Toyama, Shogo	W15-4 , W25-1, W25-2, W25-3 , W27-6, P2-087
Tian, Zhuang	ICW3-1	Toyama, Tadashi	P2-068
Tobe, Kazuyuki	P1-023, P2-285, P3-064, P3-076, P3-086, P3-180, P3-182, P3-207	Toyoda, Yuko	P2-142
Tobimatsu, Haruki	S3-6, W49-4 , P1-169	Toyohara, Issaku	P1-170
Tochihara, Mari	W31-2-3, P1-186 , P1-206, P2-071, P2-232, P3-070, P3-167, P3-219	Toyota, Tsuyoshi	W66-6
Tochimoto, Akiko	W58-2, P2-220	Trivedi, Vikas	EP1-05 , EP2-02 , EP2-08, EP2-10
Toda, Masayoshi	P3-206	Tsai, Chang-youh	ICW13-3, EP2-05
Toda, Yosuke	ICW9-5, P1-223, P3-166	Tsokos, George C	ICW5-3
Todoroki, Yasuyuki	ICW3-4, ICW8-1 , ICW11-2, ICW21-5	Tsuboi, Hideki	S3-2, S11-5, W49-1, P1-139, P1-149, P2-120 , P2-283
Toguchida, Junya	W26-1	Tsuboi, Hiroto	EL7 , W1-2, W17-3, W20-3, W26-5, W43-3 , W54-5, W76-2, W76-5, ICW12-4, ICW14-4, ICW16-3, P2-005, P2-007, P2-009, P2-111, P2-239, P2-240, P2-242
Tohdo, Satoshi	P1-100	Tsuboi, Kazuyuki	W51-6, P2-107, P3-082, P3-094, P3-173, P3-185 , P3-249, P3-256
Tohma, Shigeto	LS6 , W8-3, W10-5, W13-5, W16-2, W34-1, W36-5, W41-6, W55-5, W71-1, W71-5, W71-6, W73-5, P1-008, P1-015, P1-016, P1-017, P1-043, P1-106, P2-011, P2-055, P2-083, P2-095, P2-136	Tsuboi, Masahiko	W32-2
Toi, Norikazu	W53-6	Tsubouchi, Shiori	P1-248
Toko, Hirofumi	W1-2 , W20-3, W76-2, W76-5, ICW12-4, P2-111	Tsubouchi, Syoko	P2-291
Tokuda, Hitoshi	S19-5	Tsubouchi, Yasunori	P3-068
Tokuda, Michiaki	P2-208, P2-234	Tsuchida, Masashi	P1-140
Tokunaga, Daisaku	W15-4, W25-1, W25-2, W25-3	Tsuchida, Naomi	W31-2-2, ICW3-2, ICW12-3, P1-034, P1-179, P2-188, P2-277, P2-281
		Tsuchida, Takahiro	P2-069

Tsuchida, Toyomitsu	W8-6, P2-140	U	
Tsuchida, Yumi	S5-2, W1-5, P1-234	Ubara, Yoshifumi	W21-6, W53-4, P1-055
Tsuchiya, Haruka	S5-2 , W1-5, P1-234	Uchida, Koto	W17-6, W37-6, P1-030, P1-033
Tsuchiya, Naoyuki	W41-6, ICW15-4, P2-011	Uchida, Marina	W39-3, W59-4, W64-6, W65-5, P1-046 , P2-105, P3-090, P3-126, P3-284
Tsuda, Naonori	W57-2 , P2-200, P3-211	Uchida, Tomohisa	W9-4, P1-053
Tsuda, Reina	P1-023, P3-064, P3-076, P3-086, P3-180, P3-182, P3-207	Uchida, Yoshio	W24-3 , P1-145, P2-055
Tsuda, Tokutaro	S20-6 , P2-227, P3-196, P3-213	Uchino, Ayumi	P1-122
Tsuge, Shunsuke	P3-009	Uchio, Akihiro	W68-2, W75-5 , P1-134
Tsuji, Goh	ICW1-1	Uchiyama, Shunsuke	W3-1, P3-230
Tsuji, Hideaki	P3-091	Uda, Hiroshi	W19-1
Tsuji, Kazuya	P3-155	Uechi, Eishi	P3-057, P3-201
Tsuji, Shigeyoshi	S3-2, S11-5, MTE14 , LS19-1 , W28-5, W49-1, W50-6 , W73-1, ICW9-2, P1-149, P2-036, P3-036 W73-2, ICW1-6, ICW4-5 , ICW15-2 , P1-019	Ueda, Naoyasu	W59-5, W60-5, P3-233
Tsuji, Shoko		Ueda, Yo	ICW7-4, P1-107, P2-125, P2-278, P2-299, P3-077, P3-114, P3-181 P2-180
Tsuji, Sosuke	W31-1-6, W32-2, W32-6, W33-5, W43-4 , W48-5, W62-5, P1-037, P1-069, P2-207, P3-171	Ueda, Yusuke	W78-2
Tsuji, Yoshika	W34-2, W62-1, P3-263	Ueeda, Kiyo	W54-2, P1-153 , P3-141, P3-236
Tsujihashi, Mizuho	P2-063	Uefuji, Atsuo	P2-080
Tsujimoto, Kohei	P2-235	Uehara, Keita	P3-080, P3-224 , P3-298
Tsujimoto, Naoto	P2-128	Uehara, Koji	W72-4, P1-034
Tsujimoto, Saki	W18-4, P3-048, P3-060 , P3-267	Uehara, Takeaki	W63-6 , ICW3-6
Tsujimura, Miho	P2-053	Uejima, Yoji	W32-2, W33-5, W34-2, W37-2, W47-1, W62-1, ICW15-4, P2-122 , P3-263
Tsujimura, Shizuyo	P1-194	Ueki, Yukitaka	
Tsukada, Toshiaki	W47-1, P2-084	Uema, Takahito	P2-080
Tsukada, Yoshito	P1-214	Uematsu, Masato	W16-5
Tsukamoto, Hiroshi	P2-221	Ueno, Akiko	W4-6 , W60-2, W71-4, P3-162
Tsukamoto, Norifumi	S21-3	Ueno, Kenichi	W46-1, P2-288, P3-054, P3-127 , P3-208
Tsukida, Mayuko	P1-214	Ueno, Masanobu	ICW3-4, ICW12-2, EP1-04
Tsukui, Daisuke	W66-1, P2-003 , P3-232	Ueno, Sayaka	W66-4, P1-071, P1-072
Tsumiyama, Ken	W52-3 , W54-2, W79-6	Ueno, Shuhei	P2-179, P3-301, EP2-03
Tsumoto, Shuko	W5-1	Ueno, Yuki	P1-239, P1-241, P3-105
Tsumura, Hiroshi	P2-019	Ueta, Yoichi	P1-031
Tsuneizumi, Yoshikazu	W50-3	Uetani, Masataka	W48-2, W48-6, P1-069, P1-070
Tsuno, Hirotaka	W16-2, W26-6 , P1-008, P1-043, P2-055	Ukichi, Taro	W8-4, W64-1
Tsunoda, Shinichiro	W12-2 , W27-1, W30-4, P1-008, P1-074, P2-011, P2-203, P2-248, P3-185	Umabayashi, Hiroaki	S9-3 , W7-1, W76-3
Tsuru, Tomomi	W8-6, P1-010, P1-011	Umeda, Ai	W2-2 , W12-6, W77-6, P2-236, P3-113
Tsuruta, Daisuke	P3-019, P3-020, P3-021, P3-290	Umeda, Masataka	W47-1
Tsuruyama, Tatsuaki	W26-1	Umeda, Naoto	P2-005, P3-261
Tsushima, Hidetoshi	P1-150, P1-151, P1-165, P2-161, P2-167 , P2-185	Umegaki, Hiroyuki	EL4
Tsutani, Hiroshi	W10-5, W34-1	Umeki, Tatsuhito	W1-4
Tsutsui, Tomoko	W26-2, P1-041	Umekita, Kunihiko	W34-3 , P1-028, P1-235 , P2-219, P3-115
Tsutsumi, Akito	W47-4	Umemiya, Keiko	W33-1, P1-039, P1-233
Tsutsumi, Satoshi	W75-1, P2-123	Umemura, Kumiko	P2-197, P3-098, P3-164, P3-205, P3-221, P3-283
Tsutsumi, Tomomi	P2-086	Umemura, Masayu	W65-6
Tsutsumino, Michi	W68-4	Umibe, Takeshi	P2-022, P2-176, P3-079, P3-135
Tsuyuguchi, Yusuke	S3-4	Unno, Yukinori	W67-3
Tsuzuki, Hiroshi	W59-3, ICW10-4, ICW10-5, P1-211, P3-047, P3-210, P3-293	Uno, Yoshihiro	P2-204
Tsuzuki, Sayaka	W43-5, P2-228, P3-235, EP1-08	Ura, Takaki	P1-249
Tzu-hao, Li	ICW9-6	Urano, Fusazo	P3-194
		Urano, Takeshi	W63-1
		Urata, Shiro	P1-166

Urata, Yukitomo	W34-1, W61-6	Wakasugi, Daisuke	P3-013
Urayama, Masakazu	S3-3, W24-2, P1-003, P1-086, P2-115, P2-154, P2-171	Waki, Daisuke	W31-1-5, W59-1, W61-2, W73-4, P1-195
Urushitani, Yoshinori	W34-4, P1-236	Wakiguchi, Hiroyuki	W7-1
Ushikubo, Mari	P2-249	Wakiya, Risa	W10-4, W13-3, W20-4, W78-2 , W78-4, P3-226, P3-292
Ushio, Kazuyasu	W30-4, P1-010, P1-011	Wakui, Hideki	W18-1
Ushiyama, Satoru	W46-1, P2-288, P3-054, P3-127, P3-208	Wakura, Daisuke	P2-216
Usui, Arata	W50-2	Wakura, Reiko	W58-6, P2-216, P3-073
Usui, Masaaki	P1-068	Walker, David	ICW6-2
Usui, Takashi	P3-012	Wallace, Daniel	W31-1-7
Uto, Kenichi	W68-6	Walsh, Noreen	ICW4-6
Utsunomiya, Akira	W58-1	Wang, Guosheng	ICW8-6, ICW14-1, ICW14-3, ICW18-6
Utsunomiya, Masako	MTE12, W12-3 , W66-2, P1-184, P2-224, P2-264, P2-282, P2-296, P2-311, P3-031, P3-074, P3-081, P3-276	Wang, Qian	ICW3-1, ICW4-1, ICW19-3, ICW19-6, EP2-07
Uzawa, Yuji	W48-1, P1-045, P2-260, P3-035, P3-136	Wang, Qiaolei	W26-4
Uzuki, Miwa	P3-002	Wang, Qikai	ICW14-3, ICW18-6
V _____		Wang, Sheldon	W30-3
Van Der Heijde, Désirée	W30-3	Wang, Yiping	ICW14-1, ICW14-3, ICW18-6
Van Der Helm-van Mil, Annette H.m.	W48-2	Wang, Ziqian	ICW19-3
Van Hoogstraten, Hubert	W30-2, P1-099	Watanabe, Akane	P3-049
Van Vollenhoven, Ronald	W38-2	Watanabe, Ayano	P3-174
Visser, Ashley	PS-2, ICW16-2	Watanabe, Eiichiro	P2-053
Viswanathan, Sowmya	ICW22-3, EP3-02	Watanabe, Eri	W69-1, W69-2, P1-087, P2-015, P2-238, P3-231, P3-240
Vital, Edward M	ICW17-5	Watanabe, Haruki	W40-1, W41-5 , P2-024, EP1-02
Vsetecka, Danielle	ICW17-4	Watanabe, Hidetoshi	P1-003, P2-115
W _____		Watanabe, Hideyuki	P1-218, P3-059
Wada, Hiroyuki	P2-284	Watanabe, Hirofumi	P1-089, P2-121 , P3-112
Wada, Jun	W40-1, ICW2-4, P2-024, EP1-02	Watanabe, Hiroshi	W43-2 , W63-5, ICW15-4, P1-021, P1-183, P1-204, P2-237
Wada, Kazuteru	W30-2, P1-099	Watanabe, Kounosuke	W48-5, W48-6 , P1-070
Wada, Makoto	W9-2, W15-4, W18-2, W25-1, W25-2, W25-3, W27-6, W33-3 , W60-6, W77-1, P2-087, P2-210, P2-301, P2-303, P3-042, P3-046, P3-128, P3-170, P3-212, P3-243	Watanabe, Masahito	S11-2, ICW9-3, P1-059, P1-168, P3-016
Wada, Takashi	W31-2-5, P2-068, P3-051	Watanabe, Masashi	EP1-12
Wada, Takuma	W28-3, W55-3 , P1-082, P2-201	Watanabe, Masayuki	P1-076, P1-227
Wada, Tatsuhiko	W31-1-3, P2-189, P3-190	Watanabe, Mitsuharu	W32-4, P2-012
Wada, Yoko	W10-6, W16-3 , W21-5, W40-4, W68-3, ICW2-3, P1-013, P1-177, P1-198	Watanabe, Mitsuru	P3-196, P3-213
Wada, Yumiko	P2-099, P2-196, P3-265	Watanabe, Natsuko	W2-2, W12-6, W77-6, P2-236 , P3-113
Wakabayashi, Hiroki	P2-074, P2-163	Watanabe, Norihiko	P2-134, P2-205
Wakabayashi, Hiroshi	P1-068, P2-231	Watanabe, Rina	W12-1 , P2-108, P2-193
Wakabayashi, Ikuko	S3-3	Watanabe, Ryu	W37-2, ICW5-1
Wakabayashi, Kuninobu	W17-2, P1-024 , P1-032, P2-002, P2-034, EP3-08	Watanabe, Shinji	W21-4, W23-2 , W54-6, W69-2, P1-229
Wakabayashi, Takayuki	W6-3, W46-6 , P2-306	Watanabe, Shohei	W46-5
Wakama, Minako	P1-239, P1-241	Watanabe, Shun	W53-4
Wakamatsu, Ayako	W16-3, W21-5, W40-4, W68-3, ICW2-3, P1-013, P1-177, P1-198	Watanabe, Takashi	P3-295
		Watanabe, Tatsuo	W75-3 , P2-229
		Watanabe, Tetsuo	W19-4, P1-141
		Watanabe, Toshiyuki	W4-2, ICW3-5
		Watanabe, Tsuneo	W67-4, P2-261
		Watanabe, Tsuyoshi	W27-5
		Watanabe, Tsuyoshi	P1-054, P1-226, P2-276, P2-297, P3-107
		Watanabe, Wataru	P1-003, P2-154
		Watanuki, Satoshi	W13-1, W66-2, P1-184

Wei, Wei	ICW3-1	Yamada, Shinsuke	W53-6
Westhovens, René	ICW6-3	Yamada, Shunsuke	W50-2, P2-166
Weyand, Cornelia	ICW5-1	Yamada, Soichi	W52-2 , W74-4, P3-133
Winthrop, Kevin	W39-1, ICW6-3	Yamada, Syuji	P2-023 , P2-179
Wittmann, Miriam	ICW17-5	Yamada, Takahiro	P2-076
Wu, Brian	ICW21-3 , EP3-09	Yamada, Teruchika	W33-4, P3-149, P3-216
Wu, Jianping	ICW21-3	Yamada, Tohru	P1-190
Wu, Ming	ICW17-4	Yamada, Toshiyuki	P2-258
X		Yamada, Yusuke	P1-176
Xavier, Ricardo M	W38-2	Yamada, Yutaro	S2-4, W16-5, W16-6, W37-1 , W44-6, W68-1, ICW22-6, P3-001, P3-003, P3-004 , P3-005 , P3-006, P3-019 , P3-020, P3-021, P3-290
Xia, Weibo	EP2-07	Yamagami, Keiko	P3-195, P3-244
Xiang, Yuan	ICW14-3	Yamagata, Hiroki	P1-067
Xu, Christine	P1-099	Yamagata, Kaoru	ICW11-6, ICW16-4
Xu, Dong	ICW19-3, ICW19-6	Yamagata, Kunihiro	W41-6
Y		Yamagata, Mieko	W35-2, W40-6 , P1-050, P2-022, P2-073
Yabe, Hiroki	P1-087, P2-015, P2-238 , P3-231, P3-240	Yamaguchi, Ayako	W13-2, W51-2, W55-1, ICW3-4, ICW6-5, ICW7-1, ICW7-3 , ICW12-6, ICW19-2
Yabe, Yoko	W16-1 , ICW9-5, P1-223, P3-166	Yamaguchi, Ken-ichi	S9-6 , S14-2, P2-227, P3-196, P3-213
Yabe, Yuichiro	W71-7, P2-051, P2-109 , P2-118	Yamaguchi, Makoto	W59-2, P2-192, P3-101, P3-206
Yabuuchi, Atsuko	P3-299	Yamaguchi, Rei	W36-1, W37-4, W70-1, W70-7, P1-001
Yachi, Koji	W50-6	Yamaguchi, Ryosuke	P2-172 , EP3-03
Yachie, Akihiro	W63-1, W63-3, ICW15-1	Yamaguchi, Satoshi	P2-285
Yachie, Nozomu	MTE3	Yamaguchi, Yukie	ES13-2 , W69-1, W69-2, W69-5, P3-203, EP1-09
Yaekura, Arisa	W17-6 , W37-6, P1-030, P1-033	Yamaguchi, Yuta	W45-4 , W51-5, P3-049, P3-214, P3-311
Yagishita, Mizuki	W1-2, W20-3, W76-2, W76-5 , ICW12-4, ICW14-4, P2-111, P2-240	Yamaji, Ken	W3-6, W26-3, W44-3, W79-5, P1-020, P1-097, P1-129, P1-196, P2-187, P2-194, P2-199, P2-223, P2-246, P2-272, P3-069, P3-095, P3-103, P3-119, P3-129, P3-193, P3-234, P3-257, P3-282, P3-295, P3-307
Yagita, Masato	P3-091	Yamakawa, Noriyuki	P3-242
Yagita, Mayu	W45-4, W51-5, P3-049, P3-214, P3-311	Yamamoto, Akio	W62-6 , P1-022
Yago, Toru	P1-087, P2-015 , P2-238, P3-231, P3-240	Yamamoto, Atsuhiro	W20-5 , W22-6, W28-2, P1-208, P2-212, P3-143, P3-178
Yajima, Nobuyuki	S17-3 , LS29-2 , W21-2, W31-1-6, W31-2-2, W31-2-5, W32-6, W65-6, ICW3-2, P1-105, P1-179, P1-182 , P1-187, P1-191, P1-192, P2-188, P2-277, P2-281	Yamamoto, Kakeru	W33-6
Yajima, Takahiro	P3-200	Yamamoto, Kazuhiko	S5-2, W9-6, W52-1, W64-3, W72-1, ICW1-2, ICW1-4, ICW6-6, ICW11-3, ICW18-1, ICW18-4, ICW21-1, P1-201, P2-128
Yamabe, Toru	P3-224, P3-298	Yamamoto, Kazuko	W11-5
Yamada, Akihiro	W70-2, P1-018, P1-217, P2-257, P2-293	Yamamoto, Kei	P2-180
Yamada, Atsuhisa	W71-6	Yamamoto, Keiichiro	P1-157, P1-158
Yamada, Chiho	W56-5, P1-180, P2-306, P3-084, P3-087, P3-184	Yamamoto, Kengo	P2-164
Yamada, Harumoto	P2-153	Yamamoto, Kyosuke	P3-169
Yamada, Hidehiro	W14-5, W20-2, W41-6, P1-135	Yamamoto, Manabu	P1-113
Yamada, Hirotaka	ICW7-4, P1-107, P2-278, P3-114	Yamamoto, Mari	W13-1, P1-054, P1-226, P2-276, P2-297, P3-107, P3-139
Yamada, Hisakata	W26-2, P1-041	Yamamoto, Masahiro	P1-212, P2-025, P3-161, P3-253, P3-303
Yamada, Kazunori	W42-1, W43-6, W56-6 , W61-5, P3-009, P3-067, P3-102, P3-192		
Yamada, Kunio	P2-096, P2-114		
Yamada, Manabu	W5-5, W56-2, P1-157 , P1-158, P2-157		
Yamada, Masato	P2-053		
Yamada, Rie	P3-200		
Yamada, Risa	P2-232		
Yamada, Saeko	W52-1, ICW1-4		

Yamamoto, Motohisa	W42-2	Yamauchi, Naoto	P2-165
Yamamoto, Shotaro	P3-258	Yamauchi, Shinichi	W53-6
Yamamoto, Takuaki	P1-171	Yamauchi, Yusuke	P3-217
Yamamoto, Toshiyuki	ES9-1	Yamazaki, Hajime	W42-3
Yamamoto, Wataru	S1-3, W32-1, W36-6, W51-5, W55-2, W55-6, W66-5, W75-2, W78-6, ICW6-1, ICW7-4, P1-079, P1-231, P2-052, P3-007	Yamazaki, Hideshi	W35-1
Yamamoto, Yusuke	P1-017, P1-160, P2-291, P2-307	Yamazaki, Ikuko	W15-1
Yamamoto, Yuzuru	ICW7-4, P1-107, P2-278, P3-114	Yamazaki, Kazuko	S14-5, W7-4
Yamamura, Ayako	P2-063	Yamazaki, Kenji	W19-6, W28-4, W71-2, P1-116, P1-137, P2-046, P2-088, P3-297
Yamamura, Masahiro	W4-6, W60-2, W71-4, P3-162	Yamazaki, Miho	P2-285, P3-076, P3-086, P3-180, P3-182, P3-207
Yamamura, Yuriko	W4-6, W40-1, W71-4, P2-024, EP1-02	Yamazaki, Ryutarō	W2-3, W23-1, W23-5, W61-1, W64-4, P2-050, P3-130, P3-215
Yamana, Jiro	P1-089, P2-121, P3-112	Yamazaki, Seiko	P1-083
Yamana, Seizo	P1-089, P2-121, P3-112	Yanagawa, Kaori	W66-4, P1-071, P1-072
Yamanaka, Hajime	P1-164	Yanagida, Hidetoshi	P3-040
Yamanaka, Hideki	P3-195, P3-244	Yanagida, Takuya	W44-5, W73-3, P2-077, P3-089
Yamanaka, Hisashi	PL, W7-2, W18-6, W21-1, W31-2-3, W32-5, W36-1, W37-4, W37-5, W58-2, W66-3, W68-4, W70-1, W70-4, W70-7, W79-4, ICW6-6, ICW7-3, ICW16-1, P1-001, P1-094, P1-115, P1-186, P1-206, P2-015, P2-071, P2-220, P2-232, P2-255, P2-309, P3-070, P3-167, P3-219	Yanagida, Tamiko	W66-1, P2-003
Yamanaka, Kenjiro	W3-6	Yanagisawa, Maiko	W17-5
Yamanaka, Ryutarō	W3-2, W32-3, P1-006, P1-056	Yanagisawa, Takao	W42-4
Yamanaka, Yoshiaki	P1-031	Yanai, Ryo	W21-2, W34-6, W65-6, P1-105, P1-192
Yamane, Takashi	W79-6, P1-118, P1-230, P1-237, P2-098, P2-125, P2-130, P2-279, P3-015, P3-238	Yanaoka, Haruyuki	W52-1, W72-1, P2-227, P3-196, P3-213
Yamanishi, Yoshihiro	S12-2	Yang, Kunitaka	P1-003
Yamano, Yasuhiko	W1-3	Yang, Suran	W18-5, ICW18-3, P2-079, P2-110, P2-160, P2-256
Yamano, Yoshihisa	W45-1	Yano, Hiroyuki	P2-069, P3-145, P3-191, P3-248
Yamanouchi, Masayuki	W53-4, P1-055	Yano, Koichiro	S3-6, W49-4, P1-002, P1-163, P1-169
Yamaoka, Kunihiro	S6-3, LS16, LS32, ES5-1, W31-1-3, W38-1, W77-3, W79-2, ICW6-2, P1-202, P2-189, P3-092, P3-190, P3-229	Yashiro, Masato	W7-1
Yamasaki, Akira	W11-4, P1-012, P2-259	Yasuda, Izumi	P1-096, P2-043
Yamasaki, Masaomi	W29-5, P1-190	Yasuda, Masahiko	P1-176
Yamasaki, Satoshi	P2-014, P3-013, P3-289	Yasuda, Nobuyuki	P1-027
Yamasaki, Yoshioki	S10-3, W11-3, W14-5, W39-3, W59-4, W64-6, W65-5, P2-105, P3-090, P3-126, P3-284	Yasuda, Shinsuke	EL10, W30-1, W35-3, W62-4, ICW3-5, ICW4-3, ICW4-4, ICW8-5, ICW10-2, ICW16-6, ICW19-4, P2-215, EP3-01
Yamasaki, Yuichi	W7-4	Yasuda, Tadashi	EP1-10
Yamashita, Emi	S2-4	Yasuda, Taketoshi	P3-028
Yamashita, Fumiharu	W74-6	Yasui, Tetsuro	W49-2, W71-6, ICW10-6
Yamashita, Hiroyuki	W46-3, W69-4, P1-178, EP1-07, EP2-01	Yasumi, Takahiro	W7-1, W63-2
Yamashita, Mai	P2-278, P2-299, P3-077, P3-114, P3-181	Yasumura, Junko	W7-1, P3-296
Yamashita, Ryo	P2-076	Yasumura, Masahiro	P3-194
Yamashita, Sayuri	P3-137, P3-260	Yasuoka, Hidekata	LS5, W2-2, W12-6, W30-4, W77-6, ICW6-6, ICW21-4, P2-236, P2-245, P3-113
Yamashita, Yuka	P1-245	Yasutake, Misaki	P2-018, P2-041
Yamauchi, Kiyoshi	P2-165	Yazawa, Hiroaki	W17-5, W55-3
Yamauchi, Naofumi	P2-146	Ye, Shuang	ICW3-1
		Yingbo, Zhou	ICW14-3
		Ying-hsien, Huang	ICW20-2
		Yo, Noriaki	P1-118, P1-230, P1-237, P2-098, P2-130, P2-279, P3-015, P3-238
		Yoh, Satoshi	P2-186, P2-262
		Yokochi, Ritsuko	P1-102, P1-232
		Yokoe, Isamu	ICW10-4, ICW10-5, P3-047
		Yokogawa, Naoto	MTE12, W66-2, P1-184, P1-224, P2-224, P2-251, P2-264, P2-282,

	P2-287, P2-296, P2-308, P2-311, P3-031, P3-074, P3-081, P3-276	Yoshifuji, Hajime	S21-2, EL26 , W9-5, W32-1, W78-6, P3-012, P3-091, P3-239
Yokoi, Syunsuke	P2-197, P3-098, P3-164, P3-205, P3-221, P3-283	Yoshiga, Masayuki	W8-4, P1-025
Yokosawa, Masahiro	W1-2, W17-3, W20-3, W76-2, W76-5, ICW7-3, ICW12-4, ICW14-4, P2-009, P2-111 , P2-240	Yoshihara, Risa	W1-5, P1-234
Yokota, Kazuhiro	W54-5, W55-3, ICW2-5 , P1-008, P1-082, P2-201, P3-138	Yoshihara, Ryosuke	W54-2, W79-6, P3-141, P3-236
Yokota, Toshihiko	W31-1-5, W59-1, W61-2, W73-4, P1-195	Yoshii, Ichiro	W6-1, W6-2, P1-009, P1-038, P1-117, P1-133, P2-028, P2-065, P2-168
Yokota, Yutaka	W24-5, W75-4, P2-173	Yoshikawa, Ayaka	W23-4, W75-2 , P2-058, P2-116
Yokoyama, Hiroshi	P1-092	Yoshikawa, Hideki	S3-2, S11-5, W49-1, W55-2, W55-6, ICW2-1
Yokoyama, Satoko	W14-1	Yoshikawa, Kazuhiro	P3-179
Yokoyama, Yuichi	W41-3, W42-5, P3-185	Yoshikawa, Leo	P2-200
Yokoyama, Yusuke	W35-2, P2-073	Yoshikawa, Norie	W10-5, P2-169
Yomono, Keina	P1-102 , P1-232	Yoshikawa, Takahiro	W9-2, W47-5, W51-6 , P2-107, P2-139, P3-082, P3-094, P3-173, P3-185, P3-249, P3-256
Yoneda, Katsuhiko	W3-5, W51-1, W77-4 , P2-247, P3-121	Yoshikawa, Takeshi	P1-143
Yoneima, Ryo	P3-222	Yoshimi, Ryusuke	S14-2, W31-1-6, W31-2-2, W32-6, W72-4, ICW3-2, ICW11-1, ICW12-3, P1-034, P1-179, P1-182, P1-187, P1-191, P2-188, P2-277 , P2-281, P3-198, EP1-09
Yonemoto, Yukio	W8-5		P2-269
Yonezu, Hiroshi	P2-156	Yoshimoto, Keiichi	W56-3, ICW17-3, ICW21-4, P1-200
Yoo, Wan-hee	EP3-05	Yoshimoto, Keiko	P3-222
Yoshida, Akiko	W74-5, P3-012	Yoshimoto, Kiyomi	W31-1-2
Yoshida, Akira	W23-3, W76-4, P2-059, P2-061, P2-081, P2-091, P2-093 , P3-041, P3-075, P3-294	Yoshimoto, Ryota	W5-1, W70-6 , P2-179, P3-020 , P3-021
Yoshida, Akitsu	P3-070	Yoshimura, Hitoshi	S10-5
Yoshida, Hiroyuki	P1-054, P1-226, P2-276, P2-297 , P3-107	Yoshimura, Katsuhiko	W28-5, W61-3, W73-1, ICW9-1, ICW9-2, P1-061, P2-036, P2-067 , P3-078, P3-118
Yoshida, Ken	MTE10 , W8-4, W64-1	Yoshimura, Maiko	W10-3
Yoshida, Kenji	LS26-2 , P2-183, P2-230, P2-302	Yoshimura, Masaru	W8-3
Yoshida, Kohsuke	W17-6, W37-6, W41-3, P1-030, P1-033	Yoshimura, Motoki	S8-2
Yoshida, Koji	P1-113	Yoshimura, Noriko	W31-1-1, W31-2-4, W36-5, W73-5 , P1-064, P2-060
Yoshida, Mai	P2-187 , P2-194, P2-199, P3-129	Yoshinaga, Yasuhiko	W4-1, W13-2 , ICW3-4, ICW8-1, ICW12-1 , ICW13-5
Yoshida, Masanobu	P2-045, P2-064		W50-1 , P2-262
Yoshida, Misaki	P3-009, P3-024 , P3-102	Yoshino, Kensuke	P1-166
Yoshida, Naomi	P3-013	Yoshino, Sakurako	S18-3
Yoshida, Nobuya	ICW5-3	Yoshioka, Hiroyuki	P3-242
Yoshida, Ryochi	W52-1	Yoshioka, Kohei	W27-3
Yoshida, Shunji	W2-2, W12-6, W77-6, P2-236, P3-113	Yoshioka, Shinji	W10-2, W55-4, P1-147
Yoshida, Shuzo	P1-042 , P1-250, P2-057, P2-124, P2-196, P3-241	Yoshioka, Taro	W48-1 , P1-034, P1-045, P2-260, P3-035, P3-136
Yoshida, Tamami	P1-240	Yoshioka, Yuji	W71-7, P2-104
Yoshida, Tomohiko	W28-6 , P1-010, P1-011, P3-302	Yoshioka, Yutaka	P1-010, P1-011, P1-109
Yoshida, Tomohiro	W31-1-5, W59-1, W61-2, W73-4 , P1-195	Yoshitama, Tamami	W26-1
Yoshida, Yoshihiro	W55-3, P1-082, P2-201, P3-138	Yoshitomi, Hiroyuki	W9-6, P3-022
Yoshida, Yuji	W28-5, W61-3, W73-1, ICW9-1, ICW9-2 , P1-061, P2-036 , P2-067, P3-078, P3-118, P3-156	Yoshizaki, Ayumi	S21-1 , S21-2, S21-7, P1-089
Yoshida, Yuko	S2-4	Yoshizaki, Kazuyuki	P3-011
Yoshida, Yumi	W54-1, W69-3 , P3-096, P3-186, P3-289	Yoshizawa, Masaki	W59-5, W60-5
Yoshida, Yusuke	W4-5 , W57-4, P2-010, P2-217, P3-072, P3-131, P3-268, P3-279	Yoshizawa, Seiji	W8-3 , W10-5, W34-1
		Yoshizawa, Shigeru	W59-3, P1-211, P3-047, P3-210, P3-293
		Yoshizawa, Shoei	

You, Hanxiao	ICW4-1
Younan, Carolen	ICW22-5
Yu, Heiseki	W9-2, P2-127
Yuan, Xiang	ICW14-1, ICW18-6
Yudoh, Kazuo	P2-001
Yukawa, Kazutoshi	W4-5, W57-4, P2-010, P2-217, P3-131, P3-268 , P3-279
Yukawa, Naoichiro	P2-041
Yukioka, Masao	ES9-3, W49-6, P2-082
Yumoto, Taeko	P1-207
Yu-sheng, Chang	ICW9-6

Z

Zaiss, Mario	ICW18-5
Zanwar, Abhishek	ICW20-6
Zeisbrich, Markus	ICW5-1
Zeng, Fanxing	ICW13-2
Zeng, Xiaofeng	ICW3-1, ICW4-1, ICW19-3, ICW19-6, EP2-07
Zhang, Fengchun	ICW14-2
Zhang, Haoze	ICW14-2
Zhang, Hui	ICW5-1
Zhang, Miaojia	ICW3-1
Zhang, Mingling	ICW11-2, ICW17-1
Zhang, Mingzeng	ICW11-5, ICW11-6
Zhang, Wei	ICW3-1
Zhang, Xian	P1-204
Zhang, Xiao	ICW3-1
Zhang, Ying	W38-3
Zhang, Zhuoli	ICW3-1
Zhao, Fangyi	W44-2
Zhao, Jiuliang	ICW3-1, ICW4-1, ICW19-3
Zhao, Qianzi	ICW15-5
Zheng, Pan	ICW15-5
Zheng, Xu	ICW14-1, ICW18-6
Zheng, Yi	ICW3-1
Zhou, Yijie	W38-1
Zhou, Ying-bo	ICW18-6
Zhu, Ping	ICW3-1
Zoshima, Takeshi	P3-009, P3-067, P3-102
Zuo, Xiaoxia	ICW3-1

Modern Rheumatology Abstract Supplement

The 63rd Annual Scientific Meeting of the
Japan College of Rheumatology

Publishing date: April 1, 2019

Publishers: Japan College of Rheumatology (JCR) Modern Rheumatology Editorial Board

Hamamatsucho Empress Bldg. 3F
2-9-6 Hamamatsucho, Minato-ku,
Tokyo 105-0013, Japan
Tel. +81-3-6435-9761, Fax. +81-3-6435-9762
URL: <http://eng.ryumachi-jp.com>
E-mail: MR@ryumachi-jp.com

Production

Hidejima Inc.
Toshin Nishi-Shinjuku Bldg. 2F
7-18-16 Nishi-Shinjuku, Shinjuku-Ku, Tokyo, 160-0023, Japan
Tel. +81-3-5331-3170, Fax. +81-3-5331-3171
E-mail: gakkai@hidejima.co.jp

Copyright ©2019 by Japan College of Rheumatology

<http://eng.ryumachi-jp.com/journals/index.html>