Annals of Oncology

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Abstract Book of the
19th National Congress of Medical Oncology

Rome, Italy
27–29 October 2017

Guest Editor:

Carmine Pinto
Director, Medical Oncology, IRCCS - S.Maria Nuova Hospital, Reggio Emilia, Italy
President, Italian Association of Medical Oncology (AIOM)

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Dear Colleagues,

On behalf of the Board of Directors and of the Scientific Committee, it is a great pleasure for me to introduce the proceedings of the XIX National Congress of our Association.

As usual, the abstracts have been published in a special issue of "Annals of Oncology", the official Journal of ESMO. We continue to observe an increasing number of abstracts suggesting, once again, the presence of a widespread research activity in spite of the shortage of public funds and lack of interest of public authorities. We are pleased with the role of young oncologists. Many young oncologists are co-authors of the abstracts and several are first authors. This should be an encouragement for all of us: there is a present and also a future for AIOM.

As you can realize by reading this issue, all topics of medical oncology have been covered, including prevention, screening, translational research, simultaneous care, ethics and mutidisciplinary approaches. They will be debated in several educational and scientific sessions co-organized with several other scientific societies. We would like to highlight that the multidiciplinary approach, including supportive and simultaneous care, is a relevant part of the program of the meeting. As medical oncologists, clinicians involved in the care of the patients, we have to keep in mind that "research" does not mean to forget the daily activity in the ward as well as the ability to answer the patients' daily needs. Nevertheless, at the same time, we must remember that a research activity improves the care of cancer patients in our Units. The ability to conjugate these two aspects is the only way to improve the chance of cure for our patients.

Finally, I'd like to thank the Scientific Committee and all the reviewers for the invaluable work of the last months and I hope that all of you can enjoy the meeting and that it could be the occasion of sharing knowledge and experiences by providing an enrichment in our skills.

The Board of Directors for the years 2015-2017 includes:

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We are looking forward to seeing you in Rome.

Dott. Carmine Pinto
(President of the Congress)

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PLENARY SESSION

1* FOLFOX4/XELOX in stage II–III colon cancer: early survival data of the Italian Three Or Six Colon Adjuvant (TOSCA) trial

A. Zaniboni[1], S. Lonardi[2], R. Labianca[3], M. Di Bartolomeo[4], G. Rosati[5], M. Ronzoni[6], N. Pella[7], M. Banzi[8], M.G. Zampino[9], F. Pasini[10], P. Marchetti[11], L. Rimassa[12], E. Maiello[13], P. Bidoli[14], S. Cinieri[15], S. Barni[16], L. Ciuffreda[17], G. Beretta[18], L. Frontini[19], E. Rulli[20], A. Sobrero[21]

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Background: Six months of oxaliplatin-based treatment has been the standard of care as adjuvant therapy for stage III colon cancer and an accepted option for high-risk stage II. Given the cumulative neurotoxicity associated to oxaliplatin, a shorter duration of therapy, if equally efficacious, would be advantageous for patients and Health-Care Systems.

Methods: TOSCA was an open-label, phase III, multicenter, non-inferiority trial randomizing patients with high-risk stage II or stage III radically resected colon cancer to receive 3 months or 6 months of FOLFOX4/XELOX. Primary end-point was relapse-free survival.

Results: From June 2007 to March 2013, 3759 patients were accrued from 130 Italian sites, 64% receiving FOLFOX4 and 36% XELOX in either arm. Two thirds were stage III. At cut-off time for analysis the median time of follow-up was 62 months and 772 relapses or deaths and 456 deaths have been observed. At 8 years the RFS rate was 75% and the OS rate 80%. This analysis was done when 82% of the planned number of events was reached, with a power of 72% instead of 80%. The decision to anticipate the analysis was based on the participation to the IDEA joint collaborative analysis of studies sharing this clinical question. The Hazard ratio of the 3months vs 6 months for relapse/death was 1.14 (95%CI 0.99-1.31, p for non inferiority=0.506) and the confidence interval crossed the non inferiority limit of 1.20. The HR for survival was 1.07 (95%CI 0.89-1.29, p for non-inf.=0.249).

Conclusions: TOSCA was not able to demonstrate that 3 months of oxaliplatin-based adjuvant treatment is as efficacious as 6 months (technically 3 months were not non-inferior to six months). Nevertheless, because the absolute difference between the two treatment durations is small (less than 3% at 5 years), the decision to complete the whole 6-month program should be individualized based on toxicity and patients' attitude. Moreover these data can contribute to clarify the importance to use the appropriate schedule also for stage II patients.

This study is registered with ClinicalTrials.gov Registration Number: NCT00646607.

It was supported by a grant from AIFA (Agenzia Italiana del Farmaco) Grant Code FARM5RWTWZ.

2* Phase 3 randomized study of adjuvant anastrozole (A), exemestane (E) or letrozole (L) with or without tamoxifen (T) in postmenopausal women with hormone-responsive (HR) breast cancer. The FATA-GIM3 trial

S. De Placido[1], C. Gallo[2], M. De Laurentiis[3], G. Bisagni[4], G. Arpino[1], M.G. Sarobba[5], F. Riccardi[6], A. Russo[7], L. Del Mastro[8], A. Cogoni[9], F. Cognetti[10], S. Gori[11], A. Frassoldati[12], D. Amoroso[13], L. Laudadio[14], L. Moscetti[15], F. Montemurro[16], F. Nuzzo[3], P. Carlini[10], F. Perrone[3]

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Background: Uncertainty still exists regarding the optimal schedule of adjuvant treatment of breast cancer with Aromatase Inhibitors (AI) and no trial has ever compared all the three AI.

Patients and methods: FATA-GIM3 is a multicenter, open label, 2x3 factorial phase 3 randomized study of adjuvant A, E and L upfront (UP - for 5 years) or sequentially (SEQ - for 3 years after 2 years of T) in postmenopausal HR breast cancer pts. Two comparisons were planned: UP vs SEQ and A vs E vs L. DFS (including local or distant relapse, second breast or non-breast cancer, DCIS and death, whichever came first) was the primary end-point; 2% at 5 yrs (corresponding to a HR of 0.79) was defined as the minimum difference required to declare superiority of UP vs SEQ. With two-tailed alfa 0.05, power 80%, 669 events and the enrolment of 3600 patients were planned. Following Data Monitoring Committee advice, final analysis was performed after 5yrs median follow-up. For each comparison a Cox regression model was applied adjusted by stratification factors and stratified by the other treatment factor. Analyses were based on intention-to-treat.

Results: From 3/2007 to 7/2012, 3697 patients were enrolled at 76 centres. Median age 64, pT1 69.9%, pN0 64.3%, ER and PgR positive 88.9%, HER2 positive 8.9%, previous chemotherapy 38.3%. At 60 months median follow-up, 401 events were reported. 5yrs DFS was 89.8 with UP and 88.5 with SEQ (delta 1.32%, 95% CI -0.90-3.54; HR 0.89, 95% CI 0.73-1.08; P = 0.23). 5yrs DFS was 90.0 with A, 88.0 with E and 89.4 with L (P = 0.19).

There were no unexpected findings on side-effects in schedule comparison. Few and small significant differences were observed comparing the AI: more frequent gastrointestinal side-effects and less frequent hypercholesterolemia with E.

Conclusions: In the FATA-GIM3 trial there is a small non-statistically significant DFS advantage for UP vs SEQ. No significant difference is evident among the three AI.

Supported by the FARM5K3MEE AIFA grant from the Italian Drug Agency.

3* Final analysis of the phase III multicentric Italian study Short-HER: 9 weeks vs 1 year adjuvant trastuzumab for HER2+ early breast cancer

P. Conte[1], P. Conte[2], G. Bisagni[3], A. Frassoldati[4], A. Brandes[5], L. Cavanna[6], F. Giotta[7], M. Aieta[8], V. Gebbia[9], A. Musolino[10], O. Garrone[11], M. Donadio[12], G. Cavazzini[13], A. Turletti[14], C. Zamagni[15], S. Danese[16], A. Ferro[17], F. Piacentini[18], S. Balduzzi[19], R. D'Amico[19], V. Guarneri[20]

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Introduction: chemotherapy plus 1 year trastuzumab is the standard adjuvant treatment for HER2+ breast cancer patients (pts). The Short-HER study is an independent, non-profit study aimed to test the non-inferiority of 9 weeks vs 1 year of adjuvant trastuzumab.

Methods: HER2+ breast cancer pts were randomized to: Arm A (Long) AC or ECx4 followed by 4 courses of 3-weekly docetaxel in combination with trastuzumab, followed by 14 additional courses of 3-weekly trastuzumab; or Arm B (Short) 3 courses of 3-weekly docetaxel plus weekly trastuzumab for 9 doses followed by FEC x3. When indicated, radiation therapy and hormone therapy were started after the completion of chemotherapy. ShortHER is a non-inferiority trial with disease-free survival (DFS) as primary end-point. The sample size of 1250 pts has been estimated on the basis of an hazard ratio <1.29 for the short arm to be non-inferior. The definitive analysis was planned after 198 DFS events or a 5yr median follow up. Hazard ratio for DFS and OS (90% CI) are estimated according to the Cox model; data are also analyzed by the Bayesian approach.

Results: from Dec-2007 to Oct-2013, 1254 pts from 82 centers have been randomized. Pts characteristics are: median age 55 yrs (25-78); pts older than 60 yr 36%; stage I 40.6%, II 43.8%, stage III 15.2%; N0 53.5%, 1-3 positive nodes 30.7%, ≥ 4 15.2%. Sixty-eight% of the pts had ER+ tumors. Characteristics were balanced between the two arms.

At the time of the analysis, 189 events have occurred and the median follow up of the study is 5.2 yrs. A total of 109 Grade ≥ 2 cardiac events have been reported, 82 in arm A (long) and 27 in arm B (short) ($p < 0.0001$); grade 3-4 cardiac events were 13 in arm A and 5 in arm B.

Conclusions: Shorter trastuzumab administration significantly reduces the rate of severe cardiac toxicity. Final DFS data will be reported at the time of the meeting.

EudraCT: 2007-004326-25.

4* Cisplatin in addition to single-agent first-line chemotherapy in elderly patients with advanced non-small-cell lung cancer (NSCLC): efficacy results of a joint analysis of the multicentre, randomized phase 3 MILES-3 and MILES-4 studies

A. Morabito[1], L. Cavanna[2], A. Luciani[3], P. Maione[4], L. Bonanno[5], E. Piazza[6], S. Leo[7], S. Cinieri[8], F. Morgillo[9], M.A. Burgio[10], D. Ferrara[11], D. Cortinovis[12], F. Rosetti[13], R. Costanzo[1], C. Sandomenico[1], G. Daniele[14], S. Signoriello[15], M.C. Piccirillo[14], C. Gallo[15], F. Perrone[14], C. Gridelli[14]

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Background: The role of platinum in first line treatment of elderly patients with advanced NSCLC is still debated. We tested its efficacy in two parallel phase 3 trials.

Patients and methods: Advanced NSCLC patients, >70 years, ECOG performance status 0-1, were eligible. In MILES-3 patients with any tumor histology were randomly assigned 1:1 to cisplatin/gemcitabine (Cis 60 mg/m^2 d1, Gem 1000mg/m^2 dd1,8) or gemcitabine (Gem 1200 mg/m^2 dd1,8). In MILES-4 patients with non-squamous histology were randomly assigned 1:1:1:1 to CG, G, cisplatin/pemetrexed (Cis 60 mg/m^2 d1, Pem 500 mg/m^2 d1) or pemetrexed (Pem 500 mg/m^2 d1). Six cycles were planned. In each trial, to have 80% power in detecting a HR of death 0.75 (corresponding to 3-month prolongation of median survival), with 0.05 two-tailed α, 382 events were required. The trials were closed prematurely because of slow accrual, but a joint analysis allowed to properly perform the final analysis, according to IDMC advice. Analysis was based on intention-to treat and adjusted by trial, histotype, companion drug, stage, PS, gender, age and size of centre.

Results: From Mar 2011 to Aug 2016, 531 patients (MILES-3: 299, MILES-4: 232) were assigned to Cis-doublet (n = 263) or single-agent chemotherapy (n = 268). Median age was 75, 79% were male, 70% had non-squamous histology. Median number of cycles was 4 and 3 with and without Cis, respectively. With a median follow-up of 2 years, 384 deaths and 448 progression-free survival (PFS) events were reported. With and without Cis, median OS was 9.6 vs 7.5 months (HR 0.86, 95% CI: 0.70-1.04, p = 0.14); median PFS was 4.6 vs 3.0 months (HR 0.76, 95% CI: 0.63-0.92, p = 0.005); objective response rate was 15.5% vs 8.5% (p = 0.02). Significantly more severe hematologic toxicity, fatigue and anorexia, were found with Cis. Toxic deaths were 3 (1.1%) and 2 (0.7%), with and without Cis. QoL was not improved with Cis in the joint analysis at the common time-points (cycles 1 and 2), but in MILES-4, with a longer time of observation (cycles 1 to 6), a significant prolongation of the time to global QOL deterioration (items 29/30) was found with Cis (HR 0.53, 95% CI: 0.29-0.97).

Conclusion: Addition of cisplatin to single-agent chemotherapy does not significantly prolong overall survival of elderly patients with advanced NSCLC. However, there is significant improvement in PFS, response rate and time to global QoL deterioration.

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A - GASTROINTESTINAL (COLORECTAL) CANCERS

A1* Does bevacizumab plus chemotherapy matter in metastatic colorectal cancer patients with mucinous histology? A multicenter, retrospective analysis on 685 patients

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Bakground: In metastatic colorectal cancer (MCRC), mucinous histology has been associated with poor response rate and prognosis (Catalano et al, BJC 2009). We investigated whether bevacizumab (B) combined with different chemotherapy regimens may impact on clinical outcomes of MCRC patients (pts) with mucinous histology.

Patients and methods: The study population included 685 MCRC pts (accrual from 10/07 to 2/16) who were treated with B plus chemotherapy (FP-based: capecitabine/deGramont; OXA-based: FOLFOX/XELOX; IRI-based: FOLFIRI/XELIRI; FOLFOXIRI). Pts were classified according to the histology in mucinous adenocarcinomas (MC) and non-mucinous adenocarcinomas (AC).Prognostic factors associated with overall survival (OS) were identified using univariate and multivariate Cox proportional hazards analyses.

Results: Ninety-four (13.7%) pts had MC, male/female 401/284, median age 64 years (range, 25-86). Pts received the following regimens: B+IRI-based (MC/AC=43/263), B+OXA-based (MC/AC=18/159), B+FOLFOXIRI (MC/AC=29/130), or B+FP-based (MC/AC 4/39) regimens. More pts in the MC group had one metastatic site of disease (60.6% vs 52.3%; $p = 0.043$) and peritoneal disease (36.2% vs17.9%, $p = 0.0001$), whereas pts in the AC group had more frequently liver metastasis (76.1% vs 55.3%, $p = 0.02$). The overall response rates for MC and AC were 41.5% (95% CI, 31.5-51.4) and 62.4% (95% CI, 58.4-66.3), respectively (chi-test, $p < 0.003$). With a median follow-up of 50 months, median OS for the MC pts was 28.2 months compared with 27.7 months in the AC group (HR = 0.92; CI 95%, 0.70-1.19; $p = 0.530$). According to the first-line regimens, pts with MC treated with first-line B+OXA-based regimens had lower OS than AC pts (15.9 vs 26.1 months; HR = 0.51; 95% CI, 0.19-0.84; $p = 0.015$). No significant differences in OS were found with B+IRI-based (median OS, MC 32.7 vs AC 29.9 months, $p = 0.73$) and B+FOLFOXIRI (median OS, MC 32.7 vs AC 28.4 months, $p = 0.54$). After correcting for significant prognostic factors by multivariate Cox regression analysis, age (HR = 1.02, 95% CI, 1.01-1.03; $p < 0.0001$), resection of the primary tumor (HR = 1.55, 95% CI, 1.23-1.95; $p < 0.0001$), and number of metastatic sites (HR = 1.41; 95% CI, 1.15-1.73; $p = 0.001$) were found to be associated with poorer OS.

Conclusions: Pts with mucinous histology may benefit from the addition of bevacizumab to chemotherapy. FOLFOX and XELOX regimens may not represent the optimal chemotherapy treatment options in MCRC with mucinous histology.

A2 Combination of nivolumab (nivo) + ipilimumab (ipi) in the treatment of patients (pts) with deficient DNA mismatch repair (dMMR)/high microsatellite instability (MSI-H) metastatic colorectal cancer (mCRC): CheckMate 142 Study

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Background: Nivo, a fully human anti-PD-1 mAb, provided an ORR of 31%, durable responses (median DOR not reached), and a 12-mo OS rate of 73.8% in pts with dMMR/MSI-H mCRC (Overman M, et al. 2017). Preliminary analysis of nivo + ipi, a humanized anti-CTLA-4 mAb, demonstrated manageable safety and promising efficacy in pts with dMMR/MSI-H mCRC (Overman M, et al. 2016). Here we report interim safety and efficacy of nivo + ipi in this pt population from the Checkmate 142 study (NCT02060188).

Methods: Pts with dMMR/MSI-H mCRC who progressed on or were intolerant of ≥ 1 prior line of therapy received nivo 3 mg/kg + ipi 1 mg/kg q3w × 4 doses followed by nivo 3 mg/kg q2w until discontinuation due to disease progression or other reason. Primary endpoint was investigator-reported ORR by RECIST 1.1. Other endpoints included DOR, PFS, OS, safety, and tolerability.

Results: 84 pts with dMMR/MSI-H mCRC treated with nivo + ipi received the first dose ≥6 mo prior to the database lock (DBL; Feb 2017). Of these pts, 78.6% received ≥2 prior lines of therapy. At the time of DBL, 60.7% of pts remained on treatment, and 33 pts had discontinued therapy due to disease progression (n = 15) or TRAEs (n = 11). ORR was 54.8% and disease control rate (DCR) was 78.6% (Table). The median time to response was 2.76 mo, and 84.8% of responses (39/46) were ongoing at the time of analysis. The medians for DOR, PFS and OS had not been reached. Grade 3-4 TRAEs occurred in 24 pts (28.6%). TRAEs leading to discontinuation included acute kidney injury (n = 2), increased alanine aminotransferase, increased transaminases, necrotizing myositis, sarcoidosis, dyspnea, pneumonitis, colitis, autoimmune hepatitis, and thrombocytopenia (n = 1 each). No deaths were attributed to therapy.

Conclusions: Initial analysis of nivo + ipi in pts with ≥6-mo follow-up demonstrated a manageable safety profile and clinical activity characterized by a high DCR and encouraging survival benefit.

Table: A2

	Nivo + Ipi (n = 84)
ORR, n (%)	46 (54.8)
CR	2 (2.4)
PR	44 (52.4)
SD	26 (31.0)
PD	9 (10.7)
DCR[a], n (%)	66 (78.6)
Median DOR (95% CI), mo	NR (0.0+, 15.9+)

[a]CR+PR+SD for =12 weeks.

A3 Germline variants and clinical outcomes of high-risk stage II and stage III colon cancer patients treated with oxaliplatin and fluoropyrimidines adjuvant chemotherapy: a pharmacogenetic ancillary study to TOSCA trial

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Background: Functional germline variants (SNPs) may characterize sub-populations of cancer patients who gain different benefits from chemotherapy. We investigated 17 SNPs in 11 genes with putative impact on sensitivity to fluoropyrimidines and oxaliplatin (TS, MTHFR, ERCC1, XRCC1, XRCC3, XPD, GSTT, GSTP, GSTM, ABCC1, ABCC2).

Material and methods: TOSCA was a non-profit, Italian, multicentre, randomized, non-inferiority phase III study conducted in high-risk stage II and stage III colorectal cancer patients treated with 6 or 3 months of FOLFOX-4 or XELOX adjuvant chemotherapy. Patients who signed the informed consent were prospectively accrued in this ancillary study.

The primary and secondary endpoints were relapse free survival (RFS) and overall survival (OS), respectively. Univariate and multivariate Cox proportional hazard models were used.

Results: From July 2007 to October 2011, 524 patients were enrolled in this study. Eight patients were excluded from analysis due to major violation and 4 never started treatment. 185 and 188 patients were treated with FOLFOX-4, 68 and 71 with XELOX in 6-month and in 3-month arm, respectively. Allele frequencies of all SNPs were

consistent with Hardy-Weinberg equilibrium. 82(16%) progression and 71(14%) deaths were observed. Progression or deaths occurred in 106(21%) patients. The XRCC1 rs25487 G>A shortened significantly RFS (adjusted HR[AA vs GG] 2.02; 95%CI 1.15-3.56; p = 0.015) and OS (adjusted HR[AA vs GG] 3.07; 95%CI 1.57-5.99; p = 0.001). Interactions between SNPs and treatment duration were detected. In detail, 3-month treatment was correlated with a shorter RFS for patients with G allele in XPD rs13181 T>G and for patients with CC genotype (vs TC+TT) in ERCC1 rs11675 T>C. A better RFS and OS were identified in patients treated for 3 months with GG genotype for ABCC2 rs4148386 A>G. Finally, the GG genotype in ABCC2 rs1885301G>A increased OS in patients treated with 3 months treatment.

Conclusions: XRCC1 rs25487 G>A produced remarkable differences in RFS and OS in the studied population. Additional functional germline variants involved in the DNA repair pathways may engage a clinical impact according to the duration of the adjuvant chemotherapy program. These findings may impact on the overall chemotherapy treatment strategy of colon cancer patients. Additional prospective studies are warranted for confirming this associations and after adjustment for tumor-related prognostic factors.

A4 Dissecting primary resistance to anti-EGFRs in RAS and BRAF wt metastatic colorectal cancer (mCRC): A case-control study

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Background: Almost half of RAS and BRAF wt mCRC patients do not respond to anti-EGFRs. Different molecular alterations suggested as predictors of primary resistance have not been validated.

Material and methods: We conducted a case-control study to prospectively demonstrate the negative predictive impact of HER-2 amplification or mutations, MET amplification, NTRK/ROS1/ALK/RET rearrangements, and mutations activating MAPKs or PI3K/Akt axis. Patients with RAS and BRAF wt mCRC clearly resistant (cases) vs. clearly sensitive (controls) to anti-EGFRs were selected. Hypothesizing a prevalence of candidate alterations of 0% and 15% among controls and cases, respectively, 47 cases and 47 controls were needed to be able to reject the null hypothesis of equally prevalent alterations, with a- and b- error 0.05 and 0.20. Since hypermutated tumors may hardly rely on a single pathway for their growth, we also evaluated the predictive impact of microsatellite instability.

Results: 47 cases and 47 controls were included. Primary endpoint was met: mentioned alterations were reported in 20 (42.6%) cases and 1 (2.1%) control ($p < 0.001$). Additionally, 3 resistant patients showed *RAS* mutations at low allelic frequency. MSI-high was significantly more frequent among resistant than sensitive patients (17% vs 0%, $p < 0.001$).

Conclusions: This is the first prospective demonstration that the combined assessment of these rare alterations allows to better select patients for anti-EGFRs, while opening the way to other tailored therapies.

A5 Circulating angiogenesis-related markers as predictors of benefit from regorafenib in metastatic colorectal cancer (mCRC) patients (pts)

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Background: Regorafenib is a treatment option for refractory mCRC pts. Considering its limited clinical benefit and the extremely palliative setting, patients' selection is essential to optimize the cost-effectiveness balance. The aims of this study were to describe the modulation of selected circulating angiogenic factors by the treatment with regorafenib and to investigate their correlation with clinical outcome.

Methods: IL-8, Ang-2, PDGF, bFGF, Tie-2, sVEGFR2, sVEGFR3, PlGF, VEGF-A, VEGF-B were assessed by ELISA on plasma samples collected at baseline (d1), after 15 days of treatment (d15), at the best RECIST response (resp), and at the time disease progression (PD) in a cohort of mCRC pts treated with regorafenib, as per indication. Comparisons among concentrations of each marker at different time points were performed by using the Wilcoxon test. Markers showing significant changes were analyzed to identify correlations with outcome.

Results: One hundred and five pts were included. Median PFS and OS were 2.1 and 7.0 months (mos), respectively. As compared to d1, IL-8 and Ang-2 levels increased at PD. An early decrease at d15 was observed for PDGF, Tie-2, sVEGFR2 and sVEGFR3 levels, followed by an increase at PD. Conversely, PlGF levels increased at d15 and then decreased at PD. Baseline levels of Ang-2 and Tie-2 below the median value were associated with longer PFS (HR:0.61 [95%CI:0.37-0.83], p = 0.006; HR:0.69 [95%CI:0.43-0.95], p = 0.04, respectively) and OS (HR:0.45 [95%CI:0.26-0.60], $p < 0.0001$; HR:0.68 [95%CI:0.44-0.98], p = 0.04, respectively). With regard to Ang-2, 40 (45%) out of 89 pts with available plasma samples at d15 showed increased levels at d15 as compared to d1. Among them, 21 (53%) achieved disease control, as compared to 14 out of 49 (29%) pts with Ang-2 decreased levels (p = 0.03). Median PFS of pts with increased and decreased Ang-2 levels were 3.1 and 1.8 mos, respectively (HR:0.57 [95%CI:0.33-0.78], p = 0.004).

Conclusions: A dynamic modulation of plasma angiogenic factors occurs during the treatment with regorafenib. Low baseline Ang-2 and Tie-2 levels seem to be associated with good prognosis. The early modulation of Ang-2 levels may predict benefit from regorafenib. Since Ang-2, as an inhibitory ligand of Tie-2 receptor, promotes tumor angiogenesis, it is conceivable that the successful Tie-2 inhibition by regorafenib might lead to a compensatory increase in Ang-2 and correlate with anti-tumor activity. These results need validation in independent series.

Table: A4

Molecular alteration	Cases (Resistant patients) N = 47	Controls (Sensitive patients) N = 47
HER-2 amplification	7	0
HER-2 mutations	1 (G776V, exon 20)	0
MET amplification	4	0
NTRK rearrangements	2 (*SCYL3-NTRK1* and *TPM3-NTRK1*)	0
ALK rearrangements	0	0
ROS1 rearrangements	0	0
RET rearrangements	1 (*CCDC6-RET*)	0
PIK3CA mutations in exon 20	1 (A1035V, exon 20)	1 (H1047R, exon 20)
AKT1 mut	1 (R25C)	0
PTEN mutations	3 (L247S, R233stop and del P248, exon 7)	0
Total n. of patients with candidate alterations	**20**	**1**
Microsatellite instability (MSI-high)	8	0
RAS mutations at low allele fraction*	3 (*KRAS* G12V, exon 2, 6%; *NRAS* Q61R, exon 3, 10%; *KRAS* Q61H)	0

*by Hotspot Cancer Panel v2, (Life Technologies©), previously found wt by pyrosequencing

A6 Sidedness influences prognosis in colon cancer patients receiving an adjuvant therapy. A GISCAD analysis from three randomized trials including 5234 patients

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Background: While in the advanced setting right colon cancer is associated with a worse outcome, this negative prognostic effect has been not definitively demonstrated in the adjuvant setting. We have analyzed the outcome data from 3 large randomized trials (SITAC-1; SMAC and TOSCA) assessing adjuvant therapy in colon cancer patients with stage II and III.

Methods: In order to define the prognostic effect of sidedness we assessed three randomized trials of adjuvant therapy (SITAC, 5FU/FA vs control, 821 patients; SMAC, intraportal 5FU vs 5FU/FA, 990 patients; TOSCA, FOLFOX or XELOX three vs six months 3513 patients) carried out in Italy from 1987 to 2013 and including 5324 patients. Survival and disease-free survival, overall and in each trial, were analyzed according to right, transversum and left colon location. Right-sided was considered caecum to hepatic flexure, left-sided splenic flexure to rectum and trasversum hepatic to splenic flexure. Statistical analysis considered all randomized patients according to allocation arm, with available data on putative prognostic factors.

Analysis was planned in order to provide overall and by stage results.

Results: 5324 patients were included in this analysis, 2490 patients were males and 2834 females. Median age was 64 years. 2240 patients had a stage II colon cancer and 3084 a stage III. Right tumors were 1573 (30%), trasversum 822 (15%) and left 2929 (55%). Patients characteristics were well balanced among the three trials. In all the 5234 patients DFS was not affected by tumor location (right colon versus left, HR = 1.01; 95% CI = 0.89-1.15) while right tumor was associated to a worse OS compared to left tumor (HR = 1.21; 95% CI = 1.05-1.40).

In stage II patients there was no difference in terms of DFS and OS among the three different tumor location while in stage III patients, right colon cancer had a worse outcome both in DFS and OS than left tumor (HR: 1.37 95% CI = 1.16-1.64, $p < 0.001$).

Conclusions: This is the largest analysis demonstrating the prognostic effect of tumor location in colon cancer patients receiving adjuvant chemotherapy. The effect however is present only in stage III but not in stage II colon cancer.

A7 Survival analysis of KRAS, NRAS, BRAF, PIK3CA wild type (wt) metastatic colorectal cancer (mCRC) patients (pts) treated with FOLFIRI plus cetuximab in the CAPRI- GOIM trial

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Background: The CAPRI-GOIM trial consisted of two parts: FOLFIRI plus cetuximab in first line followed by cetuximab plus FOLFOX as second line treatment for molecularly selected mCRC pts. The primary endpoint was progression-free survival (PFS). Secondary endpoints included overall survival (OS), response rate and safety. This is an updated analysis providing the mature results for OS in KRAS, NRAS, BRAF, PIK3CA wt pts.

Methods: In the CAPRI-GOIM trial 340 mCRC pts with KRAS exon 2 wt tumors were treated in first line with FOLFIRI plus cetuximab until disease progression or unacceptable toxicity. After first line therapy progression, pts (157), who achieved a clinical response with first line treatment, were randomized to FOLFOX plus cetuximab (Arm A) or to FOLFOX (Arm B). Archival tissue samples from primary tumours were centrally assessed by next generation sequencing (NGS) with the Ion AmpliSeq Colon and Lung cancer panel. Here we report mature survival data at median follow-up of 69 months (m) (cut off date: April 30, 2017) for 98 out of the 124 RAS wt patients with NGS analysis, that were representative of the 340 intention to treat patient population.

Results: Median OS for these 98 pts was 34.0 m (95% CI 30.2–37.8) with PFS of 11.7 m (95% CI 10.3–13.1). Eighty six out of 98 pts had tumors that were KRAS, NRAS, BRAF, PIK3CA wt. In this cohort, OS was 35.8 m (95% CI 29.9–41.9) with PFS of 12.3 m (95% CI 10.7–14.0). PFS and OS were also evaluated according to tumour location (see Table 1 for results).

Conclusions: Long-term follow-up analysis of pts enrolled in the CAPRI-GOIM trial showed a median OS of approximately 36 m in KRAS, NRAS, BRAF and PIK3CA wt pts. A better prognostic outcome in terms of OS and PFS was observed in left-sided as compared to right-sided tumors.

Table: A7

Cohort	Median OS (months)		Median PFS (months)	
	Right	Left	Right	Left
RAS wt (n = 98)	33.4 (31.7-34.9)	35.8 (29.9-41.7)	9.9 (7.9-12.0)	12.3 (11.0-13.6)
KRAS, NRAS, BRAF, PIK3CA wt (n = 86)	34.0 (22.1-46.0)	35.8 (29.5-42.3)	9.9 (5.3-14.6)	12.3 (10.7-14.0)

A8 Optimization of the combination of bevacizumab with FOLFOX/OXXEL in patients with metastatic colorectal cancer (mCRC): the multicentre, randomized phase 3 study OBELICS

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Background: Bevacizumab is a humanized anti-vascular endothelial growth factor (VEGF) monoclonal antibody, approved in combination with chemotherapy in the treatment of mCRC. It is proposed that the schedule of administration might be critical and that anticipating bevacizumab to chemotherapy, might improve treatment efficacy.

Methods: mCRC patients, = 75 years old, ECOG PS = 1, having received no more than one previous treatment, with at least one measurable lesion according to RECIST, were randomized (1:1) to receive standard administration of bevacizumab (5mg/kg d1 Q14) with chemotherapy (mFOLFOX/OXXEL regimen for 12 cycles) vs experimental bevacizumab given 4 days before chemotherapy (same dose), at each cycle. Patients could receive maintenance bevacizumab (7.5 mg/kg d1 Q21) until disease progression or unacceptable toxicity in both arms. Primary end point was the objective response rate (ORR). With 80% power and 2-tailed alpha 0.05, an expected 20% increase in response rate, 230 patients were planned. With 163 events, the study also had 80% power to detect a hazard ratio (HR) 0.64 of progression-free survival (PFS). Analyses were based on intention to treat.

Results: From May 2012 to Dec 2015, 230 patients were randomised to experimental (n = 115) and standard (n = 115) arm. Median age was 62 (IQ range 53-68), 79% were PS 0, 93% were not pretreated, 53% had a single metastatic site, 54% were RAS-mutant (47% and 62% in the standard and experimental arm, respectively). ORR was 54% in both arms ($p = 0.89$). With a median follow-up of 32.4 months, 204 PFS events and 131 deaths were reported. Median PFS was 11.7 and 10.5 months (HR 0.79, 95% CI: 0.60-1.05; multivariate adjusted $p = 0.10$) and median OS was 23.7 and 29.9 months (HR 0.73, 95% CI: 0.52-1.04; multivariate adjusted $p = 0.08$), in the standard and experimental arm, respectively. 57.4% and 59.1% of the patient received at least one following treatment in the standard and experimental arm, respectively.

Conclusion: Anticipating bevacizumab to chemotherapy produced a not statistically significant prolongation of PFS and OS . Objective response rate was not improved. Supported by the Italian Ministry of Health. CT.gov NCT01718873.

A9 Histopathologic response and growth patterns of colorectal cancer liver metastases (CRCLM) in patients treated with triplets plus bevacizumab (bev) or anti-EGFRs

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Background: The histopathological response to pre-operative chemotherapy is associated with clinical outcome in patients (pts) undergoing secondary resection of CRCLM. Triple chemotherapy regimens may be preferred options in this setting. Three different histopathological growth patterns (HGPs) of CRCLM have been described: desmoplastic (i.e. with a capsule of stroma separating tumor and normal cells), pushing (i.e. with limited infiltration of normal hepatic plates by tumor cells) and replacement (i.e. with abundant infiltration of normal hepatic plates by tumor cells and vessel cooption).

Methods: Histopathological parameters of response were evaluated in specimens from 159 pts who underwent secondary resection of CRCLM, after receiving triplet (FOLFOXIRI or COI) plus bev (N = 103) or anti-EGFR (N = 56) in 5 first-line clinical studies (TRIBE, MOMA, MACBETH, COI-B and COI-E). The aims of this analysis were to evaluate the prognostic role of histopathologic response and to explore its association with clinical characteristics, and to investigate the prognostic role of HGPs and their potential different sensitivity to targeted agents.

Results: When compared with partial (TRG 3) and no (TRG 4-5) pathologic response (N = 118), major response (TRG 1-2, N = 41) was associated with longer RFS (mRFS: 28.0 versus 11.0 mos, HR = 0.57, 95%CI=0.39–0.86; p=0.007) and OS (mOS: unreached versus 42.1 mos, HR = 0.54, 95%CI=0.31-0.93; p=0.027).

No association of baseline clinical characteristics and *RAS* and *BRAF* status with major response was found. Major response was more frequent among pts treated with bev than with anti-EGFRs (OR = 2.83, 95%CI=1.20–6.65; p=0.015) and was associated with deepness of response as a continuous variable (HR = 1.02, 95% CI = 1.00–1.04; p=0.011).

In the desmoplastic HGP (N = 28) a higher percentage of major response was reported (57% vs 17% in pushing and 22% in replacement HGP, p<0.001) and a numerical advantage from anti-EGFR vs bev was evident in terms of both major response and RFS. Conversely, in the pushing HGP (N = 66) a significant benefit from bev vs anti-EGFR in major response and RFS was observed. No difference was described in the replacement HGP (N = 65).

Conclusion: Achieving deep radiologic and major histopathologic response significantly affects the outcome of pts with CRCLM. The assessment of HGPs may be useful to predict benefit from available targeted agents. To this end, the possibility to recognize HGPs by means of imaging exams should be investigated.

A10 Longer intervals after neoadjuvant therapy in locally advanced rectal cancer: a monocentric experience

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Background: Neoadjuvant chemoradiotherapy (CRT) has been proven to increase local control in rectal cancer but the optimal interval between CRT and surgery is still unclear. Some literature evidence suggest delaying surgery until 10–11 weeks or longer from the end of CRT seemed to result in the highest chance of a pathological complete response (pCR) and tumor downstaging. The aim of this study was to identify correlation between delaying time to surgery (calculated from the end of radiotherapy) and pCR rates.

Methods: From May 2010 to March 2017 110 consecutive pts with rectal cancer (stage II-III) received CRT with capecitabine 825 mg/m^2 bid concomitant with 45-50 Gy conventional fractionation external beam radiotherapy followed by radical surgery (total mesorectal excision) in our Institution. The median interval between radiotherapy and surgery was 13 weeks (range 5–18). Patients were divided in 2 groups based on time to surgery: <13 weeks (group A = 52 pts) and >13 weeks (group B = 58 pts). Statistical analysis for DFS and OS rates were calculated with Kaplan Meier nonparametric estimation from date of surgery.

Results: The mean age of patients was 64 years (range: 36-84). pCR was observed in 22.7% (n = 25/110 pts). pCR in group A was 19.2% (n = 10/52 pts) and 25.8% (15/58) in group B with statistically significant difference (p < 0.001). Good responders (Dworak TRG4 + 3) in group A were 39.6% vs 45.7% in group B. Bad responders (Dworak TRG2 + 1+0) in group A were 60.4% vs 54.3% in group B. At this time disease-free-survival rates in overall population was 90.3%, 85.2% respectively at 3 and 5 years and overall survival was 77.6%, 72.9% at 3 and 5 years. There was no statistically significant difference in DFS between group A vs group B (4 yrs DFS rate: 73.2% vs 72.2%, p = 0.920).

Conclusion: This study suggests delaying surgery beyond 13th week after the end of CRT seemed to result in the highest chance of a pCR and probably in downstaging, in accord to recent published data. The delayed surgery would seem to select a greater number of good responders. Obviously prospective randomized studies of appropriate statistical power comparing various time intervals are needed to examine the optimal timing for surgery and to plan the better management of these setting of patients.

A11 Cost-effectiveness of anti-angiogenic agents in second-line treatment for metastatic colorectal cancer. Integrating the EUROPEAN Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) with the costs of drugs

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Background: In western Countries, colorectal cancer (CRC) is the second most common cause of death from cancer. In particular, the introduction of active new anti-angiogenic agents for the second-line treatment of metastatic CRC (mCRC) is associated with a relevant increase of costs and it is therefore important to make a balance between the costs of treatment and the added value represented by the improvement of the clinical parameters of interest such as progression free survival (PFS).

Materials and methods: The analysis was conducted to assess the effect of second-line therapy with anti-angiogenic agents on the PFS and was restricted to pivotal phase III randomized controlled trials (RCTs). We calculated the pharmacological costs necessary to get the benefit in PFS, for each trial. Calculations were based on an "ideal patient" (BSA 1.8 sqm; weight 70 Kg). The costs of drugs are at the Pharmacy of our Hospital and are expressed in euros (€). We have subsequently applied the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) to the above pivotal phase III RCTs.

Results: The present analysis evaluated 4 phase III RCTs, including 3938 patients. PFS ranged from 2.7 months of bevacizumab alone in the E3200 trial to 7.3 months of the combination of FOLFOX and bevacizumab in the same trial. ESMO-MCBS reached medium score for VELOUR trial and low grade scores (grade 1 and 2) for RAISE, TML and E3200 trials, respectively. Dividing the costs of therapy by the measure of efficacy represented by PFS we found out that the lowest cost per month of PFS gained (4581 €) was associated with the use of FOLFIRI plus aflibercept; the highest cost per month of PFS gained (23 827 €) was associated with the use of FOLFIRI plus ramucirumab.

Conclusions: Combining pharmacological costs of drugs with the measure of efficacy represented by the PFS, aflibercept in combination with FOLFIRI is a cost-effective second-line treatment for patients with mCRC. The lack of correlation between PFS and OS is a well known phenomenon with the clinical use of anti-angiogenic treatment and reinforces the importance of the evaluation of PFS as a strong end-point, even on a pharmaco-economic perspective.

A12 RET rearrangements define an uncommon molecular subtype of metastatic colorectal cancer (mCRC)

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Background: RET fusions occur in < 1% of CRCs and represent new therapeutic targets, as indicated by earlier promising case reports of patients (pts) treated with tyrosine kinase inhibitors. Although the features of mCRCs harboring ALK, ROS1 and NTRK fusions were recently elucidated, the clinical and molecular landscape of RET rearranged mCRC is still largely unknown.

Methods: pts with mCRC harboring RET fusions were identified worldwide taking advantage of 1) previously published molecular case reports; 2) Italian and Korean screening collaboration; 3) Ignyta's phase 1 trial of RXDX-105 (NCT01877811); 4) Foundation Medicine Database. Clinical and molecular characteristics of RET

rearranged cases were compared with non-rearranged ones screened at 3 referral Centers in Milan, Pisa and Seoul.

Results: 22 RET rearranged (12 NCOA4-RET, 7 CCDC6-RET, 2 TRIM24-RET and 1 novel TNIP1-RET) and 236 not rearranged mCRCs pts were included. Rearrangements were more frequent in older pts ($p = 0.027$), with right sided primary tumors ($p < 0.028$), RAS wild-type ($p < 0.001$), BRAF wild-type ($p < 0.001$) and MSI-high ($p < 0.001$). All RET fusions were found in RAS and BRAF wild-type tumors and, in 43% of cases, in MSI-high ones. At a median follow-up of 31.5 months, pts bearing RET rearranged tumors had a shorter overall survival (OS) when compared to non-rearranged (HR: 4.01, 95% CI 5.64-4.74; $p < 0.001$). In the multivariable model including other significant variables (primary tumor resection and location, RAS, BRAF and MMR status), RET rearrangements retained significant association with shorter OS (HR: 2.82, 95% CI 1.21 – 6.57; $p = 0.017$), as well as primary tumor resection ($p = 0.043$). A patient showed primary resistance to FOLFOX-panitumumab, while unselective RET inhibitors (regorafenib/sunitinib) conferred only short-lasting clinical benefit. NGS molecular data and preclinical experiments with unselective/selective inhibitors in RET fusion positive PDX will be presented.

Conclusions: RET rearrangements define a new and rare molecular subtype of mCRCs associated with unfavorable prognosis, and specific clinicopathological and molecular features. The present findings in RET rearranged mCRC resemble those previously reported for ALK, ROS1 and NTRK positive ones. Since sensitivity to available treatment options including anti-EGFRs may be very limited, RET specific inhibitors such as RXDX-105 are a priority for future research.

A13 Aflibercept efficacy according to sidedness, RAS and BRAF mutations. Findings from the VELOUR trial in second line therapy of advanced colorectal cancer patients

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Background: Addition of (ziv)-aflibercept (A) to FOLFIRI in second-line therapy for metastatic colorectal cancer (mCRC) has been shown to be beneficial in phase III VELOUR trial (NCT00561470). A follow-up study (NCT01754272) was undertaken to acquire tumor samples for biomarker analyses and identify subgroups of pts with differential treatment effects. The primary results assessing efficacy according to well-established mCRC subgroups defined by RAS, BRAF status and sidedness are reported here.

Material and methods: Tissue specimens were collected for 666 pts from 1226 ITT pts. Suitable specimens were assayed for somatic mutation using NGS targeting extended RAS and BRAF genes. NGS assays with no missing values were obtained for 482 pts. Affymetrix gene chip technology was used for whole-transcriptome profiling; sidedness was extracted from available pathological reports. Differences between subgroups were assessed by interaction analysis.

Results: The treatment effects on overall survival (OS) for the 482 pts is still significant HR = 0.80 (CI 0.65-0.99), and similar to the ITT (n = 1226) results (HR = 0.82, CI 0.71-0.93). Two established ways of defining mutations (traditional KRAS exon 2 and extended RAS using NGS) show reduced treatment efficacy in mutants (see table for OS). Interestingly, BRAF mutants (which are all RAS wild types) show a trend of better outcome response. Same is seen for PFS and RR. Sidedness did not affect efficacy (HR: 0.83 (0.63- 1.1) for left and HR: 0.83 (0.54-1.3) for right).

Table: A13

Mutation	Status	N	Med OS FOLFIRI +P	Med OS FOLFIRI + A	HR 95% CI	Interaction (ratio of HR, 95% CI, p-value)
KRASex2	wt	281	11.6	14.9	0.74 (0.56-0.99)	1.21 (0.79 - 1.86)
	mut	201	10.6	12.6	0.90 (0.65-1.24)	p = 0.38
ExtRas	wt	218	11.7	16.0	0.70 (0.50-0.97)	1.39 (0.90 - 2.13)
	mut	264	11.2	12.6	0.93 (0.70-1.23)	p = 0.13
BRAF	wt	446	12.4	13.0	0.84 (0.67-1.05)	0.49 (0.22 - 1.09)
	mut	36	5.5	10.3	0.42 (0.16-1.09)	p = 0.08

Conclusion: This is the only study that evaluated the impact of RAS, BRAF and sidedness of an anti-angiogenetic drug in the second line of mCRC. Lack of significant interaction between subgroups show that Aflibercept efficacy is not impaired by RAS mutations or sidedness. However, Aflibercept seems to have a specific effect on BRAF mutated tumors. *Sanofi supported this ISS. Clinical trial information: NCT01754272.*

A14 Size does matter: comparison of activity between anti-EGFR and anti-VEGF based-treatment in RAS wild type colorectal cancer patients, stratified by size of metastatic involvement

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Background: First-line treatment for RAS wild type (WT) metastatic colorectal cancer (mCRC) patients (pts) is chemotherapy (CT) combined with anti-EGFR or anti-VEGF drugs. Several studies have been conducted to evaluate which is the best choice, without conclusive results. In this retrospective analysis we assessed whether the size of metastatic involvement (evaluated by the diameter of the greatest metastasis), could be related to different activity between the two drugs.

Patients and methods: We included RAS WT mCRC pts who received a first-line therapy with a CT doublet combined with either Panitumumab or Cetuximab or Bevacizumab. Our hypothesis is that a dimensional cut-off of 2 cm of diameter of the greatest metastatic lesion can be considered a stratifying factor, with anti-VEGF and anti-EGFR treated pts achieving improved survival respectively for metastasis $< =2$ cm and >2 cm. Other stratification factors were surgery for primary CRC and for metastatic disease (yes vs no) and site of primary tumour (left- vs right-sided). The response was assessed by RECIST criteria 1.1. Overall survival (OS) and progression free survival (PFS) were calculated by Kaplan-Meier method. Multivariate analysis was performed by Cox-regression model. Level of significance p value was set at 0.05.

Results: 156 pts were enrolled, 75% received Bevacizumab and 25% an anti-EGFR drug. The two groups were homogeneous for all the clinical characteristics analysed. Stratifying by the dimensional cut-off, we found a statistically significant improved OS for pts with $< =2$ cm metastasis in the anti-VEGF group ($p = 0.0005$) and a better but not significant OS for pts with >2 cm metastasis in the anti-EGFR group. Accordingly to our hypothesis, we defined "Pro" the group of pts who received the best treatment (metastasis $< =2$ cm treated with anti-VEGF and metastasis >2 cm treated with anti-EGFR) and "Against" the rest of population (who did not receive the best treatment). We found a statistically significant better survival in the "Pro" versus "Against" group (respectively, OS 32.3 vs 19.7 months, $p = 0.0004$; PFS 10.1 vs 8.2 months, $p = 0.003$). At multivariate analysis "Pro" vs "Against" maintained its independent role on par with surgical resection of metastases.

Conclusions: Our study suggests that optimal CT selection offered to patients should be based upon the size of the metastases. After confirmation in further prospective series, these "easy-to-assess" clinical factor could play a role in the treatment strategy process.

A15 Eph A2 expression is a predictive biomarker of poorer activity and efficacy of FOLFIRI + cetuximab in RAS WT metastatic colorectal cancer (mCRC) patients (pts) in the CAPRI GOIM trial

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Background: Eph A2 promotes tumor growth, invasiveness and angiogenesis in mCRC. Targeting Eph A2 could overcome resistance to anti-epidermal growth factor receptor (EGFR) treatment in colon cancer preclinical models.

Methods: Formalin-fixed paraffin-embedded tumor specimens from 82 RAS wild type (WT) mCRC pts treated with cetuximab + FOLFIRI as first line therapy in the CAPRI GOIM trial were assessed for Eph A2 expression by immunohistochemistry. Eph A2 levels were evaluated developing an HSCORE [1 × (% cells 1+) + 2 × (% cells 2+) + 3 × (% cells 3+)] (range: 0-300). A cut off was set by ROC analysis to define high (>50) and low (≤50) Eph A2 levels.

Results: Eph A2 expression was found in 55/82 (67%) cases. According to HSCORE Eph A2 levels were low in 54 (66%) and high in 28 (34%) samples. Eph A2 expression resulted in mostly complete membranous staining. Tumor stroma was positive in 15/82 (18%) cases. In most of these cases an intense immune infiltrate was observed. Non-tumor adjacent normal mucosa was assessable in 34/82 samples. Eph A2 was expressed in 16/34 (47%), more frequently in dysplastic epithelial areas. A significant correlation between Eph A2 expression in tumor and stroma was found ($p < 0.0001$). Eph A2 was more frequently expressed in less differentiated tumors ($p = 0.02$), as well as in left-sided tumors compared to right-sided tumors [17/28 (61%), 11/28 (39%), respectively $p = 0.04$]. Eph A2 expression was associated with higher rate of disease progression (PD) 8/28 (29%) vs 5/54 (9%) ($p = 0.02$), and with worse median PFS [8.6 m (CI95% 6.4-10.8) vs 12.3 m (CI95% 10.4-14.2) $p = 0.030$], both in left and right-sided tumours. Moreover, median OS was 28.4 m (CI95% 13.1-43.7) vs 39.8 m (CI95% 30.2-49.4), although this result did not reach statistical significance ($p = 0.23$).

Conclusion: Eph A2 levels were significantly associated with a worse PFS and an increase in PD in RAS WT mCRC pts treated with cetuximab + FOLFIRI as first line therapy in the CAPRI GOIM trial in both right and left-sided tumors. A similar trend was observed for OS. Eph A2 might represent an additional predictive biomarker of lack of efficacy in RAS WT mCRC pts treated with FOLFIRI + cetuximab.

A16 Correlation of PD-L1 staining between primitive tumor and metastasis in advanced colorectal cancer patients

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Background: Up to now, published studies have failed to demonstrate a predictive role of PD-1 or PD-L1 immunostainings in metastatic (met) colorectal cancer (mCRC) patients (pts) submitted to immunotherapy. However, in mCRC as well as in other solid tumors there is great interest on the description of concordance of expression between different sites of disease in the same pt. As data on receptor positivity are more easily obtained from primitive tumor samples, and therapy activity is tested on dimensional variation of met, we thought of interest to study the correspondence of PD-L1 expression in a matched series of primitive and surgically resected met tumors.

Patients and methods: PD-L1 immunostaining of matched primitive tumor (TP) and met (TM) samples from 50 mCRC pts retrospectively selected were obtained. Positivity was defined as moderate/intense membrane staining in at least 1% of tumor cells. Tumor infiltrate of primitive (IP) and met (IM) were also evaluated and graded according to the number of positive lymphocytes surrounding tumors (0: < 1%, 1: 1-4%, 2: 5-9%, 3: =10%). Positivity was defined as = 2.

Results: Tumor sites were (right/left/rectum): 17/20/13. Met were (liver/lung/other abdominal): 26/15/9. 3/50 TP (all right-sided) and 6/50 TM (3 liver and 3 lung) were positive. 9/50 IP and 12/50 IM (7 lung and 5 liver) were positive. PD-L1 was more frequently positive in IM of lung than liver (47% vs 19%, $p = 0.06$). The rate of concordance between TP and IP was 76% (all TP positive were IP negative), and between TM and IM was 72% (2 out of 6 TM positive were also IM positive).
The rate of concordance between TP and TM was 86% (2/3 TP positive were also TM positive), and between IP and IM was 74% (4/9 IP were also IM positive:3 lung, 1 liver).

Conclusions: An overall good correlation in PD-L1 staining between tumor cells from primitive and met was described. Tumor infiltrate (primitive or met) was more frequently positive then tumor, especially in lung metastases. However, the low number of positive samples prevents any definitive conclusion. For this reason a confirmatory analysis in a second cohort of patients from another institution is ongoing and data from the two cohorts will be presented.

A17 Image-guided SIB-IMRT for the treatment of anal cancer patients

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Purpose/objective: Concurrent chemoradiation (CT-RT) has been established as the standard of care for anal cancer patients. We explored intensity-modulated and image-guided radiotherapy (IMRT–IGRT) with a simultaneous integrated boost (SIB) approach reporting on clinical outcomes within a mono-istitutional observational study.

Material/methods: Between April 2007 and April 2015, 87 patients with biopsy proven squamous cell anal cancer were treated with SIB-IMRT. Radiotherapy was delivery using a schedule of 50.4/54 Gy to the primary tumor and involved lymphnodes and 42/45 Gy to the elective volumes. Dose prescription varied according to clinical stage, following Radiation Therapy Oncology Group (RTOG) 0529 indications. Concurrent 5-Fluorouracil and Mitomycin-C were given. Clinical data and toxicity are herein reported.

Results: A total of 87 patients (stage I 6%; II 56%; III 38%) were treated and observed for median time of 34 months (range: 9-102). CT-RT with MMC and 5-FU was administered in 90.8% of patients. One patient received MMC only, two patients 5-FU only and five patients underwent exclusive RT, after consderation of age, comorbidities and performance status. The 3-year rates of colostomy-free survival, local control, disease free and overall survival were 71% (95% CI 0.59-0.80), 69% (95% CI 0.57-0.79), 64% (95% CI 0.52-0.75), and 79% (95% CI 0.66-0.87) respectively. At the time of analysis 20/87 (23%) patients were dead and 14 death were related to cancer. Up to 23 patients recurred; ten failed locally, 7 failed both locally and distantly and 6 developed systemic failure only. Seventy-seven patients reached a clinical complete response six months after treatment (88.5%). Major acute toxicity events (≥G3) were recorded for gastrointestinal (6.9%), genitourinary (1.2%) and hematologic (neutropenia: 19.6%) aspects. Borderline significance as prognostic factors with respect to CFS were found for gender and stage.

Conclusion: Image-guided IMRT with a SIB approach concomitant to 5-FU/MMC based chemotherapy is a safe and well tolerated treatment strategy in an unselected anal cancer patient population.

A18 Efficacy of anti-EGFR antibodies combined with chemotherapy for elderly patients with RAS wild-type metastatic colorectal cancer: a systematic review and metanalysis

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The incidence of Colorectal Cancer (CRC) increases with age, reaching a peak around 70-75 years. The anti-EGFR monoclonal antibodies combined with chemotherapy represent a valid option in patients with RAS wild-type (wt) metastatic CRC (mCRC), allowing for a significant improvement in survival.

However, few data are available in literature regarding the clinical value of these drugs in the elderly population.

The aim of the study is to evaluate the efficacy of adding anti-EGFR monoclonal antibodies (Cetuximab or Panitumumab) to chemotherapy in the treatment of RAS wt mCRC older patients.

A systematic review of the published data using PubMed and EMBASE databases and the congress documents of the main national and international symposia was performed. The random effect model was used to combine the effect estimates, the I^2 and Cochran's Q index to quantify the between-study heterogeneity unexplained by sampling error.

Four randomized trials (two for Cetuximab and two for Panitumumab) have been selected among the 2765 initially identified studies. None of the studies had been specifically designed for the elderly population, so PFS and OS HR values ? were extracted from pre-specified subgroup analyses. In our meta-analysis, 605 elderly patients have been included, 289 patients treated with chemotherapy only and 316 patients with chemotherapy in combination with an anti-EGFR antibody. The meta-analysis showed a statistically significant benefit of the combination of chemotherapy and anti-EGFR against chemotherapy alone both in terms of PFS (HR 0.79, IC 95% 0.64-0.98, $p = 0.028$, $Q = 2.54$, $df = 3$, $I^2 = 0\%$) and OS (HR 0.82, IC 95% 0.68-0.98, $p = 0.032$, $Q = 0.57$, $df = 3$, $I^2 = 0\%$).

The meta-analysis of the Panitumumab studies reached statistical significance for OS and not for PFS, while none of the two for Cetuximab were significant. Sensitivity analysis confirmed the results obtained.

The addition of Cetuximab or Panitumumab to chemotherapy in elderly patients with RASwt mCRC could represent a therapeutic option in terms of efficacy. However, the available data in this subset of patient are limited. Dedicated studies are needed in order to determine the best therapeutic strategy.

A19 Multiple treatment lines and prognosis for metastatic colorectal (mCRC) patients (pts)

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Background: The proportion of pts with mCRC receiving second or further lines of treatment reported in clinical trials is considered not completely representative of clinical routine. The present retrospective analysis describes multiple lines of treatment in a consecutive cohort of pts and investigates prognostic factors for survival from diagnosis of metastatic disease.

Patients and methods: 346 mCRC pts has been considered, 173 stage IV at diagnosis, and 173 stage II or III who subsequently experienced distant and/or local relapse. Survival (S) was the time between the date of diagnosis of metastatic disease and the date of death (any cause) or last follow up. HRs and 95% CIs were calculated using univariable Cox proportional hazards models. Median S times were estimated by the Kaplan-Meier method, and p values calculated by log-rank tests (statistical significance for $p < 0.05$).

Results: The median age at the time of diagnosis of metastatic disease was 64 years. About one/third of the patients had multiple sites of disease; those with diagnosis at stage IV presented more frequently multiple sites of disease, peritoneal carcinomatosis, and massive liver deposits, whereas pts whit diagnosis of metastatic disease during follow up had significantly more lung metastases as unique site of disease. Overall, 337 pts (97.4%) received at least one treatment, 62.4% two, 41.9% three, and 23.7% four treatment lines; in the relapsed group more cases received surgery as part of first-line treatment (49.1% versus 24.8%), and more patients are still alive without progression at the time of the analysis (44% versus 34.9%). A biological drug was part of the treatment in 77.3% and 65.8% of cases in first and second line, respectively. At a median follow up of 66.8 months (range 6.7-183.8), 215 (62.1%) pts deceased, and the median S was 23.4 months (range 0.92-178.6). At univariate analysis, age >70, multiple sites of disease and peritoneal carcinomatosis negatively affected S; whereas, surgery of metastases and

isolated lung metastases predicted for significant better S.At multivariate analysis, only peritoneal carcinomatosis (HR = 1.98; p < 0.0001), and surgery of metastases (HR = 0.276; p < 0.0001)independently affect S.

Conclusions: The proportion of treated patients significantly drops from first- to forth-line. Inoperable site of metastasis and surgery of metastases are the most important prognostic factors in mCRC pts.

A20 Rechallenge with cetuximab (cet) + irinotecan (iri) in 3rd-line in RAS and BRAF wt metastatic colorectal cancer (mCRC) patients (pts) with acquired resistance to 1st-line cet + iri: the phase II CRICKET study by GONO

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Background: Clinical benefit from rechallenge with cet-based therapy in *KRAS* wt mCRC pts previously treated with the same anti-EGFR-based regimen was suggested in a retrospective study. Molecular data highlighting the dynamism of intratumoral heterogeneity under the pressure of systemic treatments may explain this finding.

Patients and methods: CRICKET (NCT02296203) is a multicenter phase II single-arm study in mCRC pts, who became resistant to 1st-line cet + iri. Main eligibility criteria are: measurable, unresectable mCRC; *RAS*/*BRAF* wt status; prior 1st-line iri-based, cet-containing regimen with at least RECIST partial response (PR), 1st-line progression-free survival (PFS) ≥6 months, and progression (PD) within 4 weeks after the last administration of cet; prior 2nd-line oxaliplatin-based and bevacizumab-containing treatment. Pts receive 3rd-line cet + iri until PD. The primary endpoint is response rate (RR) according to RECIST v1.1. Based on the Fleming single-stage design, setting p0 = 5%, and p1 = 20%, with 1-sided-α and β errors of 0.05 and 0.20, 27 pts were required. The null hypothesis P ≤ p0 would have been rejected if RECIST response had been observed in ≥ 4 pts.

Results: Between Jan 2015 and Jan 2017, 22 pts were enrolled in six centers. Pts' characteristics are: median age 70 yrs, ECOG PS 0/1-2 59%/41%, primary location right/left 36%/64%, time from diagnosis of metastases >18 mos 77%. At the time of data cut-off (Jan 15, 2017), 20 pts were evaluable for response. The primary endpoint was met. Five PRs (one unconfirmed) were reported (RR: 25%). Four SD (disease control rate: 45%) and eight PD were observed. Three pts experienced clinical PD before disease assessment. No unexpected adverse events were evident.

Conclusions: Rechallenge with cet + iri is active in some pts with *RAS* and *BRAF* wt mCRC, initially sensitive and then resistant to first-line iri-based chemotherapy + cet. Analyses on cfDNA collected at study entry are ongoing in order to verify whether the detection of markers of acquired resistance to cet may help to identify patients more likely to benefit from this strategy. Partially funded by Merck Serono SpA

A21 Metformin and risk recurrence in resected stage II/III colon cancer (CC) patients (pts): subgroup analysis from the TOSCA trial

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Background: Based on preclinical studies, metformin could display both indirect anti-cancer activity by reducing blood glucose, insulin and IGF-1 levels, and cell-autonomous effects by activating AMP-kinase (AMPK) and impairing mitochondrial metabolism. In the clinical setting, favourable cancer-related outcomes have been reported in pts with type II diabetes mellitus (T2DM) treated with metformin. However, recently published data failed to confirm a positive effect on disease free survival and overall survival in stage III resected CC pts. We performed an observational study to evaluate the impact of metformin use in pts enrolled in the TOSCA trial.

Patients and methods: TOSCA was a non-profit, Italian, multicentre, randomized, non-inferiority phase III study conducted in high-risk stage II and stage III CC pts treated with 6 or 3 months of FOLFOX-4 or XELOX adjuvant chemotherapy. Pts with T2DM were prospectively accrued in this observational study. The primary endpoint was the modified relapse free survival (mRFS), defined as the time from randomization to relapse or cancer-related death. Cancer-related survival (CRS), as defined as the time from randomization to cancer-related death, was a secondary endpoint. Fine and Gray proportional subdistribution hazard models for competing risk were used.

Results: Of 3759 pts randomized in the TOSCA trial, 1520 were screened and 142 with T2DM were included in this study. 2 pts were excluded because of major violation and 5 pts due to the lack of available data on metformin exposure. Among 135 evaluable pts, 55 (41%) received only metformin and 80 (59%) other antidiabetic medications plus/minus metformin. Regarding drug exposure, 40 out of 55 (73%) pts received metformin before, during and after chemotherapy. No difference in pts' characteristics and pathological stage between metformin users and nonusers was found. Disease relapse and cancer-related deaths were observed in 30 (22%) and 11 (8%), respectively. Relapse or cancer-related deaths occurred in 31 (23%) pts. No effect of metformin exposure was detected both on mRFS (adjusted HR 1.20; 95%CI 0.53-2.75; p = 0.65) and CRS (adjusted HR 1.71; 95%CI 0.40-7.32; p = 0.47).

Conclusions: Our findings did not demonstrate an association between metformin use and colon cancer relapse or cancer-related death in II/III stage pts treated with adjuvant chemotherapy. However, given the low number of observed events, other analyses will be needed for definitive conclusions.

A22 The role of primary tumour sidedness, EGFR gene copy number and EGFR promoter methylation in RAS/BRAF wild type colorectal cancer patients receiving irinotecan/cetuximab

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Introduction: Data from randomized trials suggested that primary tumour sidedness could represent a prognostic and predictive factor in Colorectal Cancer (CRC) patients, particularly during treatment with anti-Epidermal Growth Factor Receptor (EGFR)

therapy. However, an in-deep molecular selection might overcome the predictive role of primary tumour location in this setting.

Patients and methods: We conducted a retrospective analysis in which tumour samples from RAS/BRAF wild type (WT) metastatic CRC patients treated with second-third-line irinotecan/cetuximab were analysed for EGFR Gene Copy Number (GCN) and promoter methylation. Study objective was to evaluate the correlation of tumour sidedness, EGFR promoter methylation and EGFR GCN with clinical outcome. Median follow up duration was 14.3 months.

Results: Eighty-eight patients were included in the study, 27.3% had right sided CRC, 72.7% had left sided CRC; 36.4% had EGFR GCN<2.12 tumour, 63.6% had EGFR GCN≥2.12 tumour; 50% had EGFR promoter methylated tumour. Right Sided Colorectal Cancer (RSCRC) were associated with reduced Overall Response Rate (ORR) (4.2% for RSCRC vs. 35.9% for Left Sided Colorectal Cancer (LSCRC), $p = 0.0030$), shorter Progression free Survival (PFS) (3.0 vs. 6.75 months, $p < 0.0001$) and shorter Overall Survival (OS) (8 vs. 13.6 months, $p < 0.0001$). EGFR GCN < 2.12 tumours were associated with reduced ORR (6.2% for EGFR GCN < 2.12 vs 39.3% for EGFR GCN ≥ 2.12 tumours, $p = 0.0009$), shorter PFS (3.5 vs. 6.5 months, $p = 0.0006$) and shorter OS (8.5 vs. 14.0 months, $p < 0.0001$). EGFR methylated tumours were associated with reduced ORR (9.1% for methylated vs. 45.5% for unmethylated, $p = 0.0001$), shorter PFS (3 vs. 7.67 months, $p < 0.0001$) and shorter OS (8 vs. 17 months, $p < 0.0001$). At multivariate analysis EGFR GCN and EGFR promoter methylation maintained their independent role for ORR (respectively $p = 0.0082$ and 0.0025), PFS (respectively $p = 0.0048$ and < 0.0001) and OS (respectively $p = 0.0001$ and < 0.0001).

Conclusions: In our study an accurate molecular selection based on an all RAS and BRAF analysis along with EGFR GCN and EGFR promoter methylation status seems to be more relevant than primary tumour sidedness in the prediction of clinical outcome during cetuximab/irinotecan therapy. However, these data need to be validated with future prospective and translational studies.

A23 The prognostic impact of sidedness across all stages during the last 20 years: the "Modena Cancer Registry" experience

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Background: The importance of primary tumor sidedness and its effect on prognosis in patients (pts) with metastatic colorectal cancer (mCRC) has recently been highlighted. In early-stage disease this prognostic value is not so clear, but there is some suggestion that recurrences arising from right-sided primary tumours might be more aggressive than those arising from left-sided tumours or perhaps that they might be more resistant to chemo and biological therapies.

Methods: We performed a population-based study from Modena Cancer Registry aiming to assess the prognostic impact of tumour sidedness in pts with stage II-IV CRC treated from 1995 to 2010. We hypothesized also a potentially predictive impact in the metastatic setting analysing 3 different periods of time: 1995-2000 5-FU-based chemotherapy, 2001-2005 polichemotherapy, 2006-2015 chemotherapy + target therapy. Univariate and multivariate Cox regression analysis (adjusted for sex, tumour site, grading, number of metastatic sites and time to metastasis) were performed.

Results: During the study period, a total of 880 stage II, 777 stage III and 680 stage IV CRC pts were registered. After a median follow up of 95.3 months (range 1.1-268.0 months), the median overall survival (OS) was 108.4 months in stage II and 79.4 months in stage III while in the group of pts who died of mCRC (collected from 1995 to 2015), after a median follow up of 11.8 months (range 0.1 - 226.7 months) the median OS was 10.5 months for pts with synchronous metastases and 14.0 months for pts with metachronous disease. In the multivariate analysis of both stage II and stage III groups, OS differed significantly according to grading (stage II: HR 1.66, 95% C.I. 1.37 – 2.02, p < 0.001; stage III: HR 1.20, 95% C.I. 1.01 – 1.43, p 0.03), while sidedness had no prognostic implication (stage II: HR 1.00, 95% C.I. 0.87 – 1.15, p 0.97; stage III: HR 1.10, 95% C.I. 0.96 – 1.28, p 0.17). In the multivariate analysis of stage IV pts, OS was significantly longer for the left sided tumours (HR 1.35, 95% C.I. 1.21 – 1.51, p < 0.001) and in the metachronous group (p 0.005); the prognostic impact is confirmed independently of systemic therapies performed (1995-2000 p 0.03; 2001-2005 p 0.001; 2006-2015 p < 0.001).

Conclusions: In accordance to literature, our registry data confirm the prognostic role of sidedness in mCRC during the entire 20 year period while in the early-stage disease this impact seems not to be relevant.

A24 Mutational status and metastatic patteRn in a cohort Of ADvanced colorectal cancer patients: the ROAD study

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Background: Somatic mutation status in advanced colorectal cancer (aCRC) has an increasing role in predicting efficacy of biological therapies and outcome and could correlate with site specific pattern of metastases.

Patients and methods: We retrospectively analysed a cohort of 640 consecutive aCRC patients (pts) diagnosed at University Hospital of Udine, Italy, from January 2000 to March 2017. KRAS, NRAS, BRAF and PIK3CA status was locally determined by pyrosequencing and/or mass-Spectrometry Assay, with commercially available kits (Myriapod® colon cancer status kit, diatech pharmacogenetics, Italy). All the patients with complete molecular assessment were classified as all wild type, BRAF, RAS or PIK3CA mutated. Pearson's $?^2$ test was performed with uni- and multivariate models to test association of mutational status and site-specific metastatic spread.

Results: Overall, we detected 283 (47%) KRAS mutations, 21 (4%) NRAS mutations, 40 (7%) BRAF mutations, and 61 (14%) PIK3CA mutations. Most common mutations in KRAS gene were located in exon 2 (86%), while about 3% of mutations involved exon 3 and 5% exon 4. NRAS mutations involved equally exons 2 and 3. All BRAF mutated tumours except for one, exhibited exon 15 V600E mutations. Pts with KRAS mutations had an increased risk to develop lung metastases (odds ratio, OR 2.56, 95% CI 1.76-3.71; p < 0.001, in multivariate analyses) or central nervous system metastases (OR 2.58, 95% CI 1.15-5.76; p = 0.021, in univariate model). Instead, pts harbouring BRAF mutations had higher risk of peritoneal (OR 3.05, 95% CI 1.56-5.96, p = 0.001) and nodal (OR 2.20, 95% CI 1.21-4.66, p = 0.012) spread, in uni- and multivariate models, respectively. Liver metastases were not associated with a specific mutational status. Moreover, no associations between NRAS or PIK3CA status and metastatic sites were found. Globally pts classified as all wild type did not show a specific metastatic pattern, instead, RAS mutated had higher risk than all wild type ones to develop lung metastases (OR 2.81, 95% CI 1.75-4.50, p < 0.001).

Conclusions: Our findings suggest that molecular biology may help predicting the metastatic spread in aCRC pts. If confirmed by further studies, these observations could translate into tailored surveillance and follow-up protocols.

A25 Management of folinic acid administration in patients with metastatic colo-rectal cancer

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Since the development of 5-fluorouracil (FU) in 1957 this drug remains the agent of choice for the treatment of colorectal, cancer both in metastatic and adjuvant treatment.

There is no clear consensus about the optimal FU-folinic acid schedule and dose.

Sodium folinate acid (NALF) is a new formulation with the same pharmacological parameters as calcium folinic acid. It can be infused in one pump with 5FU without the risk of crystallization and catheter obstruction. NALF infusion and 5FU has been study with both oxaliplatin e irinotecan in patients with metastatic colorectal cancer. In our Oncology unit from January 2015 to December 2016 the patients with metastatic colorectal cancer has been treated with NALF and 5FU in combination with both oxaliplatin and irinotecan, for both adjuvant therapy, the first and second line treatments.

Totally 409 admistrations was been infused without complications confirming the safety of regimens. Table 1 resume the caratheristics of patients.

Considering the administrative management printouts, it results that the adoption of new schedules of treatment with NalF has produced for the 409 days avoided, a lower cost of 149.690,00 €equal to 4.76% of the total revenues of the biennium 2015/2016 of Oncological DH (DRG M-410).

Costs were reduced in three years 2014-2015-2016 (even if 2014 was not totally considered). The valorisation of the DH is passed from 425,08 €in 2013 (period without NalF) to 365,66 in 2016 due to the effect of the greater total number of patients treated, cancelling the differential with the repayments of the DRG (M-410 equal to 371,00 €DGR 709/2014).

Furthermore it is shown a direct saving in the use of medical devices necessary for the therapies preparation, equal to 4.058,00 €and 5.985,00 €of drug. Healthcare costs avoided direct and rationalized are equal to 159.732,00 €. (table2)

The major advantage of this combination (NALF and 5FU) appears to be the convenient and cost saving administration mode, enabling to shorten the treatment time for outpatients in ambulatory care units.

Table: A25

	Foflfox6 Mod	Folfiri	
Total Administrations	313	96	409
Male	19	10	
Female	25	8	
Adiuvant	9	0	
Metstatic	35	18	
Expenses For Medical Device Avoided	4058.28 Euro		
Differnece NALF/CALF	5985.0 Euro		
Total Gain	10043.28 Euro		
Health Costs Avoided	149690 Euro		
Avoided Costs For Setting Up Therapies	159732 Euro		

A26 Radically resected stage III colorectal cancer: sidedness and prognosis

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Background: The prognostic differences between left-sided (LCC) and right-sided (RCC) colon cancer have been described. RCC, located up to the proximal two-thirds of the transverse colon, have significantly worse prognosis. Moreover, differences in treatment sensitivity between LCC and RCC exist. The aim of our study was to investigate the prognostic significance of sidedness in radically operated stage III colorectal cancer (CRC) patients treated with adjuvant chemotherapy.

Patients and methods: 110 patients with radically resected stage III CRC were enrolled in our retrospective study. The tumor location was as follows: LCC: 67 patients and RCC: 43 patients. All patients were treated with FU-based adjuvant chemotherapy. Disease-free survival (DFS) and overall survival (OS) curves were constructed using Kaplan-Meier method, and differences were analyzed using log-rank (Mantel-Cox) test. The *p* value was bilaterally tested, and values less than 0.05 were regarded as statistically significant.

Results: In the whole group of patients, no statistically significant difference was observed in DFS and OS between the patients affected by RCC or LCC ($p = 0.51$ and $p = 0.76$, respectively). We observed disease relapse in 40 patients (36.4 percent). Median DFS in RCC group was 19 months (range 9 to 32 months), median DFS in LCC group was 21 months (range 6 to 60 months).

Conclusions: In our retrospective study, we did not observe any difference in prognosis for stage III radically operated CRC treated with adjuvant therapy according to tumor sidedness.

A27 Primary tumor site (pTS) as a key factor in adjuvant treatment decision in resected N+ colorectal cancer patients

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Background: Early-stage resected colorectal cancer is increasing due to screening programs in Italy. Although surgery is the only chance for cure, most of patients ultimately relapse thus suggesting the use of adjuvant treatment with either FOLFOX or XELOX. Primary tumor site (pTS) has been identified as prognostic factor, with a worse outcome for right-sided (RSCC) compared to left-sided tumors (LSCC) and, in RAS wild type tumors, different activity of anti-EGFR drugs. Aim of this retrospective study is to assess different outcomes for resected stage III colon cancer patients, stratified by pTS and adjuvant treatment.

Patients and methods: pN+ colon cancer patients who received XELOX or FOLFOX adjuvant treatment, stratified by pTS, were enrolled. RSCC were those arising from caecum, ascendant, transverse colon and hepatic flexure whereas LSCC were from splenic flexure, descendent and sigmoid colon. Patients who had withdrawn from treatment within 3 month time or with rectal cancer were excluded. Relapse free survival (RFS) and overall survival (OS) were calculated accordingly to Kaplan-Meier method and the association with stratification factors was assessed by log-rank test.

Results: 167 patients were enrolled, 89(54%) with LSCC and 78(46%) with RSCC. 39(43%) LSCC patients relapsed with a mRFS of 37 months, whereas 28(36%) RSCC patients had mRFS that was not reached (NR) ($p = 0.53$, HR:0.85,95%CI:0.52 to 1.38). Stratifying by chemotherapy regimen, 83(50%) patients received XELOX and 84(50%) FOLFOX. mRFS were respectively NR vs 29 months ($p = 0.047$, HR:0.49,95%IC:0.30 to 0.79). According to pTS, 36(46%) RSCC patients received FOLFOX and 42(54%) XELOX, with a mRFS of 19,8 months and NR respectively ($p = 0.017$, HR:0.41,95%IC:0.19 to 0.88). No statistically significant differences were seen in LSCC patients receiving XELOX or FOLFOX (mRFS:NR vs 34,78 months respectively, $p = 0.12$).

Conclusions: Our analysis shows that RSCC patients had lower recurrence rate and better RFS compared with LSCC, although not in a statistically significant fashion. However, this is the first time that a significantly better RFS was observed by using XELOX rather than FOLFOX as adjuvant treatment in pN+ CRC patients. This difference was only observed in RSCC, but not in LSCC. Our hypothesis is that the increased activity of XELOX vs FOLFOX in RSCC might be due to higher expression in RSCC of mechanisms of resistance to treatment with 5FU and Oxaliplatin (namely higher ERCC1 expression and more frequent MSI-H status).

A28 Survival of metastatic colorectal cancer patients at Candiolo Cancer Institute

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Background: Over the last 15 years, survival of patients (pts) with metastatic colorectal cancer (mCRC) has significantly improved. Both surgical indication and a more aggressive systemic approach may have contributed to this result.

Methods: We retrospectively collected data from 899 mCRC pts treated at Candiolo Cancer Institute from 2001 through 2016, with at least one course of chemotherapy (CT) for metastatic disease and a minimum follow-up period of two years. Since in 2007 the new molecular targeted agents were introduced in the clinical practice, pts were divided into two groups based on the year of diagnosis of mCRC, Cohort A (2001-2006) and Cohort B (2007-2014). The Cox proportional hazards regression model was used and median overall survival (mOS) was calculated using Kaplan-Meier estimate and examined by log-rank test.

Results: 788 pts with mCRC were analysed; 365 were in the Cohort A and 423 in the Cohort B.

The mOS of entire population was 32.0 months (mo), with a significant difference between the two cohorts: 29.2 mo in Cohort A vs 33.5 mo in Cohort B (HR 0.832, $p = 0.041$).

Surgical indication increased across the years (43.0% Cohort A vs 55.6% Cohort B, $p < 0.0001$), particularly for extra-hepatic surgery (21.1% Cohort A vs 33.3% Cohort B; $p < 0.0001$). As expected, surgery in addition to CT bestowed a significantly longer mOS when compared to CT alone: 58.5 versus 20.1 mo (HR 0.262, $p < 0.0001$). However, no significant changes in mOS were observed between cohorts in pts undergoing surgery (58.9 mo Cohort A vs 58.2 mo Cohort B, $p = 0.822$).

Similarly, when compared pts treated with CT alone (with or without targeted agents), we failed to demonstrate an improvement in mOS (18.9 mo Cohort A vs 20.7 mo Cohort B; HR 1.0, $p = 0.948$).

At multivariate analysis, right-sided primary tumor and synchronous metastatic disease were found independent, unfavorable prognostic factors. In these subgroups mOS has improved in Cohort B as compared to Cohort A. In particular, in pts with right-sided primary tumor mOS was 15.8 mo in Cohort A and 25.5 mo in Cohort B ($p = 0.041$). Considering only pts treated with CT alone in this subgroup, mOS was 15.1 mo in Cohort A and 22.1 mo in Cohort B ($p = 0.046$).

Conclusions: The OS improvement in mCRC pts might be correlated to a more aggressive integrated approach with a higher number of pts undergoing extra-hepatic surgery. The medical approach seems to have a more favorable impact in recent years on subgroups characterized by a worse prognosis.

A29 Colorectal cancer (CRC) progression and angiogenesis: tumor infiltrating natural killer cells as novel inflammatory orchestrators

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Background: Epidemiological studies revealed that chronic inflammation predisposes to different types cancer, including colorectal cancer (CRC). Natural Killer (NK) cells, effector lymphocytes of innate immunity primarily involved in immunosurveillance against tumors, have been recently reported to act as mediators of cancer progression. We previously reported that in Non-Small Cell Lung Cancer patients NK cells can acquire the decidual-like $CD56^{bright}CD16\text{-}VEGF^{high}PlGF^{high}IL\text{-}8^{+}IFNg^{low}$ phenotype

and promote angiogenesis *in vitro*. Here we extend our NK studies to CRC patients and analyze the molecular mechanisms involved.

Material and methods: Multicolor flow cytometry was performed using NK cells derived from peripheral blood and tissue samples of CRC patients, compared with those derived from peripheral blood of healthy control and patients with inflammatory bowel disease. Conditioned media (CM) from FACS-sorted NK were used either for secretomic profiling, by antibody membrane array or angiogenesis functional assays on human umbilical endothelial vein cells (HUVECs).

Results: We found that $CD56^{+}CD16^{-}$ NK cells predominate in CRC adjacent and tumor tissues, show decreased NKG2D surface expression and impaired degranulation abilities. NK cells from CRC patients express the decidual NK markers CD9 and CD49a, supporting the hypothesis of a pro-angiogenic/decidual-like polarization. Both secretomic and flow cytometry analysis on CRC peripheral blood NKs (TANKs) revealed statistically significant up-regulation of several angiogenesis-related factors which was specific for CRC patients. CM by FACS sorted CRC NK cells from peripheral blood and tumor tissue of CRC patients could induce HUVEC proliferation, migration, adhesion and the formation of capillary-like network structures. These functional evidences are related with molecular changes in HUVECs induced by NK CM, that include the phosphorylation AMPKα, GSKb, P70 S6 Kinase and S6 ribosomal protein. Molecularly, STAT-3 and STAT-5 pathway activation was observed in TANKs, suggesting the potential involvement of these signals in the induction of the CRC-TANK angiogenic switch. Inhibition of STAT-5 in TANKs resulted in the downregulation of many pro-angiogenic factors and inhibited the formation of endothelial network structures by NK CM.

Conclusions: Our data demonstrate that TINK/TANKS from CRC patients are switched toward a pro-angiogenic/pro-tumor phenotype and function that could be specific for CRC.

A30 Arterially directed embolic therapy (ADET) with polyethylene glycol microspheres loaded with irinotecan for refractory liver metastases from colorectal cancer

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Background: Patients with liver metastases from colorectal cancer are in 80% of cases non indicated for resection. The standard first line treatment of unresectablelivermetastases is systemic chemotherapy, however this method results in progression for 70% of patients. The indicated therapy for refractory patients is the arterially directed embolic therapy (ADET). In this study we monitored tumor response, and adverse events after ADET of colorectal cancer liver metastases with polyethylene glycol microspheres loaded with irinotecan. Secondary objectives were to monitor quality of life, time to progression and survival of patients.

Materials and methods: Patients were included in the study if: affected by CRC-LM, who were refractory to systemic chemotherapy, treated with ADET using polythylene glycol microspheres, and liver involvement >50%. Tumor response, performance status (PS), tumor marker antigens, and quality of life (QoL) were monitored at 1, 3 and 6 months after ADET. QoL was assessed with the palliative scale (PSS).

Results: We treated 50 consecutive CRC-LM patients with ADET using polythylene glycol microspheres, their tumor response one month after ADET was 43% of complete response (CR), and 52% of partial response (PR), and 4% stable disease (SD). Tumor response 3 months after ADET was CR 15%, PR 60%, SD 10% and progression disease (PD) 15%. Tumor response 6 months after ADET was PR 64%, SD 22% and progression disease (PD) 14%. QoL was> 80% PSS at each time point. Median time to progression was 3 months (2,3 – 4 range). Median follow-up was 11 months (1,3-19,2 range).

ADETs were performed with no complications. Observed side effects (mild or moderate intensity) were: pain in 22% of patients and fever in 13%, whereas 30% of patients did not complain any adverse event.

Conclusions: ADET of CRC-LM with polyethylene glycol microspheres loaded with irinotecan was effective in tumor response and resulted in mild toxicity, and good QoL.

A31 Maintenance treatment with bevacizumab in metastatic colorectal cancer: intermittent or continuous therapy? A monoinstitutional observational study

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Background: The main objective of care in patients with mCRC is survival prolongation preserving the quality of life (QoL). Optimal duration of chemotherapy (CT) is still a matter of debate, such as the treatment strategies that could be adopted (maintenance CT vs observation). Intermittent CT resulted not inferior to continuous CT in GISCAD Study. We hypothesized that bevacizumab could be administered intermittently either.

Methods: In this retrospective study we evaluated 73 patients (pts) with mCRC with stable or responsive disease after CT (FOLFIRI) and Bevacizumab as first or second-line treatment. We observed 3 groups: A (23 pts): maintenance therapy with de Gramont-Bevacizumab 2 months on/2 months off until progression (intermittent strategy); B (30 pts): no maintenance treatment; C (20 pts): induction treatment as first line followed by continuous maintenance with de Gramont-Bevacizumab.

Results: The median number of CT courses was: A 34 (range 20-56), B 12, C 22 (range 16-25). Response rate was similar in groups A and C (A:13/23, C:12/20) and lower in Group B (13/30). In Group A increase of response was observed in 6 pts in post-induction time. No increase or additional response was observed in Group B and C. Median progression free survival (PFS), was 21.2 months (m) in Group A (19-26 m), 9 m in Group B (6.6-12.9 m), 12 m in Group C (10.4-13.3 m), with statistically significant difference in favor of intermittent stratedy ($p = 0.0095$). Median overall survival (OS) was: A 60.5 m (35.6-96.2 m), B 27.2 m (19.5-39.9 m), C 22.8 m (18.6-31 m); with a statistically significant survival advantage for intermittent strategy ($p = 0.0006$). The most frequent adverse events (AEs) of all grades were: hypertension, neutropenia, thrombocytopenia, diarrhea, asthenia. No toxic death was observed. AEs of all grades were more frequent in group C (15% Grade 3-4), vs Group A and B (10% Grade 3-4).

Conclusions: According to our retrospective analysis, intermittent maintenance treatment with CT and Bevacizumab appears to be a feasible strategy in pts with stable or responsive disease. PFS and OS resulted longer in pts treated with intermittent strategy. The study has many biases: pts heterogeneity, small sample size, retrospective nature, lack of biologic and pharmacokinetic data. However we can conclude that intermittent strategy could improve pts outcome with acceptable toxicity profile and should be considered in a prospective study.

A32 How can molecular heterogeneity impact on treatment choice in advanced colorectal cancer?

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Background: Concordance between primary tumours and metastatic sites in advanced colorectal cancer (aCRC) has been widely investigated but the possible role of molecular heterogeneity among different areas of the same lesion and different lesions in the same resection specimen is still a debated issue that could influence response to targeted therapies.

Patients and methods: We reviewed a cohort of aCRC patients (pts) treated at the Oncology Department of University and General Hospital of Udine, Italy, in the last 15 years. Among 640 pts, we observed 15 challenging cases for whom several specimens for each patient were tested, showing different molecular profiles. Mutational analysis for KRAS/NRAS/BRAF/PIK3CA had been performed by pyrosequencing or MassSpectrometry Assay with Myriapod® colon cancer status kit (diatech pharmacogenetics, Italy).

Results: Among 15 controversial cases, 13 harboured mutations in KRAS or NRAS genes in at least one sample; 5 of them received an anti-EGFR treatment with some clinical benefit reported in only one patient. In 5 (33.3%) pts we demonstrated various genetic profiles in multiple lesions of the same resection specimen, in 5 (33.3%) pts discordant mutational status between endoscopic biopsy and primary resected tumour was detected, 3 (20%) pts had different mutational status between primary and several metastatic lesions, and in 2 (13.3%) cases tumours were characterized by two hystotypes differentiations (i.e. mucinous vs non mucinous) with conflicting molecular patterns.

Conclusions: Our findings draw attention to the clinical impact of molecular heterogeneity on treatment decision in aCRC. This phenomenon is probably underestimated. Discordance in molecular profile between primary tumors and synchronous metastasis could be due to the presence of different primary lesions. Thus, we recommend molecular profiling of all multiple primary lesions or different histological differentiation in the same tumour since discordances might impact on treatment choice.

A33 Dihydropyrimidine dehydrogenase (DPD) deficiency: how to translate it in clinical practice?

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Background: The DPD enzymatic activity is the rate limiting of 5FU fluoropyrimidines' metabolism. DPYD gene mutations modify its catalytic activity, but to date the impact of mutation on effective dose reduction is not known.

Materials and method: A total of 615 patients (pts) affected by GI cancer started 5 FU/Capecitabine containing regimens from December 2012 to April 2017. A total of 68 pts

with grade (G) 3-4 toxicities (34 pts), rare and persitent G2 toxicities (23 pts) and low risk adjuvant setting with comorbidity (11 pts) were planned for DPD pharmacogenetic testing on peripheral blood by Sanger sequencing. In the cohort of pts which had toxicity during treatment (57 pts), 496A>G 1601G>A, 1627A>G, 1896T>C, IVS14 + 1G>A, 2194G>A, 2846A>T polymorphisms were analyzed, while in preventive cases IVS14 + 1G>A and 2846A>T were tested.

Results: 34 pts developed G3-G4 toxicities during cycles 1-2, including leuco-neutropenia (44%), diarrhea (32%), piastrinopenia (15%), mucositis (12%), alopecia (3%), dermatitis (3%). 24 pts (70%) were DPYD deficient: 496AG (3 pts), 1627AG (8 pts), IVS14 + 1GA (1 pt), 2194GA (3 pts), 2846AT (1 pt). 10 pts presented double DYPD polymorphisms: 1627AG and 2194GA (4pts), 496AG and 1627AG (2 pts), 496AG and 2194GA (1 pt), 496AG and 1601GA (1pt), 1627AG and 2846AT (1pt), IVS14 + 1GA and 1601GA (1pt). Only the pt with IVS14 + 1GA and 1601GA polymorphisms presented life threatining complications, resolved successfully. 23 pts showed rare and persistent G2 toxicities within the first three cycles, including diarreha (57%), leuconeutropenia (39%), alopecia (30%), piastrinopenia (13%), hyperbilirubinemia (13%), dermatitis (9%). 9 pts (39%) were DPYD deficient: 496AA (3pts), 1627AA(1pt), 2194GG (1pt), 1627AA and 2194GG (2pts), 496AA and 1896AA (1pt), 496AA and 1601GG (1pt). About pts analyzed preventively, only one was DPYD deficient (1627AG) and performed therapy with dose reduction of 50%.

Conclusion: 34 on 68 pts were found to be DPD deficient and nobody died for toxic death. More than one heterozygous mutation was observed in 14 pts. Chemotherapy was discontinued in 12 adiuvant setting pts, 5 metastatic pts suspended fluoropyrimidine, while in 17 pts a toxicity improvement was seen after a dose reduction of 50% and pre-planned cycles were performed without delay. To standardize clinical practice we need extensive studies to correlate the heterozygous alleles mutation with type and grade of toxicity, the effective dose reduction or stop therapy.

A34 EPHA2 receptor is involved in in vivo acquired resistance to anti-epidermal growth factor receptor (EGFR) treatment in metastatic colorectal cancer

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Background: EPHA2 tyrosine kinase receptor is implicated in cell growth, migration, and invasiveness in a wide range of cancers. We studied its role as a potential marker of resistance to anti-EGFR drugs in colorectal cancer (CRC).

We previously demonstrated that EPHA2 was differently activated among a panel of CRC cell lines with primary and acquired resistance to cetuximab and the use of ALW-II-41-27 (EPHA2 selective inhibitor) in combination with cetuximab was able to revert this resistance in *in vitro* experiments (abstract presented at 2016 ESMO Congress in Copenhagen). Here we present the study on *in vivo* models.

Methods: EGFR dependent SW48 and LIM1215 cell lines were engrafted into nude mice and treated with cetuximab until disease progression. Once tumors became resistant (SW48-CR and LIM1215-CR) mice were randomized in groups of 10 mice each and assigned to receive ALW- II-41-27 as single agent or in combination with cetuximab, no treatment and cetuximab alone group served as control. ALW- II-41-27 was administered daily at 30 mg/kg by oral gavage and cetuximab intraperitoneally at 1 mg/kg two days a week. Treatment was performed for three weeks, then mice were euthanized and protein expression in tumors was analysed by Western Blot.

Results: The combination of the two drugs induced a significant reduction of tumor volume since the first administration. A reduction of 50% of tumor volume was found in 5 out 10 LIM1215-CR mice treated with ALW-II-41-27 as single agent. This effect was maintained after cessation of therapy and induced prolonged survival. Tumor protein analysis by WB demonstrated a strong reduction of EPHA2 expression and activation in mice treated with the combination of ALW-II-41-27 and cetuximab, accompanied by a significantly inhibition of activated pMAPK and pAKT.

Conclusions: These results highlight the role of EPHA2 as a potential therapeutic target in mCRC treatment.

A35 Colon-rectal follow-up program: a monocentric experience

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Background: Despite optimal primary treatment with adequate surgery with or without adjuvant chemotherapy 30%–50% of patients (pts) with colon cancer will relapse and most of those patients will die from their disease. Detecting relapse in advance is the main goal of surveillance after primary treatment. Data suggest a survival advantage related to intensive follow-up but the heterogeneity of the studies does not allow assessment of which kind of surveillance must be applied in our clinical practice. The objective of this study is to assess how recurrent disease presents and if it is diagnosed within scheduled multi-disciplinary interval visits.

Methods: We have evaluated retrospectivelyfollow-up data of 196 consecutive pts with colorectal cancer underwent radical surgery in our institution. Follow-up schedule includes: CEA testing every 6 months for 5 years (cutoff point of CEA was 5.0 µg/L), abdominal ultrasonography and CT scan of chest and abdomen alternated every 6 months for 5 years, colonscopy at 1, 3 and every 3-5 yearsthereafter.

Results: 196 pts (51% stage III; 49% stage II) are treated for colon carcinoma with curative intent between January 2007 and December 2014. 53 (27%) developed recurrent disease. In 48 pts (90.6%) recurrent disease was detected during a scheduled multi-disciplinary follow-up visit. Only in 5 pts (9.4%) recurrence was found during non-scheduled interval visits for symptomatic disease onset.The main relapse sites are: liver only (24.5%), lung only (24.5%), local (15,0%), peritoneum (7.5%), lymph nodes only (5,7%), multisite (22,8%).In about 65% of cases the disease was or could become potentially resettable with surgery. In 22,6% of cases recurrence was associated with a significant increase in CEA levels.

Conclusion: In this study almost all of the recurrences (90.6%) after initial curative treatment for colon cancer were found during scheduled multi-disciplinary interval visits. This follow-up schedule is in line with what the national/international guidelines suggest and seems cost/effective. However further efforts are needed to identify the best follow-up strategy for our pts.

A36 Prognostic role of aspartate aminotransferase-lymphocyte ratio index (ALRI) in patients with metastatic colorectal cancer: results from the ITACa trial

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Purpose: To investigate the role of pre-treatment aspartate aminotransferase-lynphocyte ratio (ALRI) as predictors of prognosis and treatment efficacy in patients with metastatic colorectal cancer mCRC randomized on to the prospective multicenter randomized ITACa (Italian Trial in Advanced Colorectal Cancer) trial to receive first-line chemotherapy (CT) with or without bevacizumab (Bev).

Patients and methods: 284 patients were considered for this study. The pre-treatment ALRI were evaluated to identify a potential correlation with progression-free (PFS) and overall survival (OS) in both the overall population and the two treatment arms (with or without bevacizuamb).

Results: In the overall population, observing that increased ALRI levels were associated with decreased PFS and OS ($p < 0.0001$).

At baseline, patients with low ALRI levels (<14) had a median PFS of 10.3 months compared to 8.0 months for those with high ALRI level (HR 1.43, 95% CI 1.12-1.82, $p = 0.004$). Moreover, patients with low ALRI (<14) had a median OS of 25.2 months with respect to 18.8 months for those with high baseline ALRI (HR = 1-51, 95% CI 1.17-1.96, $p < 0.001$).

Interection test involving ALRI levels and treatment efficacy in the chemotherapy plus bevacizumab and chemotherapy only groups were statisticaly significant for PFS ($p = 0.0003$) and not for OS ($p = 0.228$).

Conclusions: Our results indicate that ALRI is good prognostic and predictive markers for mCRC patients who are candidates for chemotherapy plus bevacizumab.

A37 Outcome and prognostic factors after resection of liver metastases in patients with colorectal cancer

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Background: During the last 30 years, liver surgery for metastases from colorectal cancer (CRC) has become the standard of care and an opportunity of cure in selected patients, with reported 5-year survival rates approaching 50%. However, more than 50% of patients will develop early recurrence without any long-term survival benefit. Therefore, the attention has been focused on finding prognostic factors and scores able to select patients who will benefit from surgery.

Material and methods: Medical records from 99 patients with metastatic CRC who underwent potentially curative liver resection from January 2008 to December 2014 at University Hospital of Modena were retrospectively reviewed. Aim of the study was to assess the impact of clinical and biological prognostic factors on relapse free-survival (RFS), 3-year survival and overall survival (OS). Primary or metastatic tumour samples were analysed for K-RAS (exon 2) mutations using sequencing analysis. Univariate and multivariate Cox regression analysis (adjusted for K-RAS mutational status, tumour site, resection margin, grading and time to metastases, perioperative/adjuvant chemotherapy) were performed.

Results: After a median follow up of 30 months (range 1-98), the median RFS was 10.0 months and the 3-year survival rate was 45%. In multivariate analysis, OS differed significantly according to resection margin (HR 2.40, 95% C.I. 1.29 – 4.45, p 0.006) and to time to metastases (HR 1.81, 95% C.I. 1.01 – 3.23, p 0.045). In the univariate analysis, significantly longer RFS can be predicted by FONG score (HR 1.92, 95% C.I. 1.15 – 3.20, p 0.013). KRAS exon 2 gene mutations, detected in 52/99 patients (52%), had no statistically significant interaction neither in RFS nor in OS.

Conclusions: In our single institution experience, the median overall survival following liver resection was 21 months. Only radical surgical resection (R0) can have an impact on OS. FONG liver score, which includes criteria easily available in all patients eligible to surgery, should guide patients' selection. Overall survival was not significantly shorter for KRAS exon 2 mutated patients.

A38 Focus on metastatic right-sided colon cancer: the best overall response to the first-line non-EGFR treatment correlates with better overall survival

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Background: The differences in prognosis between left-sided (LCC) and right-sided (RCC) colon cancer have been described. Moreover, tumor localization might be predictive of treatment benefit to EGFR inhibitors and their use seem to be recommendable for LCC. The efficacy of bevacizumab in RCC is less clear. The aim of our study was to investigate the correlation of the best overall response to the first-line non-EGFR treatments with RCC patients' overall survival (OS).

Patients and methods: Only patients with metastatic RCC were enrolled in our retrospective study. OS was calculated from the pathologic diagnosis of metastatic disease to death due to cancer, with participants alive or lost to follow-up at the analysis data cut-off date censored at their last contact date. The best obtained objective response to the first-line treatment have been registered. OS curves were constructed using Kaplan-Meier method, and differences were analyzed using log-rank (Mantel-Cox) test. The *p* value was bilaterally tested, and values less than 0.05 were regarded as statistically significant.

Results: From a total of 84 stage IV RCC patients, 61 (72.6%) were treated with in the first-line with chemotherapy only, the resting 23 patients (27.4%) were treated with chemotherapy and bevacizumab in the first-line. Interestingly, the best obtained objective response significantly correlated with better OS ($p = 0.000$). In particular, the median OS for RCC stage IV patients was 45.5 months if complete or partial remission was obtained as the best objective response, 43.5 months if stable disease was obtained and 14 months if progression was noted as the best objective response during the first-line treatment.

Conclusions: In our retrospective study, the best obtained objective response to first-line non-antiEGFR treatment in RCC patients significantly correlated with better OS.

A39 The acquired resistance to the combination of the anti-EGFR cetuximab and the MEK-inhibitor refametinib in KRAS mutated colorectal cancer cell lines depends on PI3K-signalling

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Background: Previous studies showed that the combination of an anti-epidermal growth factor (EGFR) and a selective MEK-inhibitor displays a significant anti-tumour activity in RAS-wild type colorectal cancers (CRCs), while the same combination partially reverts anti-EGFR primary resistance in KRAS mutated colorectal cancer cell lines. However, mechanisms of resistance to this combination are still unexplored.

Methods: We generated KRAS mutated CRC cell lines (HCT15 and HCT116) resistant to a combination of cetuximab (an anti-EGFR antibody) and BAY86-9766 (refametinib, a selective MEK1/2-inhibitor) after continuous exposure to increasing concentration of the drugs for 8 months. Resistant clones had an IC50 20-100-fold higher than the parental cells. We evaluated by Western Blot (WB) analysis and quantitative Reverse Transcriptase Polymerase Chain Reaction (qRT-PCR) the expression and activation status of a panel of receptor tyrosine kinases (RTKs) and intracellular transducers. We further analysed by MTT assay the sensitivity of these cetuximab-MEKi resistant (CM-res) cell lines to GDC-0941 (pictilisib, a selective PI3Kα inhibitor) and afatinib (BIBW 2992, an irreversible pan-HER inhibitor) either used alone or in combination.

Results: We found consistent hyperactivation of the PI3K-AKT pathway and concurrent inactivation of the MAPK pathway, coupled to the activation of multiple RTKs of the HER family such as HER2 and HER3 in resistant cells when compared to parental cells. Treatment with GDC-0941 was able to partially restore the sensitivity to the drug combination, suggesting a central role for this pathway in mediating resistance in this setting, while afatinib was not capable of reverting the resistant phenotype when used alone but showed synergistic activity when combined to GDC-0941.

Conclusions: These preliminary results suggest that PI3K activation plays a central role in the acquired resistance to the combination of anti-EGFR and MEK-i. PI3K activation depends at least in part by the activation of the HER family of RTK, but it can also be activated by other receptors. In vivo experiments on mice are currently ongoing.

A40 Prevalence of KRAS, NRAS and BRAF mutations detected by massive parallel sequencing and differential clinical outcome in metastatic colorectal cancer (MCRC) patients (pts) treated with first line FIr-B/FOx adding bevacizumab (BEV) to triplet chemotherapy

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Background: *KRAS*/*NRAS*/*BRAF* genotypes guide tailoring of first and subsequent lines of MCRC treatment strategy. First line triplet chemotherapy/BEV regimens significantly improved progression-free survival (PFS) and overall survival (OS) in MCRC patients. OS may be significantly worse in *KRAS* c.35 G > A and *BRAF* mutant (mut) MCRC. Prevalence and differential clinical outcome according to *KRAS*/*NRAS*/*BRAF* genotype was evaluated in MCRC patients treated with FIr-B/FOx intensive regimen.

Methods: Tumoral samples of 67 MCRC pts treated with FIr-B/FOx (77% overall) were analyzed through a 50 genes panel (PGM/Colon Lung Cancer) by ION Torrent. *KRAS* exons 2-4 ($KRAS_{2-4}$), *NRAS* exons 2-4 (*NRAS2-4*), and *BRAF* exon 15 ($BRAF_{15}$) were evaluated. Molecular diagnostic criteria for mutation detection: >500×sequence coverage; >1% mutant allelic fraction. Clinical outcomes (PFS and OS) were evaluated and compared by log-rank.

Results: $KRAS_{2-4}$ mut were 42 (66.7%), 4 not evaluable; $NRAS_{2-4}$ mut 13 (19.4%); $BRAF_{15}$ mut 5 (7.5%). $KRAS_{2-4}$/$NRAS_{2-4}$/$BRAF_{15}$ mut MCRC patients were 49 (77.8%), wild-type (wt) 14 (22.2%): single gene mut 40 (63.5%), $KRAS_{2-4}$ 34 (54%), and $NRAS_{2-4}$ 6 (9.5%); >1 mut genes 9 (14.3%), double mut 5 and triple mut 4, specifically double *KRAS* 1, *KRAS*/*NRAS* 2, *KRAS*/*BRAF* 1, *NRAS*/*BRAF* 1, double *KRAS*/*NRAS*1, *KRAS*/*NRAS*/*BRAF* 3. $BRAF_{15}$ mut were all atypical and concomitant with *KRAS* and/or *NRAS* mutations. Prevalence of $KRAS_{2-4}$, $NRAS_{2-4}$, $BRAF_{15}$ >1 mut samples were 19%, 53.8%, and 100% of each mut gene.At median follow-up 21 months (m), PFS and OS overall, and of $KRAS_2$ genotype were consistent with previously reported; in c.35 G > A $KRAS_2$ mut trendy worse PFS 8 m and OS 14m. Differential clinical outcome of MCRC patients wt and mut were not significantly different: $KRAS_{2-4}$, PFS 13 and 12m, OS 27m equivalently; $NRAS_{2-4}$, PFS 16 and 12m, OS 28 and 22m; $BRAF_{15}$ PFS 14 and 8 m, OS 28 and 11 m; $KRAS_{2-4}$/$NRAS_{2-4}$/$BRAF_{15}$ PFS 18 and 12m, OS 28 and 22m; more than 1 compared to 1 mut gene, PFS 11 and 14m, OS 22 and 37 m. PFS trendy worse in > 1 mut compared with *RAS*/*BRAF* wt ($p = 0.059$).

Conclusions: Clinical outcome of MCRC patients treated with FIr-B/FOx is not significantly affected by $KRAS_{2-4}$/$NRAS_{2-4}$/$BRAF_{15}$ genotype; efficacy may be increased in triple wt patients; the prevalent c.35 G > A $KRAS_2$ and $BRAF_{15}$ mut may show worse prognosis.

A41 MTHFR, TSER and DPYD gene mutation is associated with toxicity and response in pre-operative chemo-radiotherapy for local advanced rectal cancer

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Background: Radiotherapy and 5 FU based chemotherapy is the most common pre-operative regimen used for cT3-T4, N1 rectal cancer (RC). Evaluation of predictive markers of response and toxicity to radio-chemotherapy is a challenging approach for patients (pts) and drug selection. in the present experience we have analyzed the predictive role of the genetic polymorfisms (MTHFR, TSER and DPYD) on toxicity and response to pre-operative radio-chemotherapy.

Materials and methods: We HAVE enrolled sixteen patients with locally advanced RC treated with pre-operative radiotherapy and fluoropyrimidines base chemotherapy. Genetic polymorphisms of MTHFR C677T, MTHFRA 1298C, DPYD IVS 14 + 1G>A, DPYDA 2846T, DPYD T 1679 G, TSER 28 bp VNTR were analyzed by PCR and pyrosequensing of genomic DNA extracted from peripheral blood samples. Genetics markers were correlated with toxicity to treatment (chemotherapy and radio-chemotherapy) and clinical response.

Results: Patients characteristics were: male 13 pts, female 3 pts, median age 66 years, ECOG PS 0-1 all pts. We found DPYD IVS 14 + 1 G>A G/G homozygous wilde type, DPYD A2846T, T/T homozygous wilde type and DPYD T1679 g, T/T homozygous wilde type in 100% of pts, homozygous wilde type MTHFR C677T in 10% of pts, MTHFR C677T homozygous mutated in 50% of pts, heterozygous MTHFR A1298C in

60% of pts and homozygous wilde type MTHFR A 1298C in 40% of pts. G3-G4 advers events (diarrhea, neutropenia, asthenia, mucositis) were observed in 60% of pts with heterozygous MTHFR A 1298C and in 10% of pts with homozygous mutated MTHFR C 677t. treated with chemo-radiotherapy combination. DPYD homozygous wilde type was not associated with severe toxicity. Rectal surgery with TME will be performed 8 weeks after the end of pre-operative chemo-radiotherapy. We obtained 7 patological complete response and nine partial patological response. Adjuvant chemotherapy was well tolerated without G3-G4 adverse events. Three pts with patological complete respose were treated with Transanal Endoscopic Microsurgery (TEM) and they are alive without recurrence to twelve months after surgery.

Conclusion: Concomitant assesment of genetic polymorphisms of MTHFR and DPYD is promising to predict severe toxicity during preoperative chemo-radioterapy approach for pts with locally advanced rectal cancer. This result does not exclude the need to consider other non-genetic factors that might influence the individual enzyme activities.

A42 Medical management of malignant bowel obstruction: our center experience

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Background: Malignant bowel obstruction (MBO) is common in advanced cancer patients. It developes more likely in gastrointestinal or gynaecological tumors with abdominal burden, but it can arise in other cancers too. Its typical symptomps, nausea, vomiting, abdominal pain, impact negatively on patients' daily life, making MBO a very disabling condition. Surgery is a treatment option only for selected patients who meet surgical criteria. Other patients are usually treated with nasogastric tube to decompress bowel distension, fasting and supportive care. Studies showed that medical treatment with metoclopramide, octreotide and dexamethasone can significatively improve symptoms and quality of life. Octreotide has both antisecretive effects which reduce intestinal fluids improving nausea and vomiting and the power of reducing bowel motility, that can weaken abdominal cramps. Here, we report our center experience of MBO medical treatment.

Material (patients) and methods: From September 2015 to April 2017, we collected data of 20 patients hospitalized for MBO. Most patients had a gastrointestinal neoplasia (7 colorectal, 2 pancreatic, 2 gastric, 1 esophagus), 3 had ovarian cancer, 4 NSCLC and 1 head and neck tumor. 35% had vomiting episodes at presentation and no one had passage of gas/stool (G3-G4 constipation and bowel obstruction according to CTCAE v. 4). We administered intravenous injection of Dexamethasone 8 mg twice a day, metoclopramide 10-20 mg three times a day and subcutaneous Octreotide 0,1 mg every 8 hour. Evaluation measures were nausea/vomiting and abdominal pain episodes and regain of intestinal transit (according to CTCAE score v.4) during treatment with following hospital discharge.

Results: 80% of patients had a significative reduction of nausea and vomiting the same day treatment was started. Abdominal cramps disappeared within 2 days in 19 out of 20 patients. Furthermore, 13 out of 20 patients showed a recovery of intestinal transit within 3-4 days (reaching G1-G2 score of constipation-bowel obstruction) and were able to discharge from medical care unit within 7 days. All patients reported subjective improvement of their clinical condition.

Conclusions: Despite the small number of patients treated in our center, medical treatment with intravenous metoclopramide, dexamethasone and subcutaneous octreotide show to improve clinical status and to reduce symptoms in patients with MBO, giving a quick relief from nausea, vomiting and abdominal pain.

A43 Aflibercept in combination with FOLFIRI for the 2nd-line treatment of patients with metastatic colorectal cancer (MCRC): safety data from a single institute experience

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Background: In the USA and in EU, intravenously administered aflibercept (afl) in combination with FOLFIRI (irinotecan, 5-FU, leucovorin) is approved for the treatment of patients (pts) with metastatic colorectal cancer (mCRC) that's resistant to or has progressed after treatment with an oxaliplatin-containing regimen, with or without Bevacizumab (bev). The efficacy of afl in this indication was assessed in a multinational, pivotal phase 3 trial (VELOUR), in which afl + FOLFIRI significantly prolonged mOS, PFS and RR, compared with FOLFIRI alone.

Patients and methods: Between June 2015 and April 2017, 18 consecutive pts with mCRC were treated with afl + FOLFIRI based chemotherapy. The median age was 57 yrs (78% under 65 yrs and 22% ≥ 65 yrs), 11 pts male (61%), 7 female (39%); 14 (78%) resected and 4 (22%) unresected primary tumor; 13 pts (72%) with left primary tumor location, 5 (28%) with right-side; 4 (22%) showed only one metastatic site (liver), 14 (78%) more sites (≥ 2) of which 5 with peritoneal carcinosis. Most pts had previously received bev (55.5%) or anti-EGFR (22.2%) therapy. Pts received afl 4 mg/Kg intravenous + FOLFIRI every 2 weeks as second line treatment. They were evalueted for adverse event (AEs) and serious adverse events (SAEs), graded according to National Cancer Institute Common Terminology Criteria for AEs (version 4.0). A descriptive safety analysis was conducted.

Results: Pts received a median of 6.5 cycles of FOLFIRI + afl and 3 pts continued afl alone as manteinance for a median of 9 weeks. Main reported toxicities G1-2 were diarrhea (10 pts, 55.5%), asthenia (6 pts, 33.3%), arterial hipertension (5 pts, 27.7%), mucositis (4 pts, 22.2%), nausea (3 pts, 16.6%), neutropenia (3 pts, 16.6%) and proteinuria (3 pts, 16.6%). Common grade ≥3 treatment-related AEs were neutropenia (2 pts, 11.1%), diarrhea (1 pts, 5.5%) and asthenia (1 pts, 5.5%). No reported cases of gastrointestinal perforation, thromboembolism and hemorrage. No fatal events were reported.

Conclusion: In our clinical practice, afl + FOLFIRI was well tolerated, with a manageable toxicity profile. The safety results confirm the findings from the confirmatory VELOUR trial.

A44 Partial splenic embolization in chemotherapy-induced thrombocytopenia: a retrospective analysis with long term follow up

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Background: Chemotherapy-induced thrombocytopenia (CIT) may result in a chemotherapy (CT) dose delay or reduction, thus affecting dose density and intensity. Historically, partial splenic embolization (PSE) has been performed to improve hematologic parameters related to hypersplenism. In this study we reviewed our institutional experience with PSE for gastrointestinal cancer (GI) and experiencing CIT.

Material and methods: A retrospective analysis of GI cancer patients with splenomegaly undergoing PSE was performed. Mean platelet count was collected at the following time points: before CT start; at nadir pre-PSE; one week before PSE (pre-PSE); four weeks after PSE (post-PSE); and at the nadir after CT reintroduction post PSE. Time to CT re-start after PSE and the time to recurrent CIT, periprocedural laboratory values and adverse events were recorded. Wilcoxon test was adopted to exploratively compare platelet count before and after PSE.

Results: Eleven patients underwent PSE, 5 with colorectal, 3 with pancreatic and 3 with biliary cancer, 73% had metastatic disease. Baseline platelet count before initiation of CT was 146 x 109/L (range, 81-255 x 109/L). Platelet count at nadir pre-PSE was 60 x 109/L (range, 44-82 x 109/L), and pre-PSE platelet count was 78 x 109/L (range, 62-99 x 109/L). Post-PSE platelet count improved significantly (132 x 109/L; range, 67-172 x 109/L) compared with nadir pre-PSE ($p = 0.003$). The mean hospital stay was 1 day. Post-procedure abdominal pain occurred in 3 patients. All patients resumed CT and mean time to CT re-start after PSE was 43 days (range, 4-193 d). All patients exhibited recurrent thrombocytopenia. Platelet count at nadir after PSE was 54 x 109/L (range, 28-78 x 109/L) and occurred at a mean of 169 days after PSE (range, 37-664 d). No differences were observed when comparing CIT at nadir pre and post PSE ($p = 0.447$). All patients experienced CT dose delay and 82% of them experienced dose reduction after PSE.

Conclusions: Our findings underline that PSE is safe and effective to achieve short-term improvement of CIT and resumption of CT in GI patients. However, PSE does not sustain long-term adequate platelet count. Further studies may help guide patient selection by identifying characteristics that allow a sustained improvement in CIT.

A45 The regorafenib issue: focus on efficacy and safety in pre-treated metastatic colorectal cancer from a real world experience

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Background: The multikinase inhibitor regorafenib showed statistically significant survival improvements in clinical trials patients (pts) with refractory metastatic colorectal cancer (mCRC). A proper selection of pts who may most benefit of regorafenib is necessary to optimize the cost-effectiveness ratio, but it is still a challenge.

Patients and methods: We retrospectively collected data about pts with mCRC treated at our Institution with regorafenib after failure of all approved standard therapies. We analyzed data on survival, response rate and safety. Survivals were evaluated using Kaplan-Meier method. We divided pts in 3 risk groups according to the prognostic score identified by the French study REBECCA.

Results: Between August 2013 and December 2016, 16 pts with refractory mCRC received regorafenib at the initial dose of 160mg daily for 3 weeks of each 4 weeks cycle.

Pts had the following baseline characteristics: median age 62 yo; ECOG PS 0/1 9/7; tumor location right-sided/left-sided/rectum 5/7/4; KRAS wild-type/mutated 8/8. 37% of pts received 3 or more prior chemotherapy regimens for mCRC and 88% were treated with bevacizumab. At the time of our analysis all pts had progressed and 11 pts had died. No patient achieved partial response and only 2 pts had stable disease, with a disease control rate of 12%. The median progression free survival was 3.7 months and the median overall survival (mOS) was 7.4 months. The most frequent reported adverse events (AEs) were fatigue (31%), hand-foot syndrome (38%), hyperbilirubinemia (50%) and thrombocytopenia (25%). Drug-related AEs grade $<=3$ occurred in 38% of pts; discontinuation and dose-reduction due to AEs occurred in 2 and 4 pts respectively. Pts were divided in 3 risk groups according to the prognostic score proposed in REBECCA study, based on ECOG PS, KRAS mutational status, time since diagnosis of metastatic disease, number of metastatic sites, presence of liver metastases, initial dose of regorafenib: mOS was 9.2 months in low-risk group pts, 5.6 months in intermediate-risk group and 3.9 months in high-risk group.

Conclusions: Our results on efficacy and safety of regorafenib in refractory mCRC are consistent with published data, even if we observed a lower disease control rate. The REBECCA prognostic model could be a useful tool for clinicians to better select pts who may most benefit of regorafenib, thus avoiding useless and potentially toxic end-of-life treatment and reducing costs.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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B - GENITOURINARY TUMOURS

B1* CORE-URO-01 study: comparison of safety and efficacy of pazopanib in first-line metastatic renal cell carcinoma (mRCC) with or without renal failure

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Background: Pazopanib has been approved for first-line treatment of patients (pts) with metastatic renal cell carcinoma (mRCC) based on the prospective randomized trial that enrolled only pts with adequate renal function. There are no data on the efficacy and toxicity of pazopanib in pts with renal insufficiency (RI). The aim of this study is to investigate the effect of kidney function on treatment outcomes in pts treated with pazopanib for mRCC.

Patients and methods: We retrospectively analyzed the data of the mRCC pts treated with pazopanib with respect to renal function in fourteen Italian institutions from January 2010 to June 2016. Baseline glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula at the time of therapy initiation. Pts with MDRD<60 mL/min/1.73 m2 (group A) were compared with pts with MDRD=60 mL/min/1.73 m2 (group B) in terms of response rates, progression free survival (PFS), overall survival (OS) and toxicities.

Results: Two hundred and twenty-nine pts with mRCC were included in this study: 128 pts in group A and 101 pts in group B. 68% of pts were male, median age was 67 years (34-88) and median CrCl was 49,7 ml/min in group A. In group B, 64% of pts were male, median age was 64 years (38-85) and median CrCl was 74 ml/min. Pts with MDRD<60 were more likely to have had a previous nephrectomy (87% vs 79%). Median PFS was 14 months (95% confidence interval [CI] 9.4-18.5) and 17 months (95% CI 11.4-22.8), OS was 30.5 months (95% CI 8-53) and 41.4 months (95% CI 21-62) for MDRD<60 group and MDRD=60 respectively, with no statistical difference ($p = 0.6$). The disease control rate was 84% in group A, and 73% in group B ($p = 0.1$). About toxicity profile, no difference between the 2 groups was reported in terms of incidence of grade 1-2 (73% in group A vs 74% in group B, $p = 0.5$) and grade 3-4 (24% vs 33% respectively, $p = 0.2$). Dose reductions are statistically more frequent in pts in group A (66% vs 36%, $p = 0.04$), despite the same percentage of pts in both groups started at dose of 800 mg daily.

Conclusions: Although in this study it is necessary to reduce the dose of pazopanib more frequent in pts with RI, kidney function at therapy initiation does not adversely affect the efficacy and safety of pazopanib.

B2 Broad immunomodulating effect of first-line Pazopanib in metastatic renal cell carcinoma patients

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Background: The impact of tyrosine kinase inhibitors (TKIs) on tumor immunity of patients (pts) with metastatic renal cell carcinoma (mRCC) is largely unknown. We investigated the activity of pazopanib in counteracting tumor-induced immunosuppression and boosting adaptive immune response.

Methods: Sixteen mRCC pts receiving first-line Pazopanib were prospectively analyzed at baseline, 3 and 6 months for blood Immune profiling by multicolor cytofluorimetry. Gene expression analysis was performed by Illumina HT12v4 BeadChip Arrays. Data were evaluated by t-test, enrichment analysis and deconvolution algorithms.

Results: Pazopanib administration (800 mg per os/daily) was associated with a significant decrease of cell subsets involved in immunosuppression, including CD14+ monocytes, monocytic CD14+ HLA-DR^{neg} myeloid derived suppressor cells (MDSC) and CD14^{+}PDL-1^{+} cells. Similarly, low density CD15^{+} granulocytic MDSC and CD4^{+} CD25^{high} Foxp3^{+} regulatory T cells were reduced by treatment. Concomitantly, a boost of antitumor effectors, such as activated T lymphocytes (identified as CD3^{+}PD-1^{dim} T cells) and cytotoxic CD3^{-}CD16^{+}CD56^{dim} NK cells, was observed. Changes were more evident at 3 months and in pts achieving clinical benefit (69%), defined as the sum of partial response and stable disease at first restaging. Interestingly, a statistically significant increase of lymphocyte/monocyte ratio, as determined by routine blood test was also detected. Gene expression analysis confirmed the immunoregulatory effects of pazopanib. By comparing with those collected after 3 months after treatment start and pre-treatment samples, pathway-enrichment analysis revealed a coherent modulation of NK Granzyme A, IL8 signaling and other immune-related pathways. Similarly, using deconvolution algorithms, we observed an enrichment of NK and CD8+ T cell transcripts.

Conclusions: Pazopanib reshapes tumor immunity by reducing immunosuppressive cells (MDSC and Treg) and triggering T cells and NK effectors. These data provide a strong rationale for using Pazopanib both before an immunocheckpoints inhibitors and also in combination strategies based on the synergism between TKIs and immunotherapy.

B3 Impact of metabolic syndrome on clinical outcome of castration resistant prostate cancer (CRPC) patients treated with abiraterone and enzalutamide

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Background: Metabolic syndrome (MS) is a set of risk factors, including obesity, dyslipidemia, hypertension and insulin resistance, that has been implicated in the development and progression of CRPC. The study aimed to firstly assess the incidence and impact of MS on progression-free/overall survival (PFS/OS) in CRPC patients (pts) treated with abiraterone (abi) or enzalutamide (enza).

Methods: We retrospectively evaluated CRPC pts in seven Italian Institutes between March 2011 and October 2016. MS, defined by modified Adult Treatment Panel III criteria, was assessed before starting abi or enza, during treatment and follow-up. In addition, we extracted cell free-DNA from pretreatment plasma samples and performed copy number of androgen receptor (AR) by duplex TaqMan quantitative real-time PCR assay, digital PCR and targeted next generation sequencing *(Conteduca V et al. Ann Oncol 2017)*.

Results: We included 551 metastatic CRPC pts treated with abi (N = 317, 57.5%) and enza (N = 234, 42.5%). Most pts (N = 442, 80.5%) previously received a docetaxel-based regimen, and 39 (7.1%) pts also received more than two previous therapeutic lines. Eighty-three of 551 pts evaluated (15%) met MS criteria at baseline without no significant difference between abi and enza groups, whereas for 40 (8.5%) this occurred during treatment. There was no statistically significant difference for age at diagnosis, performance status, Gleason score, type of treatment and number of previous therapeutic lines between pts with (MS+) and without (MS-) MS. Baseline metabolic profile and visceral involvement were significantly associated with MS+. Moreover, we observed no correlation between MS and amplification of cell-free AR gene copy number. Median PFS was 3.7 (95% CI 3.5-4.1) for MS+ vs 8.3 (95% CI 7.4-9.2) months (mo) for MS- (HR = 2.77, 95% CI 2.12-3.61 $p < 0.0001$). Median OS was 6.9 (95% CI 5.4-9.8) and 19 (95% CI 17.4-21.6) mo in MS+ and MS-, respectively (HR = 3.43, 95% CI 2.56-4.58, $p < 0.0001$). No association was reported between the presence of MS and PSA response rate. Multivariate analysis confirmed that MS was an independent predictor of PFS (HR = 2.07, 95%1.03-4.18 $p = 0.041$) and OS (HR = 4.87, 95% CI 2.36-10.03 $p < 0.0001$).

Conclusions: The presence of baseline MS is a significant risk factor for worse survival and so to be considered for a better prognostication of CRPC pts treated with abi or enza,. A prospective evaluation is warranted.

B4 Safety and efficacy of cabozantinib for metastatic renal cell carcinoma (mRCC): real world data from an Italian Expanded Access Program (EAP)

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Background: Final results from the randomised phase III METEOR trial confirmed a survival benefit of cabozantinib over everolimus in patients (pts) with advanced clear-cell renal cell carcinoma who progressed after at least one previous antiangiogenic inhibitor. The EAP provided the opportunity to treat pts in real world clinical practice.

Methods: Data were collected from 92 pts treated with Cabozantinib across 23 Italian hospitals. Cabozantinib was available, upon physician request, from September to December 2016. Pts were aged 18 years and older, with mRCC and measurable disease, with Perfomance Status (ECOG) 0 to 2, who had relapsed after one or more prior systemic treatment. 74 pts had clear-cell RCC, while the other 18 had non-clear-cell histologies (type II papillary and chromophobe). The most frequent site of disease were: lung 54 (58%), lymph nodes 42 (45%), bone 28 (31%), liver 15 (16%) and brain 5 (5%); 43 (46%) of pts had two or more sites of disease. Cabozantinib was administered orally at 60 mg once a day in 28 days-cycles. Dose reductions to 40 or 20 mg were allowed if toxicity was encountered. Pts were monitored for adverse events (AEs) using CTCAE v.4.0. The aim of this analysis was to evaluate the safety and activity of Cabozantinib in a large unselected population.

Results: Cabozantinib was administered as second line therapy in 28 (30%) pts, as III line in 18 (19%) pts and as further lines in the remaining 46 (51%) pts. At the time of our analysis, grade 3 and 4 AEs were observed in 21% of pts. Among 91 pts, only 5 (5%) pts discontinued treatment due to AEs. The best overall response was partial in 28 cases (31%), whereas 23 (25%) pts had stable disease and 23 (25%) had progressive disease. 18 pts (18%) are not available for first response assessment. With a median follow-up of 4 months, the median progression-free survival observed was 3.5 months irrespective of the line of treatment.

Conclusions: Our data suggest that Cabozantinib is safe and active in a large unselected population treated according to everyday clinical practice.

B5 Addressing the best treatment for non-clear cell renal cell carcinoma (nccRCC): a meta-analysis of randomized clinical trials comparing VEGFR-TKis versus mTORi targeted therapies

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Aim: Non-clear cell renal cell carcinoma (nccRCC) is a heterogeneous group of tumors profoundly different in terms of morphology, genetic profile, clinical behavior and prognosis. The optimal treatment algorithm for nccRCC is still unknown and derived mainly from evidence available for clear cell RCC, being therefore represented by VEGFR-tyrosine kinase inhibitors (TKis) and mTOR-inhibitors (mTORi). We aimed to compare the efficacy of VEGFR- TKis and mTORi for the treatment of nccRCC patients.

Methods: Searching the MEDLINE/PubMed, Cochrane Library and ASCO Meeting abstracts prospective studies were identified. Data extraction was conduced according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The measured outcomes were progression free survival (PFS), overall survival (OS), and the overall response rate (ORR).

Results: Four randomized controlled trials were selected for final analysis, with a total of 332 patients evaluable for PFS. Treatment with TKi significantly reduced the risk of progression compared to mTORi (HR = 0.71; 95% CI 0.60−0.84; p < 0.0001). This difference remained significant when sunitinib was compared to everolimus in first-line setting (HR = 0.67; 95% CI, 0.56−0.80; p < 0.00001). In 332 patients evaluable for OS, no significant difference was found between TKi and mTORi (HR = 0.86; 95%CI, 0.67−1.12; p = 0.27). In the 176 evaluable patients, TKis therapy did not improve the ORR when compared to mTORi (RR = 2.21; 95% CI, 0.87−5.60; p = 0.09), even if treatment with sunitinib doubled the probability of achieving a tumor response.

Conclusions: Compared to mTORi, treatment with TKis significantly improves PFS but not OS. Furthernore, sunitinib as first-line therapy reduces the risk of progression compared to everolimus, therefore supporting the standard treatment paradigm broadly used for ccRCC. The relatively modest efficacy of available targeted therapies reinforces the need of future histological-based, molecular-driven therapeutic paradigm.

B6 Prospective translational study investigating circulating predictors of outcome to first-line pazopanib in patients with metastatic renal cell carcinoma (mRCC)

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Background: We investigated plasma levels of circulating angiogenic factors (CAFs) involved in angiogenesis in patients (pts) with mRCC treated with first-line pazopanib to assess potential biomarkers of clinical outcome.

Patients and Methods: Pts (n = 25) with mRCC receiving first-line pazopanib at Istituto Nazionale Tumori of Milan between July 2015 and February 2017 were prospectively enrolled in the study. Plasma samples were obtained at different time-points: before treatment and every 4 weeks until radiographic disease progression (PD) as per RECIST 1.1. assessed by CT scan every 12 weeks. Levels of 7 CAFs of interest including: IL-6, IL-8, SDF-1, VEGF-A, HGF, Osteopontin and E-selectin were quantified by Luminex® technology. Baseline levels and changes during treatment were analyzed for association with efficacy (progression-free survival [PFS] and objective response).

Results: 21 out of 25 pts enrolled were evaluated. The median follow up was 8 months (IQR 5.1 months). Overall plasma levels of SDF-1 (p<.0001), VEGF-A (p=.0052) and IL-8 (p=.0275) showed the highest modulation during treatment. At the end of first pazopanib cycle (week 4) plasma VEGF-A levels were significantly higher in pts with partial response (PR) than in pts with PD. IL-8 levels were significantly higher in pts with PD vs pts with PR at the time of response (p=.0481). Moreover baseline IL-8 levels were significantly higher in pts with PD vs pts with stable disease (SD) (p=.0181). Mean levels of SDF-1 (p=.0022), HGF (p=.0002), osteopontin (p<.0001) and E-selectin (p<.0001) were significantly associated with best response (PR vs SD vs PD) while IL-6 levels were significantly associated with PFS (p=.0082). The 6 months and one year estimated PFS rate was 73% and 63% respectively.

Conclusions: Treatment with first-line pazopanib is associated with variation of CAFs levels. Week 4 levels of VEGF-A as well as pretreatment levels of IL-8 showed the strongest correlation with PD suggesting that monitoring these CAFs during treatment may be useful for identifying patients likely to respond. These findings warrant further investigation in larger trials.

B7 Radium-223 with concomitant bone-targeting agents in metastatic castration-resistant prostate cancer (CRPC) patients treated in an international early access program (EAP)

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Background: The bone-targeting agents (BTAs) denosumab and bisphosphonates (BPs) are widely used in the supportive care of patients (pts) with CRPC and bone metastases. We present data on pts treated with radium-223 dichloride (Ra-223) with or without a concomitant BTA in an international EAP.Methods: This was a prospective single-arm phase IIIb study of CRPC pts with symptomatic or asymptomatic bone metastases (no visceral disease) recruited from 14 countries. Pts received Ra-223 55 kBq/kg (iv injection) every 4 weeks for 6 cycles. Co-primary endpoints were safety and overall survival (OS). Exploratory analyses investigated the effects of concomitant denosumab (no BPs) or BPs (no denosumab) on OS and symptomatic skeletal events (SSE). Results: 696 pts received at least one Ra-223 cycle. Of those, 127 (18%) pts were treated with concomitant denosumab (no BPs) and 435 (63%) without any concomitant BTAs. Key baseline characteristics are reported in pts treated with Ra-223 with or without a concomitant BTA (Table). Median OS (mOS) and median time to first SSE (mSSE) were longer in pts treated with Ra-223 and denosumab versus pts without a concomitant BTA (Table). While key baseline characteristics in pts treated with Ra-223 and denosumab were similar to pts treated with Ra-223 and BPs, adding BPs to Ra-223 did not appear to improve mOS. However, mSSE was prolonged in pts receiving Ra-223 and BPs versus pts who received Ra-223 without a concomitant BTA (Table). Conclusions: In this EAP, pts treated with Ra-223 and a concomitant BTA appeared to have longer time to first SSE than those treated without a concomitant BTA. However, improvement in OS was observed with denosumab but not with BPs. Prospective

randomized controlled studies are required to confirm the benefit of this specific treatment combination in metastatic CRPC.

Table: B7

	Denosumab N = 127	BPs N = 125	No denosumab/ no BPs N = 435
Baseline characteristics			
ECOG PS, n (%)			
0	58 (46%)	55 (44%)	144 (33%)
1	55 (43%)	54 (43%)	234 (54%)
≥2	14 (11%)	16 (13%)	57 (13%)
Pain, n (%)	123	122	413
Mild	75 (61%)	72 (59%)	218 (53%)
Moderate-severe	19 (15%)	24 (20%)	113 (27%)
None	29 (24%)	26 (21%)	82 (20%)
ALP (U/L), n	127	125	433
Median	121.0	137.0	168.0
PSA (μg/L), n	127	124	433
Median	91.2	118.5	174.6
Efficacy outcome			
Overall survival			
Median, months	NR	12.7	13.4
95% CI	NA	10.9—NA	11.7—NA
Hazard ratio (95% CI)	0.630 (0.431—0.922)	0.846 (0.584—1.226)	-
Time to first SSE			
Median, months	17.0	NR	15.8
95% CI	17.0—17.5	NA	10.9—19.1
Hazard ratio (95% CI)	0.761 (0.493—1.173)	0.498 (0.294—0.845)	-

NR/A = not reached/available.

B8 Changes in alkaline phosphatase (ALP) dynamics and overall survival (OS) in metastatic castration-resistant prostate cancer (mCRPC) patients treated with radium-223 in an international early access program (EAP)

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Background: Identifying a reliable marker of efficacy for radium-223 dichloride (Ra-223) would aid in the clinical management of mCRPC patients (pts). In exploratory analyses of mCRPC pts with symptomatic bone metastases treated with Ra-223 in the ALSYMPCA trial, OS was significantly longer in pts with a confirmed decline in ALP levels from baseline at week 12, compared with pts without a confirmed ALP decline. Here, we present data on ALP dynamics and OS and time to first symptomatic skeletal event (SSE) in pts treated with Ra-223 in an international EAP. Methods: This was a prospective single-arm phase IIIb study of CRPC pts with symptomatic or asymptomatic bone metastases (no visceral disease) recruited from 14 countries. Pts received Ra-223 55 kBq/kg iv, every 4 weeks for up to 6 cycles. Co-primary endpoints were safety and OS. Exploratory analyses investigated whether a confirmed decline (any magnitude) in ALP levels was associated with OS and time to first SSE. Results: 696 pts received at least one Ra-223 cycle. Of those, 398 (57%) pts had a confirmed decline in ALP and 298 (43%) had no confirmed ALP decline. Key baseline characteristics are shown (Table). More pts with a confirmed ALP decline (374, 94%) received 5—6 Ra-223 injections than those with no ALP decline (99, 33%). Hazard ratios (HR) for confirmed ALP decline at week 12 vs no decline suggest a strong association of ALP decline with both longer OS (HR 0.299, 95% CI 0.227—0.395) and longer time to first SSE (HR 0.474, 95% CI 0.340—0.662) (Table). Conclusions: In this EAP, which is relevant for pts currently treated in clinical practice, decline in ALP was associated with longer OS and time to first SSE.

Table: B8

	Confirmed ALP decline N = 398	No confirmed ALP decline N = 298
Baseline Characteristics		
ECOG PS, n (%)		
1	189 (47%)	159 (53%)
≥2	39 (10%)	48 (16%)
Pain[a], n (%)	380	287
Mild	217 (57%)	153 (53%)
Moderate-severe	79 (21%)	79 (28%)
None	84 (22%)	55 (19%)
ALP (U/L), n	398	296
Median	149.0	148.5
PSA (μg/L), n	398	295
Median	117.2	202.0
Hemoglobin, g/dL		
Median	12.4	11.8
Efficacy outcome		
Overall survival		
Events, n (%)	86 (22%)	124 (42%)
Median, months	NR	10.0
95% CI	NA	8.6—11.5
Hazard ratio[b]	0.299	
95% CI	0.227—0.395	
Time to first SSE		
Events, n (%)	76 (19%)	67 (22%)
Median, months	17.5	NR
95% CI	17.0—18.1	NA
Hazard ratio[b]	0.474	
95% CI	0.340—0.662	

NR/A, not reached/available.
[a]Measured from the brief pain inventory form.
[b]Calculated from Cox proportional hazards model.

B9 Bladder-sparing trimodality approach for unfit for surgery and cisplatin treatment elderly patients with muscle-invasive bladder cancer (MIBC): results from a monocentric experience

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Background: Radical cystectomy is the standard of care for localized muscle-invasive bladder cancer (MIBC). Because of the presence of severe comorbidities, a significant proportion of elderly patients (pts) is not eligible for cystectomy. Moreover, many of these pts are not fit for cisplatin treatment due to impaired renal function or peripheral neuropathy or hearing loss. Several studies showed the feasibility and efficacy of conservative approach for MIBC. We evaluated the efficacy and tolerability of maximal TURBT followed by definitive chemoradiotherapy in elderly pts with MIBC judged unfit for surgery and cisplatin treatment.

Patients and methods: At our Institution, from January 2007 to May 2015, we treated 23 elderly pts with locally-advanced (T2-4 N0-X) bladder cancer. Characteristics of pts were as follows: M18:F5, median age 74 yrs (range: 70-81 yrs), median ECOG PS 1 (range: 1-2); median Charlson Comorbidity Index was 5. After the initial diagnosis all pts received a baseline evaluation with thoracic-abdominopelvic CT and underwent maximal TURBT: pT2 disease was detected in 14 pts (61%), pT3 in 7 pts (30%) and pT4 in 2 pts (9%). Due to presence of major comorbidities and renal impairment or/and peripheral neuropathy or/and hearing loss or/and congestive heart failure all pts were considered not eligible for cystectomy and cisplatin treatment. Consequently, after maximal transurethral tumor resection, each patient received external-beam

radiotherapy (total dose 60 Gy) plus concomitant radiosensitizing weekly gemcitabine 150 mg/mq.

Results: Eight weeks after completing the concurrent radio-chemotherapy regimen, all pts were re-evaluated with cystoscopy and thoracic-abdominopelvic CT. A complete endoscopic response was reported in 18 pts (78%), five pts (22%) had residual disease (Ta-T1). After a median follow-up of 45 months, the overall 5y-OS was 61% with a 5y-DFS and 5y-specific survival of 52% and 56%, respectively. Five pts (22%) developed metastatic disease during follow-up. Toxicity was substantially manageable: grade 3 and grade 4 toxicities (cystitis/proctitis) were observed in 4 (17%) and 2 (9%) pts, respectively. No treatment-related deaths were seen.

Conclusions: In unfit for surgery and cisplatin treatment pts with MIBC, this bladder-sparing trimodality approach showed satisfactory activity with a manageable profile of toxicity and could represent a valid therapeutic option in this subgroup of elderly pts with localized MIBC.

B10 Prognostic value of systemic inflammatory biomarkers in patients with mCRPC treated with Abiraterone in pre-docetaxel setting

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Background: Systemic inflammatory biomarkers have shown a prognostic impact in several solid tumors. The aim of this study was to examine the prognostic role of baseline neutrophil-to-lymphocyte-ratio (NLR), platelet-to-lymphocyte-ratio (PLR) and lymphocyte-to-monocyte-ratio (LMR) and NLR, PLR and LMR changes at 1, 2 and 3 months in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) treated with Abiraterone Acetate (AA) in pre-docetaxel setting.

Patients and methods: We retrospectively included mCRPC pts treated with AA at two Italian hospitals from November 2012 to April 2017. NLR, PLR and LMR were evaluated at baseline and after 1, 2 and 3 months of treatment. The impact of NLR, PLR and LMR on progression-free survival (PFS) was evaluated by Cox regression analyses both in univariate and multivariate fashion. Other clinico-pathological factors, such as PSA baseline level, Time to CRPC, Gleason Score, Presence of Visceral Metastases and Bone Metastases Burden were included.

Results: Fifty mCRPC pts treated with AA were evaluated. At univariate analysis, elevated baseline NLR and PLR were significantly associated with shorter median PFS ($p = 0.01$, hazard ratio [HR]$=1.224$ and $p = 0.0001$, HR $= 1.013$ respectively); after 1 month of treatment, NLR and PLR were significantly predictors of worst PFS ($p = 0.03$, HR $= 1.320$ and $p = 0.02$, HR $= 1.012$ respectively). After 2 and 3 months of treatment, only high PLR was associated with poor prognosis ($p = 0.01$, HR $= 1.012$ at month 2; $p = 0.009$, HR $= 1.009$ at month 3 respectively). LMR didn't show any prognostic relevance. At multivariate analysis, only baseline PLR was independently associated with PFS ($p = 0.006$, HR $= 1.013$).

Conclusions: High baseline and early-assessed NLR and PLR during treatment with AA are associated with shorter PFS in mCRPC pts. PLR more than NLR may be considered as an early and easy-to-perform prognostic marker in this setting.

B11 Does dose modification affect efficacy of first-line pazopanib in metastatic renal cell carcinoma?

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Background: Pazopanib is a standard treatment for metastatic renal cell carcinoma (mRCC) and 800 mg/day is considered the optimal dose for mRCC patients (pts). However, some pts require a dose reduction due to toxicity. It remains unclear whether reduced-dose pazopanib is as effective as the standard dose.

Methods: We retrospectively evaluated treatment duration, objective response rate (ORR), progression-free survival (PFS), and discontinuation rate in consecutive pts with mRCC treated with first-line pazopanib between 2011 and 2016 at the Istituto Nazionale Tumori of Milano, Italy. Three patient groups were compared: group 1 received the standard starting dose of 800 mg/day continuously, group 2 received a dose reduced to 400 or 600 mg/day after starting with 800 mg/day, and group 3 received a reduced starting dose of 400 or 600 mg/day because of ECOG performance status = 2-3 and/or comorbidities.

Results: We included 69 pts, with 34 in group 1, 19 in group 2, and 16 in group 3. Median age at diagnosis was 62 years, and 64% were male. Overall 13% and 87% of pts were classified as Heng good and intermediate-risk respectively. In 10 and 9 pts of the group 2, the dose was reduced to 600 and 400 mg/day respectively while 12 and 4 pts in the group 3 received a reduced initial dose of 400 and 600 mg/day respectively. After a median follow-up of 13.9 months (range 0.3-43.8), 27 (39.1%) pts showed progressive disease (PD) and 3 (4.3%) pts were dead. Incidence rate of PD or death was 2.5 (95% CI: 0.6-4.4; Hazard ratio [HR]:1) per 100 person-months in group 1; 4.0 (95% CI: 0-11.4; HR: 1.45) per 100 person-months in group 2 and 3.3 (95% CI: 0-6.8; HR: 1.19) per 100 person-months in group 3. Rates of discontinuation due to PD were 28% in group 1, 42% in group 2, and 44% in group 3. ORR was 44%, 11% and 19% in group 1, group 2, and group 3 respectively.

Conclusions: Our results suggest that a reduced dose of first-line pazopanib might be less effective compared with standard dose. These data highlight the importance of the management of treatment-related side effects that may eventually lead to optimal drug exposure.

B12 Enzalutamide (E) vs abiraterone acetate (AA) in the treatment of metastatic, castration-resistant prostate cancer. Indirect comparisons and network meta-analysis for clinical practice

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Background: To compare efficacy and safety of E and AA in the treatment of metastatic, castration-resistant prostate cancer.

Methods: Efficacy and safety of E and AA were compared using the data of the PREVAIL, AFFIRM, COU-AA-302 and COU-AA-301 trials. All the data extracted from the selected trials were reported ad Hazard Ratio (HR) or Odds Ratio (OR). Overall survival was the primary end point of our analysis, all the side effects, grade III-IV side effects, serious side effects, side effects leading to treatment discontinuation or death the secondary ones. Overall survival was assessed both in the entire population and in the subgroups of patients chemotherapy-naïve or docetaxel-resistant.

Results: The outcome of 5191 patients were reviewed. 1671 patients had been treated with E, 1339 with AA and 2181 with placebo. No significant differences were observed in the eligibility of the patients in the selected trials, and the enrolled patients were considered homogeneous for the final analysis. In the indirect comparison of E vs AA no differences were observed for overall survival both in the entire population (HR $= 0.955$, IC95%$=0.796$-1.144, $p = 0.616$), and in chemotherapy-naïve (HR $= 0.947$, IC95%$=0.723$-1.24, $p = 0.692$), or docetaxel-resistant patients (HR $= 0.961$, IC95%$=0.753$-1.228, $p = 0.75$). Likewise, no significant differences were observed for all side effects (OR $= 0.414$, IC95%$=0.054$-3.196, $p = 0.463$), all grade III-IV side effects (OR $= 1.36$, IC95%$=0.253$-7.318, $p = 0.72$), all serious side effects (OR $= 0.742$, IC95%$=0.137$-4.006, $p = 0.729$), all side effects leading to treatment discontinuation (OR $= 0.743$, IC95%$=0.132$-4.193, $p = 0.736$) or death (OR $= 0.572$, IC95%$=0.089$-3.657, $p = 0.556$).

Conclusions: Although E and AA differ for pharmaceutical structure and mechanism of action, they seem to be comparable both for indication (pre- or post-docetaxel treatment in patients with metastatic, castration-resistant prostate cancer), and for efficacy or safety (both in chemotherapy-naïve and in docetaxel-resistant patients). It follows that compliance, patients characteristics and costs can play a role in the decision making process of clinical practice.

B13 Start (active surveillance or radical treatment for newly diagnosed patients with a localized, low risk, prostate cancer): an epidemiological study of the Oncology Network of Piemonte and Valle d'Aosta. Update 2017

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Background: An Active Surveillance (AS) strategy is recommended as an appropriate management for men with low risk localized prostate cancer (PC), but its diffusion, at least in the Oncology Network of Piemonte and Valle d'Aosta, is still very limited. The primary objective of the START project is to evaluate the acceptability, the safety and the cost-effectiveness of a population based program of AS, whose implementation into routine practice will be encouraged within the setting of a research framework.

Methods: Comparative effectiveness research project. All newly diagnosed PC patients fulfilling the low risk definition, resident in Piemonte or in Valle D'Aosta, will be invited to participate to this observational prospective study. All enrolled patients will receive full and clear information about their prognosis together with a balanced synthesis of the benefits and risks of the available treatments. For all patients baseline clinical, histological and psychological data, any treatment received and follow-up data (including clinical and quality of life outcomes) will be collected.

Specific objectives are:

- to encourage the diffusion of AS at a regional level, in the context of uniform and settled criteria for patients' selection and management, using standardized information about the benefits and risks of the available treatments;
- to estimate the proportion of patients in AS who remain treatment-free at 2 years;

- to compare, at a population level, the clinical outcomes, quality of life and costs associated to different treatment choices.

Results: The START protocol has been designed by a multidisciplinary panel of specialists of the Oncology Network and patients' representatives. All the regional Hospital units of Urology and Radiotherapy have been involved (34 centers participate). The project started on May 2015. 274 patients have been already enrolled: 206 chose AS, 66 radical treatments (14 radiotherapy and 52 prostatectomy) and 2 other treatments. A web-site has been implemented with both a public and a reserved area for data collection (www.start.epiclin.it).

Conclusions: A population based research framework could represent a powerful and safe strategy to effectively implement AS in the NHS. The project could have a large positive impact on the Regional Health Service to improve long term quality of life of low risk PC patients.

B14 Cardiovascular disease (CVD) markers in patients(pts) with prostate cancer(PCa) treated with GN-RH agonists(AG) or antagonist(AN): a prospective cohort study

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Background: An increased risk of CVD in men with PCa on androgen deprivation therapy (ADT) has been described and one proposed explanation is the loss of the cardioprotective property of testosterone. AG and AN are equally recommended in pts with PCa. From retrospective data, pts with preexisting CVD treated with AN appear to have a lower risk of CVD when compared to pts receiving AG. One possible explanation could be the destabilization of vascular lesions. In this observational trial we defined the behavior of some early CV risk markers in pts treated with AG or AN.

Patients and methods: We prospectively monitored PCa pts on ADT during the first year of treatment. We evaluated changes in aortic stiffness trough pulse wave velocity(PWV). Fibrinogen(FB), ICAM, Selectin, RANKL, Endothelin, proBNP and metabolic parameters changes were also measured.

Results: From June 2015 to November 2016 41 evaluable pts(22AG,19AN), were included. Most pts(36:20AG,16AN) received ADT as adjuvant treatment after surgery or concomitantly to radiotherapy. Median (m) age was 70 yrs(AG) and 71yrs(AN); m diastolic blood pressure (BP) was 80 mmHg in both groups and m systolic BP 130(AG) and 140(AN) mmHg; 14 pts in AG and 13 in AN had baseline hypertension; 6 AG and 9 AN had previous CVD. All pts had NYHA I class. Results are summarized in the table below:

Table: B14

	mPWV(m/s)		mproBNP(pg/mL)	
month	AG	AN	AG	AN
0	7.60 ±*0.51*	7.49 ±*0.49*	155.50 ±*31.36*	266.53 ±*67.98*
1	8.75±*0.90*	6.94 ±*0.41*	-	-
3	6.98 ±*0.29*	6.98 ±*0.36*	252.33 ±*91.12*	328.39 ±*62.77*
6	6.96 ±*0.32*	8.01 ±*0.75*	230.75 ±*65.24*	391.93 ±*112.09*
9	6.66 ±*0.35*	6.41 ±*0.41*	-	-
12	7.00 ±*0.44*	6.87 ±*0.57*	231.58 ±*61.24*	306.60 ±*69.65*

Preliminary results show a moderate and transient increase in the mean values of PWV at month 1 in AG and at month 6 in AN. The behavior of proBNP was comparable, while no major changes in FB levels and in the levels of the other markers on study have occurred so far (but analysis is still ongoing). No CV events were observed in either group.

Conclusions: Both AG and AN induce a moderate transient arterial and endothelial damage. Whether and how these changes can play a role in the higher incidence of CVD events reported during ADT with these compounds is not clear yet and under evaluation.

B15 A circulating miRNA signature to better stratify prostate cancer patients at diagnosis

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Background: Prostate cancer (PCa) is the most common cancer in men. Around 80% of PCas are diagnosed at an early local stage but only a subset of these will prove to be fatal. Circulating microRNAs (miRNA) may be an easily suitable biomarker target to distinguish true indolent from clinically significant early PCa thus reducing overtreatments.

Methods: Blood samples from 24 men with benign prostatic hypertrophy (BPH, n = 8), localised PCa (n = 8) or metastatic PCa (n = 8) were collected at time of diagnosis. All men had intact prostates and were naïve to any endocrine and cancer related therapy. A platform of circulating miRNAs were analysed in serum using Abcam Firefly technology. Data collected were independently verified using Taqman. The miRNAs identified as being significant in each group were then analysed in a published dataset.

Results: Serum levels of seven of the miRNAs examined were significantly different in patients with prostate cancer compared to control. A further four miRNAs could differentiate samples from the benign cohort from the metastatic cohort (miRNA-126 P = 0.008, miRNA-150 P = 0.05, miRNA-375 P = 0.007). Kaplan-Meier analysis further identified that the serum levels of four miRNAs could associate with survival rates (miRNA-21 P = 0.032, miRNA-126 P = 0.032, miRNA-150 P = 0.032, miRNA-93 P = 0.019). Examination of these miRNAs in a cohort of 280 men from The Cancer Genome Atlas (TCGA) showed that these four miRNAs had significantly different expression in patients who eventually relapse (miRNA-21 P = 0.048, miRNA-375 P = 0.021, miRNA-210 P = 0.0003, miRNA-93 P = 0.008).

Table: B15

miRNA	Mean (log2)		P Value
	Control	Cancer (n = 16, 8 localised and 8 metastatic)	
10b	0.59	0.95	0.02
125b	0.25	0.56	0.013
210	1.05	1.35	0.044
21	2.17	2.97	0.012
378a	1.19	1.39	0.04
483	0.56	0.90	0.03
93	2.72	2.65	0.033

Conclusions: Our circulating miRNAs based signature could be used to stratify men at prostate cancer diagnosis and help identify those who would benefit more from an early radical treatment. These data should be validated in a larger number of patients.

B16 CabaCy—evaluating Cabazitaxel efficaCy by patterns of treatment and disease in metastatic castration resistant prostate cancer (mCRPC) patients: a 5 years, "Real Life", mono-institutional experience

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Background: Since 2004, Docetaxel represents the standard 1st-line chemotherapy for mCRPC patients . Cabazitaxel shows an OS benefit in patients progressing during and after Docetaxel, including those refractory to Docetaxel. It also retains activity in patients progressing with new androgen receptor-targeted agents (ART) such as abiraterone or enzalutamide. A large early access program showed that Cabazitaxel has a manageable safety profile, without evidence of cumulative toxicity. We aimed at evaluating the activity of Cabazitaxel according to therapy line and disease burden.

Methods: 46 patients treated with Cabazitaxel in our National Cancer Institute were retrospectively reviewed. OS, PFS (PCWG2) and PSA response (PSA decrease =50%) were analyzed by therapy line and disease burden (bone only vs bone plus visceral disease).

Results: 10.9% of pts received Cabazitaxel in 2nd line (Doc ->Caba ->ART), 67.4% in 3rd line (Doc ->ART ->Caba) and 21.7% in 4th line or more. At Cabazitaxel initiation, median age was 70.5 years, median PSA was 104 ng/mL and 20% of pts had visceral disease. Median time to castration resistance was 18 mo. Patients were treated with Cabazitaxel (25mg/m2 q21) for a median of 6 cycles and received a median of 4 life-extending therapy lines. Overall, median OS from first Docetaxel cycle was 42.3 Mo, median PFS with Cabazitaxel was 6.2 Mo and 47,8% of pts had a PSA response with Cabazitaxel. Results by therapy line and disease characteristics are presented in the table below.

Table: B16

Setting of Disease	Outcome	Units	2 line	3 Line	4 Line +
Bone only	PFS *	Mo	7,1	6,0	5.7
	PSA Response	% Pts	75	48	37,5
Bone + Visceral	PFS *	Mo	7,7	5.5	3,7
	PSA Response	% Pts	100	50	0
Overall	PFS *	Mo	7,7	6,0	5.6
	PSA Response	% Pts	80	48,4	30

*Kaplan-Meier Survival Estimation

Conclusions: These results suggest, despite biases of a retrospective analysis, that treatment pattern could affect patients outcomes, with early use of Cabazitaxel in therapeutic algorithm being associated with higher clinical benefit compared to its administration in subsequent lines of treatment. Additional data will be presented at AIOM meeting.

B17 Abiraterone acetate (AA) in pre- and post-docetaxel (DX) setting for metastatic castration resistant prostate cancer (mCRPC): a monoinstitutional experience focused on cardiovascular events and on their impact on clinical outcomes

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Background: AA is a therapeutic option for mCRPC patients (pts). Treatment is effective in pre- e post-DX setting and it is commonly well tolerated. However it requires the concurrent administration of corticosteroids and it can induce relevant adverse events (AEs) including: fluid retention (FR), hypertension (HP), cardiac disorders (CD) and hypokalemia (HK).

Methods: We retrospectively analyzed mCRPC pts treated with AA and prednisone in pre- and post-docetaxel (DX) setting. We evaluate the incidence of AEs and the putative impact of baseline characteristics and AEs on common outcomes.

Results: We analyzed 105 pts (30 DX-naïve). Median age was 74 years, 19% of pts had ECOG 1-2 and 21.9% were symptomatic. Median PSA was 37.8 ng/ml and 52.4% of pts had a Gleason Score (GS) >7. Pre-existing CD and HT were in 37.1% and 62.9% of patients, respectively. BMI was >25 among 47.6% of pts. In the whole cohort, median OS and median PFS was 24.6 months and 14.9 months, respectively. In pre- or post-DX setting OS was 24.8 and 19.9 months while PFS 20.9 and 13.8 months, respectively. After multivariable analysis, PSA $\geq$10 ng/ml ($p = 0.007$), GS > 7 ($p = 0.008$), ECOG 1-2 ($p = 0.002$), prior androgen-deprivation therapy (ADT) $\leq$43.2 months ($p = 0.01$), and BMI >25 ($p = 0.03$) were associated with worse PFS; pain presence ($p = 0.01$), ECOG 1-2 ($p = 0.004$), prior ADT $\leq$43.2 months ($p = 0.05$), and BMI >25 ($p = 0.042$) led worse OS. Incidence of AEs was: HT 17.1%, fluid retention (FR) 4.8%, CD 8.6%, and hypokalemia (HK) 16.2%. Age $\geq$75 years predicted for the occurrence of CD ($p = 0.001$) and FR ($p = 0.03$). Pts who developed one or more AEs had not worse outcomes, in fact HK was associated with better median OS even after multivariable analysis (unadjusted $p = 0.013$; adjusted $p = 0.036$).

Conclusions: Outcomes in our series are consistent with those from pivotal trials, confirming that this treatment proves effective in "real world". This regimen was safe and well tolerated, even though pts aged 75 and over seemed to be at higher risk for cardiovascular AEs, therefore pointing at a population in need of more rigorous cardiovascular monitoring. The occurrence of cardiovascular AEs did not imply worse outcomes. Intriguingly, treatment-related HK appeared to be associated with a better OS.

B18 Safety and Efficacy of Abiraterone Acetate in Patients (pts) aged 75 or more with Metastatic Castration Resistant Prostate Cancer (mCRPC) in Both Pre-chemotherapy and Post-chemotherapy Settings: The Real Life Experience of Our Institution

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Background: Prostate cancer affects mainly elderly patients (pts) that are usually frail and subject to comorbidities. Abiraterone acetate is a selective androgen synthesis inhibitor that showed its efficacy in either CT-naive pts or those pretreated with docetaxel. Its oral administration and excellent safety profile make it a manageable treatment for elderly mCRPC patients.

Patients and methods: Since April 2013 we treated 43 mCRPC elderly pts ($\geq$75 years) with abiraterone acetate. 22 pts (51%) were pre-treated with docetaxel and 21 (49%) pts were chemotherapy-naive. The median age was 79 yrs (r. 75-86). Post-CT pts had more extensive disease with multiple mts sites, higher baseline PSA and ECOG Performance status. 18 pts (40%) had PS ECOG 2. All pts had comorbidities: 22 pts (60%) had hypertension and also diabetes was a frequent comorbidity with eight patients (19%). At baseline all pts underwent cardiac echography, octagerians 17/43 pts (40%) received also geriatric assessment.

Results: Median duration of hormonal therapy before castration resistance was 34 months (r.3-123), 14 pts (30%) received $\geq$ 3 hormonal manipulations. In post-CT group the median number of docetaxel cycles was 9 (r.2-10). Median duration of treatment with abiraterone was 11,9 months (r. 3-29,8). ORR was 44% with 9% of complete responses.12% of pts did not respond. 30 pts (70%) obtained 50% PSA reduction in 3 months (r. 1-10). Median PFS was 11,7 months, 10,9 in post-docetaxel and 13,7 in CT-naive pts. We observed mOS 26,9 months (r.3,7-45,2) in post-CT group while for CT-naive pts OS data were not mature. The treatment was well tolerated with no WHO grade 4 toxicity reported, while only 6 pts (13%) reported WHO grade 3 toxicity that led to dose reduction. In all these pts the full dosage was restored after a maximum of 2 months.In one pt the treatment was interrupted after 4 months beacause of accidental death. After progressing on abiraterone, 17 pts (40%) received at least one subsequent treatment.

Conclusions: We reported outcome of abiraterone in 43 elderly patients with mCRPC treated in our hospital. Even if almost all the pts reported numerous comorbidities and nearly a half of them had PS ECOG 2, all were able to complete the treatment with abiraterone without its premature withdrawal due to toxicity. Only a few pts required dose reduction. According to our experience abiraterone was well tolerated and it has shown to be an effective treatment option also for elderly patients.

B19 Patient (pt) characteristics and treatment patterns in the radium (Ra)-223 REASSURE observational study

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Background: Ra-223, a targeted alpha therapy, prolonged survival with good safety in metastatic castration-resistant prostate cancer (mCRPC) in the phase 3 ALSYMPCA trial. REASSURE will evaluate Ra-223 short- and long-term safety in routine clinical practice settings. This is the first planned interim analysis (median follow up 7 mos observation).

Methods: This global, prospective, single-arm, observational study enrolled pts with mCRPC with bone metastases (mets) for whom Ra-223 therapy was planned. Follow-up will continue up to 7 years after the last Ra-223 dose.

Results: 1106 pts (437 N. America, 665 Europe, 4 not recorded) enrolled from 2 Sep 2014 to 22 Sep 2016. Baseline data are available from 583 pts receiving 1st- (1L), 2nd- (2L), or $\geq$ 3rd-line ($\geq$3L) Ra-223 for mCRPC (Table). Most pts (n = 369, 63%) completed 5–6 doses (1L, 70%; 2L, 64%; $\geq$3L, 49%); median 6 doses (1L,6; 2L, 6; $\geq$3L, 4). Treatment-emergent drug-related AEs occurred in 215 pts (37%). Post-treatment grade 3/4 thrombocytopenia occurred in 14 pts (2.4%) and anemia in 45 (7.7%).

Conclusions: In routine clinical practice, Ra-223 was associated with good short-term safety. and appeared to be used in pts with less advanced mCRPC than in ALSYMPCA. The majority of pts on 1L/2L Ra-223 therapy received 5–6 doses. Ra-223 was often used with abiraterone or enzalutamide, but not chemotherapy. The 29 Italian centers involved in the study enrolled 204 pts as of March 2017. The next interim analysis in 2019 will report long-term safety and outcomes in all pts. Clinical trial information: NCT02141438.

Table: B19

Baseline characteristics and treatment patterns.

	Total pts* N = 583	1L n = 282 (48%)	2L n = 162 (28%)	≥3L n = 139 (24%)
ECOG 0–1, n (%)	451 (77)	232 (82)	118 (73)	101 (73)
No. of mets†, n (%)				
<6	165 (30)	92 (36)	37 (24)	36 (27)
6–20	302 (56)	144 (56)	90 (58)	68 (52)
>20	106 (20)	35 (14)	39 (25)	32 (24)
Superscan	40 (7)	16 (4)	15 (10)	9 (7)
ALP (U/L), median	134	112	145	167
<140 U/L, n (%)	211 (36)	105 (37)	59 (36)	47 (34)
≥140 U/L, n (%)	199 (34)	74 (26)	64 (40)	61 (44)
PSA (ng/mL), median	61	28	74	145
LDH (U/L), median	273	260	272	320
Concomitant use§, n (%)				
Abiraterone or enzalutamide	153 (26)	86 (31)	47 (29)	20 (14)
Docetaxel or cabazitaxel	19 (3)	10 (4)	5 (3)	4 (3)

B20 The TRITON clinical trial programme: evaluation of the PARP inhibitor rucaparib in patients with metastatic castration-resistant prostate cancer (mCRPC) associated with homologous recombination deficiency (HRD)

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Background: Recent data have shown that ≈20% of patients (pts) with mCRPC have a germline or somatic alteration in either *BRCA1*, *BRCA2* or *ATM* (homologous recombination [HR] genes) (Robinson et al. *Cell.* 2015;161:1215-28), suggesting these molecular markers may be used to select pts with mCRPC for targeted treatment with a poly(ADP-ribose) polymerase inhibitor (PARPi). PARPis have demonstrated preliminary evidence of antitumour activity in pts with sporadic mCRPC and an HR gene mutation (Mateo et al. *N Engl J Med.* 2015;373:1697-708). These results provide a strong rationale for investigating rucaparib in pts with mCRPC associated with HRD.

Methods: TRITON2 (EudraCT 2016-003162-13, NCT02952534) is a phase 2 study evaluating rucaparib 600 mg BID in pts (n≈160) with mCRPC who have a deleterious germline or somatic *BRCA1*, *BRCA2* or *ATM* mutation (per local and/or central testing). Pts with tumours harbouring an alteration in any of 12 other prespecified HR genes (eg, *RAD51C*, *RAD51D* or *PALB2*) will also be enrolled in an exploratory cohort. Pts must have progressed on androgen receptor (AR) signalling-directed therapy (eg, abiraterone or enzalutamide) and 1 prior taxane-based chemotherapy for mCRPC. The primary endpoint of TRITON2 is response rate (modified RECIST v1.1/PCWG3 in pts with soft-tissue disease and prostate-specific antigen response in pts with nonmeasurable disease). TRITON3 (NCT02975934) is a randomised phase 3 study evaluating rucaparib 600 mg BID vs physician's choice of treatment (abiraterone, enzalutamide or docetaxel) in pts (n≈400) with mCRPC and a deleterious germline or somatic *BRCA1*, *BRCA2* or *ATM* mutation (per local and/or central testing). Pts must have progressed on AR signalling-directed therapy for mCRPC; prior chemotherapy for mCRPC and prior PARPi are exclusions. Pts will be randomised 2:1 to rucaparib or physician's choice; the latter group may cross over to rucaparib after radiographic progression confirmed by independent radiology review (IRR). The primary endpoint of TRITON3 is IRR-confirmed radiographic progression-free survival (modified RECIST v1.1/ PCWG3 criteria). Pretreatment blood samples collected from all pts in both trials will enable development of a plasma-based companion diagnostic that predicts rucaparib sensitivity.

Results: Both TRITON2 and TRITON3 are currently enrolling pts.

Conclusions: The TRITON programme will assess the efficacy and safety of rucaparib treatment in pts with mCRPC associated with HRD.

B21 ^{223}Ra-chloride therapy: the first multidisciplinary and multicenter Italian study

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Background: Radium-223 (^{223}Ra)-chloride, a novel alpha emitter, has been shown to improve overall survival (OS), to delay skeletal-related events and to reduce pain in patients (pts) with castration-resistant prostate cancer (CRPC) and bone metastases. Our retrospective observational study is the first multidisciplinary and multicenter Italian experience in evaluating the efficacy and safety of ^{223}Ra therapy in daily medical practice.

Methods: Between August 2013 - August 2016, 83 pts with metastatic CRPC (mCRPC) received 223Ra therapy at three Italian Centers. ^{223}Ra-chloride (50 kBq/Kg or 55 kBq/kg according to NIST2015) was administered every four weeks up to the programmed six cycles of therapy. Study's endpoints were OS, progression-free survival (PFS), pain according to a numeric rating scale (NRS), biomarker response, numbers of symptomatic skeletal-related events (SSEs) and toxicity.

Results: Median age was 75 (range 53–89) years. The majority of pts had a Gleason score of 7 (n = 25), 8 (n = 16), or 9 (n = 21). Forty-one pts completed 6 cycles of treatment; 33 discontinued treatment after 1 (n = 7), 2 (5), 3 (7), 4 (5) or 5 (9) cycles. 9 were under treatment during data collection. NRS pain scores significantly improved during 6 cycles of therapy ($p < 0.000001$). Mean OS was 10.1 months; median OS had not been reached at time of reporting. Kaplan-Meier estimates for OS and PFS were 17.5 and 7.7 months, respectively. OS and PFS were significantly associated with number of 223Ra cycles; most benefit occurred in pts who received all 6 cycles. Stratifying pts according to ALP's levels (≥ 220 and < 220), a significant difference was found in two groups in terms of expected OS and PSF according to Kaplan-Meier estimation. ^{223}Ra was well tolerated, no serious adverse events occurred during treatments.

Conclusions: ^{223}Ra represents an important treatment option for pts with CRPC and symptomatic bone metastases and it seems to be useful in improving OS, PSF and level of pain; especially OS, PSF was better in pts with a lower tumour burden according to ALP's level.

B22 Radium-223 in metastatic castration-resistant prostate cancer (mCRPC): efficacy and safety in real-life experience

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Background: The ALSYMPCA trial showed that Radium-223, an a-emitter radionuclide, improved overall survival (OS) and delays skeletal complications in mCRPC patients (pts) with bone metastases.

Methods: We retrospectively analysed 32 mCRPC pts treated with 6 cycles of Radium-223. Before, after 3 and 6 cycles pts underwent bone scan, ALP, PSA and NRS evaluations. At scintigraphic, biochemical and pain assessment progression was defined as a relative increase of ≥ 25% and response as a relative reduction of ≥ 30% from the baseline value. Subgroup analyses were conducted.

Results: 91% of pts completed all 6 cycles. At scintigraphic assessment 41% had partial response, 50% stable disease with disease control rate of 91%; 41% had pain response and 34% pain

stability. 56% had ALP response and 31% ALP stability while 25% had PSA response and 16% PSA stability. Scintigraphic, biochemical and pain response/stability were associated with longer median progression free survival (mPFS) and mean OS (meOS). Skeletal related events (SRE) occurred in 3 pts with median time to SRE of 9.5 months; mPFS was 12 months and meOS 13.8 months. Pts with baseline ALP<220 (63%) experienced longer mPFS and meOS ($p = 0.004$ and $p = 0.12$). G3-G4 toxicities developed in 16%. No survival differences were observed according to previous chemotherapy and concomitant biphosphonates and denosumab. Our real-life results are in line with those reported in ALSYMPCA trial and in similar retrospective studies.

Conclusions: Radium-223 was well-tolerated and showed survival benefit and high response rate in terms of scintigraphic, biochemical and pain response.

Table: B22 Subgroup analysis

	Median PFS		Mean OS	
ALP ±220 UI/L				
• < 220	13	p = 0.004	15	p = 0.12
• ≥ 220	9		10.3	
ALP response		p = 0.45		
• PR	12		13.4	p = 0.55
• SD	12		13	
• PD	6		10	
PSA response				
• PR	11.1	p = 0.23	13	p = 0.07
• SD	9		12	
• PD	9.7		12	
Scintigrafic response				
• PR	13	p = 0.0001	16.2	p = 0.02
• SD	12		11.3	
• PD	6		6.3	
Pain response				
• PR	13	p = 0.3	13.4	p = 0.59
• SD	12		12.1	
• PD	8		10.6	

B23 Bone pain control in Castration resistant prostate cancer (CRPC): retrospective analysis of first patients trated with Radium 223

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Background: Bone metastases (mts) represent a substantial cause of morbidity in pts with CRPC with a high rate of related skeletal events (SREs). Ra223 dichloride is a targeted a-emitter that selectively binds to areas of increased bone turnover in bone mts and emits high-energy a-particles of short range. The ALSYMPCA study assessed the efficacy of Ra223 compared to placebo in terms of OS, time to first SRE and QoL in men with CRPC with symptomatic bone mts and unknown visceral mts.The aim of our analysis is to evaluate the efficacy of Ra223 in terms of bone pain control.

Patients and methods: We retrospectively collected clinical data of 12 pts affected by CRPC treated with Ra223 for symptomatic bone mts at the Department of Nuclear Medicine of our Institute from July-15 to April-17.

Serum PSA, ALP and blood count were assessed every cycle at day1 and day14. To evaluate the efficacy of treatment, at every visit we asked pts to report changes in bone pain compared to baseline and it was classified as 'increase', 'no change', 'decrease' or 'complete cessation'.

Results: From July-15 to April-17 12pts underwent treatment with Ra223 at 50kBq/kg i.v. every 4 weeks; 7 of 12 pts (58%) received all 6 expected infusions, 2pts (17%) are still under treatment, 3 (25%) died during the treatment. 2 pts were pre-treated with less then 3 lines therapy (28%), 5 pts with 3 or more lines. The most common side effects were anemia (57% G1-2, 28% G3), thrombocytopenia (42% G1, 14% G2), neutropenia (14% G2). An increase of PSA value from 1st to 6th cycle was found in 6 of 7 pts (85%) with a median? P-173ng/ml. ALP value decreased in 6 of 7 pts (85%), with a median P of 63 U/L. At the 1st Ra223 infusion, 5 pts (72%) were receiving nonsteroidal anti-inflammatory drugs (NSAIDs) + opioid drugs for pain relief, 1 pt (14%) only NSAIDs, 1 pt (14%) only opioid analgesic. 6 pts (86%) reported a decrease pain intensity since the 3rd cycle, also confirmed after the last dose; 1 pt (14%) reported no change. Antalgic drug dose was reduced in 3 of them. Choline PET or bone scan performed 1 month after the end of treatment showed 2 PD (28%) and 3 SD (42%). 2 pts didn't undergo restaging because of rapid PD and death. In 4 of the 5 living pts the first SRE was observed after 2 months, in 1 of them after 1 month.

Conclusions: In our analysis, Ra223 proved to be well tolerated and effective in terms of pain control. No PSA response was detected while ALP levels significantly decreased.

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C - BREAST CANCER

C1* Trends in the choice of first line treatment for hormone - responsive (HR+), human epidermal growth factor receptor - 2 negative (HER2-) metastatic breast cancer (MBC) patients (pts): results of a multicentric Italian observational study

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Background: Most of HR+ MBC pts are treated with both hormonal therapy (HT) and chemotherapy (CT) during the course of their disease. International guidelines indicate that HT is the preferred first - line treatment option for these pts restricting the use of CT only to pts not responsive to HT or at risk of visceral crisis.Data from observational studies indicate that nearly 50% of this pts to receive CT as first - line treatment. The present study aimed to evaluate if this behaviour does change in recent years.

Methods: All consecutive MBC pts treated at 13 centers of GIM (Gruppo Italiano Mammella) with a first - line therapy (CT or HT with or without biological therapy) from 2000 to 2016 were registered. Pts were classified in four subgroups according to the biological characteristics of their primary tumor: Luminal A (ER and/or PgR+, HER2- and Ki67 $<$ 20%), Luminal B (ER and/or PgR+, HER2- and Ki67 $\geq$ 20%), HER2 + (immunohistochemistry score of 3+ or fluorescence in situ hybridization amplified regardless of HR) and Triple - Negative (ER and PgR and HER2 negative). For the present study, we selected only Luminal A and B pts treated with at last one line of HT or one line of CT. The choice between first - line HT or CT was performed by the treating physician on the basis of pts and disease characteristics. The type of first line treatment (HT or CT) was analyzed according to four different cohorts: 2000 - 2005; 2006 - 2010; 2011 - 2013; 2014 - 2016.

Results: 1152 pts with MBC were identified and 671 (249 Luminal A, 288 Luminal B, 184 HR+ with Ki67 unknown) were included in this analysis. 481 pts were excluded for the following reasons: HER2 + (183 pts), triple - negative (85 pts) and HER2 missing (213 pts). Overall, 244 pts (37%) and 409 (62%) received CT and HT as first line treatment, respectively. Six pts (0.9%) received concurrent CT and HT and in two pts (0.3%) treatment unknown. HT was the first line treatment in 60%; 60%; 62% and 71% of pts in the 2000 - 2005, 2006 - 2010, 2011 - 2013, 2014 - 2016 cohorts, respectively (p for trend: 0.05).

Conclusions: Our results indicate an increase in the use of HT as first line treatment in HR+ MBC pts. However the percentage of pts receiving CT as first line treatment is still above that expected from adherence to the guidelines. Results from additional analysis are planned to be presented at the meeting.

C2* A Multigene Score based on gene-expression profiling as a prognostic tool in women with early stage, hormone receptor-positive/Her2-negative breast cancer

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Background: In clinical practice chemotherapy (CT) and endocrine therapy (ET) are administered sequentially in early hormone-receptor (HR) positive breast cancer (BC) patients, but the optimal timing (concurrent vs sequential) is yet to be defined. GIM 10-CONSENT is an ongoing, multicentre trial (NCT02918084) randomizing early postmenopausal BC patients to receive ET concurrently or sequentially to CT. Here we present a gene-expression profiling substudy, aiming to identify genomic signatures to stratify patients considered to be at intermediate risk of relapse according to clinical and pathological characteristics (stage I-II, G2, HER2-).

Objectives: To develop a Multigene Score (MGS) to better predict prognosis of patients with stage I-II, G2, HR+ BC.

Materials and methods: MGS was developed in silico from gene expression microarray dataset of a retrospective cohort of 948 BC cases. Training set of 583 cases was used to identify genes associated with estrogen receptor expression and cell proliferation. These genes were integrated in the MGS through Cox regression analysis and applied on a test set of 314 HR+/G2/HER2- cases with known follow-up. Kaplan-Meier curves were calculated for distant-relapse free survival. 614 patients have been enrolled so far in the GIM10 trial, and 112 samples from patients with both high-risk (G3) and intermediate-risk (G2) disease have been analysed (through RNA amplification with RT-qPCR), in order to prospectively validate the MGS.

Results: In the retrospective cohort, 66 out of 314 patients relapsed after diagnosis. 52 out of 66 cases (78,8%) were classified as high-genomic risk according to MGS, while 14 (21,2%) were classified as low-genomic risk. Among the 248 patients who did not relapsed, 146 (58,9%) were classified as low-genomic risk, and 102 (41,9%) as high-genomic risk. The prospective cohort comprises 43 patients with G3 and 69 patients with G2 disease. 29 out of 69 (42%) intermediate-risk (G2) cases were classified as high-genomic risk according to MGS. Follow-up is ongoing for the prospective validation of this classification, with the final results being available by the end of 2021.

Conclusions: We successfully stratified HR+/Her2- BC patients at intermediate-risk into two different prognostic subgroups according to a new MGS. Although this signature validation is still in progress, our data show gene-expression profiling can predict outcome in the adjuvant setting. Prospective validation of our data is ongoing.

C3 Biological and clinical effects of abemaciclib in a phase 2 neoadjuvant study for postmenopausal patients with HR+/HER2- breast cancer

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Background: Abemaciclib is a potent oral CDK4- and 6-inhibitor. NeoMONARCH (NCT02441946) was a randomized, multicenter, open-label phase 2 neoadjuvant study in postmenopausal women with early-stage HR+/HER2- breast cancer (BC).

Materials (patients) and methods: 224 patients stratified by progesterone receptor status and tumor size were randomized 1:1:1 to receive abemaciclib (150mg Q12h) plus anastrozole (1mg QD), abemaciclib monotherapy, or anastrozole monotherapy for 2 weeks, then all patients received abemaciclib plus anastrozole for 14 weeks. Abemaciclib-treated patients received prophylactic loperamide during the first 28 days of therapy, then at the discretion of the investigator. The primary objective was to assess the change from baseline Ki-67 expression after 2 weeks of therapy with abemaciclib plus anastrozole vs abemaciclib monotherapy and anastrozole monotherapy. Clinical activity and safety were evaluated as secondary objectives. The statistical design provided 80% power to detect superiority of the combination vs anastrozole, at a 1-sided alpha level of 0.1.

Results: 161/223 treated patients were evaluable for the primary endpoint. Abemaciclib plus anastrozole (n = 56) as well as in monotherapy (n = 51) significantly reduced Ki-67 expression vs anastrozole monotherapy (n = 54) at week 2 based on geometric mean change and complete cell cycle arrest (Ki-67$<$2.7%). Change in proliferation gene mRNAs at 2 weeks (Modaplex) correlated with the change in Ki-67 expression. Objective response rate was 54.7% (n = 106) for patients who completed the treatment with abemaciclib and anastrozole. Most common adverse events were diarrhea, constipation, nausea and fatigue.

Conclusion: Monotherapy with abemaciclib as well as abemaciclib plus anastrazole showed significantly higher biological activity compared with anastrozole alone and the study's primary endpoint was met. The majority of patients experienced an objective response. No new safety signals for abemaciclib when combined with anastrozole were detected. These data support continued evaluation of abemaciclib in early-stage BC.

C4 Bone health management in early breast cancer patients: an Italian Osteoncology Center experience

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Background: Bone health evaluation is important for the optimal management of early stage breast cancer (BC) both in post and pre-menopausal setting. Adjuvant endocrine

therapy (ET), including luteinizing hormone-releasing hormone (LHRH) analogues with tamoxifen (TAM) and aromatase inhibitors (AI), may affect bone health resulting in a reduction of the bone mineral density (BMD), leading to an increased risk of bone fractures. The objective of this observational study performed at an Italian Osteoncology Center was to evaluate the prevalence of vertebral fractures in pre and post women with BC treated with adjuvant ET.

Materials and methods: Data on patients (pts) with early BC were collected from 2011 to 2016 in a single Institution. We investigated the prevalence of vertebral fractures in pre and post pts treated with ET and other potential independent risk factors associated to bone fractures. To evaluate association with bone fractures and clinical factors, univariate logistic models were carried out. P-value of less than 0.05 was considered significant.

Results: A total of 1,165 women with early pre and post-menopausal BC were evaluated; for 702 (60.2%) pts treated with ET was available a X-Ray of the spine and they were included in the analysis. The median age was 61 year-old (31-86 y). A total of 124 were pre-menopausal and 578 were post-menopausal pts. Frequency of bone fractures was 17.6% in post-menopausal and, among them, the major risk of bone fractures was associated with AI treatment (OR:4.37, p:0.005); in pre-menopausal pts bone fractures incidence was 6.4% and the major risk was associated to LHRH+AI treatment (OR:2.18, p:0.307). Higher risk of bone fractures was associated with presence of back-pain (OR:1.81, p:0.006), a lower BMD (OR:2.91, p: < 0.001 for pts with BMD=2.5) and lower level of Vitamin D (OR:2.06, p:0.030 for pts with =10) in univariate analysis. Further analysis are ongoing.

Conclusions: This Italian experience confirms the importance of bone health evaluation in order to prevent bone fractures in the management of pre and post-menopausal early BC treated with ET.

C5 Efficacy of pertuzumab in combination with trastuzumab and a taxane in in first line treatment for metastatic breast cancer (MBC): a multicenter retrospective observational study

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Background: Pertuzumab (P), Trastuzumab (T) and Docetaxel (D) is standard first-line treatment in patients (pts) with HER2 + metastatic breast cancer (MBC). This multicenter retrospetive observational study was performed to evaluate the activity of P and T in combination with D or Paclitaxel (Tx) in real world HER2 + MBC pts.

Methods: We identified HER2 + MBC pts treated with P, T and D or Tx optionally followed by P, T and endocrine therapy maintenance (ETm) in hormone positive (HR+) MBC, in 17 Italian cancer centres between 09/2012 and 04/2017. Overall Survival (OS) and Progression Free Survival (PFS) were calculated by the Kaplan-Meier product-limit method. Log-rank test was used to assess differences between subgroups.

Results: 239 pts were included in our analysis. Pts characteristics: median age 53 years (range 29-80); PS 0 in 161 (67%) pts and PS 1 in 66 (28%); 138 (58%) had visceral metastases (mts), 32 (13%) only bone mts and 47 (20%) brain mts, 165 (69%) were ER/PgR +. 103 pts (43%) were metastatic at diagnosis; 183 (77) were treated with D while 56 (23%) with Tx. 229 (96) pts was evaluable for response. The ORR was 79% (CI 95% 74-84), RC 18% and RP 61%, only 10 (4%) had PD. To date, of the 89 pts treated with ETm, 25% had a further improvement of response (11 pts had RC). At median follow-up of 18 months (mo) (range 4-52), median PFS was 25 mo (CI 95%, 19-32) and 2-yrs OS was 82%. No differences in PFS were found for age ($p = 0.62$), PS ($p = 0.18$), receptor status ($p = 0.26$), visceral mts ($p = 0.32$) and chemotherapy (cht) type ($p = 0.33$), whereas number of mts site (1 vs > 1) affected PFS (29 vs 17 mo, $p = 0.01$). Moreover median PFS in naïve pts and in pts pretreated with only cht was 32 mo (CI 95% 24-36) and 22 mo (CI 95%, 12-32) respectively, whereas in pts pretreated with T it was 13 mo (CI 95%, 8-18 p 0.001). In HR+ pts ETm together with P and T had an impact on mPFS (29 vs 15 mo, $p = 0.0007$) . In pts with 2+ by IHC, ETm has determined a longer survival than no ETm (CI 95%, 27 vs 12 mo, $p = 0.009$); in HER 3 + pts no differences ($p = 0.51$). In HR neg pts Tx treatment results in a higher PFS than D (1 yrs PFS 77,8 vs 58, $p = 0.059$).

Conclusions: Our analysis confirms, in real world HER2 MBC pts, the efficacy of P, T and a taxane combination in first line treatment; in this population PFS was shorter in pts pretreated with T. ET maintenance in association with P and T in HR+ pts improved PFS. Data collection is ongoing and update results will be presented.

C6 The Pregnancy and Fertility (PREFER) study: a prospective cohort study on fertility-preserving (FP) strategies in young early breast cancer (EBC) patients (pts)

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Background: Premature ovarian failure and subsequent infertility are possible long-term side effects of chemotherapy (CT) in young EBC pts. Limited data are available on the number of pts who consider FP strategies and on the reasons for refusal of these procedures. To address the significant challenges related to fertility issues, the PREFER study was developed as a national comprehensive program aiming to optimize care and improve knowledge around this topic.

Methods: This is a prospective cohort study ongoing across several Italian centers affiliated to the GIM (Gruppo Italiano Mammella) study group. Oncologists offer the available FP strategies to young EBC pts undergoing (neo)adjuvant CT: oocyte cryopreservation (OC), ovarian tissue cryopreservation (OTC) and LHRH analogue (LHRHa) during CT. Eligible pts are premenopausal, ≤ 45 years, no previously exposed to CT and/or radiotherapy. Primary objective is to obtain data about preferences and choices of young EBC pts on the FP strategies. Secondary objectives are to evaluate the success and safety of FP strategies, hormonal changes during CT and survival outcomes. The present analysis reports preliminary results of the study including pts enrolled at the coordinating center from November 2012 to May 2017.

Results: A total of 131 EBC pts were enrolled; median age was 38.9 years (24.8-45.34). Nine pts (6.87%) refused all FP options. Reasons for refusal were no interest in fertility preservation (5 pts), previous pregnancy (3 pts), no interest in having children (1 pts). LHRHa was accepted by 120 pts (91.6%) and 27 pts (20.6%) accepted gynecologic counseling. Among these pts, 10 (7.6%) accepted OC or OTC. Main reason for refusal of cryopreservation procedures was fear of delaying cancer treatment (3 pts). No complications were observed among women who underwent OC or OTC. Median number of mature oocytes yielded and cryopreserved was 8.5 (4-13). A patient had a spontaneous pregnancy following adjuvant treatment.

Conclusions: Despite the great importance of fertility issues in young EBC pts, a minority of them (7.6%) require to access cryopreservation procedures. This is crucial information from a public health perspective and for resource allocation.

C7 Evaluation of stromal tumour-infiltrating lymphocytes (TILs) in breast cancer by Dynamic contrast−enhanced magnetic resonance (DCE-MR) imaging

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Introduction: Dynamic contrast−enhanced magnetic resonance (DCE-MR) imaging of the breast is increasingly used as an adjunct to mammography and ultrasonography (US) to improve the detection and characterization of primary and recurrent breast cancers. Correlation between morphological features, DCE-MRI and prognostic factors of breast cancer (BC), including tumor size, axillary lymph node status, histological grade, presence of vascular invasion and necrosis, ER, PR, c-erbB-2 status and Ki-67, has been previously analysed. The aim of this study was to analyse the relation between DCE-kinetic parameters of BC and the presence of stromal tumour-infiltrating lymphocytes (TILs).

Patients and methods: Patients with newly diagnosed breast cancer who underwent DCE-MRI examination within two weeks prior to surgery from January 2013 to January 2017 were selected. Patients who underwent MR imaging beyond two weeks prior to surgery or previous neoadjuvant chemotherapy (NAC), with BC histotype different from Invasive Ductal or Lobular Ccexcluded. TILs was evaluated according to the International TILs Working Group 2014 recommendation. TILs was reported as a continuous variable. Based on the TILs Score proposed by Adam et al., patients have been classified into four subgroups based on the range of TILs percentage. MR imaging was performed with a 1.5 imager ((Philips Achieva, software v. 2.6) and the post-contrast kinetic sequences were analyzed.

Results: 109 patients have been analysed. 53% tumors were poorly differentiated (G3). 25 (23%) Luminal A, 46 (42%) Luminal B/HER2 negative, 20 (18%) Luminal B/HER2 positive, 7 (6%) HER2 and 11(10%) TN subtype. Luminal tumors were associated with high values of Wash-in rate and Absolute Maximum Enhancement. On the other hand, HER2 + and TNBC tumors are characterized by slower or reduced Wash-in rate and lower values of Absolute Maximum Enhancement. Time-to-peak in TNBC and HER2 + have significantly higher values than Luminals. Brevity of Enhancement, analysed in type III curve, related to cluttered vascularization, was statistically correlated to high percentage of TILs ($p = 0.02$). Presence of TILs correlates with Area under curve higher than 500.000 and low values of Absolute Max Enhancement.

Conclusion: At the best of our knowledge, this is the first study investigating whether MRI kinetic imaging can predict the presence and the percentage of TILs in BC tissue.

C8 Brain metastases and ado-trastuzumab emtansine (TDM-1) treatment in HER2 positive metastatic patients: an Italian multicenter analysis

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Background: Ado-trastuzumab emtansine (T-DM1) is a drug-antibody conjugate whose activity has been confirmed in HER2+ advanced breast cancer (BC) patients by the phase 3 EMILIA trial. Within the 991 patients enrolled in this trial, about 10% were affected with brain metastases (BM); in this subgroup, safety and efficacy of T-DM1 were confirmed although without any PFS improvement.

Patients and methods: In an Italian, multicenter, retrospective analysis involving 303 patients with advanced BC treated with T-DM1, we analyzed 87 patients with BM (BM-group). The study wanted to evaluate the efficacy of T-DM1 on BM; furthermore we compared BM-group with the remaining 216 patients without BM (nBM-group) in terms of outcome disease. MRI was used as assessment imaging. The number of extracranial metastatic sites was 1 for 10 patients (11.5%) in the BM-group and 74 (34.3%) in the nBM-group; 2 for 23 and 93; 3 for 25 and 38; 4 or more for 29 and 11 respectively. In the BM-group, 5 patients (5.7%) had received surgery alone as local treatment for brain metastases, 13 surgery plus stereotactic radio-surgery (SRS), 4 surgery plus whole-brain radiotherapy (WBRT), 23 SRS alone, 40 WBRT alone and 2 WBRT followed by SRS. Twenty-eight patients (32.9%) and 89 (42.4%) in the BM-group and nBM-group, respectively, received T-DM1 as second line, 24 and 49 as third line and 33 and 72 as fourth line. Mean number of cycles was 6 in both groups.

Results: Among BM-group, 53 patients (60.9%) were evaluable for response. Two (3.8%) obtained brain complete response (CR), 14 (26.4%) partial response (PR) and 13 (24.5%) stable disease (SD) [brain disease control rate: 54.7%]; 24 progressed (PD) during T-DM1. Regarding extracranial metastases, overall response rate was 35.1% in the BM-group and 38.3% in the nBM-group; 6 months-clinical benefit was 50.6% and 52.3%, respectively. Median PFS was 7 months in the BM-group and 8 months in the nBM-group; when T-DM1 was given as second line, median PFS was 5 months in the BM-group and 11 months in nBM-group (p = 0.01) while as third line, in which 60% of patients received lapatinib/capacitabine before TDM1, median PFS was 12 and 13 months (p=NS), respectively.

Conclusions: T-DM1 showed a good activity on BM in BC patients. A better outcome was shown in patients previously treated with lapatinib. The identification of clinical and biological prognostic factors could be needed to better select more responder patients with BM to T-DM1.

C9 A propensity score analysis exploring the impact of adjuvant chemotherapy (aCT) in 739 patients (pts) affected by early stage pure Invasive Lobular breast Carcinoma (ILC)

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Background: In clinical practice, pts undergone surgery for early breast cancer are assigned to receive aCT according to international guidelines based upon evidences deriving from the context of trials where the most of pts included are affected by invasive ductal carcinoma. Given the lack of prospective data for the restricted context of ILC, the magnitude of the benefit of aCT for this histotype is still not sizable. Thus, the aim of this analysis was to explore the effect of aCT in a multi-center series of early stage pure ILC.

Methods: Clinical-pathological data of consecutive pts affected by resected pure ILC, diagnosed at 3 Italian Institutes, were correlated with disease-free and overall survival (DFS/OS) using a Cox model. Follow-up was analyzed and reported according to *Shuster et al.* The hazard ratio (HR) and the 95% Confidence interval (95% CI) were estimated according to a Cox model. A propensity score analysis was performed to investigate the prognostic impact of aCT. Kaplan-Meier curves were compared with Log-Rank analysis.

Results: Data from 739 pts were gathered (median age 57 years (yrs); Luminal/Triple-Negative/HER2 positive: 98%/1.6%/0.4%). At a median follow-up of 78 months, 5-/10-yrs DFS and OS were 79.4%/66.0% and 91.4%/76.5%, respectively. At the multivariate analysis, tumor-size according to TNM (HR 1.34, 95% CI 1.04-1.72, $p = 0.025$) and lymph-node status (HR 2.39, 95% CI 1.47-3.89, $p < 0.0001$) were independent predictors for DFS. Tumor-size (HR 1.87, 95% CI 0.99-3.54, $p = 0.05$), lymph-node status (HR 3.24, 95% CI 1.69-6.22, $p < 0.0001$), Ki67 (HR 2.48, 95% CI 0.95-6.42, $p = 0.06$), and age (HR 2.23, 95% CI 1.16-4.30, $p = 0.016$) were independent predictors for OS. A significant prognostic effect of aCT upon OS was found after adjusting for independent factors with the propensity score analysis, as shown:

Table: C9

Outcome	Category	5-yrs (%)	10-yrs (%)	Log-Rank
DFS	**aCT**	84.3	75.6	$p = 0.33$
	No aCT	84.7	64.0	
OS	**aCT**	94.3	87.4	$p = 0.002$
	No aCT	88.7	64.5	

Particularly, aCT significantly prolongs DFS in pts with tumor-size according to TNM >1 ($p = 0.04$). For OS, the benefit of aCT was significant in pts with tumor-size >1 ($p = 0.003$), lymph-node positive ($p = 0.02$), Ki67 >4% ($p = 0.01$) and grading >1 ($p = 0.01$).

Conclusions: Despite the retrospective design of this study, the propensity score analysis indicates that pts with pure ILC may significantly benefit from aCT in terms of long-term survival, particularly for more aggressive and larger tumors.

C10 Neutrophil-to-lymphocyte and lymphocyte-to-monocyte ratios in breast cancer

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Background: Immunity plays a central role in cancer progression and prognosis. A high neutrophil-to-lymphocyte ratio (NLR) or a low lymphocyte-to-monocyte ratio (LMR) have a negative impact on outcome and have been associated respectively with systemic inflammation and immune suppression. Aim of this study is to investigate the interaction between the immune system and breast cancer (BC) through NLR and LMR.

Methods: This retrospective study analyzed a consecutive cohort of 657 patients (pts) with a diagnosis of pT1 BC (N =), without restrictions regarding lymph node status (T1BC), or metastatic BC (MBC) (N=) treated between 2004 and 2017 at the Department of Oncology of Udine (Italy). Differences in terms of NLR and LMR among the two cohorts and between clinico-pathological characteristics in the T1BC subgroup were explored through the Kruskal-Wallis test. The prognostic impact in terms of OS in the T1BC population was investigated through uni- and multivariate Cox regression.

Results: Both NLR and LMR distributions were significantly different among the T1BC and MBC cohorts. In particular, pts with T1BC had a higher median LMR (3.9 vs 2.9; P = 0.0001) and lower NLR (2 vs 2.7; P = 0.0001). When stratifying T1BC and MBC cohorts according to molecular profile, pts with luminal B-like subtype showed significant differences in terms of both LMR (4.2 vs 3; P = 0.0001) and NLR (2 vs 2.5; P = 0.0001). In triple negative subtype, the difference between TB1C and MBC was observed for NLR (1.9 vs 3.2; P = 0.0272) only. No differences between TB1C and MBC were highlighted for the other subtypes. When focusing on the clinico-pathological characteristics of the T1BC cohort, LMR was associated with progesterone receptor (PR) expression (P = 0.0261) and marginally with the estrogen receptor (ER) expression, while NLR with tumor diameter (P = 0.0240) and marginally with grading. Furthermore, among T1BC pts, NLR had no prognostic impact in terms of OS, while LMR was associated with a better outcome also when a correction for ER, PR and HER2 status was applied (HR 0.44, 95%CI 0.28 - 0.71, P = 0.001).

Conclusions: These results suggest a role for systemic inflammation and immune-suppression in breast cancer, especially in the triple negative and luminal B-like subtypes.

C11 Updated results from MONALEESA-2, a phase 3 trial of first-line ribociclib + letrozole in hormone receptor-positive (HR+), HER2-negative (HER2−) advanced breast cancer (ABC)

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Background: In MONALEESA-2 (NCT01958021), patients (pts) with HR+, HER2− ABC who received first-line ribociclib (RIBO; cyclin-dependent kinase 4/6 inhibitor) + letrozole (LET) had a significant improvement in progression-free survival (PFS) compared with placebo (PBO) + LET at the first analysis (Hortobagyi G, et al. N Engl J Med. 2016;375(18):1738-1748). Here we report updated efficacy and safety data from MONALEESA-2, with an additional 11 months follow-up (median follow-up duration of 26.4 months).

Methods: MONALEESA-2 is a randomized (1:1) phase 3 trial evaluating RIBO (600 mg/day, 3-weeks-on/1-week-off) + LET (2.5 mg/day, continuous) vs PBO + LET in postmenopausal women with HR+, HER2− ABC with no prior therapy for advanced disease. The primary endpoint was locally assessed PFS. Secondary endpoints included overall survival (OS; key), overall response rate (ORR), clinical benefit rate (CBR), and safety.

Results: 668 pts were enrolled (RIBO + LET: 334; PBO + LET: 334). The updated PFS analysis confirmed treatment benefit from the combination of RIBO + LET (hazard ratio = 0.568; 95% CI: 0.457-0.704; $P = 9.63x10^{-8}$). Median PFS with RIBO + LET was 25.3 months (95% CI: 23.0-30.3) vs 16.0 months (95% CI: 13.4-18.2) with PBO + LET. Treatment benefit was consistent across all pt subgroups, including age, prior therapies, de novo ABC, and visceral metastasis. OS results remained immature. Common grade 3/4 adverse events (=15% of pts; RIBO + LET vs PBO + LET) included decreased neutrophils (62.6% vs 1.5%), decreased leukocytes (36.8% vs 1.5%), and decreased lymphocytes (16.2% vs 3.9%).

Conclusions: Despite a long median PFS with PBO + LET, the updated analyses confirmed that first-line treatment with RIBO + LET significantly prolongs PFS in postmenopausal women with HR+, HER2− ABC. The safety profile of RIBO + LET remains manageable.

C12 BRCA related breast cancer and sporadic tumors: same prognosis or survivorship bias?

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Germline BRCA mutations are found in about 5% of all breast cancers(BCs). They are inherited in autosomal-dominant fashion conferring BC increased risk up to 80% by age 70. Literature data are controversial about BC prognosis in BRCA carriers respect sporadic tumors patients. Aims of this study were to compare outcome among BRCA wild type(wt) and BRCA mutated BC and to investigate relationship between BRCA mutations and main standardized prognostic factors.

Pathologic and clinical features were recorded in all consecutive women with BC referred to perform genetic counseling, which resulted eligible for BRCA genetic testing between 1996 and 2015 at our Institution. Differences within the groups were analyzed using Chi Square Test.Cox univariate proportional hazard regression model was used to evaluate prognostic factors on relapse-free (RFS) and overall survival (OS).Level of significance p value was set at 0.05.

A total of 485 patients were included, 160(32.9%) hosted BRCA pathogenic mutation: 84(52.5%) BRCA1, 76(47.5%) BRCA2. At diagnosis, median age was 45.9 years (range18.3-84.4) and 254 patients (52.3%) developed BC earlier. BRCA related tumors had higher Ki67 and grading than wt one ($p = 0.001$), BRCA1 had a significantly strong association with triple negative phenotype ($p < 0.0001$) and stage II-III ($p = 0.03$). No variable showed prognostic impact on RFS and OS in BRCA1 tumors. In BRCA2 group, small tumor size and negative node status were confirmed as prognostic factor of RFS ($p = 0.037$, $p = 0.021$ respectively) and OS ($p = 0.001$, $p = 0.006$, respectively). There were no differences in RFS between wt patients and BRCA1 and BRCA2 carriers ($p = 0.96$ and $p = 0.91$, respectively) and OS between BRCA1 carriers and wt at 10 years ($p = 0.44$) from diagnosis or later ($p = 0.38$). Differently, in the first 10 years BRCA2 tumors reported worse prognostic trend ($p = 0.044$), which was lost later ($p = 0.10$).

BRCA2 tumors had more frequent node involvement and higher stage than others maybe because younger age at diagnosis, outside current mammographic screening range. Common prognostic factors do not have significant impact in BRCA1 patients. Comparing BRCA1/2 and wt patients prognosis no significant differences emerged because some kind of compensation between the high mortality in the first years in TNBC and the higher mortality after the first 10 years post diagnosis in luminal. It is like each prognostic factor would be "mitigated" by extended follow-up, survivorship bias and received specific treatments for subtype.

C13 Relevance of immunohistochemical (IHC) surrogate reclassification of pT1 breast cancer in luminal-like subtypes: a 15-years long-term observational retrospective study

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Background: Molecular BC subtypes may improve risk assessment in order to individualize therapeutic strategies. However, gene expression tests are often too expensive and not available in real-life clinical practice. The aim of study was to discover whether IHC surrogate reclassification of BC into molecular subtypes provides precise information regarding outcome compared to conventional prognostic factors.

Methods: We reviewed the records of 511 patients with pT1 BC treated at single Oncology Unit between1995 to 2010. We reclassified tumors of patients into five IHC surrogate intrinsic tumor subtypes: Luminal A-like, Luminal B-like HER2-, Luminal B-like HER2+, HER2-enriched, TN. Primary end-points was to evaluate at 15-years of follow-up (FU) distant metastases free survival (DMFS), disease free survival (DFS) for each subgroup of Luminal-like tumors.

Results: On overall population, the 15-ys DMFS rate was 95% for Luminal A−like, 65% for luminal B−like HER2-, and 41% for Luminal B−like HER2+ tumors ($p = 0.036$); DFS was 78% for Luminal A−like, 57% for Luminal B−like HER2-, and 18% for Luminal B−like HER2 + ($p = 0.006$). In the cohort of 440 Luminal-like tumors, the Kaplan-Mayer curves showed that disease recurrences occurred mostly in luminal B-like BC patients later after five years of FU. At a long-term FU, low expression of PRs ($\leq 20\%$) was associated with recurrence events both in terms of DMFS (68% vs 87%; $p = 0.018$) and DFS (50% vs 73%; $p = 0.025$). The same trend resulted for HER2 overexpression with a DMFS of 41% vs 74% ($p = 0.014$) and a DFS of 14% vs 60% ($p = 0.002$). In BC tumors with Ki-67 rate = 20%, the analysis showed a significant difference only for DMFS rate at 15-years (63% vs 86%, $p = 0.042$). Multivariate analysis confirmed that the main independent prognostic factors involved for delayed distant recurrences were low expression of PR (HR = 2.27; $p = 0.04$) and HER2 overexpressed (HR = 2.46; $p = 0.03$). Only HER2 overexpression was the independent prognostic factor (HR = 2.55; $p = 0.003$) for DFS.

Conclusion: Despite the notable limitation of retrospective analysis, our results confirmed the utility in clinical practice of IHC-surrogate reclassification of BC. In patients with pT1 Luminal-like tumors, low PR expression, HER2 overexpression and high Ki67 rate are the main prognostic factors for long-term outcome. Finally, our long-term results seem to suggest the appropriateness of an extend follow-up for women with Luminal B-like breast cancer subtype.

C14 From the CLEOPATRA study to real life: preliminary results from the G.O.N.O. SUPER trial

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Background: Approximately 20% of breast cancers (BC) are HER-2+. Trastuzumab (T) has dramatically changed the outcome of HER2+ BC patients (pts), both in early and in advanced settings. Pertuzumab (P), combined with T and taxanes, significantly improved progression free survival (PFS) and overall survival (OS) in the phase III CLEOPATRA study. In order to verify the results of the trial in unselected pts, we performed a multicenter, retrospective-prospective, observational study, in HER-2+ metastatic BC (MBC) pts.

Methods: We analyze the outcome of all HER-2+ MBC pts treated with P+T and taxanes, as first line therapy since the availability of P in Italy, at 14 general and university hospitals.

Results: Up to May 10th data from 180 HER-2+ MBC pts were recorded. Main pts' characteristics were: median (M) age 55 y (28-79), M ECOG PS 0 (0-2), ER/PgR positive 125 pts (69.4%), 45 pts (25%) received neo/adjuvant chemotherapy (CT) + T and 62 pts (34.4%) adjuvant endocrine therapy. Most common metastatic sites: bone 106 pts (56.3%), liver 79 pts (43.8%), lung 48 pts (26.6%), soft tissues 106 pts (56.3%). Sixty-one pts (33.8%) had bone and/or soft tissues disease only; 91 pts (50.5%) had metastatic disease on presentation. M number of metastatic sites was 2 (1-8). 118 pts (65.5%) and 62 pts (34.4%) received docetaxel (D) and paclitaxel (P) respectively. M number of CT cycles was 6 for both drugs (D range 2-12; P range 1-18). Up to now 18 pts are still on CT and 115 on maintenance; ORR is 76.1% (40 and 97 pts obtained CR and PR respectively), 7 pts experienced PD during CT; 85 pts (47.2%) received endocrine therapy during maintenance. M PFS is 14.9 months (0.2+ - 42+). Among hematological toxicities leucopenia (any grade) was recorded in 37 pts (20.5%), neutropenia (any grade) in 42 pts (23.3%) and febrile neutropenia in 7 pts (3.8%). Two pts interrupted CT due to symptomatic drop of left ventricular ejection fraction (LVEF); 9 pts interrupted maintenance P, 8 due to drop in LVEF and 1 due to rash. Diarrhea, nail changes, nausea, stomatitis, alopecia, rash, neurotoxicity and arthro-myalgia were the most common non-hematological toxicities.

Conclusions: Our preliminary results highlight the activity and safety of the combination of CT plus P and T in unselected HER2+ MBC patients. The study is ongoing and updated results will be presented.

C15 Time to surgery after neoadjuvant chemotherapy for early breast cancer

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Background: In early breast cancer (BC) patients, a delay between surgery and adjuvant chemotherapy (CT) has been associated with worse outcome, but little is known about timing-related consequences in the neoadjuvant setting. The aim of this study was to evaluate the impact of the interval between the end of neoadjuvant CT and surgery (CTTS) on relapse free survival (RFS) and overall survival (OS).

Patients and methods: This study retrospectively analyzed a series of 469 consecutive BC patients receiving neoadjuvant CT at the Department of Oncology of Udine (n = 222) and at the Istituto Nazionale Tumori of Milan (n = 247), between 2004 and 2015. CTTS was defined as the time between the last CT administration and surgery. The impact on outcome measures was investigated through Cox regression.

Results: The study population consisted of the following subtypes: Luminal-like (53.69%), HER2-positive (29.26%) and triple negative (17.05%). Median follow-up was 55.07 months (mo). Estimated RFS at 24 and 60 mo was 83.6% and 65.8%. Estimated OS at 24 and 60 mo was 96.4% and 88.2%, respectively. Median CTTS was 1.08 mo (25%-75% range: 0.89 - 1.2 mo). No statistically significant differences were observed in terms of RFS and OS between CTTS > 1 vs < 1 mo (HR 1.28, 95%CI 0.89-1.85; HR 1.18, 95%CI 0.72-1.98, respectively). On multivariate analysis, grade 3 and Ki67 > =20% were associated with worse RFS (HR 2.09, 95%CI 1.31-3.33; HR 2.77, 95%CI 1.30-5.91, respectively); additionally, a pathological complete response was associated with better RFS (HR 0.23, 95%CI 0.09-0.56). On the other hand, tumor grade and Ki67 were marginally associated with OS. In the subgroup analysis for CTTS, no statistically significant differences were observed after stratification for the main clinico-pathological features. Of interest, a trend for interaction was observed in favor of patients with N3 nodal status who underwent surgery within 1 month.

Conclusions: This study explored the impact on RFS and OS of the interval between the end of neoadjuvant CT and surgery. Despite the exploratory purpose of the analysis, the results suggest that an interval greater than 1 month was not significantly detrimental in terms of both RFS and OS. Further investigations are needed in high risk patients (eg. patients with N3 lymph node involvement).

C16 Metronomic chemotherapy (mCHT) in HER2-ve advanced breast cancer (ABC) patients (pts): old drugs, new results. The multicenter VICTOR-6 study

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Introduction: mCHT is the minimum biologically effective dose of a chemotherapeutic agent, given at regular dosing regimen with no prolonged drug free interval, that leads to anti-tumor activity. Old regimens included Cyclophosphamide-Methotrexate (CM), whereas in the last years new regimens, such as Vinorelbine (VRL) and Capecitabine (CAPE)-based have been developed. Aim of this observational retrospective ongoing study is to describe the use of mCHT in ABC pts across 5 years and the clinical characteristics of the pts together with efficacy of old (CM-like) vs new (VRL/CAPE-based) metronomic regimens.

Methods: We retrospectively identified from clinical records those HER2-ve ABC pts who have received any kind of mCHT in the years 2011-2015, alone, or in combination with a non-metronomic drug. Standard statistical approaches were used for describing the sample characteristics. Logistic and non proportional hazard analysis were used to identify factors associated with response, and time to treatment failure and survival, respectively. This preliminary analysis focuses on Response Rate (RR) and Disease Control Rate (DCR).

Results: From June 2011 to December 2015, 431 pts have been identified till now and 404 are fully evaluable. Median age at mCHT start was 67 years. 80% were HR+ and 68.2% had visceral disease. 113 pts (27.9%) received CM, 182 (45%) VRL-based and 111 (27.4%) mCAPE-based regimens. mCHT use increased over the time from 17% (2011) to 24.6% (2015). Overall Response Rate (ORR) was 26.6%, 14.2% in the CM group and 31.4% in the VRL/CAPE group and 33.3% in the VRL one. Median time to mCHT failure was 5.6 months (5.2-6.2). Median OS was 21.8 months (18.1 – 24.6). TTF and OS according to the type of mCHT is detailed in Table 1.

Table: C16

	ORR, n/N (%)	DCR, n/N (%)	TTF (range)	OS (range)
CM	16/113 (14.2%)	76/113 (67.2%)	4.8 (4.1-5.8)	18.9 (14.1-26.6)
CAPE-based	32/111 (28.8%)	74/111 (66.6%)	5.8 (4.8-7.0)	21.8 16.6-29.4)
VRL-based	60/182 (33.0%)	149/182 (81.9%)	6.2 (5.5-7.1)	22.5 (17.4-27.8)

At univariate analysis, Hazard Ratio for Time to mCHT Failure of new regimens (CAPE- and VRL-based) in comparison to old ones (CM) was 0.77 (95%CI: 0.61-0.96, p = 0.02). Multivariate analysis showed similar results: HR:0.81 (95%CI: 0.63-1.03; p = 0.09).

Conclusion: The use of mCHT in the treatment of HER2-ve ABC pts has deeply changed across the last 5 years, new metronomic regimens have demonstrated an ORR comparable to that produced by standard regimens with a low incidence of severe side effects.

C17 The HERBA trial: a retrospective study on patients (pts) with HER2-positive (HER2+ve) breast cancer (BC) and brain metastases (BMs)

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Background: Approximatively 25-45% of pts with HER2+ve BC will develop BMs during the course of the disease. The management of BMs from HER2+ve BC is based on a multi-modal approach including symptomatic therapy, stereotactic radiotherapy (SRT), whole brain radiotherapy (WBRT), surgery and systemic therapy, but there is not a standardized treatment. The aim of this study is to evaluate treatment and outcome of a large real-life cohort of HER2+ve BC pts with BMs.

Patients and methods: Data of 154 HER2+ve BC pts diagnosed with BMs from 1st January 2005 to 31st December 2014 were retrospectively collected from 14 Italian institutions. Pts were divided into 2 cohorts according to the year of diagnosis of BMs, as it follows: period A (between 2005 and 2009) and period B (between 2010 and 2014). Survival data were analyzed by Kaplan-Meier curve and Log-rank test was used for comparison.

Results: 47 pts (31%) had only 1 BM, 37 pts (25%) had 2-3 BMs, and 70 pts (44%) had > 3 BMs. 74% of pts developed BMs after other systemic metastases had diagnosed. 82 pts (53%) received WBRT, 35 pts (23%) received SRT, 26 pts (17%) received surgery, 126 pts (82%) received systemic therapy and 112 pts (73%) received anti-HER2

treatment. 63 and 91 pts were diagnosed with BMs in period A and B, respectively. No difference was observed in terms of local therapy between the 2 periods. There was an increased use of anti-HER2 treatment from period A to B (67% vs 73%), with a relative reduction in the trastuzumab use (48% vs 40%) associated with an increased use of lapatinib (19% vs 31%) and other anti-HER2 agents (0% vs 6%). Median OS from the diagnosis of BMs was 24.5 months, with no significant difference between pts diagnosed in period A (25.2 months) and those diagnosed in period B (21.5 months; $p = 0.42$). As expected, mOS was significantly shorter (14.1 vs 27. 4 months; $p = 0.03$) for pts with multiple BMs (>3) as compared with those with oligo-BMs (1-3). There was no significant difference in terms of mOS between pts with and those without previously diagnosed systemic metastases (23 vs 27 months; $p = 0.469$) and this data suggest that the occurrence of BMs is a predominant prognostic factor for HER2+ve BC pts.

Conclusions: The development of BMs negatively affect the prognosis of pts with HER2+ve mBC, with a mOS of about 24 months. Despite an improvement in the management of HER2+ve mBC over the last decade, the outcome of pts with BMs has not changed from 2005-2009 to 2010-2014.

C18 Strategy of monitoring metastatic breast cancer (M-MBC) in clinical practice: more or less intensive?

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Background: Optimal strategy of M-MBC has never been formally studied. There is no evidence of clinical benefit of intensive M-MBC. On the contrary, emotional harms due to fear of progression disease have been reported by patients during monitoring of the disease outcome. Aim of this study was to describe strategy of M-MBC in a real world scenario, identifying predictors of intensive M-MBC.

Methods: We conducted a retrospective analysis on a consecutive series of 382 women with MBC, treated from 2010 to 2016 at the Department of Oncology of the Academic Hospital of Udine, Italy. Demographic and clinico-pathological data observed during the first 3 lines of therapy were collected together with number of performed exams [tumor markers (TM) and imaging]. Multivariable analysis was performed to identify factors associated with intensive M-MBC (defined as 1 or more exams in a 3-month period).

Results: Median follow-up was 44 months (mo). Median Progression Free Survival (PFS) was 10 mo at 1st line (L), 5 mo at 2nd L, and 4 mo at 3rd L. Near 92% of cases performed baseline scan within 2 mo before starting therapy. At least one TM test was performed in a 1.9-, 1.5- and 1.2-month median period at 1st, 2nd and 3rd L, respectively. At least one second-level scan (TC/RM) was performed in a 2.8-, 2.4- and 3.2-month median period at 1st, 2nd and 3rd L, respectively. PET-TC was performed only in 31, 7 and 6 cases at 1st, 2nd and 3rd L, respectively. Factors associated with intensive M-MBC are summarized in the table. Marital status, region, employment, comorbidity, performance status, type of therapy, tumor burden were not associated with decision making. PFS was significantly worse in case of intensive M-MBC (HR 2.65, 95%CI 2.03-3.48).

Conclusion: TM testing and scans were frequently ordered in M-MBC, even outside clinical trial. Strategy seemed to be little influenced by clinico-pathological characteristics.

C19 Monitoring metastatic breast cancer (M-MBC) during treatment: a GIM (Gruppo Italiano Mammella) survey

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Background: With the lack of clear indications from international guidelines, the most appropriate strategy for M-MBC is perceived as one of the practice performance gaps in cancer care. M-MBC influences first and foremost patient's life and it strongly impacts on the use of resources both in terms of drugs and diagnostic exams. The aim of this survey is to disclose oncologists' approach on M-MBC, identifying areas of controversies, if any.

Methods: The analysis was conducted using an online survey under the umbrella of GIM. In particular, through the mailing list of GIM members, each survey recipient was invited to share his/her own method and to rate the importance of clinico-pathological features for M-MBC planning through a 0-100 scale. Chi-square tests, and Fisher exact tests were used as appropriate.

Results: A total of 256 (51%) recipients completed the survey. Most of them were specialists (78%) and around 50% had been involved in M-MBC for over 10 years. Respondents identified the possibility to avoid toxicity (42%) or unnecessary costs (34%), or an earlier PD detection (25%) as primary goals of M-MBC. Almost all of respondents stated to perform CT/MRI scan (not PET/CT nor RX/ECO) within 2 months before treatment start (1 month: 48%; 2 months: 46%); an additional brain CT/RM was performed in HER2-positive/triple negative (TN) cases by 51% of respondents or in presence of symptoms by 80%. More than 70% declared to perform CT-scans every 6 months (3 months for TN cases or expensive drugs). About 95% choose to monitor CEA/Ca 15-3 level even if not elevated at baseline. The most relevant factors influencing the M-MBC strategy were the presence of TN disease (73), the contraindication for exam (69), the presence of clinically measurable disease (68), and treatment safety profile (67), while patients' socio-economical status (16) or logistics (26) were less relevant. M-MBC was considered to influence quality of life with a score of 69/100 and survival with a score of 39/100. Only 18% thought that strategies of M-MBC were defined by guidelines and 70% called for literature data. Negligible differences were observed according to institution type, title, age or geographical location.

Conclusion: The study describes the attitude of Italian oncologists on M-MBC. The potential consequences for breast cancer patients need prospective studies on M-MBC, also in order to support guidelines implementation.

Table: C18

		1st L OR [95%CI]	2nd L OR [95%CI]	3rd L OR [95%CI]
TM use	Elevated TM at diagnosis	6.23 [3.53-10.6]	9.27 [2.80-30.6]	16.4 [3.9-68.6]
	Frequent oncology office visit*	1.60 [1.26-2.02]		
	High educational level		5.29 [1.47-19.1]	
	Senior prescriptor			9.7 [2.31-40.9]
CT/RM use	Frequent oncology office visit*	3.07 [2-4.72]	2.28 [1.32-3.95]	
	Presence of cutaneous/subcutaneous metastases		0.34 [0.12-0.98]	
	Luminal A type		0.22 [0.06-0.78]	
	Age >65 years		0.33 [0.13-0.82]	

*Volume in any 1 month.

C20 First prospective multicenter Italian study on the impact of the 21-gene recurrence score (RS) in adjuvant clinical decisions for ER+/HER2- early breast cancer (BC) patients

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Background: The Breast-DX Italy prospective study evaluated the impact of the 21-gene RS on adjuvant treatment decisions for early BC patients. **Methods:** The study was conducted in 9 centers of the Veneto Region (2 hub and 7 spoke). All consecutive patients with ER+/HER2-, T1 to T3, N0 to N1 early BC who met protocol-defined clinicopathological criteria for "intermediate risk" were included. Pre-RS and post-RS physicians' treatment recommendations.

Results: From November 2014 to August 2016, n = 124 N0 and n = 126 N1 patients were enrolled (65% at hub and 35% at spoke centers). The majority had PgR + (86%), G2 (71%) and pT1c (63%) BC. Median age was 55 yrs, median Ki67 was 20% (range 2-70%). The distribution of RS was: <18 (61%), 18-30 (32%) and >30 (7%). Main factors associated with higher RS were G3, low PgR expression and high ki67. The addition of chemotherapy (CT) to hormonal therapy (HT) was initially recommended for 48% of the patients (38% of N0 and 57% of N1 patients; 54% and 37% of patients enrolled at hub and spoke centers, respectively). The post-RS recommendation changed from the pre-RS recommendation for 40 patients, mostly from CT+HT to HT (n = 30; n = 25 with low and n = 5 with intermediate RS). Change was more frequent for N1 patients (Table). Of the 72 N1 patients initially recommended to CT+HT, 28% had a post-RS indication to HT alone. From pre-RS to post-RS, the recommendation to CT-HT was reduced from 48% (120/250) to 40% (100/250), McNemar's $p < 0.0016$, more evidently for N1 patients and at Hub centers.

Conclusions: Pre-RS indication to HT alone was frequent, in particular for N0 patients. The use of the 21-gene RS further contributed in sparing CT administration, more so for N1 patients and at hub centers. The impact of the RS when used at discretion of the clinicians is currently under investigation in the prospective ROXANE study.

Table: C20

Change in Pre-RS to Post-RS recommendation	N0 (n = 124)	N1 (n = 126)	Total (n = 250)
Any change; n(%)	15 (12%)	25 (20%)	40 (16%)
HT to CT+HT	5 (33%)	5 (20%)	10 (25%)
CT+HT to HT	10 (67%)	20 (80%)	30 (75%)

C21 Expression and clinical-pathological correlations of the androgen receptor (AR) in a series of ER and PgR negative breast cancers undergoing surgery: our center experience

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Background: Many evidences have shown that the direct action of AR-mediated androgens is the main mechanism used to influence tumor growth.

Unlike ER and PgR, AR is commonly expressed in high invasive breast cancers (BC), high-grade ductal BCs, in mutated BRCA BCs, in breast Paget's disease and also in apocrine differentiated BCs where it is greater the hyper-expression of c-erbB-2. In the basal subtype of invasive BC, AR expression is commonly lost.

From a prognostic point of view, in a cohort of negative ER BCs patients, the majority younger than 50 years old, AR's positivity is associated with a significantly longer disease free survival, with a recurrence risk of only the 33% when compared with negative AR cases.

Materials and methods: We consecutive analyzed 220 ER and PgR negative BC cases undergoing surgery between 1 January 2009 and 31 December 2015, with the aim of investigating the expression of AR and its correlation with relevant clinical and pathological parameters. Median follow-up time is 36 months.

Results: We had 159 triple negative and 61 HER2 positive BC. In 20 pts we find apocrine-like histology. Positivity for AR was found in 39.1% of cases. 40 pts had recurrence and 30 pts died due to BC disease. In the univariate analysis, we did not find any statistical correlation between AR expression and menopausal status, disease stage, p53 expression, BRCA mutational status, disease-free survival, and mortality. There is, however, a close correlation between AR and apocrine-like histology (p = 0,0001) and HER2 positivity (p = 0,0001). From the multivariate analysis emerges that only the stage of BC disease influences relapse (p = 0,0021) and mortality (p = 0,045).

Conclusions: According to current literature data, AR expression is a relatively common feature of ER and PgR negative invasive BC. Our investigations confirm the correlation between AR expression, HER2 status, and apocrine-like histology. However, differently from what has been shown in the recent meta-analysis, in our study, no prognostic differences emerge between positive and negative AR cases.

C22 Assessment of critical factors related to return to work in women after breast cancer

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Background: New diagnostic, surgical and therapeutic techniques allow an increasing number of women to return to their family and working life after breast cancer. According to AIRTUM 2016, in Italy, 692.955 women live after a breast cancer diagnosis. The workplace is one of the most important concerns felt by women who've had breast cancer. In fact, work represents for them a confirmation of an active and productive role. A CENSIS 2013 report suggests that 10% of those women lose their job after cancer. It is due to voluntary resignation, dismissal or other reasons. Meanwhile, the women who continue to work have to face other professional problems.The present research aims to identify the main critical factors related to return to work, focusing on physical, psychological and relational issues and identifying the predictors of a problematic reintegration.

Materials (patients) and methods: This descriptive observational study uses an ad hoc questionnaire to explore the variables detected in scientific literature as negative factors for job reintegration after the therapeutic pathway.

The main risk factors were verified by multivariate statistical analysis. Study cohort: 1578 women with breast cancer resident in the area of Ausl Bologna. They have had cancer surgery in a public or private structure. Average age: 55 years (July 2014).

Results: 47% of women came back to work presenting problems of varying nature and severity. It was possible to identify the four homogeneous groups of problematic factors that are predictive for a problematic return to work: 1. live alone; 2. needs for non-oncological post-surgery treatments; 3. physical and psychological problems related to the return to work; 4. long duration of absence from work after surgery. It is also proved that even receiving maximally invasive treatments (mastectomy, DA, chemotherapy) represent a negative predictive factor.

Conclusions: Returning to work is problematic for about 50% of women. This suggests the importance to set up personalized rehabilitation programs in order to counteract the chronicity of physical and psychological diseases and the consequent disability. Probably, information on pre-intervention status and psycho-social vulnerability should be evaluated within breast units as well as clinical and biological parameters, affecting the result of the treatments. Collaboration between territorial oncology and associations of oncological patients could be an important contribution in this direction.

C23 Stromal peritumoral and intratumoral infiltrating lymphocytes: how immunity influences prognosis in triple negative breast cancer

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Background: Triple negative breast cancer (TNBC) is an aggressive subgroup of breast cancer (BC) with poor clinical outcome. The lack of target therapies switches attention on the role of immune interaction between host and tumor. Tumor-infiltrating lymphocytes (TILs) is a biomarker of immunogenity that in TNBC can correlate with DFS and OS. The aim of our study was to evaluate the prognostic role of TILs and its association with clinicopathological parameters in TNBC.

Materials and methods: Nine-three consecutive patients with primary diagnosis of TNBC referred to our institution between January 2009 and December 2015 were enrolled. We collected their clinicopathological data. In each tumor sample the pathologist evaluated stromal intratumoral TIL percentage (area of stroma occupied by infiltrating lympochytes) and stromal peritumoral TIL percentage (percentage of stroma lymphocytes encountered in entire circumferential invasive tumor front). Lymphocytes predominant breast cancer (LPBC) were the ones with TILs higher than 60%. TILs were correlated with clinicopathological data, OS (time between diagnosis and death or last follow up) and DFS (time between diagnosis and relapse either as local recurrence or distant metastasis). All data were analyzed by Chi square test. Kaplan-Meier curves for OS and DFS were applied. Univariate and multivariate Cox proportional hazard models were conducted to correlate between TIL, OS and DFS. Level of significance p value was set at 0.05.

Results: We found a significant association between stromal intratumoral TIL and stromal peritumoral TIL (p = 0.0082). A significant difference was also seen in LPBC subgroup (p = 0.0001 95% CI 3,4761-33,5857). There was no significant correlation between both intratumoral and peritumoral TIL and the clinicopathological data examined. Peritumoral TIL was significantly associated with OS (p = 0.0119 95% CI 1,7109-75,541) and DFS (p = 0.0113 95%CI 1,5723-34,8046), the latter regardless of

TIL percentage of expression. Intratumoral TIL did not demonstrate significant correlation with DFS, unless a TIL percentage =1% (p = 0,029 95%CI 1,1266-10,3296), nor with OS. At the multivariate analysis TIL did not show a significant correlation with OS and DFS.

Conclusions: Peritumoral TIL correlates with DFS and OS in TNBC. This is an intriguing data not enough considered in literature yet which suggest that the location of TIL may help to stratify prognostic BC subgroups to guide future therapeutic decisions.

C24 Prognostic value of tumor-infiltrating lymphocytes in small HER2-positive breast cancer

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Background: Standard treatment for patients with small, node-negative, human epidermal growth factor receptor type 2 (HER2)-positive breast cancer (BC) is still controversial. No data are available on the prognostic role of tumor-infiltrating lymphocytes (TILs) in this subset of patients.

Methods: Patients with have been selected. Hematoxylin and eosin (H&E) slides from node-negative, pT1 a-b HER2-positive BC surgical specimens were retrieved from pathology archives to assess TILs and their association with outcome.

Results: TILs were evaluated in 205 patients with HER2 positive, pT1 a-b tumors who underwent breast surgery between 1997 and 2009. At a median follow-up of 11 years, we did not observe any association between the presence of TILs, either assessed as a continuous variable or dichotomously (<50 vs > =50%) and outcome.

Conclusions: TILs cannot be used as a prognostic biomarker in pT1a-b HER2-positive BC. Additional biomarkers are needed for selecting patients with stage I HER2-positive BC candidate to adjuvant therapy de-escalation.

C25 Fulvestrant (FUL) as first-line therapy in HR+ve, HER2-ve advanced breast cancer (ABC) patients (pts): when clinical practice comes earlier than clinical trials. Results from the GIM-13 AMBRA study

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Introduction: Hormone receptor positive tumors represent the most common form of breast cancer. Endocrine therapy (ET) represents the main initial therapeutic strategy for these patients and has been associated with significant clinical benefits. One of the available therapeutic strategy is FUL; in a Phase II study, FUL demonstrated improvements in time to progression (TTP) and overall survival (OS) in comparison to anastrozole (ANA). In a recent Phase III trial, comparing FUL vs ANA as 1st-line therapy, PFS was significantly longer in the FUL group than in the ANA group (16 = 6 vs 13 = 8 months). The benefit in PFS seems to be limited to patients without visceral sites of disease. Aim of the present analysis is to describe pts' characteristics and outcome treated with FUL in a real-life setting.

Patients and methods: We used data of the HR+ve pts of the AMBRA study, a longitudinal cohort study, describing the choice of first and subsequent lines of treatment in HER2-ve MBC pts, treated with FUL in any line of therapy to describe pts' characteristics and outcome in terms of ORR (CR+PR) and DCR (ORR+SD) and time to treatment change (TTC).

Results: So far, 791/1500 pts have been registered into the AMBRA study, 673 of them (85%) with HR+ MBC: 197 (29.3%) pts received FUL in any setting and 125 (18.6%) as 1st-line therapy. Median DFI was 74 months (14-420). Main sites of metastasis were bone in 69 pts (55.2%) and viscera in 43 (34.4%). ORR was 24% in the whole population, 24.6% and 18.6% in pts with bone and visceral metastases, respectively. Median TTC was 14.63 months (range 1.17-96.70) in the whole population, 3.8 months in pts with visceral involvement and 25.7 in those with bone disease.

Conclusions: Our data are very close to those obtained in the FALCON trial and strongly support the use of FUL as 1st-line therapy mainly in pts with metastatic disease limited to bone.

C26 BRCA1/BRCA2 mutations in a Mediterranean population (Apulia Region) with breast or ovarian cancer: a single center experience

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Background: Approximately 5-10% of breast (BC) and ovarian cancers (OC) are hereditary, and are characterized by aggressive disease and early age of onset. Mutation of BRCA1 or BRCA2 genes are present in 30% of hereditary BC and OC. BRCA1/2 mutations substantially increase the lifetime risk of developing BC and OC. The purpose of our study is to describe the percentage of BRCA mutations in patients (pts) with BC or OC treated in our institution.

Materials (patients) and methods: Three hundred seventy-seven pts (372 women and 5 men) with BC (n = 313; 83%), with OC (n = 60;16%) or BC plus OC (n = 4; 1%) were included in the analysis. We collected data about primary site of cancer, baseline clinical characteristics, BRCA1/2 status and family history of cancer in an anonymized dedicated database. DNA was extracted from the pts peripheral blood. We used multiplex ligation-dependent probe amplification (MLPA) to screen mutations in BRCA1 and BRCA2.

Results: Of the 377 pts analyzed, 68 (18%) were BRCA1/BRCA2 mutated, 39 (10.3%) at BRCA1 gene and 27(7.1%) at BRCA2; only one subject (0.3%) had both BRCA1 and BRCA2 mutations. Among BC pts, 56 (17.6%) had triple negative (TN) disease and BRCA1/2 mutations were present in 20 (35.7%) of these: 17 TNBC pts had BRCA1 (85%) and 3 (15%) BRCA2 mutation. In 377 pts the most frequent BRCA 1/2 mutation was c.5266dupC (n = 29; 42.6). In TNBC pts c.5266dupC mutations constitutes about 88.2% of the BRCA1 pathogenic mutations.

Conclusions: Different ethnic and geographical Countries have different BRCA1/2 mutation spectrum and prevalence. Very few data have been published regarding on geographical distribution in families with BRCA1/2 mutations in Italy, and particularly in South of Italy. The BRCA1 mutation c.5266dupC was originally described as a founder mutation in the Ashkenazi Jewish (AJ) population; however, this mutation is also present in Europe, Brazil and North America. The high incidence of c.5266dupC mutation in our pts may be linked to international migration flows. Understanding genetic predisposition to develop BC and OC may contribute to refine more cost-effective prevention and screening measures in a high-risk population.

C27 Estrogen receptor mutation: a new strategy to overcome endocrine resistance

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Background: Around 75% of breast tumours express estrogen receptor (ER+). Endocrine therapy (ET) is a cornerstone in the treatment of both early and metastatic disease, but its effectiveness is limited by the developing of acquired resistance and more rarely by de novo resistance. Understanding the mechanisms of resistance to ET represents a challenge. Recently acquired mutations in ESR1, have been associated with resistance to aromatase inhibitor (Ai) therapy in hormone-refractory metastatic breast cancer (MBC).

Materials and methods: We retrospectively collected data of 85 patients (pts), treated at our Institution between 2007 and 2015, diagnosed with ER+ HER2- MBC, previously exposed to ET both in adjuvant or metastatic setting, whose tissue samples were available from primary (N = 40) and metastatic tumor (N = 45). We performed sequencing of DNA tissue to detect hotspot ESR1 mutations at codons 536-538 using Sanger sequencing and next-generation sequencing (NGS). Moreover, we collected blood samples from 7 pts to detect ESR1 mutational status in circulating cell free DNA (ccf DNA) using E-Ice-COLD for the amplification of ESR1 region and droplet digital PCR (ddPCR) or NGS to analyse the amplicons.

Results: We detected no mutations in primary tumor and 6 somatic mutations in 45 of metastatic specimens (overall 13,3% frequency). In our population, the most frequent mutation was the Y537S (3 pts) and in 2 pts D538G: all data were confirmed at NGS analysis. In one case a Y537C mutation was detected using only Sanger method. Blood samples from 7 patients were collected a long time away from the biopsy of metastatic lesions, after exposition at further lines of therapy. In 2 pts respectively L536H and Y537S mutation has been detected in plasma and none mutation in metastasis, in 1 pts a Y437C was found in metastasis but not in ccf DNA, 1 pts presented Y537S both in plasma and metastatic tissue and 3 pts either in plasma or in tissue were ERS1 wild-type. We observed an increase incidence of ESR1 mutations according to the number of endocrine lines administrated: 8,8% in pts with one line, vs 33% in pts with more than 3 lines of ET.

Conclusions: With the limitation of the retrospective nature of the study and the small population, our data confirm that ESR1 mutations are frequent in patients who

progress after ET with Ai. Their early detection and monitoring in plasma across metastatic history might help in the choice of best treatment.

C28 Role of DCE-MR imaging of the breast in predicting breast cancer subtypes: where are we going?

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Background: Dynamic contrast−enhanced magnetic resonance (DCE-MR) imaging of the breast is increasingly used as an adjunct to mammography and ultrasonography (US) to improve the detection and characterization of primary and recurrent breast cancers. Correlation between morphological features, kinetic parameters of DCE-MRI and prognostic factors of BC has been previously analysed, providing conflicting results. Aim of the study is to expand the evaluation of the dynamic characteristics of MRM, analyzing potential correlation with the histopathologic and immunohistochemical characteristics of breast cancer to orient the subsequent clinical and therapeutic management of patient.

Patients and methods: Between January 2012 and June 2016, 95 consecutive patients with histopathologically confirmed invasive breast carcinoma underwent MR imaging were elegible. Patients with rare forms of breast cancer (different from invasive ductal/lobular carcinoma) were excluded. In patients with multifocal, multicentric or bilateral carcinoma, the largest lesion was analysed.

Results: The immunohistotype was shown to be significantly related with Maximum Enhancement ($p = 0.05$), Time to peak ($p = 0.04$) and Wash-in rate ($p = 0.01$). Furthermore, ER status correlates with Maximum and Relative Enhancement ($p = 0.004$ and $p = 0.028$, respectively), Wash-in rate ($p = 0.0018$) and Area under curve ($p = 0.006$). In addition, PR status and vascular invasion were significantly related to Time to peak ($p = 0.048$ and $p = 0.02$, respectively). Type of RMN curve doesn't show any significant association in relation to the histological, immunohistochemical and locoregional features of BCs.

Conclusion: Our analysis demonstrated that Max Enhancement Absolute and Relative, Time to Peak, Wash-in rate and Area under the curve, which dependent from tumoral grading and intra and peri-lesional vascularization, significantly correlate with several prognostic factors, like ER status, immune-profile and tumoral vascular invasion. Thus, they can potentially predict the intrinsic aggressiveness of the lesion and improve molecular characterization.

C29 Small luminal-like breast cancer: determinants of adjuvant chemotherapy use

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Background: The use of adjuvant chemotherapy (CT) in small luminal-like breast cancer (BC) is still heavily debated. International guidelines identify endocrine therapy (ET) as the backbone of adjuvant treatment for these patients (pts), while the addition of CT should be limited to high-risk cases. The aim of this study was to evaluate the association between patient- or disease-related factors with the prescription of adjuvant CT.

Methods: This retrospective study analyzed 601 consecutive pts with pT1 (≤ 2 cm) luminal-like BC treated between 2004 and 2015 at the Department of Oncology of Udine (Italy). No restrictions were applied regarding lymph node status. The cut-off point of 1% was used to define ER and/or PgR positivity. Factors influencing the prescription of CT were investigated through uni- and multivariate logistic regression with odds ratio (OR) calculation. Prognosis was explored through Cox regression.

Results: By multivariate analysis, lymph node involvement was highly associated with CT prescription (OR 16.17, 95% CI 7.61-34.33, $P < 0.001$ for pN1; OR 6.17, 95% CI 2.25-16.92, $P < 0.001$ for pNmi). Tumor size drove towards the use of CT among pts with pT1c tumors (OR 13.45, 95% CI 1.58-114.31, P 0.017) but not in pts with pT1b BC (OR 1.95, 95% CI 0.21-17.47, $P = 0.549$). In addition, a higher CT use was observed in pts with luminal B-like disease (OR 3.26, 95% CI 1.84-5.77, $P < 0.001$), in presence of grade 3 (OR 11.54, 95% CI 3.81-34.90, $P < 0.001$), grade 2 (OR 3.11, 95% CI 1.40-6.90, $P = 0.005$) and Ki67 >14% (OR 1.04, 95% CI 1.02-1.06, $P < 0.001$). Counterparty, the increase in ER expression (OR 0.98, 95% CI 0.97-0.99, $P = 0.033$) and pts with age > 60 years predicted a lower use adjuvant CT (OR 0.10, 95% CI 0.04-0.22, $P < 0.001$). Regarding CT, no differences in DFS or in OS were observed between treated and untreated pts (HR for DFS 1.32, 95% CI 0.70-2.48, $P = 0.380$; HR for OS 1.006, 95% CI 0.455-2.227, $P = 0.987$).

Conclusions: Nodal status, tumor size, histological grade, disease sub-type, Ki67, ER and age are determinants of adjuvant CT prescription in pts with small luminal-like BC. Prospective studies are needed to identify which patients could safely avoid CT without influencing prognosis.

C30 Neutrophil-to-lymphocyte ratio in metastatic breast cancer patients: relationship with tumor characteristics and survival

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Introduction: The neutrophil-to-lymphocyte ratio (NLR) is a good reflection of inflammation, which plays an important role in tumor progression and metastasis. The presence of an elevated NLR has been recognized as a poor prognostic factor in various tumors, including breast cancer (BC); however, its prognostic value was still little explored in patients (pts) with metastatic breast cancer (mBC).

Patients and methods: Clinico-pathological features and treatment outcome of 595 consecutive mBC pts treated at the Department of Oncology of Udine, Italy, between 2004 and 2014, were retrospectively analyzed. NLR was calculated from the blood count performed before first line therapy starts. Differences in NLR according to clinico-pathological characteristics were investigated through chi-square test. Cox regression was used to determine the prognostic impact of NLR.

Results: Some tumors characteristics have been statistically significant associated with higher NLR in mBC pts: high histologic grade ($P = 0.009$), ductal histotype ($P = 0.02$), ER negativity ($P = 0.003$), PgR negativity ($P = 0.0001$), high Ki-67 ($P = 0.03$). No statistical differences in NLR was found between HER2-positive and HER2-negative disease ($P = 0.33$). Among subtypes, luminal HER2+ BC were associated with lower NLR, while triple-negative BC with higher NLR ($P = 0.004$). No statistical differences in NLR were observed according to visceral disease ($P = 0.13$) nor according with bone-only disease ($P = 0.24$). At univariate analysis, a NLR ≥ 2.64 (median value of the whole population) was associated with worse progression-free survival after first line therapy (HR 1.41, 95%CI 1.11-1.79, $P = 0.005$) and with worse overall survival (HR 1.76, 95%CI 1.32-2.36, $P < 0.0001$); however, the statistical significance was lost at multivariate analysis ($P = 0.08$ and $P = 0.13$, respectively). Interestingly, a subgroup analysis revealed a significant prognostic value of NLR in HER2-positive subtype (HR 4.89, 95%CI 1.13-21.23).

Conclusions: In our cohort study, although a high NLR did not represent an independent prognostic factor at multivariate analysis, it turned out to be associated with peculiar pathological features of BC. Further efforts are needed to establish the appropriate cut-off value of NLR, as well as to identify the BC subtypes in which the prognostic role of this easy to collect parameter could be more useful.

C31 Insights from a long-term follow-up evaluation of early breast cancer (BC) outcomes by tumor subtype (TS)

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Background: Immunoistochemistry (IHC)-based classification of BC is mostly used in common practice and provides surrogate definitions of intrinsic molecular subtypes with validated prognostic significance. We aimed at evaluating the impact of TS on long-term BC mortality.

Materials and methods: We used a retrospective cohort of women diagnosed with early BC between 1985 and 1990. Surgical samples underwent centralized pathology review and IHC re-assessment for ER, PgR, HER-2 and Ki67 expression. Multivariate Cox and Fine-Gray's proportional hazard regression models assessed associations of TS with overall survival (OS) and breast cancer-related survival (BCRS), adjusting for menopausal status, tumor (T) size, nodal status and receipt of adjuvant treatment.

Results: Of 200 patients, 42.0% had Luminal A-like, 32.5% had Luminal B-like/Human epidermal growth factor (HER)2-negative, 8.5% had HER2-positive and 17.0% had triple negative BC. At the time of diagnosis, 68.5% of patients were post-menopausal, 53.0% had $T > 2$ cm, and 47.5% had node-positive disease. Over a median follow-up of 18.7 years (range 0.3-32.0), we recorded 140 death events, of which 75 were BC-related. Median OS was 18.5 years (95% confidence interval [CI] 15.8-21.2). Luminal A-like tumors experienced the longest absolute median OS (21.2 years [95% CI 17.4-24.9]), although no statistically significant differences in the hazards of death for all causes were observed across subtypes. Luminal B-like/HER2-negative subtype was significantly associated with worse BCRS vs. Luminal A-like (adjusted hazard ratio [HR]=1.86 [95% CI 1.09-3.16]). After multivariate analysis, T size >2 cm (HR [95%

CI] 1.71 [1.03-2.84]) and positive nodal status (HR [95% CI] =2.19 [1.03-4.65]) predicted BCRS, whereas post-menopausal status was significantly associated with BC-unrelated survival (HR [95% CI] 3.82 [1.93-7.55]).

Conclusions: Using contemporary definitions of TS, Luminal A-like cancers seem to have a better prognosis even after thirty years since diagnosis, particularly when compared to Luminal B-like/HER2-negative tumors and with respect to BCRS. This finding is relevant when assessing the need and duration of adjuvant treatments especially among postmenopausal patients, who may also carry a burden of age-related comorbidities exposing them to a higher risk of death due to non-BC related causes. T size and nodal status still hold a major independent prognostic association with survival outcomes.

C32 Efficacy of extended aromatase inhibitors for hormone-receptor−positive breast cancer: a literature based meta-analysis of randomized trials

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Background: Endocrine treatment, in particular with aromatase inhibitors (AIs) for 5 years is nowadays the preferred adjuvant treatment for hormone-receptor−positive breast cancer. However, very few data are available on efficacy of the extending approach with AIs up to 10 years as adjuvant treatment. We performed a meta-analysis to assess the real impact on the disease-free survival (DFS) of extended adjuvant therapy with AIs.

Methods: A literature-based meta-analysis of randomized controlled trials (RCTs) in accordance with the preferences for reported items in systematic reviews and meta-analyses guidelines was undertaken. Relevant publications from PubMed, the Cochrane Library, and abstracts from meetings were searched. The primary endpoint was DFS, the secondary was the overall survival (OS); moreover, a subgroup analysis was performed to elucidate the role of nodal involvement on the primary endpoint.

Results: The pooled analysis from the RCTs of AIs revealed a significantly increased DFS (hazard ratio (HR) for DFS: 0.72, 95%CI: 0.61-0.84; P < 0.0001, I2=50%). The subgroup analysis according to nodal status revealed that the greater DFS benefit with extended AIs was achieved in patients with positive nodal status (HR = 0.61 and 0.69 in node negative and node positive patients, respectively). With regards to OS, the pooled analysis revealed no improvement in OS related to the use of extended adjuvant endocrine therapy with AIs (HR = 1.01, 95%CI: 0.87-1.16; P = 0.95, I2=0%).

Conclusion: This analysis confirmed the efficacy of extended treatment with AIs in the adjuvant setting on DFS for hormone-receptor−positive early breast cancer and no impact on OS. A greater DFS efficacy was observed in women with positive nodal status.

C33 Nab-paclitaxel (Nab-P) in HER2-ve advanced breast cancer (ABC) patients (pts): focus on luminal cancers. Results from GIM13 - AMBRA study

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Background: Two randomized studies demonstrated that Nab-P produces a significantly higher overall response rate (ORR), longer Time to Progression (TTP), and greater overall survival (OS) in ABC pts treated with second-line or greater therapy compared with patients who receive conventional Paclitaxel. However, few data are available in the real-life setting, especially for the weekly schedule (wNab-P).

Patients and methods: AMBRA is a longitudinal cohort study, aiming to describe the choice of first and subsequent lines of treatment in HER2-ve ABC pts receiving at least one CHT (SABCS 2016, P5-15-07 & P5-14-09) in the years 2012-2015. For the present analysis, we focused on the use of Nab-P in Luminal tumours, describing efficacy results according to pts' characteristics.

Results: So far, 791/1500 pts have been registered into the study, 107 (13.5%) received Nab-P in any line of treatment and 88 (82.2%) were Luminal tumours. Median age was 56 years. Seventeen pts (19.3%) received Nab-P as 1st line therapy, 38 (43.2%) as 2nd-line, the remaining as 3rd-line or greater. Most pts (40, 45.5%) received the every 3 weeks (Q21) schedule, whereas 27 pts (30.7%) were treated with the weekly (wNab-P) schedule (days 1,8,15 Q28) at different doses: 100 mg/mq: 9 (33.3%), 125 mg/mq,: 13 (48.1%); 150 mg/mq: 3 (11.1%). The remaining received different schedules or doses. Median number of cycles received was 5 (1-17) and median duration of treatment was 3.5 months in the whole population. No difference has been observed in terms of number of cycles or duration of treatment according to the schedule.

Conclusion: Our results are similar to those obtained in a recent large real-life study, confirming that Nab-P is one promising option also for pts with Luminal tumours.

C34 Long term results of ASTER study, a single Institution phase II trial of sequential chemotherapy (CT) for operable breast cancer (BC)

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Background: Efficacy of anthracycline- and taxane-based CT for neoadjuvant (NA) and adjuvant (A) treatment (tx) of operable BC has already been established, although no clear superiority of a CT regimen has ever been demonstrated. ASTER study was designed to investigate safety and efficacy of a peri-operative sequential approach, with the intent of reducing both the duration and the total dose of CT. Herein we report the long term results of the study in a single Institution cohort of patients (pts).

Materials and methods: ASTER study enrolled pts with cT2-3 N0-1 or pT1-2 N1-3 BC, from 11/2008 to 08/2011. Tx consisted in Doxorubicin 60 mg/sm IV bolus + Paclitaxel 200 mg/sm IV 3 hours infusion q21 (AT) x 3 cycles followed by Cyclophosphamide 600 mg/sm IV bolus + Methotrexate 40 mg/sm IV bolus + 5-Fluorouracil 600 mg/sm IV bolus d1,8 q28 (CMF) x 3 cycles, in either NA or A setting. Toxicity was graded according to Common Terminology Criteria for Adverse Events (CTCAE) v. 3.0. Progression free and overall survival (PFS and OS, respectively) were estimated according to Kaplan-Meier method.

Results: 330 pts were enrolled, with a median age of 51 years (range 23-72). 78% of cases was treated in A setting. 65% of pts received breast conservative surgery, 78% underwent axillary dissection. Most cases presented estrogen and/or progesterone receptor positivity (75% and 67%, respectively); 18% of pts presented HER2-positive BC, 16% triple negative disease. At a median follow-up of 80 mos (range 2-107), median loco-regional and distant disease free survival (DFS), as well as median overall survival (OS), were not reached. Outcome data are detailed in the table below.

Table: C34

Follow-up (years)	Loco-regional DFS (%)	Distant DFS (%)	OS (%)
1	99.6	98.4	99.6
5	97.1	90.2	94.9
7	95.9	88.8	91.2

No cases of long term or delayed toxicity were observed.

Conclusions: CT with AT x 3 -> CMF x 3 is confirmed safe and effective at 7 years follow-up. With intrinsic limits of a retrospective parallel, these results appear comparable to those reported in regulatory trials of most commonly used anthracycline and taxane-based regimens. No specific safety concerns emerged after prolonged follow-up (e.g. neurotoxicity, cardiac dysfunction, secondary neoplasm). Indeed AT x 3 -> CMF x 3 may be considered an appropriate regimen for NA and A tx of operable BC.

C35 Pathogenetic mutations in BRCA related triple negative breast cancer

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Background: Triple negative breast cancer (TNBCs) are about 12−24% of breast tumours and to date, chemotherapy is the only therapeutic chance. Their tendency to a visceral metastatic dissemination leads to poor outcome within 5 years after diagnosis.

About 10-16% of TNBCs harbor a Breast Related Cancer Antigens (BRCA) germline mutation and 70% of breast cancers developed in BRCA1 germline mutation carriers are TNBCs, resulting in a "haploinsufficiency of homologous recombination". We present detected BRCA mutations in patients with TNBCs at our Istitution.

Patients and methods: A total of 147 women affected by TNBCs were selected for genetic counseling and underwent BRCA genetic testing between 2002 and 2016 to our Institution. Risk assessment was performed according to the clinical criteria of Modena and using BRCApro tool (total score ≥10%). However, women under the age of 50 have also been tested, taking into account that triple-negative phenotype is now considered a sufficient requirement. BRCA genes were investigated by sequencing and Multiplex Ligation Probe Amplification (MLPA). We referred mainly to the Breast Cancer Information Core committee (BIC) (www.research.nhgri.nih.gov/bic/) and the IARCs databases (http://brca.iarc.fr/LOVD/) and to the ClinVar archive.

Results: Of all sample, 81 (55%) TNBCs patients were BRCA mutation carriers. Among them 44 (54%) showed pathogenetic variants: 18 in-frame deletions, 4 point mutations and 1 large deletion of several exons. According to the literature, most of the TNBCs (n = 35; 80%) was associated with BRCA 1 mutations, mainly involving exons 5 (300T>G) and 11 (962del4, 3901delT). Three founder mutations were detected: two commonly encountered in Askenazite Jews (185delAG; 5382insC) and one in Poland (300T>G); this was also, the most frequent pathogenetic mutation in our BRCA1 carriers. Among BRCA2 mutations, 9106C>T is one of the most common in Italy, frequently reported in early-onset male breast cancer as well as ovarian cancer.

Conclusions: Our study describes a consecutive series of TNBCs referred for genetic counseling and tested for BRCA germline mutations, with a high detection rate (55%). The identification of three of the most common BRCA1 mutations worldwide (185delAG, 5382insC, 300T>G) makes our data collection representative. Interestingly, our results show the high prevalence of TNBCs in BRCA1 mutation carriers, confirming the close link between genotype and phenotype.

C36 Nab-paclitaxel in clinical practice: data from the MANTEL study

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Background: Metastatic breast cancer (MBC) is an incurable disease. The main goals of treatment are palliation, symptoms control, preserving QoL and prolonging survival. New drugs have contributed to ameliorate the outcome of MBC patients (pts) by increasing response rates (RR) progression free survival (PFS) and, in some setting, overall survival (OS). Taxanes are the most effective drugs in the management of MBC. Nab-Paclitaxel (Nab-P), a solvent-free albumin-bound taxane with high tumor retention, showed antitumor efficacy, and limited toxicity in MBC pts. Aim of the present study is to evaluate the activity and safety of Nab-P in clinical practice.

Methods: MANTEL is a retrospective, multicenter, observational study, designed to collect clinical data of MBC treated with Nab-P since its availability in Italy.

Results: Up to date 149 cases were collected from 9 centers. Main patients' characteristics are: median age 59 y (32-82) including 45 pts over 65, median ECOG PS 1 (0-3), ER/PgR positive 134 pts (89.9%), Triple Negative 12 pts (8%); 101 pts (67.8%) received neo/adjuvant CT. Most common metastatic sites were: bone 104 pts (69.8%), liver 78 pts (52.3%), soft-tissues 82 pts (55%), lung 48 pts (32.2%), CNS 7 (4.7%); median number of organs involved: 2 (1-5), median number of previous chemotherapy regimens for advanced disease: 2 (0-9). Data on activity showed an ORR of 30.2%: 4 CR (2.8%), 41 PR (27.5%), 36 SD (24.1%), 58 PD (38.9%) and 10 NE (6.7%), CB was observed in 62 pts (41.6%). Median number of cycles administered was 5 (1-15). Seven pts are still on treatment. Median PFS is 4.3+ months (1+ - 34), median OS 11+ months (0.7+- 46.4). G3-4 leucopenia was observed in 8 pts (5.3%), G3-4 neutropenia in 13 pts (8.7%), anemia (all grades) in 53 pts (35.5%); 68 pts (45.6%) experienced neuropathy (G3 in 6 pts), 94 pts (63%) fatigue (G3 in 4 pts) and 20 pts (13.4%) G1-2 arthro-myalgia. 101 pts (67.8%) received standard every 3-w schedule, 37 pts (24.8%) required dose reduction due to toxicity.

Conclusions: Nab-P is feasible in unselected MBC pts. ORR and PFS are comparable to the data reported in the pivotal study. No concerns about toxicity in this real life population, including large number of elderly and heavily pretreated pts. The study is ongoing.

C37 First-line bevacizumab in combination with weekly paclitaxel for metastatic breast cancer: efficacy and safety results from a routine oncology practice analysis

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Background: First-line bevacizumab plus paclitaxel therapy for human epidermal growth receptor factor 2 negative (HER2-) metastatic breast cancer (MBC) demonstrated a median progression-free survival (PFS) of around 11 months in few pivotal randomized phase 3 trials (E2100, TURANDOT, and CALGB 40502). However median overall survival (OS) did not significantly differ between treatment arms.

Patients and methods: We analysed a series of MBC patients treated between 2008 and 2016 at our Department using bevacizumab plus paclitaxel regimen as first line (bevacizumab 10 mg/kg on days 1,15 q28 plus paclitaxel 90 mg/mq on days 1,8,15 q28). Primary endpoints were efficacy outcomes measured as PFS, overall response rate (ORR), clinical benefit rate (CBR), and OS on the whole series, and on selected subgroup of patients. CBR was defined as the percentage of patients who have achieved complete response, partial response or stable disease > =6 months. Toxicity profile of the treatment was recorded following the NCI CTCAE, version 4.

Results: We overall evaluated a series of 97 patients. The median PFS was 9 months (range 2-68); no significant differences were shown in patients previously treated with taxanes in (neo)adjuvant setting (p = 0.42), and endocrine treatment for the MBC (p = 0.53). The best ORR was 25% (24/96 cases), and the CBR was 72.9% (70/96 cases). No significant difference emerged in terms of presence of visceral disease (9 vs 19 months; HR 1.1 95%CI 0.67 to 1.9; p = 0.63), triple negative (8 vs 13 months; HR 1.5 95%CI 0.74 to 4.67; p = 0.19), age (<65 vs > =65 years; p = 0.25), and time to failure from adjuvant treatment (< =18 vs > 18 months; p = 0.12). The median OS was 26 months (range 2-111). Patients showing a PFS longer than 18 months evidenced a significant OS improvement (21 vs 75 months; p < 0.0001). Eleven grade 3 AE were reported: hypertension (5.1%), neutropenia (5.1%), and peripheral neuropathy (1%).

Conclusions: In our experience bevacizumab plus paclitaxel regimen as first line chemotherapy for HER2- MBC confirmed the efficacy results of pivotal trials. The regimen is highly effective and overall well-tolerated. Patients with prolonged PFS (>18 months) resulted in a significant better OS. Therefore, there is a strong need for studies aiming to identify predictive factors for response to treatment.

C38 Hair loss prevention by scalp cooling device in early breast cancer patients: the Poliambulanza experience

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Background: The most effective regimens for breast cancer are often complicated by alopecia. The chemotherapy-induced hair loss (HL) is one of the main reasons for patients (pts) to refuse chemotherapy. The scalp-cooling device (SCD), causing cutaneous vasoconstriction, reduces the drug concentration to the hair follicles and, in some studies, the HL. We report our preliminary experience with SCD in reducing chemotherapy-hair loss (CT-HL) and related distress in breast cancer pts undergoing adjuvant (adj) CT.

Materials (patients) and methods: From March 2016 to March 2017 we prospectively selected pts with for stage I-III breast cancer and eligible for HL-inducing adj treatments. The regimens used were: paclitaxel (P) for 12 weeks plus trastuzumab (T) for 1year, docetaxel-cyclophosphamide (TC) and doxorubicin-cyclophosphamide (AC) both for 4 cycles. The HL grading and the treatment tolerability has been evaluated during CT every 21 days through the DEAN's scale by pts and operators (op) and the administration of a comfort analogic scale. We administered Hospitality Anxiety depression scale questionnaire at the baseline and at the end of treatment to assess CT-HL related distress.

Results: Among the 46 patients identified, 27 accepted SCD. The median age was 56 (36-76). 22 (81.4%) pts received TC, 3 (11.1%) AC, 2 (7%) P weekly plus T. 24 (89%) completed the treatment whereas the 3 pts (11%) treated with AC interrupted prematurely the SCD use for inefficacy: grade (G) 3 HL after 2 cycles. At last cycle of CT, of 24 pts, 3 pts (12.5%) reported a G 4 HL, no pts reported a G 0, 11 (45.8%) a G 2, 5 (20.8%) a G 1 and 5 a G 3. Concurrently, the op described a G 4 in no pts, G 0 in 1 patient (3.7%), G 2 in 16 (59.3%), G 1 in 4 (14.8%), G 3 in 3 (11.1%). The evaluation of the concordance between the HL G reported by pts and op was not statistically significant with the Cohen test. On the contrary a statistically significant reduction in anxiety and an increasing in depression was described with the Wilcoxon test. The treatment was quite well tolerated in the majority (81.5%) of pts, with a better tolerability during the cycles succession. There was no serious adverse device related events.

Conclusions: In our study the SCD results in a reduced CT-HL in taxane-based CT and is associated with a well tolerability. Furthermore it suggests a discordance in HL perception between pts and op.

C39 We are all Jews of somebody: migration and genetic. The story of Jewish settlements in Italian Salento

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Background: Hereditary breast cancer (BC) has become a popular topic in recent years; in this setting the availability of early detection is key to survival. Approximately 5-10%

of BC are hereditary, and are characterized by aggressive/bilateral disease and early age of onset. The aim of our observational study was to describe the percentage of BRCA mutations in patients (pts) with BC treated in Medical Oncology Department (MDO) of Brindisi, Italian Salento.

Materials (patients) and methods: A total of 317 consecutive pts (312 women and 5 men) were tested for analysis, according to national AIOM guidelines 2016. All pts had BC diagnosis and 4 pts (1,5%) had both BC and ovarian cancer (OC). Data about baseline characteristics, treatment, BRCA1/2 status and family history of cancer were collected according to the local Ethical Committee guidelines. We used multiplex ligation-dependent probe amplification (MLPA) to screen mutations in BRCA1 and BRCA2 in serum DNA samples.

Results: Of the 317 pts analyzed, 55 (17.3%) were BRCA1/BRCA2 mutated, 31 (9.8%) at BRCA1 gene and 23 (7,2%) at BRCA2; only one subject (0,3%) had both BRCA1 and BRCA2 mutations. Furthermore, 56 pts (17,6%) had triple negative (TN) disease, and BRCA1/2 mutations were present in 20 (35.7%) of these: 17 TNBC pts had BRCA1 (85%) and 3 (15%) BRCA2 mutation. The most frequent mutation was c.5266dupC; this alteration represented 83.8% (n = 26) of the BRCA1 mutations and 47.37% of all mutations identified. In TNBC pts, the c.5266dupC mutations constitutes about 88.2% (n = 15).

Conclusions: Few data have been published regarding on anthropological and geographical distribution in families with BRCA1/BRCA2 mutations in Italy, and particularly in Mediterranean population. The BRCA1 c.5266dupC mutation was first described in the Ashkenazi Jewish (AJ) population; however, this alteration is also present in Europe, Brazil and North America. The high incidence of c.5266dupC mutation in our pts may be linked to the presence in Salento of Jewish communities in the Middle Age. Actually there is no knowledge of organized Jewish settlements in this Area. Different ethnic and geographical regions have different BRCA1/2 mutation prevalence: understanding genetic predisposition to BC may contribute to definition of more cost-effective screening measures in population.

C40 PerTe: efficacy and safety of pertuzumab in "real life setting" for the neoadjuvant treatment of HER2-positive breast cancer patients

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The standard preoperative systemic therapy for HER2+ breast cancer(BC) patients(Pts) includes chemotherapy(CT) and trastuzumab(T), increasing pathological complete response rate(pCR). In Jun 2015 the EMA approved Pertuzumab(P) in neoadjuvant regimens for HER2+BC. Two phase II trials have evaluated pertuzumab-plus-trastuzumab—based therapy in the neoadjuvant setting. In NeoSphere trial, the use of dual HER2-targeted therapy combined with docetaxel was associated with a significantly improved pCR. In TRYPHAENA study low rates of symptomatic systolic dysfunction were noted and there was no evidence that P increased the rate of cardiac dysfunction.

PerTe is an observational pilot study, aimed to evaluate efficacy and safety of P for the Neoadjuvant Treatment of HER2+BC pts. The medical records of 2 different Italian Institutions were reviewed to identify Pts treated with P+T+CT as neoadjuvant therapy from Jul 2015 to day. Twenty patients were treated according 2 different CT regimens, based on the clinical practice of belonging institution. The 50% of Pts received ECx4 followed by P+T+weekly Paclitaxel for 12, and the remaining 50% received P+T+Docetaxel (for 6 cycles). Our primary objective is to evaluate the pCR rate, defined as the absence of any residual invasive cancer on haematoxylin and eosin evaluation of the resected breast specimen and all sampled ipsilateral lymph nodes. The secondary objective is to evaluate the safety profile of dual HER2 blockade.

Up to now 20 pts treated with dual HER2 blockade completed the study treatment. 60% of pts had a ductal infiltrating carcinoma(CDI) Luminal B HER2+, while the remaining 40% had a CDI HR negative and HER 2+.

The 70% of pts received radical mastectomy. The pCR was achieved in 85% of pts. The remaining 25% achieved a partial response(3pts), all these pts had high level of ER/PgR and low ki-67 and 2 of them did not receive TCH; one of them experienced a disease recurrence. No cardiac toxicity was detected.

Addition of P to T+CT in neoadjuvant setting seems to be beneficial and not to increase the rate of cardiac dysfunction, regardless of CT regimen used. Levels of ER/PgR and different CT regimens seems to produce different pathological response. Up to now other pts are on treatment and we are going to involve more institutions in order to collect a larger sample.

C41 The APE1/NPM1 axis in triple negative breast cancer: prognostic and therapeutic implications

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Background: Heterogeneity and absence of a molecular target are a challenge in triple negative breast cancer (TNBC). Apurinic/apyrimidinic endonuclease 1 (APE1) is a pivotal enzyme of the Base Excision Repair (BER) pathway, while Nucleophosmin (NPM1) is involved in ribosome biogenesis and cell proliferation. We previously demonstrated that NPM1 stimulates BER activity in cells through direct protein interaction with the N-domain of APE1. Aim of the study was to explore the utility of APE1, NPM1 and their interaction as both a prognostic factor and a novel therapeutic target.

Methods: Cell line models used were based on the HCC70 and HCC1937 TNBC cells. Cell viability after platinum-based treatment, protein levels and their localization were analyzed through MTS assay, Western Blotting and immunofluorescence analysis (IF), respectively. A retrospective analysis of 129 consecutive TNBC patients was conducted. Correlations between cytoplasmic APE1 (cAPE1), nuclear APE1 (nAPE1) and NPM1 were evaluated through Spearman's test. Associations with clinico-pathological features were investigated and the prognostic impact of APE1 and NPM1 was explored in an early TNBC subset.

Results: HCC70 and HCC1937 cell lines were differentially responsive to platinum-based treatment. An up-regulation of NPM1 was observed in HCC70 cells only, while APE1 levels were unaffected in both TNBC cell lines. IF data showed a relocalization of APE1 and NPM1 to the nucleoplasm after treatment with cisplatin and carboplatin, independently from the cell line used. APE1 inhibition caused a significant sensitization to cisplatin in HCC70 cells, but not in HCC1937 cells. When analyzing the retrospective cohort, higher levels of NPM1 significantly correlated with higher levels of nAPE1 ($P < 0.0001$), but not with cAPE1. Counterparty, higher levels of cAPE1 significantly correlated with lower levels of nAPE1 ($P < 0.0001$). No associations were observed between both nAPE1 or cAPE1 and baseline clinical characteristics, while significantly lower levels of NPM1 were found in stage pT3 or pT4 ($P = 0.047$) tumors and among patients who developed distant localization in the whole clinical history ($P = 0.011$). Levels of nAPE1 higher than 80% predicted a favorable prognosis in terms of event free survival (HR 0.42, 95%CI 0.42-0.16, $P = 0.026$).

Conclusions: APE1 and NPM1 are promising prognostic factors and therapeutic targets in TNBC. Inhibitors of APE1, NPM1 and their interaction are currently under further investigation

C42 The ENDOPREDICT® molecular test for breast cancer prognosis: clinical-pathological correlations and therapeutic implications on a selected cohort of patients

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Background: Gene signatures of prognosis are emerging for treatment strategies in breast cancer (BC), based on individual risk profile. These molecular tests are useful for patients who are affected by estrogen receptor (ER) positive/HER2 negative BC of indefinite prognosis. We focused on Endopredict® (Myriad Genetics), a multi-gene test, which gives both a molecular fingerprint of the tumors (the "EP score") and a score obtained by combining the EP score with the tumor size and number of metastatic lymph nodes (LN) (the "EPclin score"). EPclin score discriminates between patients having "low risk" or "high risk" of relapse within 5 years. To verify the utility of this test in clinical practice, we decided to: (i) correlate EP score and EPclin score with clinical-pathological features; (ii) test the ability of the EPclin score to influence therapeutic choices.

Materials and methods: From July 2014 to December 2016, we selected in Piedmont Region a cohort of 56 ER+/HER2- BC patients at intermediate risk of recurrence (tumor size < 3 cm; LN involvement from 0 to 3; Ki67 15-30%), for which the eligibility to chemotherapy (CT) was not univocal. For each case, clinical and pathological data were recorded. EndoPredict® was performed on each case and EP score and EPclin score were noted. We correlated both scores with clinical and pathological data. The data base was then submitted to 26 oncologists, who indicated the therapeutic option [hormonal treatment (HT) *versus* HT + CT] before and after the Endopredict® results.

Results: EP score was related with LN status (p 0.008), tumor grade ($p < 0.001$) and progesterone receptor (PgR) expression (p 0.007); EPclin score was related with tumor grade ($p < 0.001$), PgR (p 0.033) and Ki67 (p 0.009). In 11 cases the risk was assessed as "high" according with EP score and "low" with EPclin score; while in 3 cases the risk was "low" by EP score and "high" by EPclin score. Treatment agreement was low when

oncologists were blind to Endopredict® results (Cohen's K: 26%; Z: 26.47) and improved following the results of the molecular test (Cohen's K: 58%; Z: 24.32). The therapeutic indication changed from HT to HT + CT for 9 patients and from HT + CT to HT alone for 6 patients.

Conclusions: Both EP score and EPclin score correlate with grade and PgR expression. EPclin score gives a more comprehensive estimation of the risk of relapse and improves the agreement between oncologists in the subgroup of patients for whom the therapeutic protocol is not univocal.

C43 Everolimus-exemestane (EE) vs palbociclib-letrozole (PL) or palbociclib-fulvestrant (PF) in the treatment of metastatic HR+, HER2- breast cancer. Indirect comparisons with network meta-analysis for daily clinical practice

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Background: To compare the efficacy of EE to PF or PL in the treatment of metastatic HR^+, $HER2^-$ breast cancer pre-treated or untreated with aromatase-inhibitors (AI) for advanced disease.

Methods: An indirect comparison with a network meta-analysis comparing EE with PL or PF in the treatment of metastatic HR^+, $HER2^-$ breast cancer pre-treated or untreated with AI for advanced disease was performed. The Progression-Free-Survival (PFS) was the primary end point of all our indirect comparisons. The indirect comparison was performed both for patients pre-treated with AI and for patients never treated with AI for advanced disease. Efficacy data were expressed as Hazard Ratio (HR) and 95% Confidence Interval (95CI), assuming an α-error of 5% as index of statistical significance.

Results: All the data of the BOLERO-2 trial, the Bachelot et al network meta-analysis (Breast Cancer Treat Rep 2014), the PALOMA-2 and the Paloma-3 trial were analyzed and indirectly compared in a network meta-analysis. 2 orders of comparison were performed: EE vs PL for patients never treated with AI for advanced disease and EE vs PF for patients pre-treated with AI for advanced disease. The pooled HR and 95%CI were respectively 0.597 (0.355-1.005, p = 0.89) and 1.1 (0.7-1.6, p = 0.97) for EE vs PL (never treated with AI) and EE vs PF (pre-treated with AI). No major reasons of clinical and methodological heterogeneity were detected in an independent qualitative analysis, while a moderate quantitative heterogeneity was detected using the I^2 test.

Conclusions: Till today EE and PL or PF represent active treatments for patients with metastatic HR^+, $HER2^-$ breast cancer treated or untreated with AI, and no direct comparisons between EE and PL or PF exist in literature. Although our data have not the power to detect any definitive difference in PFS between EE and PL or PF (probably with the exception of EE vs PL, where a trend in favor of EE could be hypothesized), EE, PL or PF seem to be comparable in terms of PFS; it follows that the better safety profile or the economic profile could help physicians in daily clinical practice.

C44 Role of inflammation parameters in locally advanced breast cancer: the debate is still open

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Background: Neoadjuvant chemotherapy (NCT) is the standard treatment strategy for locally advanced breast cancer (BC). Data about clinical utility of blood-derived inflammation parameters as prognostic factors are robust in early BC, while their use in neo-adjuvant setting warrants investigation. Recently, a novel inflammatory parameter, named Systemic mmune-Inflammation Index (SII), obtained by analyzing the neutrophil, lymphocyte and platelet counts, has been proposed as a prognostic factor in some solid tumours as hepatocellular carcinoma, renal cancer and lung carcinoma. Our study aims to investigate the prognostic and predictive value of the SII in locally advanced BC patients treated with NCT.

Patients and methods: Data of consecutive patients undergoing NCT for locally BC (stage II-III) between January 2007 and April 2017 were retrospectively reviewed. Pre-treatment SII was calculated by multiplying the absolute platelet (P) and neutrophil (N) counts and dividing by the absolute lymphocyte (L) count. Patients were divided in two groups epending on the cut-off value of SII, calculated by ROC analysis. SII was then correlated with clinical-patological features of BC and with the patologically complete response by $\chi 2$ test. Relapse-free survival (RFS) and overall survival (OS) were estimated using Kaplan-Meier method. Level of significance p value was set at 0.05.

Results: A total of 120 patients were enrolled in the study. Median age was 53 years (range 28 – 75 years). The Hormonal Receptor (HR) status was positive in 73 patients (60.8%) and negative in 47 (39.2%); 45 of them (37.5%) presented HER2-positive tumors; 28 patients (23.3%) presented pCR. The best SII cut-off was $\geq$790 vs. <790 as defined by the ROC analysis. The value of SII showed no correlation with pathological complete response, RFS and OS. However, based on $\chi 2$ test, low level of SII was related with low pre-chemotherapy MIB-1 proliferation index (p = 0,01). No additional statistically significant relation between the value of SII and other clinical-patological features of BC were found.

Conclusion: In our study SII did not show a significant prognostic and predictive impact in patients with locally advanced BC. However, based on the recent results obtained by the use of anti-Programmed death-1 (PD-1)/PD-ligand 1 (PD-L1) agents, the research for reliable inflammatory biomarkers will be a major focus in future years.

C45 The role of ribociclib in hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2−) early breast cancer: the EarLEE adjuvant clinical trials program

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Background: In the phase 3 clinical trial MONALEESA-2, the CDK4/6 inhibitor ribociclib in combination with letrozole prolonged PFS versus letrozole plus placebo in postmenopausal women with HR+, HER2− advanced breast cancer (BC) and no prior therapy for advanced disease (HR = 0.56, 95%CI: 0.43-0.72; $P = 3.29 \times 10^{-6}$; Hortobagyi et al. N Engl J Med 2016). Although adjuvant endocrine therapy (ET) reduces the risk of recurrence of early BC (EBC), it is not yet known if the addition of ribociclib to ET would provide a benefit in this setting, where disease recurrence is common in patients with adverse clinical and pathologic features. EarLEE-1 (NCT03078751) and EarLEE-2 (NCT03081234) will examine the efficacy and safety of ribociclib plus ET versus placebo plus ET as adjuvant therapy in patients with high- and intermediate-risk EBC, respectively.

Trial design: In these double-blind, placebo-controlled, phase 3 trials, women and men with fully resected, HR+, HER2− EBC are being randomized 1:1 to ribociclib (600 mg/day, 3 weeks on/1 week off for ~24 months) plus ET or placebo plus ET. Adjuvant ET may include tamoxifen, letrozole, anastrozole, or exemestane for = 60 months with ovarian suppression for premenopausal women (in EarLEE-2, ovarian suppression is per investigator discretion). High-risk EBC is defined as AJCC 8th ed Prognostic Stage Group III, or > 2 mm residual disease in axillary lymph nodes and > 10 mm in breast after neoadjuvant chemotherapy. Intermediate-risk EBC is defined as AJCC 8th ed Prognostic Stage Group II. Randomization is stratified by menopausal status, geographical region, and risk factor. Prior adjuvant chemotherapy is optional in EarLEE-2 and is an additional stratification factor; patients eligible for EarLEE-1 must have completed (neo)adjuvant chemotherapy. Eligible patients must have tumor tissue from the surgical specimen, adequate bone marrow and organ functions, normal serum electrolytes, QTc interval < 450 msec, and must have completed and recovered from acute toxicities of adjuvant radiotherapy (if indicated) and adjuvant chemotherapy (for patients in EarLEE-1; per investigator discretion in EarLEE-2). The primary endpoint for both studies is invasive disease-free survival. Secondary endpoints include recurrence-free survival, distant disease-free survival, overall survival, quality of life, and safety. Global recruitment of ~2,000 patients (EarLEE-1) and ~4,000 patients (EarLEE-2) is ongoing.

C46 Prognostic value of lymph node ratio in early breast cancer: a restrospective single institution analysis of clinical-pathological characteristics and outcomes

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Background: Nodal involvement is recognized as negative prognostic factor in early breast cancer (BC), but the role of lymph node ratio (LNR) is less defined.

Methods: In our retrospective single institution study we analyzed the association between LNR and risk of recurrence in 96 BC patients (pts) who underwent to surgery as first disease treatment and reported local or distant recurrence. We collected patient demographics, tumour characteristics, initial clinical stage and treatment received.

LNR was defined as the number of positive lymph nodes divided by the number of dissected lymph nodes. DFS and OS rates were calculated according to Kaplan Meier methods and findings were tested for significance by the log-rank test.

Results: We obtained a median LNR of 0.18 (range 0-1). We compared pts with a LNR=0.18 (n = 57, group A) with pts with LNR > 0.19 (n = 39, group B). Tumor characteristics were similar among two groups: luminal A 23 (40%) versus 12 (32%); luminal B 22 (39%) vs 19 (50%), luminal B HER2 positive 3 (6%) vs 7 (8%), HER2 positive 2 (3%) vs 0 (0%), triple negative 7 (12%) vs 4 pts (10%) respectively. 34 pts of group A

(87%) and 41 (72%) of group B received adjuvant chemotherapy. All pts with hormone receptor positive BC were treated with adjuvant hormonal therapy in both groups. 12 pts (21%) of group A reported local recurrence as first invasive event versus 6 pts of group B (15%); 9 pts of group A and all pts of group B developed distant metastasis. In overall population DFS was 53.6 months (95% CI; 40.4 − 66.8), no statistically significant different was noticed among two groups: 56.2 mos group A, 49.8 group B ($p = 0.3$). OS was 120.2 mos, (95% CI; 112 − 311.9) with statistically significant difference among two groups: 137.7 mos group A, 98.7 mos group B ($p = 0.03$).

Conclusions: the study demonstrated that a LNR > 0.19 was associated with a significant increased risk of death, independently from tumor characteristics or type of treatment received. Despite the limitations of a retrospective study on a small sample of pts, results obtained should encourage to identify a more accurate cut-off for LNR that could help clinicians for therapeutic decisions or follow up programs.

C47 Potential miRNAs involved in molecular pathways mediating the anticancer effects of short term starvation in breast cancer cells treated with doxorubicin

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Background: In recent years, increasing evidences showed that several types of dietary approaches restricting food intake, including Short Term Starvation (STS), may exert a protective role against aging and other age-related pathologies as well as cancer. Interestingly, the dietary restriction showed significant anticancer effects able to prevent cancer onset, slow its progression and improve therapy response. Since recent studies showed that miRNAs may modulate sensibility/resistance to antiblastic therapy, the aim of our study was to investigate the STS-induced molecular changes in breast cancer cells treated with doxorubicin, focusing our attention on miRNA expression profile.

Materials and methods: Vitality assays were used to assess the effects of STS on cell proliferation. Using a TaqMan Low Density Array A human microRNA microarray analysis, the expression profile of 377 miRNAs was analyzed in healthy and malignant breast cells, MCF10A and MDA-MB-231 respectively, treated for 24h with 1μM doxorubicin under STS conditions for 48h. In addition, the expression of mRNAs and miRNAs specifically induced by STS was analyzed in MCF-7, MDA-MB-231 and SkBr3 cells using Real-time PCR analyses.

Results: *In vitro* cell vitality assays showed that STS, in association with doxorubicin treatment, significantly reduces breast cancer cell proliferation and viability, whereas it appears to protect healthy breast cells from chemotherapeutic treatment. Microarray analysis showed that a subset of miRNAs involved in molecular pathways related to drug sensitivity/resistance was found to be differentially expressed in breast cancer cells following the doxorubicin treatment and STS. Finally, expression analysis of hypothetical miRNA gene targets involved in therapy response have confirmed the coherence of our results.

Conclusions: This work establishes, for the first time, an interesting link between anticancer effects of STS and miRNA expression changes in doxorubicin-treated breast cancer cells, suggesting the potential involvement of some miRNAs in molecular pathways mediating the effects of STS in breast cancer.

C48 Response rate by molecular subtypes and p53 expression in neoadjuvant therapy for breast cancer with TAC regimen: a single-centre experience

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Background: Pathologic complete response (pCR) is a surrogate of survival in breast cancer (BC), although its value seems to be restricted to specific subtypes. The aims of our study were to determine the response rate (RR) and pCR according to BC subtypes and p53 expression in neoadjuvant setting.

Materials and methods: From January 2000 to December 2016 we retrospective analyzed 87 consecutive patients (pts) treated with TAC regimen (docetaxel 75mg/mq, doxorubicin 50mg/mq, cyclophophamide 500mg/mq, d1q21) for locally advanced BC between 2004 and 2016. RR > 50% and pCR (defined as no evidence of residual cancer or residual in situ component only in the primary tumour and lymph-nodes) were compared to St. Gallen 2015 molecular subtypes and p53 expression, considered positive with a nuclear staining>10%.

Results: 87 patients (pts), median age 44.7 years (24-78), were classified as follows: luminal A 13.7% (12/87), luminal B-HER2-ve 29.8% (26/87), luminal B-HER2+ve 10.3% (9/87), HER2+ve 4.5% (4/87), triple negative 40.2% (36/87). p53 was negative in 49% pts and positive in 51%. All pts received 6 cycles of TAC regimen before surgery that was conservative in 37 cases (42.5%) and modified or radical mastectomy in the others. After surgery patients HER2+ve underwent adjuvant treatment with Trastuzumab for an year. RR was 75.8% (67/87) and pCR 19.5% (17/87). pCR rate by molecular subtypes was: luminal A 0%, luminal B-HER2-ve 11.7% (2/17), luminal B-HER2+ve 17.6% (3/17), triple negative 70.5% (12/17).p53 expression was determined in 77/87 pts. RR was 77.5% in p53+ve tumours and 69% in p53-ve, pCR was 50% in both p53+ve and p53-ve. At a median follow-up of 55.5 months (15-104), 74 pts are still alive. All pts that achieved pCR are alive and disease free at a median follow-up of 63 months (24-102).

Conclusions: Our results are in agreement with the literature. TAC regimen is highly effective in neoadjuvant setting especially in triple negative BC. p53 expression doesn't seem to be an independent predictor for response.

C49 Early assessment of chemotherapy-related cardiovascular toxicity in patients with breast cancer

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Background: Chemotherapy used for the treatment of breast cancer (BC) is commonly complicated by cardiac damage and may also deteriorate vessels function, leading to an impaired cardiovascular coupling. Cardiac toxicity is generally evaluated by assessing left ventricular (LV) ejection fraction (EF). Recently, myocardia deformation imaging has been proposed for the detection of subtle systolic dysfunction. However, few studies have analyzed the effects of anticancer drugs through an integrated evaluation of heart and vessels. The aim of the study was to evaluate myocardial and arterial function early after anthracyclines administration.

Patients and methods: 35 women (mean age: 54±10) with localized or metastatic BC and without history of heart disease were enrolled. All patients received anthracyclines (epirubicin, 500 mg/mq or doxorubicin 600 mg/mq) and, in different percentages, further antiblastic therapy: 5-fluorouracil (500 mg/mq, 35.7%), docetaxel (75 mg/mq, 42.9%), cyclophosphamide (600 mg/mq, 89.3%) and trastuzumab (loading dose of 8 mg/kg, followed by 6 mg/kg, 25%). Patients were evaluated at time 0, 3 and 6 months after the start of the therapy. We used global longitudinal strain (GLS, EchoPac), as marker of preclinical LV systolic dysfunction, and pulse wave velocity (PWV), augmentation index (AI), and β-stiffness, derived by echotracking software (Aloka, Japan) as markers of arterial stiffness, measured on the carotid arteries. The ANOVA analysis was used for comparing the data.

Results: Although volumes, EF and BNP were not altered significantly after cancer therapy, GLS and troponin I were instead modified since the first 3 months (Tab. 1). Also, both carotid PWV and β-stiffness index increased at 6 months. Results were not affected by the type of anticancer drugs associated with antracyclines.

Conclusions: A combined evaluation of cardiac and vascular function should be early started in patients receiving anthracyclines. The identification of early markers of cardiac damage from cytotoxic drugs remains of crucial clinical relevance.

Table: C49

	Baseline pre-treatment	3 months	6 months	P
BNP, pg/mL	43.6±37.1	55.1±69	42.6±22.01	ns
Troponin I, ng/L	0.014±0.008	0.046±0.06*	0.03±0.01**	*0.03;**0.01
EDV, ml	77.8±19.5	77.2±16.9	74.8±17.8	ns
ESV, ml	32.3±19.4	32.5±16.9	30±11.3	ns
EF, %	60.2±7.2	58.2±6.5	61.7±6.1	ns
GLS, %	-20.5±2.9	-18.1±2.1*	-15.98±4.1**#	*<0.001; **0.008; #0.02
β index	10.9±3.8	11±3.7	12±2.1*	*0.03
PWV, m/sec	10.4±3.3	10.7±3.6	11.6±2.8#	#0.013
AI	15.2±5.7	14±5.7	15.9±4.3	ns

ns: not significant.

C50 Differential gene expression patterns in HER2 positive metastatic breast cancer patients according to hormone receptor status

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Background: HER2 positive breast cancer (HER2+ BC) is a heterogeneous disease. Presenting features, patterns of recurrence and survival of HER2+ BC can differ according to hormone receptors (HR) status. The purpose of this study is to highlight different gene profile and molecular pathways between HR+ and HR- metastatic HER2+ BCs.

Materials and methods: 34 HER2+ metastatic BC patients were included: 18 patients with HR+/HER2+ and 14 with HR-/HER2+. Data regarding tumor characteristics, treatment information and clinical outcomes were collected. The expression of 770 genes and 13 molecular pathways were evaluated by means of *Nanostring PanCancer pathway panel* performed on BC formalin-fixed paraffin-embedded tissues from diagnostic core biopsy or surgical resection specimen.

Results: Gene expression analysis identified 118 genes with significantly different expression in the two cohorts. All but one of these genes were over-expressed; only the gene CACNG6 was down-regulated in HR+/HER2+ group. In particular, 93 genes were over-expressed in HR-/HER2+ while 24 were overexpressed in HR+/HER2+. Most of these genes encoded growth factors, pro- or anti-inflammatory interleukins and DNA repair factors. 62% of these genes were involved in PI3K, MAPK and RAS pathways (32, 22 and 18, respectively). PI3K, MAPK and NOTCH pathways were differently expressed between HR+/HER2+ and HR-/HER2 + ($p = 0.003$, $p = 0.0018$, $p = 0.02$, respectively). All these three pathways were overexpressed in HR-/HER2+ BC. In particular, all the significantly different expression genes in NOTCH pathways were overexpressed in HR-/HER2+ group.

Conclusions: This genome expression analysis identified a gene expression profile able to differentiate HR+ versus HR- HER2+ metastatic BC. The overexpression of PI3K, MAPK and NOTCH pathways in HR-/HER2+ BC could justify its more aggressive behaviour. The validation of this HER2+ BC profile needs further investigation.

C51 Use of scalp-cooling device to prevent alopecia for breast cancer patients receiving chemotherapy: a single-Institution prospective study

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Background: Previous studies have suggested that scalp cooling may prevent chemotherapy-induced alopecia, a common adverse event with a relevant impact on quality of life.

Patients and methods: Two DigniCap scalp cooling system devices are available at the Istituto Oncologico Veneto. The PROTECT prospective observational study evaluated the performance of scalp cooling for patients with breast cancer receiving different adjuvant/neoadjuvant chemotherapy schedules. Scalp cooling was initiated 30 minutes prior to each cycle, with a scalp temperature maintained at 3-5 °C, throughout chemotherapy and for 90 to 120 minutes afterwards. Patients' questionnaires were administered every 3 weeks during treatment and at 3 weeks from the last cycle. Success of scalp cooling was defined as self-reported hair loss$\leq$50% according to Dean scale.

Results: From may to december 2016, 40 patients were included in these treatment cohorts: $n = 10$, Docetaxel-Cyclophosphamide q3w x4 (TC); $n = 10$, Paclitaxel qw x12 (Txl); $n = 10$ Epirubicin-Cyclophosphamide q3w x4 followed by Txl qw x12 (EC-Txl); $n = 10$, Txl qw x12 followed by EC q3w x4 (Txl-EC). HER2 + ($n = 11$) patients received trastuzumab. Success rate at 3 weeks from the start of treatment was 85% (34/40). Three patients in the TC and 3 in the EC-Txl cohort reported a hair loss >50%. Full assessments have been completed so far in the TC, Txl and EC-Txl cohorts (3 patients in the Txl-EC cohort are still undergoing chemotherapy). Rate of final scalp cooling success was 18/30 (60%). No failure was reported in the Txl cohort. Failure was reported by 6 patients in the TC and 6 patients in the EC-Txl cohort and led to premature scalp cooling discontinuation in 1 and 3 patients, respectively. Two more patients discontinued scalp cooling in these cohorts: 1 patient due to chemotherapy toxicity and 1 patient in the EC-Txl cohort due to low scalp cooling tolerability. Most frequent cooling-related symptoms were: chill(26/30), heavy head(18/30), scalp pain(14/30), headache(13/30); respective mean highest scores (in a self-reported scale of 1 to 4 with 4 as the worst) were: 3.04, 2.39, 2.64, 2.54. Mean final patient's judgment on scalp cooling performance (on a scale of 1 to 7, where 7 is the best) was 6.7, 5 and 4.6 in the Txl, TC and EC-Txl cohorts, respectively.

Conclusions: Use of scalp cooling system for chemotherapy-induced alopecia prevention was successful in the majority of patients, but relevant difference was observed across treatment groups.

C52 Scalp cooling: a real opportunity to prevent alopecia in breast cancer women undergoing chemotherapy?

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Background: Hair loss is one of the most distressing side effects of chemotherapy. Recent clinical trials demonstrated the efficacy of scalp-cooling in preventing and reducing the risk of chemotherapy-induced alopecia (CIA), but factors predicting outcome are still undefined.

Patients and methods: Data on women with breast cancer stage I-IV who used the Paxman scalp-cooler during chemotherapy at Ferrara Oncology Unit were prospectively collected. Efficacy and safety of scalp-cooling device were assessed using clinicians-reported data and patients direct interviews. Alopecia was graded according to the Dean's Scale: a score of 0 to 2 (hair loss < 50%) was considered successful. Correlation between categorical variables was assessed using chi-square test and Fisher's exact test.

Results: From March 2015 to April 2017, 48 women with a median age of 53 underwent scalp-cooling during chemotherapy for breast cancer. 5 patients (pts) were treated in neoadjuvant setting, 29 in adjuvant setting and 14 in advanced setting; 27 pts received anthracycline-based chemotherapy, 13 taxane-based chemotherapy, 5 both anthracyclines and taxanes and 3 other regimens. Median scalp-cooling cycles were 3 (range 1-14). Hair preservation was reported in 17 women (37%). According to literature data, women treated with taxane-based chemotherapy had higher rate of hair preservation than women treated with anthracycline-based chemotherapy (54% vs 31%), even if the correlation between chemotherapy regimen and hair loss wasn't statistically significant in our analysis. Different variables (such as age, BMI, smoke, menopausal status, comorbidities, previous chemotherapy, neutropenia) were tested, but only neutropenia G3-4 during treatment resulted significantly related to hair loss (chi-square 4.9, p 0.049). Early interruption of scalp-cooling occurred in 26 pts, due to hair loss < = grade 3 (21 pts) or intolerance (5 pts). 15 pts reported adverse events, all graded < = 2, the most common being headache, cold sensation and mild cranial pressure. 14 pts had to use a wig, even if 5 of them experienced alopecia G1-2. No scalp metastases were reported, but follow-up data are still immature.

Conclusions: Our analysis suggests that scalp-cooling has a moderate efficacy in reducing CIA and is well-tolerated. Further clinical trials are needed to determine exact indications for scalp-cooling and to improve the efficacy and adherence, to reduce side-effects and to define the best cooling procedure.

C53 Oral etoposide in heavily pretreated metastatic breast cancer: a retrospective analysis of efficacy and safety

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Background: The therapeutic approach to heavily pre-treated Metastatic Breast Cancer (MBC) is challenging and suspended between activity and side effects which need to be minimal in a palliative setting. In this context, data from few retrospective and prospective phase II trials showed that oral etoposide (VP-16) is active in MBC. However heavily pre-treated patients were rarely recruited. The aim of our study was to assess efficacy and safety of oral etoposide in this unfavourable subset of MBC patients.

Patients and methods: We retrospectively analysed 110 patients with MBC, who received 50 mg/day oral etoposide in 20-day cycles with 1-week of rest between 2003 and 2017. Median number of previous treatments was 7 (range 2-14). Clinical benefit rate (CBR, including complete response, partial response and disease stabilization for more than 6 months), Overall Survival (OS) and Time To Progression (TTP) were evaluated. Side effects were recorded.

Results: Patients received a median of 5 cycles of oral etoposide. CBR was 27.3%; median TTP and OS from the start of treatment were 4 (range 3.5-4.5) and 10.6 (range 8.4-12.8) months respectively. Interestingly, etoposide activity was unrelated to the number of previous lines and type of metastatic involvement; there were no statistical differences according to Estrogen Receptors (ER) or HER2 status, but patients with a ER+/HER2+ MBC had a trend towards a longer TTP ($p = 0.068$). Oral etoposide was well tolerated with only two patients discontinuing therapy due to toxicity and no treatment related deaths.

Conclusions: To our knowledge, this is the biggest retrospective study showing that low dose oral etoposide is a valuable option for MBC patients who failed multiple prior treatments with a significant clinical activity and manageable side effects.

C54 CompLEEment-1: phase 3b study of ribociclib + letrozole for the treatment of hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2−) advanced breast cancer (ABC) in patients with no prior endocrine therapy (ET) for ABC

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Background: CDK4/6 inhibitor ribociclib was recently approved in the United States in combination with letrozole for the treatment of HR+, HER2− ABC in postmenopausal women with no prior therapy for advanced disease, based on the significantly prolonged PFS versus placebo plus letrozole observed in the pivotal phase 3 MONALEESA-2 trial (Hortobagyi et al. NEJM 2016). The phase 3b CompLEEment-1 study will further evaluate the safety and efficacy of ribociclib plus letrozole as first-line therapy in an expanded patient population.

Trial design: In this open-label study, men or women of any menopausal status with HR+, HER2− ABC will receive ribociclib (600 mg/day, 3 weeks on/1 week off) +

letrozole (2.5 mg/day); men and premenopausal women will receive concomitant goserelin (3.6 mg subcutaneous implant every 28 days). Treatment will continue until disease progression or unacceptable toxicity. Patients are limited to = 1 line of chemotherapy and no prior ET for advanced disease; patients receiving (neo)adjuvant ET with a nonsteroidal aromatase inhibitor must have a disease-free interval of > 12 months. Exclusion criteria include Eastern Cooperative Oncology Group performance status >2, or prior CDK4/6 inhibitor treatment. Planned hematologic and chemistry laboratory assessments will be completed every 2 weeks for the first 2 months, then monthly to Cycle 6, and as clinically indicated to Cycle 36. Tumor assessments are recommended every 12 weeks or at intervals per local standard of care during the treatment phase. The primary outcome is safety and tolerability. Secondary outcomes include time to progression, clinical benefit rate, overall response rate, safety, and patient-reported outcomes (PROs). Adverse events and drug-drug interactions will be monitored using CT Scholar; PROs will be collected for female patients using the FACT-B questionnaire to better understand health-related quality of life and treatment side effects. Global recruitment of the planned ~3,000 patients is ongoing, with the majority occurring in Europe. Clinical trial NCT02941926.

C55 Safety and efficacy of the treatment with Nab-paclitaxel in mEtastatic bREast cancer In elDerly patiEnts: NEREIDE study

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Background: Recommendations for management of metastatic breast cancer (MBC) in elderly patients (pts) are limited because of this subgroup of pts are largely underrepresented in clinical studies and this treatment is largely based on limited retrospective subgroup analyses.

Patients and methods: This is an observational, retrospective, multicenter study conducted in 11 Oncology Sicilian Centers. The aim of this study was to assess the safety and efficacy of nab-paclitaxel (nab-P) treatment in pts with HER2 negative MBC with age ≥ 65 years. We evaluated 70 HER2-negative MBC pts. The intrinsic molecular subtype was: Luminal A (18.8%), Luminal B HER-2 negative (62.5%) and Triple negative (18.8%). The most common type of metastatic sites was: visceral plus bone (31.4%), bone (15.7%), lung (10%), visceral plus lymph nodes (10%). The 23% of pts received treatment with nab-paclitaxel in fourth metastatic line. 87.1% of all pts received nab-paclitaxel at doses 260 mg/m2 every 3 weeks and 12.9% received nab-P 125 mg/m^2 weekly. 28.6%, 25.7% and 26.2% of pts received previous treatment with taxanes in the neoadjuvant, adjuvant and metastatic setting, respectively. The primary end-point was to investigate the safety of nab-paclitaxel treatment. The secondary end-points were to evaluate progression free survival (PFS) and overall survival (OS). PFS and OS curves were estimated using the Kaplan-Meier method. Tumor response was assessed according to RECIST v1.1 and safety profile according to CTCAEv4.0.

Results: Median (m) age of pts who received Nab-P: 67 years (65-83). mECOG PS: 1 (range 0-2). The m cycles administrated was 6 (range 1-21). 35.5% of the pts had a dose reduction and 11.5% interrupted treatment for toxicity. Adverse events (Grade 2-3) were observed in 47% of the pts. The main toxicities were fatigue (61.5%), neuropathy (53.8%) and leukopenia (39.1%) and occurred in the 85.7% of pts treated with 3-weekly Nab-P. 6.3% of pts had a complete response, 25% had a partial response and 39.1% had a stable disease. Median PFS was 6 months (95% CI 2-38) and median OS was 40.5 months (95% CI 7-255).

Conclusions: Our real-life study showed that the treatment with nab-paclitaxel is an effective and well-tolerated regimen in MBC elderly pts, even if previously treated with other taxanes. In particular, our data indicate that the weekly Nab-P can be safely administered in elderly MBC pts.

C56 Electrochemotherapy in the treatment of cutaneous metastases from breast cancer: a multicenter cohort analysis

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Background: The management of breast cancer (BC) skin metastases represents a therapeutic challenge. Electrochemotherapy (ECT) combines the administration of bleomycin with temporary permeabilization induced by locally administered electric pulses. Preliminary experience with ECT in BC patients is encouraging.

Methods: A total of 125 patients with BC skin metastases who underwent ECT between 2010 and 2013 were enrolled onto a multicenter retrospective cohort study of the GISEL group (Gruppo Italiano Senologia ed Elettrochemioterapia). The treatment was administered following the European Standard Operative Procedures of Electrochemotherapy. Tumor response was clinically assessed adapting the Response Evaluation Criteria in Solid Tumors, and toxicity was evaluated according to Common Terminology Criteria for Adverse Events 4.0. Cox regression analysis was used to identify predictive factors.

Results: Response was evaluable in 113 patients for 214 tumors (median 1 per patient, range 1−3). The overall response rate after 2 months was 90.2%, while the complete response (CR) rate was 58.4%. In multivariate analysis, small tumor size ($P < 0.001$), absence of visceral metastases ($P = 0.001$), estrogen receptor positivity ($P = 0.016$), and low Ki-67 index ($P = 0.024$) were significantly associated with CR. In the first 48 h, 10.4% of patients reported severe skin pain. Dermatologic toxicity included grade 3 skin ulceration (8.0%) and grade 2 skin hyperpigmentation (8.8%). Tumor 1-year local progression-free survival was 86.2% (95% confidence interval 79.3−93.8) and 96.4% (95% confidence interval 91.6−100) in the subgroup of those with CR.

Conclusions: In this study, small tumor size, absence of visceral metastases, estrogen receptor positivity, and low Ki-67 index were predictors of CR after ECT. Patients who experienced CR had durable local control. ECT represents a valuable skin-directed therapy for selected patients with BC. A new prospective protocol has been recently approved by the coordinator centre of Padova for an observational multicentre study on BC patients treated with ECT. GISEL group is open to new centres interested in giving their contribution to the study.

C57 Bald is beautiful: no more. The stigma of alopecia during chemotherapy: Brindisi Oncology Department experience

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Background: The cancer treatments often bring with it body image challenges, causing low self-esteem and contributing to worsen the quality of life (QoL). Chemotherapy (CT)-induced hair loss (HL) is one of the most emotionally distressing side effects of several breast cancer (BC) treatments. The DigniCap system (DCS), using the scalp cooling system, has been shown to reduce CT-induced alopecia (A) in a multicenter prospective trial. The purpose of this prospective observational study was to describe our experience.

Materials (patients) and methods: From February 2016 and April 2017, 40 consecutive early stage BC pts who received anthracycline and/or taxane-based treatment were enrolled, post local Ethics Committees approval. A nurse and a psychologist were dedicated for these pts. A/HL has been graduated according to the Dean's scale: G0= no HL; G1 < 25% HL; G2=25−50% HL; G3=50−75% HL; G4 >75% HL.

Results: A total of 40 women were enrolled; median age was 49 years (range 31-64). Seventeen pts (42.5%) received 4 courses of EC (epirubicin at 90 mg/m2 and cyclophosphamide at 600 mg/m2 intravenously on day 1, with 21 days between cycles) followed by 12 courses of Paclitaxel 80 mg/m2 intravenously once a week); 21 (52.5%) received 4 courses of EC and 2 pts (5%) Paclitaxel (P 80 mg/m2 intravenously once a week) and concurrent Trastuzumab (2 mg/Kg intravenously; loading dose 4 mg/kg) for 12 consecutive doses. Full preservation of the hair (G0) was observed in 6 pts (15%), G1 in 15 pts (37.5%) and G2 in 7 pts (17.5%) (Table 1). Twenty-eight pts (G0-2=70%) did not need a wig or other hair piece to mask their hair loss during the chemotherapy period; only 6 pts (15%) used wig or head cover.The majority of pts tolerate DCS very well. Among G3 DCS-related side effects, coldness (n = 11, 27.5%), neck pain (n = 4, 10%) and headache (n = 3, 7.5%) were the main toxicity.Overall, 4% (n = 4) of pts discontinued DCS because of unsatisfactory hair preservation (n = 3; 7.5%) and cold discomfort (n1; 2.5%).

Table: C57. A/HL according to the Dean's scale

ALOPECIA/HL	G0	G1	G2	G3	G4
n (%)	6 (15%)	15 (37.5%)	7 (17.5%)	10 (25%)	2 (5%)

Conclusions: Our results confirm previous evidences, showing that DCS is a good chance to keep hair during CT. Further trials are needed to refine pts selection and to improve the effect and tolerance.

C58 Eribulin mesylate in advanced breast cancer: retrospective review of a single institution experience

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Purpose: Eribulin is a non-taxane microtubule inhibitor, which can be used after anthracycline and taxane treatment in patients with metastatic breast cancer (MBC). The purpose of this study was to investigate the efficacy and safety of eribulin monotherapy in heavily pretreated MBC patients.

Materials and methods: This was a single institution retrospective analysis of MBC patients treated with eribulin from August 2012 to May 2016. These patients had received at least 2 lines of prior therapy for metastatic disease. Patients received standard doses of eribulin and were monitored for responses.

Results: Forty-four patients were included in this analysis who received at least one cycle of eribulin were identified. Median patient age was 58 years (range 43-76). All were pretreated with anthracyclines and taxanes and 72% with capecitabine. Brain metastases were present in 9 (20%) patients at the time of initial eribulin administration. Most patients were heavily pretreated with a median of 3 (range 2-7) previous chemotherapy lines prior to eribulin and had significant visceral involvement (median 3 organs). A median of 5 cycles of eribulin was delivered. There were no complete responses; partial responses were 20% (9/44) with a 54,5% of disease control rate (25/44), progressive disease was seen on eribulin in 44,5% (19/44) patients. The median progression-free survival was 4.5 months (95% CI 2.8- 6,2) and median overall survival was 12 months (95% CI 7.8-16.4). Only one patient experienced grade 3 neurotoxicity. Three patients (6,8%) stopped eribulin due to fatigue grade 3. No hypersensitivity reactions and no toxic deaths were observed.

Conclusion: Eribulin monotherapy is an effective and safe regimen for MBC patients. In our experience, eribulin maintains its activity out of clinical trials, without unexpected toxicities.

C59 Efficacy and safety of the combination of pertuzumab (P) plus trastuzumab (T) plus docetaxel (D) for HER-2 positive metastatic breast cancer (MBC) in pretreated patients (pts) with trastuzumab in the neo/adjuvant setting: a retrospective real-life study

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Background: The discovery of new anti-HER2 targeted therapies has significantly improved the outcomes in the metastatic setting. However, the population enrolled in clinical trials is not always representative of the clinical practice. Moreover, only 7% of breast cancers (BCs) present as metastatic disease at the first clinical observation. In most cases, metastatic disease is diagnosed in pts with a history of BC already treated in the neo/adjuvant setting. This latter subgroup is largely under-represented in clinical trials.

Methods: This is a multicenter, observational, retrospective study conducted in 6 Oncology Italian Centers. The aim of this study was to assess in real-life the efficacy and safety of dual HER2 blockade as 1st line in Trastuzumab-pretreated pts in the neo/adjuvant setting. Primary end-points: progression free survival (PFS) and overall survival (OS). Secondary end-points: response rate and cardiac safety. PFS and OS curves were estimated using the Kaplan-Meier method. Tumor response was assessed according to RECIST 1.1 and safety with CTCAE v4.0.

Results: We evaluated 35 HER2-positive MBC from November 2013 to December 2016, 60% with tumors Luminal B, 40% HER2-enriched. The most common metastatic sites were: lung (20%), lymph nodes (14.3%) and liver (11.4%). Median (m) age: 50 (range 20-71), mECOG PS 0 (range 0-1). At a m follow-up of 55.6 months (mos) (range 6-170), all pts were evaluable for efficacy and safety. The m number of cycles administrated was 6 (range 2-10). The mPFS was 12 mos (95% CI 2-38). The mOS was 15.2 mos (95% CI 2-36). 14.3% of pts had a complete response, 60% a partial response and 25.7% a stable disease. m baseline LVEF was 65%, m final LVEF 61%.

Conclusions: Our preliminary data confirmed the efficacy and no increase in cardiac toxicity of the combination Pertuzumab, Trastuzumab and Docetaxel in Trastuzumab-pretreated pts, mirroring the PFS data but not the OS reported in the Cleopatra study. A longer follow-up for OS is needed for a comprehensive evaluation of the antitumor activity of dual-HER2 blockade in Trastuzumab-pretreated pts.

C60 Cardiac safety of adjuvant non-pegylated liposomal doxorubicin combined with cyclophosphamide and followed by paclitaxel in older breast cancer patients

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Background: To investigate the cardiac safety of adjuvant Non-Pegylated Liposomal Doxorubicin (NPL-DOX) combined to Cyclophosphamide (CTX) and followed by weekly Paclitaxel, in older patients (≥ 65 years) with diagnosis of high risk breast cancer. The main end point of this prospective study was the detection of early episodes of symptomatic congestive heart failure (CHF).

Methods: The cardiac function was evaluated by left ventricular ejection fraction (LVEF) measurements with repeated echocardiograms, performed 2 weeks before the beginning of chemotherapy and every 6 months, until 30 months after the study entry; then yearly for at least 5 years.

Results: Median cardiac follow up period was 40.5 months (range, 18.6-66 months). Forty-seven patients were enrolled from two Italian Divisions of Medical Oncology. Final results revealed no early episodes of symptomatic CHF within the first 12 months from the enrolment. Only two cardiac events were observed: an episode of atrial flutter after the first cycle of NPL-DOX and CTX, with a quick return to normal rhythm, and a grade 3 (scored to NCI-CTCAE, version 3.0) CHF episode, 18 months later chemotherapy start. No other relevant toxicities were reported. Median LVEF values remained the same for all the period of time (60%), with minimal changes within the 10° and 90° percentiles, when compared to baseline. For the survival assessment, after a median follow up of 40.5 months (range, 18.6-66 months), eight patients (17%) experienced disease relapse. Five patients with distant relapse, died for progression of disease.

Conclusions: This adjuvant combination including NPL-DOX in elderly patients, resulted in a low rate of cardiac toxic effects. Comparative trials should be encouraged to confirm these findings.

C61 Early male breast cancer: a single center experience

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Background: Male breast cancer(MBC)is an uncommon disease.Clinical behavior is generally more aggressive than women's BC.The best treatment is not well defined;most of MBC reviews are retrospective from single Institutions.Mastectomy is considered the best surgical therapy.Common adjuvant endocrine therapy(HT)is Tamoxifen(TAM)for endocrine responsive disease.Therapy with Aromatase Inhibitors(AI)is used when Tamoxifene is contraindicated in association with LH-RH.Several chemotherapy(CT)regimens are used(Antracicline based or not).

Materials: We reviewed data regarding patients(pts)with early MBC diagnosed in our Oncology Unit from January 1991 to March 2016.

Results: We collected data of 53 pts.Median age was 67years(33-86).30 pts were pT1,13pT2,0 pT3,10 pT4;25 pts were N0,24 N+, 4 Nx.Histology:invasive ductal carcinoma in all pts.Median size:2,3 cm(0,7-11); median ki67:31%(2-70%).Grade:G3 in 17 pts, G2 in 32 pts, G1 in 4 pts;46 pts were ER+ve and PgR+ve and 6 pts were ER+ve and PgR-ve.3 pts were triple-ve.14 pts were HER2 2+ve;35 pts were HER2-ve, HER2 status of 5 pts is unknown(diagnosis before 2005).All pts underwent radical mastectomy and received adjuvant treatments.27 pts received CT(antracicline, taxanes and CMF).50 pts received adjuvant HT(33 pts received TAM, 2 pts received TAM for 2years and IA for 3 years and 15 pts received an AI and LHRH).6 high risk pts received adjuvant radiotherapy(RT).None of the pts who received djuvant RT presented local

recurrence.Seven pts of 47 pts(15%)who hadn't received RT in adjuvant setting had local recurrence:4 of them underwent surgery and RT and also with systemic therapy (HT or CHT or both) 3 pts were treated only with chemotherapy;2 pts had controlateral recurrence, that was surgically removed, followed by RT.Nine pts had distant recurrence and were treated with CT.At a median follow-up of 10 years(1-25 years)23 patients (43%) are alive; the median DFS and OS are 78 months and 97 months, respectively.

Conclusions: Our patients presented at an older age, earlier stage and presented an aggressive disease. Prognosis is not well defined but the clinical course seems aggressive.MBC treatment has been extrapolated from experience treating breast cancer. Further prospective multicenter studies are needed to determine the best treatment and it is very positive that EORTC in 2014 started a prospective international registry.

C62 Safety and efficacy of non-pegylated liposomal doxorubicin (NPLD) in HER2 negative metastatic breast cancer (mBC) patients (PTS) as second-line (2L) and beyond: a restrospective single institution analysis

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Background: NPLD has shown comparable efficacy but lower risk of cardiotoxicity, compared to conventional anthracyclines, in mBC pts. Up today, its label indication is limited to the first-line treatment, however, in daily clinical practice, it is widely used in pretreated pts, where limited data exist.

Materials and methods: we retrospectively collected all consecutive, HER2 negative, mBC pts treated at our institution with NPLD 60 mg/mq iv every 21 days in 2L or beyond. We reported cpts characteristics, outcomes and adverse events (AEs).

Results: Between Nov 2010 to date, we identified 42 pts. Median age: 52 years (range 34 - 73). Molecular subtypes: luminal A 17 (40%); luminalB 20 (48%); triple negative 5 (12%). 18 pts (43%) were previous exposed to anthracyclines (anthra): 16 (38%) pts in neo/adjuvant and 2 pts (5%) in metastatic setting. 10 pts (24%) received adjuvant radiotherapy on the left breast and among them 6 pts (14%) were treated with anthra. NPLD was administered as: 2L in 14 pts (33%); third-line (3L) in 12 pts (29%) while 16 pts (38%) received it after three or more lines. 36 pts (86%) had visceral disease. Median number of cycles was 5 (range 1 - 11). Overall 40 pts were evaluable. Partial response was reported in 7 pts (17,5%) and 13 pts (32,5%) had stable disease with a clinical benefit of 50%. 20 pts (50%) showed a progressive disease (PD) as best response. Median PFS was: 5,3 months (mos) (range 0,7-18,3) in 2L, 3,9 mos (range 0,7-11,36) in 3L and 4,4 mos (range 0,7-18,7) in fourth-line and beyond. There was no difference in mPFS between patients previously exposed or not to anthra: 5,1 mos (range 0,7-18,7) vs 5,6 mos (range 0,69-12,93) respectively ($p > 0.05$). AEs were mild: nausea G1-2 in 19 pts (45%), fatigue G1-2 in 18 pts (43%), vomiting G1-2 in 7 pts (20%), skin toxicity G1-2 in 7 pts (20%), mucositis G1 in 12 pts (29%) and anemia G1 in 11 pts (26%). The most common G3-4 AEs was neutropenia observed in 12 pts (28%). An asymptomatic reduction in the left ventricular ejection fraction (LVEF) of G1 was shown only in 2 pts (5%). One of them received previous anthra.

Conclusions: with the limitation of the retrospective nature of the analysis, our single institution, real life experience demonstrate that NPLD is effective and safe in mBC pts, also as 2L or beyond, irrespective of previous exposure to anthracyclines.

C63 Efficacy and safety of everolimus and exemestane for metastatic breast cancer patients: a real-life experience of three Oncology Departments

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Background: Everolimus and exemestane regimen for metastatic breast cancer (MBC) is an effective and widely adopted treatment in hormonal receptor positive (HR+) and human epidermal growth receptor factor 2 negative (HER2-) patients. The pivotal phase 3 BOLERO-2 trial showed a significant progression-free survival (PFS) improvement in patients previously treated with nonsteroidal aromatase inhibitors (4.6-months prolongation in median PFS). Conversely, adding everolimus to exemestane did not confer a significant improvement in the secondary endpoint overall survival (OS). Many other experiences reported results in patients mostly endocrine-treatment naive or treated with tamoxifen only. Therefore, the real-life translation of these evidences is still debated.

Patients and methods: We evaluated the efficacy rates obtained from a cohort of consecutive treated patients at three different Oncology Departments. We compared our PFS and OS results to the outcomes showed in the BOLERO-2 trial (published as a pre-planned interim analysis after 359 observed PFS events), in order to evaluate if applicable also in out-of-trial real-life series. Adverse events were graded according to the NCI CTCAE, version 4.0.

Results: We overall analysed 95 patients. The median age of patients was 51 years (range 30-86). 70 patients (73.7%) received previous adjuvant endocrine treatment; 35/70 patients were treated with adjuvant aromatase inhibitors. Median PFS was 6 months (BOLERO-2 trial showed a local-assessed PFS of 6.9 months). Visceral disease (62/95; 65%) showed a significant worse outcome compared to bone metastases group of patients ($p = 0.043$). Concerning age, median PFS was 7 months ($<=$65 years) versus 6 months (>65 years), no significant ($p = 0.61$). If used in I-II line of chemotherapy the median PFS showed a significant improved outcome (8 months versus 5 months in case of > 2 line; $p = 0.03$). The OS of our series was 20 months; patients affected by visceral disease at time of treatment had a comparable median OS compared to the bone metastases group of patients (17 versus 15 months; $p = 0.64$).

Conclusions: Real-life use of everolimus plus exemestane regimen in our clinical routine practice supported the BOLERO-2 trial outcomes, confirming the expected efficacy in several subgroups of patients affected by HR+/HER2- MBC patients.

C64 Alopecia/hair loss in all patients treated with trastuzumab and paclitaxel: myth or reality?

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Background: The treatment for patients (pts) with small, node-negative, human epidermal growth factor receptor type 2 (HER2)-positive breast cancer (BC) is controversial. In January 2015, Tolaney et al. published on the NEJM data about pts undergoing chemotherapy schedule for node-negative, HER2-Positive BC with adjuvant Paclitaxel (P) and Trastuzumab (T) without anthracyclines. The authors observed the most common side effects and described that Alopecia (A)/Hair Loss (HL) was expected in the vast majority of pts. However, data regarding its real incidence were not collected. Based on this lack, in our center we gathered data about A/HL in pts treated with adjuvant P and T.

Materials (patients) and methods: From December 2015 to April 2017, 28 consecutive early stage HER2-positive BC pts were treated with adjuvant P and T schedule in our center. The treatment consisted of intravenous administration of 80 mg of P per square meter of body-surface area weekly for 12 weeks and a loading dose of 4 mg of intravenous T per kilogram of body weight on day one, followed by 2 mg per kilogram weekly, for a total of 12 doses. The main goal was to analyze the HL/A grading in pts treated with this schedule using the Dean's scale: G0= no HL; G1 < 25% HL; G2=25−50% HL; G3=50−75% HL; G4 >75% HL. This scale is the most common way to measure the degree of chemotherapy-induced A/HL.

Results: A total of 28 pts were treated with this schedule; median age was 59 years (range 36-76). All grades of A were observed in 93% (n = 25): G1 in 5 pts (18.5%), G2 in 12 pts (43%), G3 in 9 pts (33.3%). No pts had G4 HL. Full preservation of the hair (G0) was observed only in 2 pts (7.4%).

Table: C64. HL according with Dean's scale

HL	n (%)
G0	2 (7.4)
G1	5 (18.5)
G2	12 (43)
G3	9 (33.3)

Conclusions: Data collected in our experience confirm that this schedule causes a gentle-to-average A/HL in the vast majority of pts (93%, n = 25). Nevertheless 19 pts (68%) experienced a non-severe A/HL, which does not require the use of wigs, scarfs or headgears. In the light of these data, it would be useful to deepen this topic for improving the selection of which pts can better benefit from the Scalp Colling device in order to prevent A/HL.

C65 Are anti-HER2 agents the best choice in metastatic breast cancer with an HER2 positive switch from primary tumour? A retrospective multi institution analysis of clinical-pathological characteristics and outcomes

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Background: Approximately 6% of breast cancer change HER2 status at the time of recurrence, this change could be observed in both directions. HER2 switch can influence therapeutic decisions, even if no data are at the moment available about this specific subgroup.

Methods: Between 1991 to date we retrospectively identified all consecutive patients (pts) with HER2 positive metastatic breast cancer, proved by a biopsy on a secondary lesion, who had a primary tumour without HER2 expression.

Results: We obtained clinical and pathological data from 22 BC pts. 21 pts (95%) underwent surgery for primary tumor; histology: ductal carcinoma 19 (90%) pts, medullar carcinoma (5%) 1, unknown 1 (5%). Stage at first diagnosis: stage I 2 (9%), stage IIA 5 (23%), stage IIB 5 (23%), stage IIIA 3 (14%), stage IIIC 2 (9%), stage IV 1 (4%), while in 4 pts (18%) no data were available. 14 pts (64%) received adjuvant chemotherapy (12 anthracycline-based; 2 CMF) and 16 (73%) adjuvant hormonal therapy (12 Tamoxifen; 4 Aromatase Inhibitor). 4 pts (18%) received neoadjuvant treatment and among them no pCR was observed. No pts was treated with anti-HER2 agents in adjuvant/neoadjuvant setting. We observed a mDFS of 25.95 months (mos); range 0-285. All pts received a first line treatment for the metastatic disease: 2 chemotherapy alone, 2 trastuzumab (T) + hormonal therapy, 6 chemotherapy + T (3 vinorelbine + T, 3 paclitaxel + T) 12 pertuzumab (P)+ T + taxanes. We noticed a mPFS of 17.2 mos, range 2.9 − 77.7 mos; but a mPFS of 10.89 mos for pts treated with P+T+taxanes. 15 to 22 received T-DM1 as a subsequent therapy; 9 of them as second line therapy. mPFS was 3.88 mos (range 2.0 − 12.2 mos); and was consistently lower for pts (n = 9) previously treated with P+H+taxanes: 2.81 mos (range 2.0 − 12.2 mos). Most of pts (n = 10) showed a progressive disease as best response.

Conclusions: Our real-world study showed a lower efficacy of anti-HER2 agents for treatment of metastatic HER2 positive breast cancers that changed HER2 status at the time of recurrence. Particularly most of pts did not benefit from a treatment based on T-DM1, suggesting that the use of the antibody-drug conjugate may not be an adequate therapeutic option in this specific subgroup.

C66 Taxane-rechallenge in HER2-positive breast cancer patients who develop an oligo-progression during pertuzumab-trastuzumab maintenance therapy

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Background: Breast cancer is a heterogeneous disease that develops from different cellular lineages and progresses along multiple molecular pathways, resulting in a wide variability in treatment response. In addition to the variability between the different subtypes of the breast cancers, there is a coexistence of multiple cancer clones in the same patient. Currently the first-line therapy for HER2 breast cancer patients is represented by the combination of pertuzumab, trastuzumab, and a taxane agent followed by pertuzumab plus trastuzumab maintenance therapy. After a disease relapse during pertuzumab and trastuzumab maintenance therapy, the standard of care consists in a different second-line therapy as the antibody drug-conjugate trastuzumab emtansine or the combination of capecitabine plus lapatinib. No data about rechallenge of a taxane agent during pertuzumab and trastuzumab maintenance therapy have been reported in literature. It is possible that some chemosensitive clones of breast cancer cells in the context of a polyclonal disease, result not completely controlled by exclusive treatment with anti-HER2 target therapy, growing again after stopping a line of chemotherapy. We hypothesized that these chemosensitive clones could benefit from the rechallenge of a taxane agent obtaining a new disease control.

Materials and methods: In our center we have evaluated the rechallenge of a taxane in 4 cases of HER2-positive breast cancer with oligo-progression during the pertuzumab and trastuzumab maintenance treatment.

Results: Four HER2−positive breast cancer patients with complete response after docetaxel, pertuzumab and trastuzumab therapy and oligo-progression evidence during pertuzumab-trastuzumab maintenance therapy, received three mounts of weekly paclitaxel. The imaging evaluation with total body tomography documented three (3/4) complete response and one progression (1/4). Responder patients are currently continuing maintenance therapy with a variable period between 12 and 18 months. The one case progressed during the rechallenge of a taxane is now undergoing a second-line therapy with the antibody-drug conjugate trastuzumab emtansine.

Conclusions: Rechallenge with taxanes in breast cancer patients who developed an oligo-progression during pertuzumab-trastuzumab maintenance therapy appear to be effective and seems to be a reasonable option, especially in patients with good tumor response at first-line chemotherapy.

C67 Anti HER2 treatment (H) in the elderly: a "real life" retrospective analysis

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Background: Anti HER2 treatment with Trastuzumab, Lapatinib or TDM1 (H) has positively modified the outcome of HER2 positive breast cancer. However, only few data are available in patients (pts) over 65y, cause the small amount of such patients enrolled in clinical trials. Some recommendations suggest that also elderly pts benefit from this kind of therapy, but the risk of cardio-toxicity seems to increase with age.Our aim is to analyze efficacy and toxicity of H in the elderly.

Patients and methods: Since 2010 in our Oncological day hospital we treated 20 pts over 65y with H: 15 of them were over 70y, 6 over 75y and one 83y. Seven pts were treated for metastatic disease, 3 of them received more than 1 H and 1 patient received 3 different drugs. Thirteen pts were treated in adjuvant setting. H was associated with chemotherapy in 11 pts, anthracycline were omitted in order to reduce the risk of cardiotoxicity. In hormonal receptor positive pts H was associated with Aromatase Inhibitor. Comorbidity were present in 50% of pts: hypertension, diabetes and dyslipidemia, two pts (76y and 83y) had in anamnesis a congestive heart failure; all symptoms were well controlled by pharmacological therapy. All pts were monitored with echocardiography at the beginning of therapy, then every three-four months during treatment.

Results: The treatment duration ranged from 2 to 85 months, on average of fifteen months. We observed reduction in LVEF in four patients treated with iv Trastuzumab, symptomatic only in two of them. All of them recovered to normal range by stopping anti HER2 therapy. In metastatic setting all pts but one had partial or complete response long lasting. Three of the four patients that stopped Trastuzumab were treated in 2010-2012. In the last three years we have improved our collaboration with cardiologist and all pts HER2 positive >65y were offered a cardiological evaluation besides echocardiography, for better selecting patients. Since then we had to stop only one Trastuzumab in a 79y patient with an asymptomatic reduction of LVEF.

Conclusions: The result of our analysis is consistent with the small amount of literature data, suggesting that anti-HER2 therapy is effective and feasible also in elder pts. A very important focus is the selection of patients and an accurate cardiac monitoring in order to early recognize any sign of toxicity that could affect patient's treatment and quality of life.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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D - GASTROINTESTINAL (NON-COLORECTAL) CANCERS

D1* Randomized phase 2 trial of peri- or post-operative chemotherapy in resectable pancreatic adenocarcinoma

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Background: Pancreatic ductal adenocarcinoma (PDAC) has a remarkable trend to metastasize early. Accordingly, there is a strong rational to investigate preoperative chemotherapy in patients with resectable disease. We conducted a multicenter randomized phase 2 trial (PACT-15; NCT01150630) to assess the role of combination chemotherapy in perioperative setting.

Methods: Treatment-naïve patients with 18-75 yr, KPS>60 pathologically confirmed stage 1-2 resectable PDAC were randomized to surgery followed by 6 cycles of adjuvant gemcitabine 1000 mg/m21,8,15q4w (arm A), or PEXG (cisplatin 30 mg/m2, epirubicin 30 mg/m2, and gemcitabine 800 mg/m2 1,15q4w and capecitabine 1250 mg/m2/day 1-28) (arm B), or to 3 cycles of PEXG before and 3 after surgery (arm C). The primary endpoint was 1 year event-free survival (EFS); the secondary endpoints were EFS, overall survival (OS), and the difference in pathological findings between arm A+B and arm C. With 24 eligible patients in each group (H0 20%; H1 40%; a 10%; b 20%) $\leq$ 16 events of 24 would support further evaluation of experimental therapy.

Results: Between September 2010 and April 2015, 88 eligible patients were randomized in 9 Italian centers (arm A: 26, B: 30, C: 32). Basal patients and tumor characteristics are reported in the first table. Failure was observed (A/B/C) in 22/23/21 patients; 1-year EFS was 6/26 (23%); 15/30 (50%); 21/32 (66%). Median EFS was 4.9; 12.4; 18.9 months (A vs C p = 0.002). 19/22/18 (A/B/C) patients died; 3-year OS was 35%/42%/55%. Median OS was 20.5, 25.1, not reached at 33 months (A vs C p = 0.022). Pathological results are summarized in the second table. Main G3-4 toxicity (A/B/C) was: neutrophils 23/38/54%; fatigue 4/7/6%; anemia 0/10/21%; vomiting 0/0/6%.

Table: D1*

	A	B	C
Enrolled	26	30	32
Female	12 (46%)	17 (57%)	7 (22%)
KPS	24 (92%)	27 (90%)	25 (78%)
Basal CA19.9 >5 ULN	9 (35%)	16 (53%)	16 (50%)
Median age (range)	65 (37-74)	68 (49-75)	64 (39-75)

	A+B	C
Resected	49 (88%)	27 (84%)
Intraoperative metastases	7 (13%)	2/32 (6%)
Postoperative metastases	10/56 (18%)	3/32 (9%)
Grade 3	29/49 (59%)	6/27 (22%)
T1	2/49 (4%)	4/27 (15%)
No	13/49 (27%)	13/27 (48%)
Ro	16/49 (33%)	15/27 (56%)
Median size	2.5 cm	2.0 cm

Conclusions: Patients receiving perioperative chemotherapy had significant improvement of EFS and OS as compared to those receiving adjuvant treatment. This trial provides the strongest piece of evidence currently available in favor of preoperative chemotherapy in resectable PDAC.

D2 Metformin effects on clinical outcome in advanced HCC patients receiving sorafenib: validation study

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Background and aims: In 2005 we published a paper where we have assessed the outcome of patient with HCC treated with metformin (M) and sorafenib(S). The data show a better PFS e OS in patients that receiving only sorafenib.The aim of this study was to validate the prognostic significance of M in patients with HCC treated with S.

Methods: 280 patients with HCC consecutively treated with S twice daily between March 2008 and August 2016 were included in the study. Patients who had been taking insulin(I) for at least 5 years at the time of the HCC diagnosis were considered "patients with diabetes treated with I" whereas those who had been on M at for at least 5 years when HCC was diagnosed were considered "patients with diabetes treated with M".

Results: The median PFS of all patients was 3.6month(95%CI:3.1-4.4)and medianOSwas10.7month(95%CI:9.1-12.8).In patients treated chronically with M the treatment with S was associated with a median PFS of 1.9months(95%CI1.8-2.3)compared to 3.7 months (95% CI 3.1-4.6) for patients without DM2 and compared to8.4months(95%CI5.3-11.4)for patients treatment chronically with I($P < 0.0001$)In patients treated chronically with M the treatment with S was associated with a median OS of6.6months(95%CI4.6-8.7)compared to 10.8 months(95%CI9.0-13.1)for patients without DM2 and compared to 16.6 months(95%CI14.5-25.5)for patients treatment chronically with I(P=0.0001).M effects on clinical outcome were also investigated in relation to ORR. Patients treated chronically with M showed a higher percentage of progression at the first CT re-evaluation than those patients treatment with I and patients without DM2(75.8%vs14.7%vs38,8%, respectively).Considering the overall population, the risk of progression, was higher in DM2 patients taking M compared with patients without DM2(HR = 1.91,95%CI1.28-2.8). Regarding the risk of survival, similar results were observed (HR = 1.70, 95% CI 1.14-2.55).Considering the overall population, the risk of progression was lower in DM2 patients taking I compared with patients without DM2 (HR = 0.65, 95% CI 0.48-0.89), similar results for survival (HR = 0.62, 95% CI 0.44-0.87).Considering diabetic patients only, the risk of progression was higher in patients taking metformin than in those taking insulin (HR: 2.91; 95% CI: 1.84−4.6), similar results for survival (HR: 2.74; 95% CI: 1.69−4.43;).

Conclusions: These findings could be explained by an increased tumor aggressiveness and resistance to S in patients treated with M.

D3 Randomized phase 2 trial of nab-paclitaxel plus gemcitabine, ± capecitabine, cisplatin (paxg regimen) in metastatic pancreatic adenocarcinoma

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Background: The recommended phase 2 dose of nab-paclitaxel (150 mg/m2) in combination with cisplatin, capecitabine, and gemcitabine (800, 30, and 1250 mg/m2 every 2 weeks, respectively; PAXG regimen) were determined in a phase 1b trial. Now we report the final results of a randomized phase 2 trial of PAXG or nab-paclitaxel-gemcitabine (AG) in metastatic pancreatic adenocarcinoma (NCT01730222).

Patients and methods: Previously untreated patients with pathologic diagnosis of metastatic pancreatic adenocarcinoma, 18-75 years, Karnofsky Performance Status = 70 were eligible. Primary endpoint was the progression-free survival rate at 6 months (PFS6). With 42 eligible patients in each group, a PFS6 in = 25 of 42 would support further evaluation of the PAXG regimen.

Results: Between Apr 2014 and June 2016, 83 patients (Table 1) were randomized at a single Institution to receive PAXG (arm A; N = 42) or AG (arm B; N = 41). PFS6 was 31/42 (74%), and 24/41 (59%), respectively. PFS at 1 year and median PFS was 26% and 8.1 for arm A and 7% and 6.8 months for arm B. One-year survival was 62% and 41%, respectively. Median survival was not reached at 13.5 months for arm A and was 11.2 for arm B. PAXG regimen did not increase grade 3-4 extra-hematological toxicity as compared to AG.

Table: D3

Baseline Characteristic		PAXG	AG
Number		42	41
Male/female		20/22	23/18
KPS	90-100	34 (81%)	26 (63%)
	70-80	8 (19%)	15 (37%)
Age	median	66	63
	range	44-75	29-75
Biliary stent		9 (22%)	8 (19%)
Ca19.9	>ULN	32 (76%)	31 (76%)
	median	1413	1546
Neutrophil/Lymphocyte >5		15%	21%

Conclusions: The results show that addition of cisplatin and capecitabine to the AG backbone is feasible and linked with improved disease control. The PAXG regimen warrants further exploration in this setting of patients.

D4 Impact of phospho-Akt expression on the clinical outcome and activity of gemcitabine and Akt inhibitors in pancreatic ductal adenocarcinoma

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Background: Pancreatic ductal adenocarcinoma (PDAC) is among the most lethal solid tumors. Despite extensive preclinical and clinical research, the prognosis of this disease has not significantly improved, with a 5-year survival rate around 7%. There is an urgent need to better understand the molecular pathology of PDAC in order to improve patient selection for current treatment options and to develop novel therapeutic strategies. The PI3K/AKT/mTOR pathway plays a crucial role in PDAC: activation of Akt is a frequent event and has been correlated to poor prognosis and resistance to chemotherapy. Against this background, effective blockage of Akt signaling can lead to programmed cell death and inhibition of tumor growth. Several inhibitors of Akt under investigation include perifosine, which prevents Akt translocation to the cell membrane, MK-2206 which is an Akt allosteric inhibitor and BEZ-235 which is a dual PI3K/mTOR inhibitor. The aims of this study were to investigate 1) the prognostic role of Akt in PDAC tissues and 2) the molecular mechanisms underlying the interaction of Akt inhibitors with gemcitabine in PDAC cells and primary cultures.

Materials and methods: Immunohistochemistry of tissue microarrays with specimens from radically-resected patients (n = 100) revealed a correlation between high phospho-Akt1 expression and worse outcome. Patients with low expression had a median overall survival (OS) of 16.2 months (95%CI, 14.8-20.1), while patients with high expression had a median OS of 12.0 months (95%CI, 9.0-14.9, P = 0.03).

Results: Akt inhibitors synergistically enhanced the antiproliferative activity of gemcitabine in the LPC028 primary cells, characterized by high expression levels, while this combination was antagonistic in LPC006 cells, characterized by low expression levels. Inhibition of Akt decreased cell migration and invasion, which was additionally reduced by the combination with gemcitabine. However, the combination of Akt inhibitors with gemcitabine significantly increased apoptosis, associated with induction of caspase-3/6/8/9, PARP and BAD, and inhibition of Bcl-2 and NF-kB in LPC028, but not in LPC006 cells.

Conclusions: Our results support the analysis of phospho-Akt as a new biomarker both for PDAC prognosis and for the development of new therapeutic approaches. In particular, perifosine interact synergistically with gemcitabine in cells with phospho-Akt overexpression.

D5 Second-line treatment efficacy in elderly vs. non-elderly advanced gastric cancer patients: an Italian multicentre real-world study

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Background: Gastric cancer incidence rises with age, but elderly patients (pts) are scarcely represented in clinical studies. Therefore, the treatment of elderly population with advanced gastric cancer (AGC) remains a challenge, being difficult to translate trials' results into standard management.

Patients and methods: Baseline parameters, tumour features, and treatment data of 868 AGC pts treated with at least 2 lines of therapy at 19 Italian institutions were retrospectively analysed. Characteristics of elderly [≥70 years at second-line (2L) start] and non-elderly pts were compared using 2-tailed Fisher exact test or chi-squared test. The Cox proportional hazards regression model was used to identify prognostic factors. Progression-free survival (PFS) and overall survival (OS) were calculated using Kaplan-Meier estimation and examined by log-rank test.

Results: Overall, median OS was 13.6 months, median 2L OS 5.8 months and median 2L PFS 2.8 months. The elderly accounted for 31.8% of the population. No statistical difference in gender prevalence between age groups was found (P = 0.19). G3-G4 tumours were more frequent in non-elderly pts (P = 0.016). Intestinal type was found more often in the elderly (P = 0.02). There was no statistical difference in HER-2 status (P = 0.38) and TNM stage at diagnosis (P = 0.23) between age groups. At stage IV diagnosis, liver metastases were more frequent in elderly (P = 0.02), while the rate of peritoneal/ovarian metastases was higher in non-elderly pts (P = 0.002). In both groups, median number of cycles received in 2L was 4 and a similar percentage of pts received further therapy lines (P = 0.17). Elderly had similar 2L PFS (HR 0.86, P = 0.1), 2L OS (HR 0.87, P = 0.065) and OS (HR 0.86, P = 0.13) compared to non-elderly pts. In the elderly, 1st-line PFS≥6.2 months was associated with longer survival, while ECOG PS 2 negatively impacted on prognosis (Table 1).

Conclusions: Our large cohort study, while highlighting some differences in tumour features, did not show any statistical survival difference between age groups, indicating that age per se should not limit the use of 2L therapy in AGC pts. Toxicity analysis is ongoing.

Table: D5. Multivariate analysis (elderly pts)

VARIABLE	2L PFS			2L OS			OS		
	HR	95%CI	P	HR	95%CI	P	HR	95%CI	P
ECOG PS 1 vs 0	1.25	0.93-1.67	0.14	1.35	1.00-1.81	0.051	1.26	0.90-1.77	0.17
ECOG PS 2 vs 0	2.62	1.79-3.84	<0.0001	2.57	1.74-3.80	<0.0001	2.33	1.54-3.51	<0.0001
1st-line PFS ≥6.2 vs < 6.2 months	0.79	0.61-1.02	0.066	0.69	0.53-0.90	0.006	0.24	0.18-0.33	<0.0001
Haemoglobin at 2L start ≥11.5 vs < 11.5 g/dL	-	-	-	-	-	-	0.78	0.59-1.04	0.097

D6 Family history of pancreatic cancer in BRCA1/2 testing criteria

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BRCA1/2 mutation carriers have an increased risk for breast cancer (BC), ovarian cancer (OC), prostate cancer and pancreatic cancer (PC). On this basis, the NCCN Guidelines include prostate and PC among the BRCA testing criteria. However, in Emilia Romagna region, BRCA diagnostic test is exclusively offered to patients affected by BC or OC, according to the Modena Criteria (MC), or to healthy women with BRCAPro> 40%. The aim of this study was to compare the rate of positive BRCA test in families with PC, classified according to NCCN guidelines or MC.

We retrospectively analyzed families with family history of PC registered in the archive of our Family Cancer Clinic. Analysis of BRCA1/2 mutation was evaluated in these families and the BRCA mutation detection rate was calculated according to both selection criteria. We also evaluated age at diagnosis and overall survival of patients affected by PC.

435 families with at least one diagnosis of PC have been identified. 393 families had PC and BC and/or OC cases and were included in our analysis. 218 (55.5%) of these families were candidate to BRCA testing according to the MC, whereas 357 (90.8%) of families were candidate according to the NCCN Guidelines. 143 (65.6%) of families selected according with the MC underwent BRCA test, identifying 19 BRCA1 mutations and 16 BRCA2 mutations (detection rate 24.5%). 164 (45.9%) of families with the NCCN Criteria underwent the test with the identification of the same mutations (detection rate 21.3%). Mean age at PC diagnosis was lower in patients with family history of BC and/or OC (65.8 years) and in BRCA mutated families (65.7 years) than in general population (72 years). One-year OS rate was higher in patients with family history of BC and/or OC (41.3%) and in BRCA mutated families (50%) than in general population (23%). 5-year OS is around 7.2% for patients with PC in general population, whereas it is slightly decreased in our patients with family history or BRCA mutation in the family.

Our retrospective study confirms the high rate of positive BRCA1/2 test in families with PC associated to BC and/or OC. The NCCN Guidelines compared to the MC did not increase the BRCA mutation detection rate. Notably, PC diagnosed in families with history of BC and/or OC or BRCA mutation showed younger age at diagnosis and better 1-year OS. We are planning to test all the remaining families selected by NCCN guidelines to increase the rate of BRCA mutation in this group of patients.

D7 Ang-2 polymorphisms in relation to outcome in advanced HCC patients receiving sorafenib

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Background: Sorafenib, an oral multikinase inhibitor, represents the standard care for advanced hepatocellular carcinoma. Angiopoietin-2 (Ang-2) is a crucial angiogenic factor. By binding to its receptor Tie2, Ang-2 cooperates with the VEGF pathway to maintain normal physiological functions. In the presence of VEGF, Ang-2 destabilizes blood vessels and promotes vascular sprouting. In cancers, Ang-2 is linked to not only angiogenesis but also invasive and metastatic phenotypes. Although sorafenib exerts no significant activity against Tie2, the predictive value of Ang-2 has been explored in 2 studies. Llovet et al conducted a large biomarker study based on SHARP study. The authors found that a high baseline plasma Ang-2 level was an independent factor for poorer OS but not for reduced sorafenib efficacy. Conversely, in a small retrospective study, a high serum Ang-2 level was associated with a lower DCR and poorer PFS. The actual role of Ang-2 in predicting sorafenib efficacy warrants further investigations. Polymorphism analysis seems to have more advantages than protein or gene expression analysis. Gene expression analysis is performed on biological material collected at a specific time in the natural history of the disease. It is also subject to the influence of a number of laboratory biases. Conversely, polymorphism analysis can be performed at any time during the course of the disease, is not substantially influenced by laboratory biases and is less expensive. In our study we analysed the role of ANG-2 polymorphisms in relation to clinical outcome in patients with hepatocellular carcinoma treated with sorafenib.

Methods: We analyzed 135 patients with hepatocellular carcinoma treated with sorafenib. Peripheral blood samples or FFPE tumor tissues were available for DNA extraction and genotyping analysis. Nine *Ang-2* polymorphisms were analyzed by direct sequencing or Real Time PCR method.

Results: With regard to Ang4 rs55633437 was observed that patients carrying the allele GG were associated with a better PFS and OS. The variants GG were associated with a median OS of 16.9 months vs 6.5 months of variants GT and TT ($p = 0.016$). The variants GT and TT were associated with a median PFS of 2.94 months vs 4.67 months of variants GG ($p = 0.03$). These data were confirmed by multivariate analysis.

Conclusions: Ang4 rs55633437 could represent prognostic markers in patients with advanced hepatocellular carcinoma treated with sorafenib.

D8 Biliary tract carcinoma and chronic viral hepatitis in Italy: the GICO (Gruppo Italiano COlangiocarcinoma) experience

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Background: Chronic hepatitis (hep) is an established etiologic factor of biliary tract carcinoma (BTC) in Eastern countries, mostly in intrahepatic cholangiocarcinoma (IHC), whereas in Western world the lower prevalence of hep has prevented a clear correlation so far. A possible prognostic role is still matter of debate.

Methods: A cohort of 830 advanced BTC patients (pts), treated in 12 Italian centers, was retrospectively analyzed by the Gruppo Italiano COlangiocarcinoma (GICO). Hep status was assessed through the collection of anamnestic findings, serology (HBsAg, HBcAb, HCV Ab), and molecular test (HCV RNA, HBV DNA).

Results: Hep status was available for 562 pts (67.7%); of these, 50 (8.9%) were labeled hep-positive (hep+). Among the 273 IHC pts with hep status available, 35 were positive (14 hep B, 21 hep C), resulting in a significantly higher hep prevalence in IHC than other BTC sites (12.8 vs 4.9%, $p = 0.001$). Among IHC pts, no significant differences were found between hep+ and hep- in relation to nodal involvement (62 vs 69%), metastatic disease (66 vs 67%) or mean number of metastatic sites (1.5 vs 1.7) at diagnosis. Hep+ pts were older than hep- (median 68.4 vs 64.4 years). At time of start of first-line chemotherapy (CT1), IHC hep+ pts shown significantly higher mean levels of leucocytes (8500 vs 6900 c/mmc, $p = 0.012$), neutrophils (5800 vs 4200 c/mmc, $p = 0.008$), neutrophiles-to-lymphocytes ratio (NLR, 4.1 vs 2.9, $p = 0.043$), platelets-to-lymphocytes ratio (167 vs 123, $p = 0.014$), but were not characterized by a higher prevalence of leucocytosis, neutrophilia, lymphocytosis or thrombocytosis. Median CEA was higher in hep+ pts (3.3 vs 1.5 ng/ml, $p < 0.0001$), but the fraction of abnormally high levels was halved (25 vs 51%, $p = 0.009$); median Ca19.9 was unaffected by hep status. Hep did not affect either progression-free survival to CT1 (median 4.4 months in hep+ vs 3.6 in hep-, HR 0.86, $IC_{95\%}$ 0.59−1.27) or overall survival (11.2 months vs 11.3, HR 0.81, $IC_{95\%}$ 0.53−1.24).

Conclusions: The higher prevalence of hep in IHC pts suggests an epidemiological nexus between these two entities. Albeit in hep+ IHC pts there was an increased pre-treatment NLR, hemocromocytometric analysis failed to reflect at systemic level a supposedly more pronounced local inflammatory background. Hep+ IHC doesn't show evidence of an accelerated carcinogenesis, such as worse clinical-radiological presentation or younger age at diagnosis, nor is characterized by worse survival in treated pts.

D9 Estimation of 12-weeks life expectancy in patients (pts) with metastatic gastric cancer (mGC) candidated for second-line treatment: the "Gastric Life" nomogram

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Background: The estimation of life expectancy of mGC pts in the second-line setting may be biased by the absence of objective prognostic tools to be used for the enrollment in clinical trials and for the

decision making in the everyday practice. The availability of evidence-based second-line treatment options highlights the need of a prognostic tools that may assist clinicians in refining pts' clinical selection in the salvage setting. The aim of this study was to

build a nomogram for predicting the individual 12-weeks overall survival (OS) of mGC pts starting a second-line treatment.

Materials and methods: At 26 Italian Institutions, 320 mGC pts receiving second-line chemotherapy, ramucirumab or paclitaxel-ramucirumab were used as developing set. Putative prognostic variables (age, gender, ECOG PS, T resection, Lauren's histotype, primary anatomic site, synchronous presentation, number and location of metastatic sites, PFS and response to 1-line, LDH, neutrophils/lymphocytes ratio) were selected using a random forest model and included in a Cox multivariable model from which the nomogram was derived. The nomogram performance was evaluated by means of calibration plot and discriminative ability (Harrell's C index).

Results: Three variables were selected and included in the nomogram: ECOG PS, neutrophils/lymphocytes ratio and peritoneal involvement. The model discriminative ability index was 0.712. The internal calibration plot did not show any significant differences between the observed and the predicted 12-weeks OS probabilities. External validation analysis is currently ongoing.

Conclusions: Our nomogram may be a useful tool to predict the 12-weeks life expectancy in mGC pts candidates for second-line therapy. Based on 3 easy-to-collect variables, "Gastric Life" nomogram may help clinicians to refine pts' selection for second-line treatments and assist researchers for the enrollment in clinical trials.

D10 Prognostic impact of nutritional support in patients affected by locally advanced or metastatic pancreatic cancer (PC) undergone chemotherapy

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Background: Patients affected by PC frequently present nutritional disorders that may influence their quality of life and prognosis. In addition to the disease, the systemic treatment may contribute to the malnutrition status of these pts. Few studies investigated the role of nutritional support during treatment of PC pts. Therefore, the aim of this analysis was to assess the nutritional status and the prognostic value of nutritional intervention in pts affected by advanced PC undergone chemotherapy.

Materials and methods: Pts affected by locally advanced or metastatic PC, undergone chemotherapy, receiving nutritional counseling at the AOUI of Verona between July 2013 and October 2016 were included. Nutritional status was assessed by Malnutrition Universal Screening Tool (MUST), Body Mass Index (BMI), weight loss in the past 6 months (WL), presence of symptoms that may affect food intake and energy intake. Descriptive statistics was adopted. Clinical, pathological and nutritional data were prospectively correlated to Overall Survival (OS) using a Cox model.

Results: Data from 109 pts (47 males [43.1%] and 62 females [56.9%]) were gathered (median age 63 years, median follow-up 8 months). At baseline, in seventy pts (64.2%) the MUST was $^{3}2$, significantly correlated with the PS (ECOG) ($p < 0.0001$), the median WL was 11.5% (range 0−35.4) and most patients suffered from early satiety (78%), loss of appetite (83.5%), dysgeusia (87.2%), dyspepsia (66.1%) and diarrhea or constipation (69.7%). The oncologist initially prescribed the nutrition counseling in only 33% of cases. At multivariate analysis, the time between the diagnosis of PC and the nutritional counseling (HR 2.22, $p = 0.017$), the Performance Status (HR 1.38, $p = 0.075$), the surgery of the primary (HR 5.89, $p = 0.005$) and the response to the first line (HR 5.9, $p = 0.03$) were significant predictor for OS. Furthermore, a weight gain more than 2% (cut-off defined by the Maximally selected Log-Rank statistics analysis) from the baseline weight was correlated with the time between the diagnosis and the nutritional intervention ($p = 0.021$): in pts receiving nutritional support within 3 months from diagnosis, a 2% weight gain was associated with a 2-year OS benefit (50.3% vs 33.0%, $p = 0.04$).

Conclusions: These data suggest that the nutritional support may impact on prognosis of pts affected by advanced PC undergone chemotherapy. External validation is ongoing.

D11 Early changes in plasma levels of mutant KRAS DNA as a sensitive marker of response to chemotherapy in pancreatic cancer

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Background: Pancreatic cancer (PDAC) is still lacking of good markers to monitor tumor response and chemotherapy represents the gold standard to treat advanced disease. Ca19.9 is the only one approved, however, it has several limitations in sensitivity and specificity. Since mutations of KRAS occur in more than 90% of tumors, its detection and variations in circulating free tumor DNA (cftDNA) could represent a biomarker to monitor chemotherapy response.

Material and Methods: Twenty-seven advanced PDAC patients given first-line 5-fluorouracil, irinotecan and oxaliplatin or gemcitabine and nab-paclitaxel were enrolled. Three ml of plasma were collected 1) before to start chemotherapy (baseline), 2) at day 15 of treatment and 3) at each clinical follow-up. CftDNA was extracted and analysed for KRAS mutations (^{mut}KRAS) by digital droplet PCR to monitor its variation and to compare its predictive role respect to Ca19.9.

Results: A total of 27 patients with locally advanced (n = 4) and metastatic (n = 23) PDAC were included in this prospective study. Median PFS and OS were 7.4 and 11.5 months, respectively. Nineteen patients displayed a ^{mut}KRAS in baseline plasma, and there were no significant statistically differences in median PFS and OS in patients with baseline positive or negative cftDNA ^{mut}KRAS (median PFS: 7.4 months *vs.* not reached, $p = 0.24$; median OS: 11.5 months *vs.* not reached, $p = 0.16$). Monitoring ^{mut}KRAS cftDNA during treatment and correlation with outcome were possible in 25 patients. There was a statistically significant difference in PFS and OS in patients with increase *vs.* stability/reduction of cftDNA in the sample collected at day 15 (median PFS 2.5 vs 7.5 months, $p = 0.03$; median OS 6.5 vs 11.5 months, $p = 0.009$). None of the other parameters (sex, age, stage, PS, primary tumor location, baseline CA19.9) was significantly correlated with PFS or OS. Moreover, ^{mut}KRAS cftDNA variations were deeper than those of Ca19.9, suggesting that ^{mut}KRAS cftDNA can be more accurate and sensible biomarker (Table 1).

Conclusions: The results of this study support the hypothesis that ^{mut}KRAS in plasma may be used as a new marker for monitoring treatment outcome and disease progression in PDAC, suggesting that cftDNA ^{mut}KRAS changes are associated with tumor response to chemotherapy.

Table: D11. Comparison of ^{mut}KRAS cftDNA and Ca19.9 is a patient undergoing progression of disease (PD).

	Baseline	2 weeks	8 weeks - PD
^{mut}KRAS cftDNA (copies/ml)	200	290	2800
Ca19.9 (U/ml)	2600	2000	1500

D12 Whole-exome sequencing analysis identifies recurrent mutation rate in BAP1 gene in intrahepatic cholangiocarcinoma patients exposed to asbestos

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Background: The past three decades have registered a progressive worldwide increase in incidence of intra-hepatic cholangiocarcinoma (ICC), a malignancy arising from the biliary tree within the liver. Recently, in two case-control studies (one retrospective and one prospective), we observed a 4.8- and a 7-fold, respectively, increased risk of ICC in workers exposed to asbestos. These findings strongly suggest a putative role of asbestos in ICC carcinogenesis and, possibly, in its increasing incidence.Since the identification of environmental diseases is gaining increasing attention because of their high impact on public health, the present study aimed to identify putative molecular biomarkers of asbestos-driven ICC carcinogenesis.

Material and methods: A total of 22 ICC patients were enrolled. For each patient, data on established or suspected ICC risk factors were collected; asbestos exposure was assessed by modified ReNaM questionnaire. On the basis of modified ReNaM questionnaire, patients were divided in two groups: asbestos-exposed and the control group of not-exposed. Whole exome sequencing (WES) was performed on DNA from 22 tumors and matched blood samples. Somatic single nucleotide variants, insertions and deletions were identified and functionally annotated. Mutated genes of interest were selected according to the frequency of mutations within the asbestos-exposed patients' subgroup and based on *a priori* knowledge about cancer-related genes, with particular attention for those ones already reported to be mutated with high recurrence in malignant pleuric mesothelioma (MPM), a classic model of asbestos-related cancer.

Results: According to ReNaM questionnaire, 10 (45%) out of 22 ICC patients resulted exposed to asbestos. WES analysis revealed a frequency of 27% (6 over 22) of somatic mutation in BRCA1 associated protein -1 (BAP1), corresponding to 5 over 10 of asbestos-exposed ICC patients (50%) and to 1 over 12 of not exposed (5%). According to chi-square test, BAP1 alterations were significantly associated with asbestos exposure (p-value= 0.0289).

Conclusions: BAP1 mutation occurred with a high recurrence rate in asbestos-exposed ICC patients and, as already reported in MPM, could serve as a putative candidate for genetic alterations associated with asbestos exposure in this malignancy. Further studies based on a larger patients population are needed to confirm this preliminary finding.

D13 Analysis of DPYD and UGT1A1 genotype in patients with advanced pancreatic cancer treated with modified FOLFIRINOX

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Background: Modified FOLFIRINOX (mFOLFIRINOX) is a standard treatment in advanced pancreatic cancer (aPC). Because of the presence of either loss-of-function mutations in DPYD (c.1679T>G, IVS14 + 1G>A, c.2194G>A, c.2846A>T) or UGT1A1*28 variant associated with reduced UGT1A1 expression, deficiency of DPD and UGT may result in drug accumulation and severe toxicities caused by fluoropyrimidines and irinotecan, respectively.

Material and methods: The present study analyzes the association between DPYD and UGT variants and adverse drug reactions (ADRs) in aPC patients (pts) treated with mFOLFIRINOX. Blood samples were collected from 104 pts, and analyses of DPYD c.1679T>G, IVS14 + 1G>A, c.2194G>A, c.2846A>T and UGT1A1*28 were performed by automatic sequencing. Statistical analysis was performed by chi-square, Mann-Whitney and Spearman's rho tests on SPSS v.23s.

Results: Non of the pts was carrier of the c.1679G and c.2846T alleles. Only one IVS14 + 1GA was found and 8 pts had c.2194GA genotype. ADRs grade (G) =3 were neutropenia (42.3%), diarrhea (7.7%) and stomatitis (7.7%). The statistical analysis of the IVS14 + 1GA has not been performed due to the extremely low frequency of the mutant allele (0.96%), however IVS14 + 1GA patient experienced G4 hematological and gastrointestinal ADRs after the first cycle. We observed a trend toward significant association between c.2194GA genotype and the risk of thrombocytopenia ($p = 0.080$) and hand-foot syndrome (HFS) ($p = 0.096$). The UGT1A1*28 allele was found in 56 (54.4%) pts (*1/*28, n = 38; *28/*28, n = 18) and it was correlated with the risk of developing thrombocytopenia ($p = 0.006$) and neutropenia ($p = 0.044$). Moreover, this risk increased as the number of *28 alleles increased (*28/*28 > *1/*28 > *1/*1, $p = 0.003$). No significant correlation with diarrhea was found.

Conclusions: Our data confirm that DPYD IVS14 + 1A is associated with life-threatening toxicities and that the c.2194A allele could be possibly associated with thrombocytopenia and HFS, but validation in larger cohorts is needed. UGT1A1*28 allele is associated with a higher risk of G3/4 thrombocytopenia and neutropenia, and should be implemented in routine practice to personalize treatment in aPC.

D14 Prognostic factors in unresectable biliary tract cancer: a GICO (Gruppo Italiano COlangiocarcinoma) retrospective analysis

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Background: Faced with a general background of a poor prognosis, individual histories of patients (pts) with advanced biliary tract cancer (aBTC) may vary to a considerable extent. However, low incidence and heterogeneity of this group of neoplasms prevented an unambiguous and consistent identification of clinical and laboratory features, useful to estimate the expected prognosis and to allow the prediction of the benefit of chemotherapy (CT).

Methods: The Gruppo Italiano COlangiocarcinoma (GICO) conducted a retrospective study of different variables at the time of beginning of 1st line CT in a cohort of aBTC pts treated since 2001 in 12 Italian centers, and analyzed their impact on overall survival (OS) and progression-free survival (PFS) through Cox proportional hazards model.

Results: The demographic and clinical characteristic of the 830 collected histories were: 65.3 years median age, 47.6% female, 90.4% ECOG PS 0-1, 8.9% chronic viral hepatitis-positive, 69.2% lymph-nodes positive (N+) and 43.4% metastatic (M1) at diagnosis; gallbladder (21%) and ampullary (6%) cancer, intrahepatic (51%), distal extrahepatic (14%) and hilar (8%) cholangiocarcinoma; 36% underwent prior curative intent surgery, 29% 2 lines of systemic CT, 16% at least 3 lines. Median PFS to 1st line CT of the whole cohort was 4.0 months (mo; $IC_{95\%}$ 3.6-4.4), and OS was 10.3 mo ($IC_{95\%}$ 9.4-11.2). At multivariate analysis, factors significantly associated to an impaired PFS ($p < 0.05$) were: above-median levels of CEA (HR 1.43), leucocytes (HR 1.87), AST (HR 1.65), INR (HR 1.48), and ECOG PS > 1 (HR 1.31), whereas only M1 status at diagnosis (HR 2.19) predicted worse OS, with marginal significance observed for above-median CEA (HR 1.49, $p = 0.061$) and leucocytes (HR 2.05, $p = 0.057$). Primary site, prior curative intent surgery, prior R0 surgery, low neutrophil-to-lymphocyte ratio, low platelets-to-lymphocyte ratio, low Ca19.9, positively correlated with survival only at univariate analysis. Lymphocytes levels, hepatitis status and age did not affect survival.

Conclusions: Prognosis prediction upon easily accessible data proved feasible in a large cohort of unselected pts with aBTC. However, few variables meaningfully correlated with survival indexes. The analysis will be implemented with the identification of the most informative cutpoints for each continue variable and the building of a prognostic model.

D15 Combination of duligotuzumab, anti HER3 antibody or taselisib, PI3K INhibitor with trastuzumab shows synergetic antitumoral activity in HER2 positive gastric cancer cells

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Introduction: The anti-HER2 monoclonal antibody trastuzumab is central to the treatment of HER2-positive gastric cancer (GC); however, its responses are limited due to some poorly understood mechanisms of resistance. The aim of this study was to asses the antitumortal activity of Duligotuzumab, an anti HER3 antibody or Taselisib, a Pi3k inhibitor combined with Trastuzumab in a panel of HER2 positive human gastric cancer cell lines (GCG), to improve anti HER2 treatment efficacy.

Methods: We evaluated *in vitro* the effect of Duligotuzumab, Taselisib and Trastuzumabin single agent and in combination treatments in HER2-positive GCG (NCI-N87, KATOIII, OE19) and in negative HER2 GCC (MKN28), throughproliferation, migration and apoptosis assays. We also investigated the effect of combined treatment on downstream intracellular signaling, by western blot analysis.

Results: After establishing, through a dose response curve, the IC50 for each drug used (≈ 0.5 μM), a significant synergistic effect of Duligotuzumab, Taselisib and Trastuzumab treatments in HER2-positive GCG was observed by reduction of proliferation and migration in KATOIII, OE19 and N87 cell lines; the same effect was found analyzing the apoptotic rate. At cellular level, in particular in KATOIII and OE19 cell lines, the combined treatment with Duligotuzumab or Taselisib plusTrastuzumabcompletely inhibited the activation of proteins downstream of HER3, PI3K and MAPK pathways.

Conclusions: Targeting both HER2 and HER3 or HER2 and PI3K with the combination of anti-HE3 antibody or pi3k inhibitor with Trastuzumab may result in an improved treatment effects on HER2-positive GCG. These important findings can be utilized to facilitate the design of future clinical trials.

D16 Immune inflammation indicators as predictors of releaps or new HCC in patients treated with direct-acting antiviral (DAA) for hepatitis C

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The impact of DAA- based treatment on the incidence of hepatocellular carcinoma (HCC) in patients with cirrhosis and particularly on the incidence of HCC recurrence after successful curative treatment, has emerged as a controversial issue with potential clinical implications. Recently, studies have shown unexpected high HCC recurrence rate of 27%-29% among patients treated with resection or ablation, who received DAA therapy. The mechanism that could explain the high rate of tumor relapse after DAA treatment is one of the main issues rising from these studies. Microenvironment and viral induced inflammation play a key role in chronic liver injury and tumor initiation. In contrast, the immune system has also an anti-tumor function several infammation and immune-based prognostic scores, such as lymphocyte count, neutrophil-lymphocyte ratio (NLR), and systemic immune-in ammation index (SII), have been developed to predict survival and recurrence in cancers, including HCC. Herein, we evaluated the potential role of SII, NLR and PLR as predictors of releaps or new HCC in patients treated with DAA. AQ2

Methods: We analysed 439 consecutive cirrhotic patients without HCC and 92 patients with previous HCC. Information on neutrophil, lymphocyte and platelet counts from hematologic blood tests carried out at baseline (the day before the start of treatment).

Results: During 24-week follow-up, HCC was detected in 60 of 92 patients with previous HCC and 29 of 439 patients without previous HCC. In patients with previous HCC the increase of NLR was associated with a early releapse of HCC (HR 1.104854, 95% CI 1.017-1.199, $p = 0.04$). In patients without previous HCC the value of NLR, SII and PLR not was associated with early releapse of HCC. In this patients the increase of AST (HR 1.004751, 95% CI 1.000782-1.008736 $p = 0.019$), lymphocyte (HR 0.4732381, 95% CI 0.2611029-0.8577245, $p = 0.014$) and platelet (HR 0.9854803, 95% CI 0.977689-0.9933337, $p < 0.0001$)and decrease of albumin (HR 0.2708681, 95% CI.1353519-0.542065 $p < 0.0001$) was associated with early releapse.

Conclusion: Overall, the high rate of HCC recurrence after DAA treatments in patients with prior HCC suggests that a close follow-up of these patients remains mandatory. The NLR represent potential prognostic indicator in patients with previous HCC,

differently for patients without previous HCC where the risk of releapse is due to the stage of cirrhosis.

D17 Transarterial radioembolization versus chemoembolization for hepatocarcinoma patients: a meta-analysis of randomized trial

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Introduction: A novel technique of loco-regional treatments for HCC is called transarterial radioembolization with yttrium-90 (TARE), which induces tumor necrosis by means of injection of glass or resin microsphere loaded with yttrium-90. TARE, which is in fact a novel form of liver-directed brachytherapy. Although several studies comparing the two locoregional techniques have been recently published, whether there is a clear superiority of one treatment over the other is still debated. In this study, we performed a meta-analysis to compare the efficacy of TARE and TACE in treating patients with unresectable HCC and we considering only the three randomized study.

Materials and methods: Randomized controlled studies that included patients with intermediate hepatocellular carcinoma were included in to the analysis.

Results: A total of 3 studies published from 2014 to 2016 were analyzed, which included 49 HCC patients treated with TARE and 48 who underwent TACE. A significant between the trials' heterogeneity was detected for PFS (I2 test 78%), while no heterogeneity was detected for the other outcomes. OS at 1 year was similarity between the two treatment groups (OR = 1.21, 95%CI: 0.51-2.83, P = 0.67). Overall survival at 1 year was 63.2% for TARE compare to 66.6% for TACE. For PFS at 1 years the data were not statistical significant between two treatment (OR = 0.25, 95%CI: 0.02-3.03, p = 0.28). We also analysed progression disease, disease control rate and transplanted patients. For progression disease and disease control rate not statistical significant was detect. For progression disease the OR was 0.61 (95%CI: 0.14-2.70, p = 0.51) and for disease control rate the OR was 1.80 (95%CI: 0.51-6.30, p = 0.36). For transplatate patients the OR was 0.68 (95%CI: 0.23-2.01, p = 0.49). In the group treatment with TARE the ttransplanted patients were 30% compared to 20.8% of patients treatment with TACE.

Conclusion: Our meta-analysis reveals that TARE and TACE show similar effects in unresectable HCC patients in terms of OS, disease control rate, patients transplantate and progression disease. However, important evidence emerging from the various studies and this meta-analysis is that TARE seems to have a greater down-staging compared to TACE especially in early-stage patients.

D18 Early loss of skeletal muscle mass (LSMM) as prognostic factor in metastatic pancreatic cancer (PC) patients

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Background: PC patients (pts) have multiple risk factors for sarcopenia and LSMM that in turn may cause more intense treatment toxicities, reduced response to cancer therapy, prolonged hospital stay, impaired quality of life, and worse prognosis.

Material and methods: we retrospectively analyzed 127 consecutive metastatic PC pts treated at the Department of Oncology of Udine between Jan 2012 and Mar 2017 to evaluate if baseline sarcopenia and/or early LSMM (measured at first radiological evaluation and compared to baseline) may impact on overall survival (OS). Baseline sarcopenia was defined according to Prado's criteria (SMI < 53 cm2/m2 for men with BMI >25, 43 cm2/m2 for men with BMI<25 and 41 cm2/m2 for women). Skeletal muscle area was measured as cross-sectional areas (cm2) using CT-scan data through the PACS image system. Skeletal muscle index (SMI) was calculated as cross-sectional area of muscle (cm2) at the L3 level divided by the square of the height (m2). Early LSMM during first-line chemotherapy was defined as a decrease in SMI >10% from baseline at first evaluation. Characteristics between two pts groups (sarcopenic and not) were compared with chi-square test. Survival outcomes were estimated with Kaplan-Meier curves. Uni- and multivariate Cox regression analyses for OS were conducted to explore the prognostic impact of LSMM.

Results: At baseline, 67 pts (53.1%) were >70 years old and 72% had ECOG PS > =. Sarcopenia was reported in 62 pts (81%). Of note, 80 (63.4%) were evaluated by a nutritionist, 75 (59.5%) had a nutritional supplementation and 39 (35.8%) had a BMI>25. Out of 127 pts, 56 (44%) had a CT-scan at first evaluation, and one third of them (32.1%) had an early LSMM. Median OS was 9.52 months. In univariate analysis, older age (HR 1.5, p = 0.05), ECOG PS > =1 (HR1.57, p = 0.046), and early LSMM (HR 2.49, p = 0.009) were all significantly associated with worse OS. Instead, high lymphocyte-to-monocyte ratio (LMR) at baseline (HR 0.79, p = 0.015) and the nutritionist evaluation (HR 0.65 p = 0.038) were associated with longer OS. In multivariate analysis, only LSMM >10% was significantly associated with worse OS (HR 2.44 p = 0.015).

Conclusion: Early LSMM >10% may negatively influence the outcome of metastatic PC pts, probably due to systemic inflammation. Further prospective investigations are needed to confirm these preliminary data.

D19 Locoregional treatments and sites of metastatic involvement in metastatic gastric cancer patients: do they influence survival?

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Background: Despite newly active drugs, metastatic gastric cancer (MGC) patients' prognosis has not improved considerably, thus suggesting that different therapeutic approaches, such as locoregional treatment of metastases, should be considered. Aim of this study is to assess the role of several factors in MGC such as metastatic site, tumor subtype and type of treatment received (systemic vs. local).

Patients and methods: 184 patients with metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma who received at least one line of palliative therapy with a chemotherapy doublet or triplet were retrospectively evaluated. Stratification factors were histotype according to Lauren classification, sites of metastases, second-line chemotherapy (yes vs. no) and locoregional treatment of metastases (yes vs. no). Survival analysis was calculated by Kaplan-Meier method and stratifying factors by log-rank test. Multivariate analysis was performed by Cox-Model. Level of significance p value was set at 0.05.

Results: In the whole group, median overall survival (OS) was 8.32 months (95%CI: 7.02-9.41) and median progression-free survival (PFS) was 4.16 months (95%CI: 3.24-5.08). Lung metastases vs. other sites of metastatic involvement and intestinal subtype were significantly correlated to OS (HR:0.27, 95%CI: 0.14-0.50, p = 0.0133 and HR:0.48, 95%CI: 0.34-0.68, p = 0.0006, respectively). A trend towards a better PFS was also observed (HR:0.49, p = 0.10 and HR:0.72, p = 0.08, respectively). Second line chemotherapy or locoregional treatment of metastases (surgery or radiotherapy) also resulted related to better OS (HR:0.52, 95%CI: 0.37-0.74, p < 0.0001 and HR:0.35, 95%CI: 0.24-0.52, p < 0.0001, respectively). Multivariate analysis confirmed an independent significant role as predictor of better OS only for locoregional treatment (Exp(B):0.32, p = 0.0007) and for 2nd line treatment (Exp(B):0.53, p = 0.0002).

Conclusions: Although at the univariate analysis our study would suggest a positive prognostic role of lung involvement in MGC patients, multivariate analysis revealed that this difference might be related to use of other treatment modalities and a higher percentage of patients receiving 2nd line treatment. Locoregional treatments, although out of proper indication for most patients, should be offered in cases of favourable features such as single site of metastatic involvement, high probability of achieving R0 resection and long disease-free interval.

D20 Multidisciplinary approach and nutritional impact on the patient with pancreatic cancer

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Background: Early nutritional assessment and nutritional status play an important role in patients' prognosis and quality of life. The A.O.U. City of Health and Science of Turin (Città della Salute e della Scienza di Torino), together with the Oncology Network of Piedmont and Valle d'Aosta (Rete Oncologica Piemonte-Valle d'Aosta), established on one side the Reception and Services Center (CAS), that aims at taking care of patients trough the involvement of different health professionals and on the other side the Interdisciplinary Treatment Groups (GIC) that define more appropriate treatment paths for each patient. Early reports of pancreatic cancer patients to the Dietetics and Clinical Nutrition Unit may positively affect medical and surgical treatments.

Material and methods: 61 patients with pancreatic cancer were investigated for nutritional status, food intake and health status. The aim of the study was to evaluate whether a multidisciplinary approach and an early nutritional intervention can improve patients' outcome and quality of life. Patients were examined from January 2015 to December 2017, each of them for a minimum of 6 months, depending on their nutritional and health status.

Results: During 6 months of follow up, weight remained almost unvaried, starting from a body mass index (BMI) of 23,2 (+/- 3,3) at T0 and ending with a BMI of 23,1 (+/-2,6) at T2, **(but weight loss percentage varied from 11,9 (+/- 6,5)at T0 to -1,8 (+/-4,9) at T2**.) Calories intake varied from 1308 kcal (+/- 363) at T0 to 1670 kcal (+/- 408) at T2 and proteins intake varied from 52 (+/-17) at T0 to 68 (+/- 18) at T2. 21% of patients needed oral nutritional supplements and 8% of patients started parental nutrition after the first nutritional assessment at T0, while at T2 35% of patients needed oral nutritional supplements and 20% started or continued parental nutrition.

Conclusion: The early nutritional assessment and the multidisciplinary approach showed a reduction in the percentage of the weight loss, due to an increase of calories and proteins intake (oral food) together with an increase in oral nutritional supplements. Serum proteins and albumin changed from 6,2 mg/dl (+/- 0,6) and 3,2 mg/dl (+/- 0,6) at T0 to 6,3 mg/dl (+/- 0,5) and 3,4 mg/dl (0,6) at T2.

D21 Prediction of overall survival after 3 months of treatment using the NLR-over-the-time curve in pancreatic cancer patients

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Background: High NLR is an established adverse prognostic feature in pancreatic cancer, however his change over the time during the entire course of the disease and its ability to precisely predict survival have never been investigated.

Methods: We analysed 2975 blood cell counts from 85 metastatic pancreatic cancer patients to build a NLR-over-the-time-curve from the beginning of the disease history until death. The shape of NLR-over-the-time-curve was evaluated and the minumum timepoints needed to predict the entire curve was assessed using the error-vs-partial-measurmnets function.

Results: The NLR-over-the-time-curve was found to have a clear rectilinear shape in all analyzed patients. The best fitting linear curves proved to have a coefficient of determination, namely "R-squared", about of 24-25% for nearly all patients. In order to investigate how linear extrapolations of initial (partial) data can predict the whole phenomenon, we compared such extrapolations with the final best fitting curve in terms of R-squared and considered the prediction to be adequate when the corresponding R-squared attained the same final value of the best fitting curve. Overall, the R-squared of 24-25% could be attained in as early as three months of blood cell count measurements. Since the near-end-of-life NLR was > 4 in 95% of cases, then a precise overall survival prediction was possible using NLR values assessed during the first three months of patient management.

Conclusion: Building the NLR-over-the-time-curve is a precise tool to predict overall survival in pancreatic cancer patients. Future studies need to understand how interventions to change the slope of the curve (such as anti-inflammatory therapies) may impact on prognosis.

D22 Prognostic factors associated with survival and recurrence in resectable gastroesophageal cancer: retrospective analysis of 338 patients operated at the Hospital of Cremona in ten years' time

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Background: Surgical resection remains the only curative treatment for non-metastatic gastroesophageal (GE) cancer. A large cohort of GE cancers derived from a high-volume Italian center was analyzed to describe clinical outcomes and prognostic factors.

Methods: 338 patients (pts) diagnosed with GE cancers who underwent curative resection from 2007 to 2016 were considered. Variables analyzed were: age, sex, tumor location, histology, tumor (T), nodal status (N), resection margin status (R), grade (G), (neo) adjCT, adj CTRT, neutrophil/lymphocyte ratio (NLR) and lymphadenectomy status (D1-D2-D3) . Statistical analysis was performed according to intention to treat principle.

Results: Included pts were 131 women (39%) and 207 men (61%), median age 75 years. Adenocarcinomas (Lauren intestinal type) accounted for 69% (232 cases), 76 cases were diffuse carcinomas (22%) and 30 of mixed histology (9%). In 182 cases TNM stage was I or II (54%), 128 pts had stage III (38%) and 28 stage IV (8%). Median overall survival (mOS) was 33.8 mo and median disease free survival (mDFS) 24 mo. Adj CT was administered in 98 cases (29%); 93 pts (28%) had adj CTRT and 26 (8%) neoadj CT. D2 or D3 lymphadenectomy was performed in 182 pts, 54%. Median NLR was 2.52. Statistically significant variables for mOS and/or DFS at univariate analysis were: age, T, N, R, G, stage, tumor location, NLR and adjuvant chemotherapy. Pts with proximal disease (GE junction-cardias, 41 patients, 12%) had the poorest survival (mOS 17.1 vs 36.4 months for others, $p = 0.0025$). A low NLR was associated with higher mOS (44. vs 27.8 months for NLR over median value, $p = 0.0016$). Results of multivariate analysis are shown in Table 1.

Conclusions: Despite a short follow-up, our analysis performed on a large cohort of consecutive pts showed the prognostic value of R for both mDFS and OS. Moreover, disease stage and adj CT administration were significantly correlated with mOS. A longer follow-up is needed to achieve more conclusive data.

Table: D22. Multivariate analysis for mDFS and OS

Variable	mDFS (p value)	mOS (p value)
Sex	n.s.	n.s.
Tumor location (GE-cardia vs others)	n.s.	n.s.
Histology (Lauren)	n.s.	n.s.
T (1-2 vs 3-4)	n.s.	n.s.
N (0 vs 1-2-3)	n.s.	n.s.
R (0 vs 1-2)	0.033*	0.001 *
G (3-4 vs 1-2)	n.s.	n.s.
Stage (I-II vs III vs IV)	n.s.	0.012 *
NLR (> vs < median value)	n.s.	n.s.
Lymphadenectomy (D1 vs D2-D3)	n.s.	n.s.
Adj CTRT (no vs yes)	n.s.	n.s.
Neoadj CT (no vs yes)	n.s.	n.s.
Adj CT (no vs yes)	n.s.	0.001 *

*: statistically significant; n.s.: not significant

D23 Treatment and outcome for small bowel adenocarcinoma (SBA): a real life experience of two Italian centres

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Background: Small bowel adenocarcinomas (SBA) are rare tumours with an increasing incidence. The duodenum is the most common primary location. They are often sporadic, but Crohn's disease and genetic syndromes have been indentified as risk factors. Bowel occlusion and bleeding are common at clinical presentation. Surgical resection represents the best option for resectable tumours. The role of adjuvant treatment has not yet been established by randomised trials and in metastatic disease, the best treatment is fluoropirimidine and platinum based chemotherapy.

Patients and methods: In this retrospective observational study we enrolled patients with histological diagnosis of SBA treated at two Italian Hospitals. Their clinical courses and outcome were evaluated considering tumour location and treatment received. According to Kimora Classification we divided duodenum-ampullary carcinoma in intestinal and bilio-pancreatic type.

Results: 39 patients were evaluated. Median age at diagnosis was 66 years (range 29-88); male/female 21/18. According to tumour location we identified 3 duodenum adenocarcinomas (8%), 30(77%) duodenum-ampullary adenocarcinomas (23(59%) intestinal and 7(17%) biliary type), 3(8%) jujunal and 3(8%) ileal adenocarcinomas. At diagnosis the majority of the cases were stage II (16;41%) and G3 (15;23%) adenocarcinomas, while 8 pts were metastatic/unresectable. 20 of 31 early stage resected patients received adjuvant chemotherapy, mainly fluoropirimidine based (17;85%). 13 of them showed relapse of the disease. Overall, in the cohort of the resected patients we observed a median DFS of 14 m and a median OS of 33 m. 7 of the 8 unresectable/metastatic pts received a 5FU and oxaliplatin based first line chemotherapy and 1 of the 8 underwent a definitive chemoradiation for unresectable primary tumour. The unresectable/metastatic group showed a median PFS of 9 m and a median OS of 26 m. In the subgroup of resected ampullary adenocarcinoma OS was longer for intestinal type respect to biliary type with a median value of 40 m and 17 m respectively.

Conclusions: According to literature data, our analysis confirm the poor prognosis of SBA at all stages. Ampullary intestinal adenocarcinoma may have a better prognosis than ampullary biliary type. Fluropyrimidine based chemotherapy could be an option in the adjuvant setting and its combination with oxaliplatin could be a valid treatment for unresectable SBA.

D24 Small bowel adenocarcinoma (SBA) is a rare and heterogeneous disease: results of a retrospective analysis

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Background: Small bowel adenocarcinoma (SBA) is a rare disease representing about 1-3% of all gastrointestinal malignancies. Risk factors for SBA include inflammatory bowel disease and hereditary colorectal cancer syndromes. Moreover, SBA is sometimes associated with colorectal cancer. Because of its rarity, SBA biology and clinical course

are not as explained as other gastrointestinal cancer. Moreover, data from clinical trials on advanced SBA and adjuvant treatment are lacking.

Patients and methods: In this retrospective study we analyzed clinical data of 30 patients diagnosed with SBA in two Italian institutions between 2004 and 2016. Demographic and clinical data were collected and patients' outcome were analyzed.

Results: Median age of the patients was 69 years. Twenty-one patients were male (70%) and nine female (30%). Primary tumor site was duodenum in eighteen patients (60%), jejunum in eight patients (26.7%) and ileum in four patients (13.3%). Two (6.7%) patients had inherited genetic syndromes (Hereditary non polyposis colorectal cancer and familial adenomatous polyposis).Twenty-one patients underwent surgery and fifteen patients received adjuvant chemotherapy mainly with FOLFOX (66.7%), XELOX (13.3%) or 5-fluorouracil (5-FU) (13.3%). Thirteen patients received first line chemotherapy for advanced disease. Regimens included FOLFOX (61.5%), XELOX (7.7%), FOLFIRI (7.7%), 5-FU + Mitomycin C or Cetuximab (23.1%). Overall response rate was 36.4%, disease control rate of 45.5%. Median Progression Free Survival (PFS) was 6.43 months while median Overall Survival (OS) was 9.73 months. Lower ECOG PS was significantly associated with longer OS (ECOG PS 0-1 vs 2-3: 17.07 months vs 2.03 months, $p = 0.045$). Six patients received second line chemotherapy, mainly with FOLFIRI regimen. Overall survival of patients with advanced duodenal tumors was numerically shorter compared to patients with tumors of jejunum or ileus (median OS 6.42 months vs 21.5 months vs 17.1 months respectively, $p = 0.46$).

Conclusions: Combination chemotherapy with 5-FU and oxaliplatin represent an active regimen in the treatment of SBA. ECOG PS is a prognostic factor in patients with advanced SBA treated with first line chemotherapy. Nevertheless, prognosis of this disease is poor if compared with colorectal cancer. In particular duodenal location showed a trend for worst survival, comparable to what observed in gastric cancer.

D25 HER2 negative metastatic gastric cancer (mGC): a retrospective analysis on the efficacy of doublet or triplet chemotherapy (CT) as a first-line therapy in the clinical practice

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Background: The best regimen of CT for patients (pts) with Her-2 negative mGC is still under debate. Although several studies supported a benefit in terms of overall survival (OS) of triplet CT regimens versus doublet one, this superiority appears small and accompanied by increased toxicities. On these bases, we evaluated in the clinical practice the outcome of pts with mGC treated with triplet or doublet CT regimens as first-line therapy.

Methods: We retrospectively analyzed 165 consecutive pts with Her-2 negative mGC treated at our Department from 2012 to 2015 (median age 61 yrs; PS 1: 48.5%; G3: 52.7%; peritoneum metastasis: 40%; $\geq$ 2 metastatic sites: 48.1%; FOLFOX-4: 85 pts; ECX: 50 pts; mDCF: 30).

Results: Median number of cycles was 5.5 (range 1-10) for FOLFOX-4 and 5 (range 1-9) for ECX/mDCF. ORR was 30.5% for FOLFOX-4 and 44.1% for ECX/mDCF. Median TTP was 5.2m and 6.5m for FOLFOX-4 and ECX/mDCF regimens, respectively. Median OS was 9.4 m for FOLFOX-4 and 10.9 m for ECX/mDCF regimens. Grade 3-4 vomiting (11.6%), neutropenia (18.6%), HFS (6.9%) and diarrhea (6.9%) occurred more frequently in ECX/mDCF regimen, while peripheral neuropathy (7.5%) was more common with FOLFOX-4.

Conclusions: In our analysis, both Folfox-4 and ECX/mDCF are active and safe in the palliation of Her-2 negative mGC. Triplet chemotherapy regimens appear more active than doublet one, but offer only a slight improvement in OS with an increased G3-G4 toxicity; therefore the choice of a triplet should be reserved to pts with symptomatic tumors, bulky disease or unresectable locally advanced disease at the diagnosis.

D26 Gemcitabine/nabpaclitaxel in elderly patients with metastatic or locally advanced pancreatic adenocarcinoma: a retrospective analysis on the efficacy and safety profile

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Background: Gemcitabine/nabpaclitaxel is a polychemotherapy active regimen currently used as first-line treatment of patients with metastatic pancreatic adenocarcinoma and a good performance status (PS). This combination treatment significantly improves progression free survival (PFS) and overall survival (OS) in all population, but few data are available in elderly patients. Therefore, we carried out a retrospective analysis to evaluate efficacy and safety profile of gemcitabine/nabpaclitaxel in a cohort of elderly patients.

Methods: All patients over 70 years old with a diagnosis of metastatic pancreatic adenocarcinoma treated with gemcitabine/nab-paclitaxel at our Department between 2014 and 2016 were retrospectively reviewed. The primary objective was to evaluate the safety and efficacy of this regimen in the elderly population.

Results: Forty-six patients with a median age of 73 years (range: 70-79) were included in this analysis: males: 19 (41%); PS2: 6 (13%); primary location: head 26 (57%); biliary stent:14 (30%); previous surgery: 5 (11%); adjuvant chemotherapy 5 (11%). Overall response rate (ORR) was 33.3%; median progression-free survival (PFS) was 7 mo (95% CI 5.89-9.10) and median overall survival (OS) was 12 mo (95% CI 10.7-16.13). Treatment was well tolerated. No grade 4 toxicity was reported. Grade 3 toxicity included neutropenia in 5 pts (10%), peripheral neuropathy in 2 pts (4.3%), thrombocytopenia in 2 pts (4%), diarrhea in 3 pts (6.5%), nausea and vomiting in 1 pt (2.1%), and fatigue in 2 pts (4.3%). No significant difference in terms of efficacy and safety was recorded with a cohort of 50 pts under 70 years of age: ORR: 36.6%; median PFS 6.7 mo (95% CI 5.966-8.034), and median OS 10.5 mo (95% CI 7.864-12.136). Finally, pain control was achieved in 15 of 24 patients (62.5%) with a performance status improvement of 10% according to the Karnofsky scale.

Conclusion: Although pancreatic cancer mostly affects elderly people, clinical trials often include few elderly pts. These data suggest that combination of gemcitabine plus nab-paclitaxel is effective and safe in an unselected population of elderly pts showing no differences in outcome between older patients and younger patients treated with this combination.

D27 Comparative effects of Folfirinox and Gemcitabine/nab-paclitaxel as first and second line chemotherapy for metastatic pancreatic cancer: single choice or sequence

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Background: Gemcitabine/nab-paclitaxel and Folfirinox are standard of care of treatment of metastatic pancreatic cancer as first and second line in patients with good performance status or "fit". Progression-free survival shows similar data in both chemotherapy regimens. No data on the better treatment sequence is available.

Methods: We have retrospectively analyzed 43 patients with histological diagnosis of metastatic pancreatic adenocarcinoma and an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1. 23 (53,5%) and 20 (46,5%) of 43 patients received Folfirinox and Gemcitabine/Nab-paclitaxel as first line chemotherapy respectively. Only 19 (44,1%) patients, after progression disease, started second line chemotherapy. 8 patients received Folfirinox, whereas 11 patients were treated with Gemcitabine Nab-paclitaxel as second line regardless of prior chemotherapy. The sequence of chemotherapy Folfirinoxàgemcitabine/Nab-paclitaxel versus Gemcitabine/Nab-paclitaxelà Folfirinox was administered to 10 patients 5 for both, respectively.

Results: Median Progression-Free Survival was 5 months in the Folfirinox group as compared with 6 months in gemcitabine Nab-paclitaxel group (hazard ratio for disease progression, 0.83; 95% CI, 0.34 to 1.32; P value = 0.95). No difference between the two groups were identified in first line. The median of progression-free survival in second line was 2.5 months in the Folfirinox group and 4 months in the Gemcitabine/nab-paclitaxel. Hazard ratio for second disease progression was 0.62; 95% CI, 0.24 to 1.00; P value = 0.03. The median overall survival in patients with the sequence of chemotherapy Folfirinoxàgemcitabine/Nab-paclitaxel versus Gemcitabine/Nab-paclitaxelà Folfirinox was retrospectively 8 months and 11 months.

Conclusion: In this retrospective study, similar progression-free survival we observed between Folfirinox group and Gemcitabine/Nab-paclitaxel group in first line metastatic pancreatic cancer. These data need to be confirm in prospective randomized trial.

D28 Pancreatic cancer: sharing a nutrition education project with the patients and their care givers

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Background: Improving nutrition does not just mean to follow a strict diet, but also to discover new habits, becoming able to improve our own well-being. In the therapeutic diagnostic pathway of pancreatic cancer, it is important to involve not only the medical and nursing staff, but also the family members: together it is possible to settle and share behaviors to maintain a good health, exploiting energies from food.

Material and methods: In March 2016, the Medical Oncology and the Dietology Service of the City of Health and Science of Turin (Citta' della Salute e della Scienza), with the support of a private Association for pancreatic cancer patients, presented the project "Pancreatic cancer: nutrition education in the therapeutic pathway for patients

and their care givers". It provided a multidisciplinary training course for medical and nursing staff, a cooking class for patients and their families and a database of involved patients.

Results: In November 2016, the 1st edition of the course "The nutrition management of the patient with pancreatic cancer" was opened to the oncology, radiotherapy surgery and medical and nursing staff. The course was organized in a 8-hour study day. At the end of each session, an interactive discussion allowed the professionals to debate about the key points of the event. In the same month, the cooking class was organized too, involving for four hours 15 patients and their family members, with dietitians, oncologists and dieticians as well. The practical course was held in an equipped kitchen, after a brief lesson about food, spices, various types of cooking and food preservation. All the participants got a brochure with dietary advice and recipes presented during the course. All participants were asked to write a feedback about the event.

Conclusion: In recent times there has been an increase of the attention on the links between food and health from patients and family members. It is necessary to convey to the patient and to the care giver a message that follows validated guidelines, with the aim of improving the quality of life. We believe that some decisions on medical actions affecting patients and their families can be shared with the Patient Associations. The success of this small project (we have told you) convinced us to continue in the patients undergoing high enteric gastrointestinal cancer, with a further study with the involvement of the Oncology Network Piemonte-Valle d'Aosta and other hospital companies.

D29 Does second-line therapy affect the outcome of the patients with cholangiocarcinoma? A single institution experience

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Introduction: Metastatic cholangiocarcinoma (MC) remains at poor prognosis with median overall survival lower than 10 months. In these patients, chemotherapy constitutes the only treatment strategy. After progression to a first-line chemotherapy, there is no established second-line therapy for these patients. Indeed, literature data suggest limited activity of most second-line agents without a specific drug. The purpose of this study is to evaluated in our experience the actual role of first and second-line chemotherapies comparing to the literature date.

Materials and methods: We retrieved data of 20 consecutive MC patients referred to our Department between January 2012 and December 2016. Follow-up was closed on January 2017. We analyzed clinical data: age, Karnofsky performance status (KPS with cut-off of 80%), diagnosis (radiologic or biopsy), clinical symptoms, first-line chemo with gemcitabine plus cisplatin (GP) or oxaliplatin (GemOx) and second-line when done. Median Overall survival (mOS) was calculated using the Kaplan Mayer method.

Results: At the diagnosis median age was 70.8 years (range 33 to 84). Jaundice was the main symptom (30%), following abdominal pain and other clinical manifestations (25%). Histological diagnosis was present in 17 pts (85%). Only 17 pts (85%) received a standard chemotherapy (CT) with a doublet GP or GemOX. 9 pts (45%) were treated with second line chemo. mOS in the entire population was 8.67 (Interquartile Range [7.0-21.5]) and 6.9 [4.43-9.70] months (mo) respectively. Those who received first-line CT had a mOS of 6.97 [3.63-9.67] vs 13.2 [8.17-23.1] mo with second-line ($p = 0.05$, log-rank test). No significant statistically differences were found in terms of OS between first-line GP and GemOX treatments. ($p = 0.17$, log-rank test).

Table: D29

	N = 20	%
Age > 70	10	50
KPS > 80	12	60
Jaundice	6	30
Abdominal pain	5	25
Weight loss	1	5
GGT increase	3	15
Other	5	25
Biopsy	17	85
1°-Line		
GP	7	35
GemOx	10	50
XelOx	1	5
Gem	2	10
2°-Line		
GP	1	5
Capecitabine	4	20
FOLFIRI	2	10
Gem	2	10
None	11	55

Conclusions: Despite the small number of patients and with the limits derived from retrospective analysis, our experience confirms literature data regarding the role of second-line CT in selected patients in good clinical conditions.

D30 Nab-paclitaxel plus gemcitabine in the treatment of metastatic pancreatic cancer: our experience

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Background: Pancreatic cancer (PA) is the fourth most fatal cancer for both man and women. Many of patients(pts) with metastatic disease are often not included in clinical trials due to comorbidity such as diabetes, jaundice, etc.and poor performance status at diagnosis. These patients are the most treat in our clinical practice and they have few opportunities for cure. Von Hoff D. et all. (2013) published the data of the phase III MPACT study showing a statistically significant benefit of the nab-paclitaxel plus gemcitabine vs gemcitabine alone in terms of OS (8,5 vs 6,7 months) and PFS(5,5 vs 3,7months) as first line treatment for metastatic disease with acceptable toxicity.

Materials and methods: From September 2015 to May 2017 we collected the data of 26 unselected metastatic pancreatic cancer pts treated with nab-paclitaxel 125mg/mq and gemcitabine 1g/mq on days 1,8,15 q 28 days cycle, as first line treatment. Median age was 64 year (range 46-78); 9pts (34%) were over 70 years old. 9pts(34%) were male and 17(65%) female. PS 0: 10pts(38%), PS1:10pts(38%), PS2:6pts(23%). NLR was > 5 in 6pts(23%). They received a median of 15 drug administrations (range 1-32).

Results: The treatment was well tolerated. No toxic death or grade 4toxicity were recordedHematologic G3 toxicity included: Neutropenia 4pts (15%), Thrombocytopenia 4pts(15%). Non Hematologic G3 toxicity included: Neuropathy 1pts (3%), Asthenia 2pts (7%). ORR was 38%(10/26), DCR(PR+SD) was 53%(14/26), median PFS was 6 months (range 1-12), median OS was 9 months (range 2-18). 38%(10/26) of pts received a second line treatment.

Conclusion: We believe that nab−paclitaxel plus gemcitabine is an active and discreetly tolerated schedule and that the literature data can be reproduced in clinical practice in unselected pts with metastatic disease.

D31 Efficacy and safety of Nab-paclitaxel plus gemcitabine in metastatic pancreatic cancer

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Background: Nab-paclitaxel is a solvent-free, taxane-based antiblastic drug approved for the treatment of metastatic pancreatic cancer, as first line therapy in association with gemcitabine.* This retrospective analysis examines clinical benefit and toxicities in a group of consecutive MPC.

Patients and methods: Until Jan. 2017 we analyzed 18 consecutive patients affected by metastatic pancreatic cancer. Nab-paclitaxel was given intravenously at dose of 125 mg/mq in association with gemcitabine 1000 mg/mq on day 1-8-15 q.28 for 3 cycles, and until progression for responders. Clinical benefit was defined as disease control rate (DCR), classified by radiologic evaluation every 3 months. We also evaluated mTTP for responders and overall survival.Toxicity was recorded every cycle.

Results: We recorded 18 pts (1 F + 17M) on average 57 years old (41-76). All patients were caucasian, with adenocarcinoma, 3 stage III + 15 stage IV, PS 0-1, Metastatic lesions were 6 in liver, 4 in lung and 5 in peritoneum. Biliar duct stents were performed in 7 pts. The median number of CT cycles was 5 (range: 1-9). At first clinical/radiological evaluation after three cycles the DCR was 56% (7 pts RP; 5 pts NC). The responders continued CT until progression disease, with 3 pts that underwent local RT also and five pts underwent to second line treatment with 5FU or Oxaliplatin. Peripheral neuropathy G3 was the major toxicity in 20% of cases. We observed only 4 cases of neutropenia (grade 3-4) that required G-CSF treatment, and 3 cases of anemia G3 that required blood trasfusions. Fatigue G 1-2 was 20% e Thrombocytopenia G 2 was 10% The median time to progression in 7 responders pts was 5 months (range 2-8 months). Median OS was 12 months with 50% pts live at 1 year, 25% at 18 months and 11% at 2 y.

Conclusion: This retrospective study shows the efficacy, clinical benefit and tolerability of nab-paclitaxel associated with gemcitabine in MPC with only mild neurological and ematological toxicity.

*Von Hoff DD et al. Gemcitabine plus nab-paclitaxel is an activeregimen in patients with advanced pancreatic cancer: a phase I/II trial. J Clin Oncol 2011; 29:4548-54.

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E - THORACIC CANCERS

E1* Crizotinib in ROS1 rearranged or MET deregulated non-small-cell lung cancer (NSCLC): final results of the METROS trial

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Background: Crizotinib is an orally active inhibitor of receptor tyrosine kinases effective in NSCLC with ALK rearrangement. Recent data showed that the drug is dramatically effective in patients with *ROS1* rearrangement ($ROS1^+$), with promising activity also in individuals with *MET* exon 14 mutations (MET^{Ex14}) or *MET* amplification (MET^{FISH+}).

Material and methods: The METROS is an Italian multicenter prospective phase II trial designed to assess the efficacy and safety of crizotinib in $ROS1^+$ or MET^{Ex14} or MET^{FISH+} advanced NSCLC patients who failed at least 1 standard chemotherapy regimen. The co-primary end-point was response rate (RR) in cohort A ($ROS1^+$: centrally confirmed ROS1 rearrangement) and cohort B (MET+: centrally confirmed MET^{FISH+} defined as ratio MET/CEP7 >2.2 or locally confirmed MET^{Ex14}). Eligible patients received crizotinib at the standard dose of 250 mg BID orally.

Results: At the data cut-off of April 30th, 2017, both cohorts completed accrual. Among 498 screened patients, 51 accounted for the intent-to-treat population (ITT) and received at least 1 dose of crizotinib. Among them, 26 resulted $ROS1^+$, 16 MET^{FISH+}, 8 MET^{Ex14} and 1 had $MET^{FISH+/Ex14}$. Notably, 3 MET^{Ex14} patients had concurrent *KRAS* mutation. Cohort A included individuals with adenocarcinoma histology, median age of 55 years (range 29-86), predominantly female (61%) and never smokers (54%). Cohort B included older subjects (median age 68, range 39-78), predominantly current/former smokers (68%) and with adenocarcinoma (92%). In both cohorts crizotinib was mainly offered as second line treatment (74%). In ITT population RR, median progression free-survival (PFS) and overall survival (OS) were 65%, 17.2 months (mos) and not reached in cohort A and 20%, 3.1 mos and 5.3 mos in cohort B, respectively. For cohort B, responses were numerically higher in MET^{FISH+} than in MET^{Ex14}, with evidence of rapid progression in patients carrying $MET^{Ex14/KRAS}$. At present, 2 MET^+ patients are not evaluable yet. Therapy was generally well tolerated with adverse events consistent with the known safety profile of the drug.

Conclusions: The METROS is the first prospective trial confirming remarkable efficacy of crizotinib in $ROS1^+$ NSCLC. *MET* deregulated lung cancer is a very aggressive disease, requiring additional and innovative therapeutic approaches.

E2 ASTRIS, a real world treatment study of osimertinib in patients (pts) with EGFR T790M positive non-small cell lung cancer (NSCLC): preliminary analysis of the Italian cohort

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Background: Osimertinib is an oral, irreversible, CNS active, EGFR tyrosine kinase inhibitor (TKI) selective for both EGFR-TKI sensitising and T790M resistance mutations. ASTRIS is the international phase IIIb study that followed US FDA and EMA approval in NSCLC T790M pts. We report results from the first predefined interim analysis of the italian ASTRIS cohort (NCT02474355).

Methods: Pts received osimertinib 80 mg once daily. Eligible pts had Stage IIIB/IV NSCLC harbouring a T790M mutation determined by local validated molecular test, received prior EGFR-TKI therapy, had WHO performance status (PS) 0 – 2, acceptable organ and bone marrow function and no history of interstitial lung disease (ILD) or QTc prolongation. Asymptomatic, stable CNS metastases were permitted. The primary efficacy outcome is overall survival; other outcomes included investigator-assessed response rate (RR), progression-free survival, time to treatment discontinuation and safety events.

Results: From study start (18 Sept 2015) to data cut-off (DCO; 3 Nov 2016), 439 pts received osimertinib from 25 italian sites with a median follow-up of 4.6 mths (<1 – 14 mths) median age 65 yrs (33–92 yrs), 69% female, 85% WHO PS 0/1, 53% had only one prior EGFR TKI. 159 pts of 339 (47%) pts had CNS involvement at enrollment. All pts tested positive for T790M, identified from tissue/cytology in 153 pts (35%), plasma ctDNA in 275 pts (63%) and other specimens in 10 pts (2%). Most frequent concomitant mutations to T790M were Del19 (58%), L858R (21%) and Exon 20 insertion (14%). The molecular testing methods most commonly used were Therascreen (45%) and Roche cobas (17%). In pts evaluable for response, the investigator-assessed RR was 60% (173/288; 95% CI 54,66). Median duration of exposure was 4.4 mths (<1–13 mths). Adverse events (AEs) leading to dose modification and treatment discontinuation were reported in 59 (14%) and 23 (5%) pts, respectively. Serious AEs were reported in 46 pts (11%) and AEs leading to death in 14 pts (3%). ILD/pneumonitis-like events were reported in 5 pts (1%); no QTc prolongation was reported.

Conclusions: ASTRIS, the largest reported clinical study of osimertinib in Italy for T790M-positive NSCLC, demonstrates disease response activity similar to that observed in the AURA program with no new safety signals.

E3 Subgroup analysis of patients (Pts) refractory to first-line (1L) chemotherapy from REVEL, a randomized phase 3 study of docetaxel (DOC) with ramucirumab (RAM) or placebo (PBO) for second-line (2L) treatment of stage IV non-small-cell lung cancer (NSCLC)

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Background: In the phase 3 REVEL trial, RAM+DOC for 2L treatment of advanced NSCLC significantly improved overall survival (OS), progression-free survival (PFS) and objective response rate (ORR), independent of histology. Pts refractory to 1L therapy have a poor prognosis and are challenging to treat; we report relevant outcomes in such pts, including those with adenocarcinoma, from REVEL.

Material (patients) and methods: Refractory pts had progressive disease as best response to platinum-based treatment. Pts were randomized (1:1) to DOC 75mg/m2+ RAM 10mg/kg or PBO every 21 days. Assessments included: response [RECIST v1.1]; treatment-emergent adverse events (TEAEs) [NCI-CTCAE, version 4.0]; quality of life (QoL) [Lung Cancer Symptom Scale (LCSS)].

Results: Of 1253 REVEL pts, 29% were refractory (including 17% with refractory adenocarcinoma). Baseline characteristics of refractory pts were balanced between treatment arms (Table 1). RAM+DOC improved OS, PFS and ORR in refractory pts overall and the subgroup with adenocarcinoma (Table 2). No new safety concerns or increased detriment in QoL were identified in either group of refractory pts (Table 3).

Table 1: E3

Baseline characteristics, n(%)	RAM+DOC n = 178	PBO+DOC n = 182
Age, median (range), years	63(23-84)	60(29-87)
Male	137(77)	127(70)
ECOG PS		
0	53(30)	50(27)
1	125(70)	132(73)
<9 months since prior therapy	156(88)	154(85)
Histology		
Nonsquamous	130(73)	130(71)
Adenocarcinoma	111	101
Squamous	46(26)	50(27)

ECOG PS, Eastern Cooperative Oncology Group performance status

Table 2: E3

Subgroup	Overall			Adenocarcinoma		
	RAM+ DOC n = 178	PBO+ DOC n = 182	HR (95% CI)	RAM+ DOC n = 112	PBO+ DOC n = 101	HR (95% CI)
Median OS, m	8.3	6.3	0.86(0.68, 1.08)	8.5	6.2	0.79(0.57, 1.09)
Median PFS, m	4.0	2.5	0.71(0.57, 0.88)	4.0	2.6	0.63(0.47, 0.85)
ORR	23%	13%		20%	15%	

CI, confidence interval; HR, hazard ratio; m, months

Subgroup	Overall		Adenocarcinoma	
	RAM+DOC n = 178	PBO+DOC n = 182	RAM+DOC n = 111	PBO+DOC n = 101
Total LCSS score, time to deterioration HR (95%CI)	0.77 (0.51,1.17)		0.81 (0.47,1.41)	
TEAEs, n(%)				
Any	173(97)	171(95)	108(97)	101(100)
Grade ≥3	131(74)	126(70)	82(74)	73(72)
Serious	80(45)	84(47)	47(42)	48(48)
Leading to discontinuation	9(5)	7(4)	6(5)	4(4)
Leading to death	11(6)	17(9)	4(4)	11(11)

Conclusions: The effect of RAM+DOC for treating pts with advanced NSCLC refractory to 1L therapy appears consistent with that for the intent-to-treat population. The benefit/risk profile for refractory pts, including pts with refractory adenocarcinoma, suggests that RAM+DOC is an appropriate treatment option even in this difficult-to-treat population.

E4 Molecular profile characterization and impact on clinical outcome in metastatic NSCLC patients enrolled in MOSCATO 01 trial

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Background: The choice of anti-cancer treatments in non-small cell lung cancer (NSCLC) is currently based on both histological and molecular subtype. The goal of our analysis is to describe molecular profiles and clinical outcomes of the metastatic NSCLC patients (pts) cohort enrolled in the MOSCATO 01 trial.

Methods: Pts were identified within the MOSCATO 01, a trial that aimed for personalizing the treatment on the basis of the molecular alterations (MA) identified by targeted Next Generation Sequencing (tNGS), Whole Exome Sequencing (WES), array Comparative Genomic Hybridization (aCGH) and RNA sequencing [Massard et al Cancer Discovery 2017].

Results: 110 NSCLC pts with a representative fresh tumor biopsy were evaluable and for 105 (described in table 1) a molecular portrait was obtained.

Of these pts, 57 (54%) had an actionable MA and 30 pts (29%) received a MA-based therapy, either in a clinical trial (23) or an off-label target therapy (7). Pts received EGFR TKi (7), inhibitors of MET(5), FGFR (4), BRAF (3), MEK (3), HER2 (2), MTOR (1), NOTCH (1), ALK (1), ROS1 (1), RET (1) and MDM2 (1).

In the group of pts with MA-based therapy the PFS2/PFS1 > 1.3 ratio was achieved for 23% of pts (7/30), median (m) PFS2 was 2.2 (0.9-26.6), mOS was 13.9 (3.1-58.6) months.

Not oriented pts (47) were treated with chemotherapy (20), target therapy (16) or immunotherapy (11). Their mOS was 12.2 (1.7-60.2) months.

Conclusions: This study confirms the relevance and feasibility of molecular screening and provides a rich description of the molecular landscape of a metastatic NSCLC population. Further analyses to better understand the immunological features and epigenetic landscape of our cohort are currently ongoing.

Table: E4

	Molecular Portrait, N = 105 (100%)	MA-based therapy, N = 30 (29%)	Non MA-based therapy, N = 47(45%)
Age at inclusion			
Median	59	59	59
Range	32-83	36-78	32-76
Sex			
Male	50(48%)	15(50%)	19(40%)
Female	55(52%)	15(50%)	28(60%)
ECOG Performance Status			
0	26(25%)	9(30%)	9(19%)
1	49(47%)	14 (47%)	21(45%)
2	2(2%)	0	1(2%)
missing	28(26%)	7(23%)	16(34%)
Histology			
Squamous cell carcinoma	11(10%)	2(7%)	4(8%)
Non squamous cell carcinoma	94(90%)	28(93%)	43(91%)
Smoking			
Never smoker	32(30%)	8(27%)	15(32%)
Former smoker	45(43%)	13(43%)	20(43%)
Current smoker	17(16%)	6(20%)	7(15%)
Molecular status at diagnosis			
EGFR mutated	18(17%)	4(13%)	11(23%)
Exon19	10(10%)	3(10%)	4(9%)
L858R	5(5%)	0	5(11%)
T790M	2(2%)	0	1(2%)
other	2(2%)	1(3%)	1(2%)
ALK translocated	3(3%)	0	2(4%)
KRAS mutated	12(11%)	3(10%)	7(15%)

E5 Integrating programmed cell death ligand 1 (PD-L1) and neutrophil to lymphocyte ratio (NLR) as predictive panel of response to nivolumab in non-small cell lung cancer (NSCLC)

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Background: Cost-effectiveness and viability of new predictive markers for immunotherapy limit their application in clinical practice. This retrospective study explores PD-L1 expression and NLR as an easy feasible panel to predict benefit to Nivolumab.

Methods: Out of 108 pre-treated NSCLC pts included in the Nivolumab expanded access program, 71 (66%) were evaluable for PD-L1 expression on archival tissue samples by immunohistochemistry (clone E1L3N, Cell Signalling Technology) and NLR on baseline blood cell count. PD-L1 positivity was defined as expression on $\geq$ 1% of tumor cells, while NLR was considered as high (NLR>3) or low (NLR<3). Progression free survival (PFS) was estimated by Kaplan Meyer method; the combined predictive value of PD-L1/NLR for PFS and overall survival (OS) was assessed using multivariate Cox proportional hazard models.

Results: Pts were mostly males (63%), smokers (86%), with adenocarcinoma (76%); *EGFR* + (10%), *K-RAS* + (33%). Median PFS and OS to Nivolumab were 5.52 months (mo) (95% [CI] 4.5-8.05) and NR (95% [CI] 7.4-NR), respectively. 1-y OS was 51%. PFS to Nivolumab was not affected by PD-L1 status (PD-L1 >1% 13.2 mo, 95% [CI] 3.4-NR vs PDL1 <1% 6 mo, 95% [CI] 3.35-14.21; p= 0.51). High NLR significantly predicted poorer PFS than low NLR (NLR>3: 2.5 mo, 95% [CI] 2-5.29 vs NLR<3: 8.61 mo, 95% [CI] 4.86-23.02, p<0.001). Although median OS was not reached at the time of analysis, 25th percentile survival rate favored low NLR (NLR<3: 6.84 mo, 95% [CI] 4.98-7.88 vs NLR>3: 2.89 mo, 95% [CI] 2.5-4.3, p<0.001). Patients were divided in two cohorts according to combined PD-L1/NLR (cohort1: PD-L1+/low NLR, cohort 2: PD-L1-/high NLR). In the multivariate analysis, PFS to Nivolumab was significantly longer in cohort 1 (Cohort 1: 13.26 mo, 95% [CI] 3.42-NR vs Cohort 2: 2.5 mo, 95% [CI] 1.45-6.08, p < 0.0001). OS is available only for cohort 2 (OS 3.29 mo 95% [CI] 2.76-5.16).

Conclusions: This retrospective study supports NLR as predictive biomarker for survival to immunotherapy and shows how the combined use of PD-L1/NLR can predict longer PFS to nivolumab treatment. This feasible panel may be routinely applied to select pts for immunotherapy avoiding more complex and expensive methods.

E6 Randomized phase 1b/3 study of erlotinib plus ramucirumab in first-line EGFR mut + stage IV NSCLC: phase 1b safety results

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Background: Ramucirumab, an antiangiogenic IgG1 VEGFR2-targeted monoclonal antibody, and erlotinib, an EGFR tyrosine kinase inhibitor, are both active in advanced NSCLC. This global phase 1b/3 study (NCT02411448) will assess safety, tolerability and efficacy of the combination of ramucirumab with erlotinib in previously untreated patients with *EGFR* mutation-positive stage IV NSCLC. Here we report phase 1b safety results.

Methods: Eligible patients with ECOG PS 0-1, an activating *EGFR* mutation, and previously untreated stage IV NSCLC received ramucirumab 10 mg/kg intravenously on day 1 of repeating 14-day (± 3 days) cycle and erlotinib 150 mg orally daily. Treatment continued until disease progression or unacceptable toxicity. The primary objective of part A was to assess the safety and tolerability, in terms of dose limiting toxicities (DLT), of adding the recommended dose of ramucirumab for phase 3 (part B) to standard dose erlotinib. Data were analyzed separately for Japan (JP) (cohort 1) and US/EU (cohort 2). The DLT assessment occurred during the first 2 cycles (approximately 28 days).

Results: As of Dec 16th, 2015, 14 patients were treated in the phase 1b part of this trial and 12 were DLT evaluable (6 JP; 6 US/EU). Overall, 6 grade (Gr) 3 treatment-emergent adverse events (TEAE) were noted, with at least one TEAE in 5 patients; no serious adverse events or Gr 4-5 TEAEs occurred. In the JP cohort the median age was 73 (64-79), 57% had ECOG PS 1 and 29% had a history of smoking. Four patients (57%) experienced a Gr 3 TEAE, of which one was a DLT (elevation of alanine aminotransferase) while the others (hypertension [n = 2], dermatitis acneiform, and diarrhea) were not DLTs. In the US/EU cohort the median age was 71 (31-83), 86% had ECOG PS 1, and no patients had a history of smoking. One patient experienced Gr 3 TEAE of rash; no DLTs were observed in this cohort.

Conclusion: Enrollment on the phase 1b portion of this trial is complete and the safety results were consistent with previous combinations of antiangiogenic/erlotinib in this patient population. No unexpected toxicities were identified. Phase 3 enrollment has been initiated maintaining the dose of ramucirumab at 10 mg/kg Q2W.

E7 A retrospective analysis of patients (pts) with non-small-cell lung cancer (NSCLC) with uncommon or complex epidermal growth factor receptor (EGFR) mutations treated with tyrosine kinase inhibitors (EGFR-TKIs): clinical features and outcome

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Background: The discovery of EGFR-activating mutations (EGFRm) in about 10-15% of lung adenocarcinomas in European populations and the introduction of oral EGFR-TKIs have expanded the treatment options for patients with non-small cell lung cancer. Three defined regions (exons 18, 19 and 21) in the EGFR gene are commonly mutated. Exon19 deletions of 15−18 pb represent more than 50% of EGFR mutations, and the exon 21 point mutation at the residue L858R represents more than 30%. However, there are a number of relatively rare EGFRm whose associations to EGFR TKIs are not well clarified. This is an observational study investigating epidemiology, clinical features and treatment outcome of NSCLC pts harbouring rare/complex EGFRm.

Material and methods: 2,093 NSCLC pts, enrolled from 2010 to 2016, were considered for EGFR mutational analysis performed by (SSCP)-Sanger sequencing, Real-Time-PCR, Pyrosequencing or MALDI-TOF (Sequenom)

Results: 294 NSCLC pts (14%) harbored EGFRm, out of which 32 (10.8%) rare mutations (27 cases with single mutation and 5 cases with complex mutation). EGFR single mutations included: 9 point mutations (E709 and G719 codons) in exon 18, 12 insertions and 1 point mutation (S768 codon) in exon 20 and 5 point mutations (H835 and L861 codons) in exon 21. EGFR coexisting point mutations were: E709A+G719D, E709K+G719C and E709K+G719X in exon 18; R776H+T790M in exon 20 and G719C + S768I in exon 18 and 20, respectively. Among these 32 pts, 15 received and were evaluable for first-line TKIs treatment. Analyzing clinical features median age was 71 year old, with slight majority of men (9 vs 6); smoking history was negative in half of pts.

At the diagnosis, almost all pts (12/15) presented metastatic stage, with most common metastasis sites bone, pleura and brain (respectively 26.6%, 26.6% and 20%). Response Rate and Disease Control Rate (DCR) were 40% and 53%; median Progression Free Survival (PFS) was 5.5 months with brain as major site of progression (40%). Significantly more than 70% of patients do not undergo to second line of treatment. The median Overall Survival (OS) was 6.7 months.

Conclusions: The analysis emphasizes the peculiar clinical features and lower TKIs sensitivity of uncommon/complex compared with common EGFRm and the clinical need to identify the better therapeutic strategy.

E8 Efficacy of ceritinib administered to patients with crizotinib-refractory, ALK-positive, advanced NSCLC within the Italian compassionate use program

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Background: Ceritinib is an effective treatment for patients (pts) with anaplastic lymphoma kinase (ALK)-positive advanced non-small cel lung cancer (NSCLC) who progress on crizotinib. We assessed the efficacy of ceritinib administered within a compassionate use (CU) program.

Patients and methods: This collaborative study involved pts with crizotinib-refractory, ALK-positive, advanced NSCLC treated at multiple Institutions. The clinical data of pts for whom ceritinib was requested as CU at the recommended dose of 750 mg/d without food were collected and analyzed.

Results: Twenty-five Centers took part to the study, for a total of 70 pts who received at least one dose of ceritinib from July 2014 to March 2017. Pts characteristics were as follows: median age 56 years (22-86), 67/70 (95.5%) adenocarcinomas, 36/70 (51.5%) female, 47/70 (67%) never smokers, 14/70 (20%) ECOG PS $\geq$ 2, 17/70 (24.5%)

pretreated with ≥ 2 lines of chemotherapy, 49/70 (70%) metastatic to the brain. Median time on prior crizotinib was 359 days (51-1644). The starting dose of ceritinib was 750 mg/d in 63/70 (90%) pts. The most common any grade treatment-related adverse events (TRAEs) were nausea and/or vomiting (60%, 7% grade 3 or 4), diarrhea (50%, 1.5% grade 3 or 4), ALT and/or AST elevation (47%, 18.5% grade 3 or 4) and fatigue (57%, 8.5% grade 3 or 4). Unusual TRAEs considered to be drug-related consisted of an increase in serum creatinine in 2 pts. Dose reduction due to TRAEs occurred in 31/63 (49%) pts who started at 750 mg/d. Of them, 17/63 (27%) pts reduced to 600 mg/d, 8/63 (12.5%) pts to 450 mg/d, and 6/63 (9.5%) pts to 300 mg/d. Permanent dose discontinuation due to toxicity occurred in 4/70 (5.5%) pts. Of the 61 evaluable pts, 27 (44.5%, 95%CI: 31.5-57.6) responded to treatment, the median duration of response being 11.2 months. At a median follow-up of 6.7 months (<1-26), the median progression-free survival (PFS) was 7.2 months, with 6- and 12-month PFS rates being 54.5% and 31.5%, respectively. No statistically significant difference in terms of PFS was observed between pts with (n = 38) or without (n = 32) dose adjustements (8.2 months vs. 4.2 months, respectively, P = 0.20).

Conclusions: Ceritinib CU program in Italy confirms the efficacy of the drug in a "real-world" setting, with a safety profile that is similar to that observed in clinical trials. A high rate of dose adjustments due to TRAEs was observed, which, however, did not appear to affect the activity of the drug.

E9 Compliance to diagnostic and therapeutic pathways and innovative drug recommendations in advanced non-small cell lung cancer: preliminary results from the MOST study

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Background: Evidence-based diagnostic-therapeutic pathways (PDTA) and innovative drugs recommendations are needed in order to promote high-quality and high-value cancer care, particularly in case of 'me too' drugs with the same indication such as gefitinib (G), erlotinib (E) and afatinib(A) in EGFR mutated (EGFRm) Non-Small Cell Lung Cancer (NSCLC).

Patients and methods: The primary aim of the MOST (Multicenter prospective observational study on EGFR TKIs as first-line treatment of EGFRm NSCLC) study was the assessment of Veneto Oncology Network centers compliance to NSCLC PDTA and recommendations on A as first-line treatment of metastatic EGFRm NSCLC. Secondarily, we evaluated treatment outcome, safety profile, budget impact of G, E and A in a 'real world' practice. Selection criteria for first-line treatment choice were also explored. Data about the diagnostic pathway of non-squamous NSCLC patients and first-line treatment of EGFRm cases were collected in the time-frame of 12 months and followed in the observation period of 18 months. The compliance of the participant centers to PDTA and treatment recommendations was assessed through specific indicators and benchmarks aiming at evaluating their quality and adequacy.

Results: Fourteen centers were recruiting at the time of this preliminary analysis on the first 182 evaluable patients. All non-squamous NSCLC cases underwent EGFR mutation analysis (benchmark 100%). Median time frame between histological sample acceptance and EGFR results was 16 working days (wd) (benchmark 10 wd). In 124(68%) cases EGFR analysis was performed automatically without physician request. EGFRm (*N*=47) NSCLC patients who received EGFR TKIs as first-line treatment were 45 (96%) (benchmark 90% or more). Among these patients 26(58%) received G, 8(18%) received E and 11(24%) received A (benchmark for A 10%-30%). In the first 26 evaluable patients, response rate was 50% for A and G and 67% for E. We observed definitive treatment interruption for adverse events in 1(9%) patient receiving A (benchmark 8%), 1(13%) patient receiving E (benchmark 6%), and no patient receiving G (benchmark 6.9%).

Conclusions: Compliance to the diagnostic pathway of NSCLC should be improved in the clinical practice, particularly the timing of molecular tests. So far, treatment recommendations were followed. Primary, secondary and exploratory endpoints results on a wider sample size will be presented at the conference.

E10 Results of an integrated multi-platforms analysis in squamous cell lung carcinoma (SqCLC) revealed PI3K/RICTOR-mTORC2 axis as a potential prognostic biomarker and druggable target

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Background: We built a risk classification model for resected SqCLC (R-SqCLC) based on clinicopathological predictors to discriminate patients' (pts) prognosis (*Pilotto JTO 2015*) and we externally validated this model in a pts' cohort of > 1,300 R-SqCLC (*Bria WCLC 2016*). To identify potentially druggable modulators we performed an integrated multi-platforms genome analysis of prognostic outliers and we selected *PI3K/RICTOR-mTORC2* axis (*Pilotto WCLC 2016*) as the main candidate. Here we present the results of transcriptome, we validate our genomic findings in an external cohort and we enhance our rationale with in vitro studies.

Material and methods: Next Generation Sequencing (NGS) analysis of somatic mutations (SM) and copy number alterations (SCNA) was performed (Ion AmpliSeq Lung & Colon Cancer Panel: 22 genes, a SqCLC customized panel: 20 genes, the Ion AmpliSeq Comprehensive Cancer Panel: 409 genes). Transcriptome libraries were prepared using the AmpliSeq Transcriptome kit and sequenced on an Ion Proton. In vitro experiments were performed using the SqCLC cell line H-1703 (Rictor amplified-6 copies). PF-05212384 (PI3K/mTOR), AZD2014 (mTORC1/2), MK-2206 (panAkt), everolimus (mTOR) and chemotherapeutic drugs (Docetaxel, Gemcitabine) were tested. Cell viability was assessed by crystal violet assay and the half maximal inhibitory concentration (IC50) was estimated.

Results: Main results of 97 pts (Training/Validation: 60/37) are presented in the table.

Table: E10

	Gene	Training Set [%]	Validation Set [%]
SM	*TIE1*	4 [6.7]	2 [5.4]
	PTEN	6 [10]	4 [10.8]
	PI3KCA	3 [5]	3 [8.1]
SCNA Gains	*RICTOR*	14 [23.3]	13 [35.1]
	PI3KCA	26 [43.3]	17 [45.9]
SCNA Losses	*PTEN*	19 [31.7]	5 [13.5]
	TSC2	7 [11.7]	8 [21.6]

Regarding the transcriptome, poor prognosis pts (n = 17) showed a majority of repressed (n = 63) than overexpressed (n = 27) genes compared to good prognosis (n = 17). Top genes (fold expression change>8) with higher expression in poor prognosis were XAGE1C, SCGB1D2, PPP1R1B and EREG. The in vitro results support a significant inhibition of H-1703 cells proliferation by Gemcitabine, Docetaxel, PF-05212384, MK-2206 and AZD2014 with IC50 values of 0.4 nM, 0.45 nM, 10 nM, 66 nM, 110 nM, respectively.

Conclusions: A multi-step genomic analysis of R-SqCLC is technically feasible and it allows investigating the differential profiles of pts stratified according to prognosis. The *PI3K/RICTOR-mTORC2* axis emerged as the main candidate and our in vitro results justify pursuing mTOR inhibition, focusing on mTORC2, in RICTOR-aberrant tumors.

E11 The close link between anxiety and cluster symptoms in lung cancer patients during first-line chemotherapy: further data from a dedicated WALCE (Women Against Lung Cancer in Europe) survey

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Background: Lung cancer (LC) patients refer a simultaneous incidence of physical and psychosocial symptoms defined cluster symptoms (CS). Preliminary results currently under evaluation for publication showed an association between anxiety and chemotherapy induced nausea and vomiting (CINV). As among CINV predictors, anxiety is a modifiable factor, once having identified subjects at higher risk, this toxicity could be prevented. With this additional analysis of the survey we aimed to identify the factors associated with anxiety during chemotherapy in stage IV LC patients undergoing first-line treatment.

Material and methods: The WALCE survey investigated in 11 Italian centers, at four consecutive evaluations (T0, T1, T2 and T3) and by means of a Numerical Rating Scale, the following items: anxiety, lack of self-confidence, fatigue, lack of appetite, pain, somnolence, dyspnea, general status, and lack of trust in treatments. Depending on the value assigned to the anxiety item, anxiety was categorized as absent (0), mild (1-3), moderate (4-7), severe (8-10). The evaluated items number was too high to be included in a multivariate model, thus factor analyses were run at each time point. The factor scores obtained were included as covariates (together with sex, age class and chemotherapy scheme) in the multivariate logistic ordinal models, run at T0, T1, T2 and T3 evaluating the risk factors for anxiety.

Results: 188 patients completed the questionnaire at T0, 164 at T1, 138 at T2 and 101 at T3. The global incidence of anxiety was equal to 90%. The factor analyses showed that behind the considered variables, there were two latent factors composed by the same items at each evaluation: factor 1 (physical CS), composed by fatigue, somnolence, dyspnea and lack of self-confidence, and factor 2 (psychological CS), composed by lack of trust in treatments, general status and lack of appetite. Only physical CS was associated with an increased risk of pre-chemotherapy anxiety, while during chemotherapy, both physical and psychological CS seemed to exert an influence on anxiety development at T1, T2 and T3.

Conclusions: To date, there is no clear cause-effect relationship between CS and anxiety, however, their linkage and simultaneous intensity growth is well demonstrated during chemotherapy. More attention should be paid to the detection of CS and anxiety in LC patients during first-line chemotherapy.

E12 Prospective generation of PDTX (patient derived tumor xenografts) and molecular profiling of NSCLC (non small cell lung cancer)

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Background: The generation of "xeno-patients" is a valuable tool to prospectively reproduce *in vivo* molecular mechanisms underpinning cancer progression, by recapitulating human cancer heterogeneity. Furthermore, this method allows to overcome intrinsic limitations of *in vitro* models. In NSCLC, xeno-patiens have been described from early and late stages, with heterogeneous results. The project aims to confirm the reliability of this model in NSCLC and to prospectively characterize their genetic profile.

Materials and methods: From February 2014 to September 2016, 125 early stage (I-III) NSCLC patients who underwent radical lung resection and 14 metastatic NSCLC patients were enrolled. Written informed consent was required. Fresh intact tissue (from surgery or radio-guided biopsy) was collected and kept in serum free medium, embedded in 20% matrigel and subcutaneously engrafted into NSG and NOD SCID mice, within 24 hours from sample collection.

Next Generation Sequencing was conduced on explanted paraffin embedded samples after first passage. Multigenic mutational analysis of hot spot regions of 52 genes (Oncomine Focus Assay) was conducted on 21 out of 30 engrafted samples.

Results: The engrafted samples were 125 from radical lung resections and 14 from TC-guided biopsies. Histologically, early stages samples were found as adenocarcinoma (65%), squamous carcinoma (28%), sarcomatoid carcinoma (2%), LCNEC (3%) and carcinoid (2%). In late stage samples, the main observed histological subtypes were adenocarcinoma (43%), squamous carcinoma (21%) and SCLC (14%).

The engraftment rate was equal to 23.2% in surgical samples and 7.1% in biopsy samples. Engraftment was significantly higher in squamous histology ($p < 0.005$) without correlation with clinical characteristics (age, sex, smoking status, stage). NGS showed high concordance between cancer tissue and corresponding PDTX in terms of polymorphic and mutational variants. Non-synonimous somatic variants were found to overlap in tumors and PDTX, whereas low allelic frequency variants (<10%) were lost in PDTX.

In the PDTX transition new somatic variants were not acquired; in six cases, the PDTX showed higher allelic frequency of mutated oncogenic drivers (KRAS, PIK3CA, FGFR2, MET).

Conclusions: NGS showed high concordance between NSCLC samples and PDTX, retaining their genetic characteristics. These data confirm the reliability of this model in NSCLC, providing the rationale for further population-based translational studies.

E13 DNA amount comparison between cytologic and histologic samples for epithelial growth factor receptor (EGFR) testing in non-small-cell lung cancer (NSCLC) patients: a single institution experience

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Background: In EGFR-mutated advanced NSCLC patients (pts) the identification of the specific mutation is mandatory to design the proper therapeutic algorithm. Abundant histologic tumour specimens are usually preferred for mutational analyses in regarding small and cytologic specimens. Unfortunately, these ones still represent the only available material for several patients. We aim to compare the DNA amount extracted from cytologic and histologic samples for EGFR tests performed in a single Institution.

Methods: Positive EGFR tests performed at San Luigi Hospital from 2008 to 2015 were included. Information about pts' characteristics, type of mutation, sample details and DNA amount for EGFR test were collected. The comparison of median DNA amount was performed using the independent T test, while the chi-square test was used for the evaluation of cytological sample ratio over time.

Results: We collected 152 tests performed on 136 EGFR mutated pts. The median age was 66 yrs [range 32 – 86], 80 (58.8%) were females, 135 (99.3%) adenocarcinoma, 120 (88.2%) never or former smokers, 95 (69.8%) presented a metastatic disease at diagnosis while 41 pts presented a localized or locally advanced disease. Eighty-five pts (62.5%) harboured a mutation in exon 19; 39 (28.7%) in exon 21, 4 (2.9%) in exon 20 and 1 (0.7%) in exon 18; 7 pts (5.2%) presented a double mutation and in 3 pts (2.1%) a de novo T790M mutation was detected. Thirty-six pts performed at least one re-biopsy at EGFR TKI progression and 15 cases showed the acquired T790M mutation. In the overall population, the proportion of cytologic samples was equal to 50.7%, with a significant increase from before 2011 to 2015 ($p = 0.004$). Any significant difference in extracted DNA amount neither between cytologic and histologic samples (61.25 ng/ml ± 52.97 vs 71.42 ng/ml ± 75.47, $p = 0.348$) nor between specimens derived from bronchoscopy and thoracic biopsy (64.07 ng/ml ± 57.53 vs 52.31 ng/ml ± 42.39, $p = 0.233$) was detected.

Conclusions: In this retrospective evaluation, no difference in DNA amount availability for EGFR analysis was detectable in cytologic or histologic specimens. This result supports previous data showing a similar sensibility in EGFR detection in both types of samples, confirming the indication to perform the less invasive procedure in specimen obtaining. Our institution progressively increased the number of cytologic samples over time, showing to get more confident with this analysis over time.

E14 Efficacy of platinum-based chemotherapy in EGFR WT nonsquamous advanced non-small cell lung cancer (NSCLC) patients: association with KRAS mutation and thymidylate synthase (TS) levels

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Background: Preclinically, KRAS mutation has been associated with enhanced dependency on the folate metabolism in non-small cell lung cancer (NSCLC). Whether this phenomenon is related to increased sensitivity to anti-metabolites and/or lower thymidylate synthase (TS) levels in KRAS mutant patients (pts) is unknown.

Patients and Methods: Pts with EGFR WT nonsquamous advanced NSCLC were retrospectively evaluated at one Center. Only pts with a known KRAS mutation status

who were treated with platinum-based chemotherapy as first-line were eligible. One-step RT-PCR was used to evaluate the expression of genes potentially associated with treatment outcome (including TS, ERCC1, RRM1 and BRCA1) in pts with available tissue.

Results: KRAS-mutant pts who received platinum/pemetrexed (85/136, 62.5%) had shorter progression-free survival (PFS) (4 vs. 6 months, $P = 0.05$) and overall survival (OS) (8 vs. 20 months, $P = 0.0019$) compared to those who received platinum/gemcitabine (51/136, 37.5%). Similarly, a significantly lower overall response rate (28.2% vs 47%, $P = 0.02$) and disease control rate (50% vs. 72.5%, $P = 0.01$) was observed for platinum/pemetrexed compared with platinum/gemcitabine. No significant differences in PFS and OS were observed in the KRAS WT group according to the type of platinum-doublet received. When focusing only on pts treated with platinum/pemetrexed, a shorter PFS (4 vs. 6 months, $P = 0.01$) and OS (8 vs. 16 months, $P = 0.0065$) were noted for KRAS-mutant pts. On the other hand, among pts treated with platinum/gemcitabine no differences in terms of PFS and OS were observed according to KRAS mutation status. TS, ERCC1, RRM1 and BRCA1 levels were assessed in 93 KRAS-mutant and 93 KRAS WT pts. Pts with KRAS mutation had significantly lower mean expression levels of TS ($P = 0.036$) and higher mean expression levels of ERCC1 ($P = 0.05$) while no differences in terms of RRM1 and BRCA1 mean expression levels were observed. In unselected pts those with low TS and RRM1 levels, as assessed by ROC analysis, had a significantly higher probability to bear a KRAS mutation ($P = 0.02$ and 0.04, respectively).

Conclusion: In EGFR WT nonsquamous advanced NSCLCs a poor outcome on platinum/pemetrexed was reported for KRAS-mutant pts, which could not be justified based on TS expression levels. Rather, activation of the KRAS pathway may drive resistance to platinum/pemetrexed regardless of TS levels. Whether platinum/gemcitabine represents the best option in KRAS-mutant pts should be assessed prospectively.

E15 Programmed death ligand 1 (PD-L1) expression status as prognostic factor in early stage non-small cell lung cancer (NSCLC)

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Background: Therapeutic strategies against PD-1/PD-L1 have proved efficacy in NSCLC. PD-L1 status is a predictive marker of immunotherapy efficacy in first-line setting. This study explores its potential prognostic role in early stage surgically resected NSCLC (NCT03078959).

Methods: PD-L1 expression was evaluated in a cohort of 289 surgically resected IA-IIIA stage NSCLC samples by immunohistochemistry using the SP263 clone (Ventana). Tumors were considered PD-L1 positive (PD-L1+) if $\geq$ 50% of tumor cells expressed the ligand. PD-L1 status correlation to clinical characteristic, progression free survival (PFS) and overall survival (OS) were studied with Chi Square, Fisher Exact Test and Kaplan Meier analysis.

Results: Patients were mostly males (79%), former or current smokers (81%), with median age of 69 years, non-squamous histology (68%) and high-grade tumors (55%). PD-L1 positive tumors were 18.7% (54/289). There was no significant correlation with sex, age, smoking status and histology. PD-L1 expression was mostly limited to grade 3 tumors (G1 vs G2 vs G3: 0 vs 13% vs 25%, p = 0.005). In the whole cohort no statistical difference was noted both in median PFS (PD-L1+ vs PD-L1-: NR vs 63.2 mo, p < 0.152) and OS (PD-L1+ vs PD-L1-: 47.5 movs 32.2 mo, p = 0.5). When the survival analysis was restricted to grade 3 tumors, PFS was significantly longer in PD-L1+ tumors (PD-L1+ vs PD-L1-: NR vs 61 mo, p = 0.046). OS was not affected by PD-L1 status.

Conclusions: PD-L1 is mostly expressed in high grade NSCLC. HighPD-L1 expression is a prognostic marker for PFS but not for OS in the subset of G3 tumors. Further studies are needed to confirm PD-L1 correlation to grading in the metastatic setting and to evaluate whether grading could represent a surrogate biomarker for sensitivity to immunotherapy.

E16 Prognostic impact of hyponatremia in patients affected by advanced non-small cell lung cancer (NSCLC) with bone metastases (BMs)

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Background: In recent years, due to the development of new treatment options, the outcome of patients with metastatic non-small cell lung cancer (NSCLC) has improved. However, hyponatremia and bone metastasis still correlate with poor prognosis. Some studies suggest that hyponatremia is associated with higher risk of osteoporosis and bone fracture, but no data are available about the relationship between hyponatremia and bone metastasis. Aim of this study is to investigate the prognostic role of hyponatremia in patients with bone metastases (BMs) due to NSCLC.

Material and methods: NSCLC patients' data were retrospectively collected. Survival curves were estimated using Kaplan-Meier method, and comparisons were made using chi-square test. Age, gender, tumor stage, histology, Eastern Cooperative Oncology Group-Performance Status (ECOG-PS), smoking history and presence of hyponatremia were included in the Cox analysis to investigate their prognostic relevance.

Results: 647 patients with advanced NSCLC were enrolled; of them 440 (68%) were male. Median age was 72y (range 32-93y). A total of 264 patients (41%) presented with BMs, which were synchronous in 170 patients (26%) and metachronous in 94 (15%).

At diagnosis, hyponatremia was described in 105 (16%) patients, a total of 237 (37%) patients developed hyponatremia during the first line. Median overall survival (OS) was 15,9 (95% CI 14,1-17,9) months for patients without BMs, 11.4 (95% CI 9,4-13,4) months for patients with BMs, while mOS was 16,3 (95% CI 14,6-18,0) months for eunatremic patients and 10.3 (95% CI 7,6-12,8) months for patients with hyponatremia.

Considering the two variables, mOS was 10.1 (95% CI 4,3-15,9) months for patients with BMs and hyponatremia, 11.9 (95% CI 11,4-12,4) for patients with hyponatremia without BMs, 13.1 (95% CI 12,0-14,2) for eunatremic patients with BMs, 17.1 (95% CI 15,2-19,1) months in eunatremic patients without BMs (*p*: 0.0020). Metachronous BMs appeared earlier in hyponatremic patients (3.73 vs. 5.76 months, *p*: 0.0187). At multivariate analysis in the whole population, ECOG-PS$\geq$2, IV tumor stage, male sex, hyponatremia and BMs were independent prognostic factors for worst OS. In patients with BMs, smoking history, IV tumor stage were independent prognostic factors for worst OS.

Conclusions: Our study suggests that hyponatremia represent an important prognostic factor and it should be necessary considered in order to optimize the management of NSCLC patients with BMs.

E17 Updated report of an observational clinical registry (REGCLIN-MM) on malignant pleural mesothelioma (MPM)

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Background: In 2012, the CCM (Centro Controllo Malattie) supported a project aimed at creating a collaborative network among centers with significant diagnostic rate of MPM. An observational study (REGCLIN-MM) was activated providing information about recruitment, clinical characteristics, treatment modalities and outcomes. Data were collected in a web-based registry. Preliminary results were previously reported (IMIG 2016) and here we provide an updated analysis.

Patients and methods: The study enrolled MPM patients (pts) diagnosed and treated in 12 participating centers. The most relevant clinical and treatment parameters were collected and registered. The analysis were made using SAS (v 9.2).

Results: From 1/2010 to 1/2017, overall 846 pts were included, 248 (29%) females and 598 (71%) males, median age 70 (range 91-27, IQR 64-76).

Information about asbestos exposure was available for 673 (80%): environmental 129 (19%), professional 388 (58%), hobby/domestic 12 (2%), unknown/undeterminable 144 (21%). Histology was epithelioid in 658 (78%), biphasic in 90 (11%), sarcomatoid in 78 (9%), not specified in 20 (2%). Diagnosis was obtained through pleuroscopy/thoracoscopy in 657 (78%), CT-guided biopsy in 149 (18%), other modalities in 13 (1%) and not specified in 27 (3%). Pleurodesis was performed on 242 pts (29%) whereas 167 (20%) pts underwent surgery within a multimodal approach consisting of EPP in 13 (8%), P/D in 126 (75%), undefined in 28 pts (17%). Radiotherapy was delivered to 171 pts (20%). Treatment within a clinical trial was offered to192 (23%) pts. Chemotherapy was administered to 643 (76%) pts and was the only treatment for 442 (52%), 567 (67%) received pemetrexed in combination with cisplatin/carboplatin as first line, 53 (6%) pemetrexed alone and 23 (3%) other drugs. With a median follow-up of 12,7 (IQR 6,8-21,23) months median overall survival (mOS) is 22,8 (95%CI 20,3-26) months for epithelioid MPM and 9,5 (95%CI 8,1-11,7) for non-epithelioid.

Conclusion: This study demonstrates that sharing data through a web-based registry among high-volume centers for MPM is feasible. A high proportion of pts received active treatment and a relevant percentage of them were included in clinical trials. The mOS compares very favorably with historical data. This web-based registry may represent either a good platform for translational research or could be used to integrate the information collected by the Italian epidemiological registry ReNaM.

E18 Clinical features of never smoker patients with lung squamous cell carcinoma: a retrospective multicenter study

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Background: Squamous cell carcinoma of the lung (LSCC) is the second most common histological subtype of non-small cell lung cancer (NSCLC) having smoking habit as the major risk factor. LSCC in non-smokers is an exceptional finding possibly related to professional exposure and subsequent carcinogenesis even though clinical and biological landscape is largely unexplored.

Methods: This is a retrospective multicenter study investigating clinical features of never-smoker LSCC patients (pts) referred to three Italian Centers between 2010 and 2016. Relapse (RFS) or progression free (PFS) and overall (OS) survival curves were calculated by Kaplan-Meier method. Cox regression proportional hazards model was used to estimate the impact of covariates on OS.

Results: Among 810 LSCC pts, 39(4,8%) occurred in never-smokers; our case series included 21 males and 18 females with a median age of 63 years. ECOG PS was 0-1 in 31(79%) pts. Median Charlson Comorbidity Index (CCI) was 7. Two(5%) pts referred second-hand smoking history and 13(33%) occupational exposure. Additional tumor history was reported by 18(46%) patients: head and neck (*N*=5), basocellular skin (*N*=5), breast (*N*=2), lung (*N*=2), prostate (*N*=1) cancer and leukemia (*N*=1). Molecular characterization was performed in 13(33%)pts: in two different pts were found a KRAS mutation and an ALK rearrangement, respectively; an EGFR mutation has been identified in 2 pts. Median time from symptoms appearance and diagnosis was 7 weeks. Thirteen (33%) pts showed a limited stage, while the other 26(67%) showed advanced/metastatic disease at the diagnosis. Nineteen(49%) pts received a first-line palliative chemotherapy (pct), mostly platinum-based doublets plus gemcitabine (*N*=11) or taxane (*N*=3), achieving a response rate and disease control rate of 37% and 58% respectively. Three patients harbouring a druggable molecular alteration were treated with gefitinib (*N*=2) and crizotinib (*N*=1), achieving partial response. Median RFS in resected patients (*N*=9) was 21 months. Median PFS and OS after first-line pct were 5 months and 8.5 months respectively, without covariates impact.

Conclusions: Never-smoker LSCC pts represent a rare subgroup characterized by more females, younger age and a not negligible CCI and second-tumor history compared with the known features of smoker LSCC. Molecular assessment should be considered. Treatment outcome after pct for advanced disease is still dismal as for most LSCC pts.

E19 Comorbidity scores as predictive tools for nivolumab toxicity in patients with advanced non small cell lung cancer (NSCLC): preliminary results of a prospective multicenter study

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Background: Recent advances in lung cancer therapy are notable for the introduction of a novel class of drugs, the immune checkpoint inhibitors, among which nivolumab, an anti-programmed cell death 1 monoclonal antibody, is the first approved for clinical practice. Boosting the immune system leads to a unique constellation of inflammatory toxicities known as immune-related adverse events (irAEs) that may warrant the discontinuation of therapy and/or the administration of immunosuppressive agents. No data are available regarding possible patient − related predictive factors for these irAEs. This study aims to assess the association of Charlson Comorbidity Index (CCI) and Cumulative Illness Rating Scale (CIRS) scores with toxicities in patients with advanced NSCLC treated with nivolumab according to current indications.

Methods: We used Spearman's (rho) method and logistic regression analysis to evaluate whether an association exists between CCI and CIRS scores and probability to develop toxicities as measured by Common Toxicity Criteria v 4.03.

Results: From September 2015 to January 2017, 54 patients have been enrolled; the median age was 69 years (range 54 − 83). The majority had a metastatic disease (stage IV in 74%, stage IIIC in 26%); 45% had received = 2 lines of chemotherapy. The baseline median CCI was 4.29 ± 2.39 (1 − 9; 95% CI 3.34 − 5.24) and the baseline median CIRS was 19.07 ± 9.19 (6 − 35; 95% CI 15.43 − 22.71). Analysed groups, where higher scores express more severe comorbidity load, were CCI < 3 (n = 25) and > = 3 (n = 29), CIRS comorbidity index < 4 (n = 24) and > = 4 (n = 30) and CIRS severity index < 2 (n = 26) and > = 2 (n = 28). The correlation between CCI and CIRS was moderate/high (rho= 0.64; 95% CI for rho: 0.346 − 0.821, P = 0.0003). Having CCI > = 3, CIRS comorbidity index > = 4 and CIRS severity index > = 2 increased the probability of having any grade toxicity (OR = 2.0, P = 0.04) and, in particular, grade 3 and 4 toxicity (OR = 5.5, P = 0.007).

Conclusions: In patients treated with nivolumab for advanced NSCLC, the presence of comorbidity seems to affect the probability of having irAEs.

E20 Circulating immune-profile as predictor of outcome in advanced NSCLC patients treated with Nivolumab

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Background: Detection of predictive markers of anti-PD-1/PD-L1 antibodies activity is of pivotal interest in non-small cell lung cancer (NSCLC). This study aimed to identify a circulating immuno-profile as predictor of outcome in NSCLC patients treated with nivolumab.

Methods: A peripheral blood immuno-profile evaluation was performed at baseline (T0), after 2 (T1) and 4 cycles (T2) of bi-weekly nivolumab in advanced pre-treated NSCLC patients from two Italian Institutions. First tumor assessment was performed after 4 cycles and then every 2 months. FACS analysis of lymphocyte subpopulations [CD3, CD4, CD8, NK (CD56), Treg (FOXP3) and MDSC] was performed. Absolute and % changes of lymphocyte subsets together with their functional and proliferative activity were assessed. Quali-quantitative leucocyte composition at baseline and its variation during therapy were correlated with tumor response and survival.

Results: In the overall population of 54 treated patients, baseline Neutrophil-to-Lymphocyte ratio and NK count, lymphocyte count and CD4 variations during therapy showed a statistically significant prognostic role ($p < 0.001$; $p = 0.012$; $p < 0.001$; $p = 0.010$, respectively). Among 31 patients (squamous carcinoma, n = 17; adenocarcinoma, n = 14) in which all 3 time-points samples were available, 19 were *responders* (response and stable disease) and 12 *non-responders*. In *responders*, absolute numbers of total NK and NKCD56dim subset were higher at baseline and their increase between T0 and T1 was statistically significant ($p < 0.05$). *Responders* also displayed increased cytotoxic capability as shown by a higher baseline expression of CD3ζ, perforin and granzyme in NKCD56dim subset. No significant variation was documented in absolute number and functional activity of CD4+ and CD8+ lymphocytes. A higher percentage of CD8+PD-1+ cells at baseline was observed in *responders*, while *non-responders* showed a statistically significant increase in the absolute number of MDSC during therapy ($p < 0.05$).

Conclusions: The number and function of NKs and the frequency of PD-1 expression in CD8+ cells could represent predictive peripheral immuno-biomarkers for nivolumab treatment in advanced NSCLC.

E21 Nivolumab in non-small cell lung cancer: is there an upper age limit?

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Introduction: Recent scientific evidence has led to extensive use of immunotherapy in the treatment of non-small cell lung cancer (NSCLC) patients (pts) pretreated with platinum-based chemotherapy regimens. The checkpoint inhibitor Nivolumab (Opdivo® BMS ™) has shown superior efficacy to standard 2nd-line chemotherapy with greater tolerability, which results in improved quality of life. Aging involves physiologic changes and immunosenescence, aging-related loss of immune function, may have a negative impact on clinical benefit and effectiveness of immunotherapy. The objective of our study was to evaluate disease treatment response, to estimate the incidence and diversity of immune-related adverse events (IrAEs) in pts receiving Nivolumab and to check the relationship with age-associated immune dysregulation.

Material and methods: From May 2015 to April 2017, 92 NSCLC pts were treated with nivolumab as a single agent, after disease progression to one or more chemotherapy lines, at a dose of 3 mg/kg every two weeks. Clinical examination and evaluation of adverse reactions were performed every 2 weeks. CT scans was performed every 8-12 weeks to assess tumor treatment response. The study population was divided into two different age groups, under 70 years and over 70 years older. Two aspects of adverse event patterns were measured: incidence rate and different types of adverse events in each of the pts age groups.

Results: Of 92 pts 41 were age <70 yrs (45%) and 51 were >70 yrs (55%). ORR in pts group <70 yrs was 43% (PR 23%, SD 20%), similar to that found in older pts group (PR 14%, SD 29%). The incidence of IrAEs was 36% in the first group, 32% in the second group. Most common irAEs among pts >70 were endocrinopathies (11%), colitis (7%) and rash (7%). Some adverse events, such as endocrinopathies and fatigue, appeared most frequently in the pts group <70 yrs (16% and 10% respectively).

Conclusions: Immunotherapy represent a valid therapeutic option for NSCLC patients but currently there is little known about the safety of nivolumab in elderly patients that may still respond appropriately to checkpoint inhibitors. The obtained data suggest that nivolumab is well tolerated and there is no significant differences between the two age-groups in terms of efficacy and tolerability. The inclusion of greater number of elderly patients in registration clinical trials will provide helpful informations to clinicians on the safety of immunotherapy in patients aged 70 yrs and older.

E22 Baseline absolute neutrophil count (ANC), derived neutrophil-to-lymphocyte ratio (dNLR) and platelet-to-lymphocyte ratio (PLR) and outcome in non small cell lung cancer (NSCLC) treated with nivolumab or docetaxel: a preliminary analysis

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Background: Nivolumab (N) is a novel therapeutic option in NSCLC, with a significant survival gain compared with Docetaxel (D). However, predictive biomarkers are lacking and no strategies have been adopted to date for optimal patients (pts) selection. The presence of systemic inflammation has been correlated with poor outcome in many cancer types. We aimed to evaluate whether there is a correlation between some indicators of inflammation and response in pts treated with N or D.

Methods: 28 consecutive pts with NSCLC receiving N were analyzed. Baseline white cell count (WBC) and ANC were collected and correlated with tumor response. 34 NSCLC pts treated with D were used as controls. An ANC $\geq$ 7500 cell/μl was defined neutrophilia. dNLR was calculated as: ANC/(WBC-ANC). PLR ratio was defined as platelet count (PLT)/lymphocyte count. dNLR $\geq$3 and PLR $\geq$160 were defined high. PLT $\geq 450 \times 10^3$/μL was defined as thrombocytosis.

Results: Baseline characteristics: median age 68 years (range 45-82); sex M 77%; histology squamous 40%, adenocarcinoma 48%, and 12% mixed histology/NOS. Smoking status: 90% smokers/former smokers. Among non-squamous pts, 16.2% were EGFR mutated and 8.1% were KRAS-mutated, with an equal distribution in both treatment groups. Lines of therapies: range 2-8 in N group and 2-3 in D group. Overall response rate (ORR): 12.5% with N vs. 9% with D; 8.3% of pts with N experienced unconventional responses. Baseline neutrophilia (18% with N and 26% with D) and thrombocytosis (3.5% and 3%, respectively) were not associated with response (ORR 0%). High dNLR was associated with no response to N, but not with D (ORR 0% and 12.5%, respectively), whereas high PLR correlated with low treatment response in both groups (ORR 8.3% and 0%, respectively). Among refractory pts (i.e. progressive disease as best response), a higher incidence of thrombocytosis (7% and 5%), neutrophilia (28.5% and 40%), high PLR (75% and 50%) and high dNLR levels (28.5% and 55%) were detected compared with the overall population.

Conclusions: The results of this preliminary study suggest that indicators of inflammation such as baseline neutrophilia, thrombocytosis and high dNLR are usually associated with a dismal prognosis and low efficacy of both chemotherapy and immunotherapy. Given their relative easy estimation, baseline evaluation of these indicators may be included together with other predictive biomarkers in the baseline evaluation of pts candidate for immunotherapy.

E23 Surgery in multimodal management in non-metastatic small cell lung cancer: a retrospective monocentric series

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Background: Combined chemo-radiotherapy currently represents the standard treatment for stage I-III Small Cell Lung Cancer (SCLC), with 5-year survival rate of 20%. Recent retrospective analysis reported benefit from surgery followed by adjuvant platinum-based chemotherapy. No randomized trials investigated any clinical markers to select patients eligible for surgery.

Patients and methods: A series of 365 patients with SCLC treated from 1996 to 2015 has been retrospectively evaluated. Patients with metastatic disease or lacking clinical data were excluded from the analysis. Among 86 evaluable patients, 61 underwent surgery and 25 chemo-radiotherapy. Clinical, surgical and radiological data were reviewed and related with outcome.

Results: Median follow-up for resected patients was 44 (2.6-216.4) months. Median overall survival (OS) and relapse-free survival (RFS) of resected patients were 62.3 (95% CI: 40.5-84.1) and 11.2 (95% CI: 6.9-15.4) months respectively. Mortality of surgery was 0%, morbidity was 23%. Univariate and multivariate analysis reported pN2 stage (p 0.04) and surgical margins (p 0.03) as significant prognostic factors. Median OS and RFS of non-resected patients were 13.4 (95% CI: 5.3-21.5) and 8.3 (95% CI: 4.4-12.7) months. Median OS of pN2 surgically resected patients and cN2 non-resected patients were 30.3 (95% CI: 7-36.9) and 16.3 (95% CI: 0.2-32.4) months respectively. The difference was not statistically significant.

Conclusion: Surgical therapeutic approach was feasible, safe and related to long-term survival. Mediastinal nodal involvement and non-radical surgery significantly worsened survival and patients with mediastinal nodal involvement should be considered as a different prognostic group and systematic specific staging should be performed when considering radical-intent surgical approach. Prospective trials are warranted to select patients eligible for a multimodal approach.

E24 Overall survival (OS) of selected patients (Pts) with non-small cell lung cancer (NSCLC) receiving nivolumab beyond progression

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Background: Nivolumab is currently available for previously treated advanced NSCLC on the basis of improved OS over docetaxel. However, a relevant proportion of Pts experience early progressive disease (PD) during treatment; it has been observed that some of these Pts report clinical benefit in spite of radiologic PD and might take advantage from receiving nivolumab beyond progression. Our aim is to evaluate the outcomes of Pts with advanced NSCLC receiving nivolumab beyond PD observed at the first response assessment (early PD).

Pts and methods: Pre-treated NSCLC Pts received nivolumab at 3 mg/Kg every 2 weeks. Response was assessed every 4 administrations by response evaluation criteria in solid tumors (RECIST) v.1.1 and immune-related response criteria (irRC); Pts experiencing PD were re-evaluated after 2 additional administrations to confirm PD. Early PD was defined as PD at the first assessment with subsequent confirmation. Pts reporting clinical benefit (improved or stable clinical conditions) in spite of confirmed PD could continue the treatment. The Pts who kept receiving nivolumab in spite of early PD (continuation-Pts) were then compared, in terms of survival, with those Pts who stopped nivolumab at early PD (discontinuation-Pts) and with those Pts who did not experience early PD (non-early PD); Log Rank p-values (p) were reported.

Results: 53 Pts were evaluable for response. RECIST classified 29 Pts as early-PD; among these, 10 Pts were continuation-Pts and 19 were discontinuation-Pts. irRC classified 26 Pts as early PD; among these, 9 Pts were continuation-Pts and 17 were discontinuation-Pts. Median OS of the whole Pts population was 10.0 months. Continuation-Pts at RECIST had longer OS compared to discontinuation-Pts (12.9 vs. 4.4 months; $p = 0.003$); continuation-Pts at irRC had longer OS compared to discontinuation-Pts (12.2 vs. 4.3 months; $p = 0.018$). Although median OS of non-early PD Pts was not reached at the time of the analysis, no statistically significant OS difference between continuation-Pts and non-early PD Pts was observed regardless of the employed response assessment criteria for defining early PD (RECIST: $p = 0.527$; irRC: $p = 0.205$).

Conclusions: While early PD on treatment is commonly seen as a negative prognostic factor, our results suggest that Pts reporting clinical benefit from nivolumab in spite of early PD might achieve prolonged survival, comparable non-early PD Pts. These findings are consistent between RECIST and irRC.

E25 First-line platinum-based chemotherapy in elderly patients with NSCLC: determinants of therapeutic choice and outcome

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Background: The role of platinum-based chemotherapy (PBC) as first-line treatment (1LT) for elderly patients (Epts) with advanced non-small cell lung cancer (NSCLC) is still debated, mainly due to limited data on Epts in prospective randomized trials. This study aimed at identifying clinico-pathological factors associated with PBC prescription and the corresponding outcome.

Methods: We analysed a consecutive series of 169 EGFR and ALK wild-type NSCLC Epts (age $\geq$70) treated with first-line PBC or single-agent chemotherapy (SAC) for stage IIIB-IV disease at the Department of Oncology of Udine (Italy), from January 2010 to March 2017. Data on clinico-pathological features, comorbidities and hospitalisation during 1LT were collected. Association analyses were conducted through logistic regression. Prognosis was explored with a Cox's regression model. Kaplan-Meier analysis and log-rank test were used to compare overall survival (OS) among subgroups. A landmark analysis at 63 days (day 1 cycle 4 of PBC) was performed in the PBC group, after stratifying Epts for having received or not at least 4 cycles of PBC (4PBC vs < 4PBC).

Results: Median age was 75 years (range 70-90) and PBC was prescribed to 112/169 Epts (50.9% received <4 cycles and 42% cisplatin). During 1LT 69/169 Epts were hospitalized (in 56.5% of cases for toxicities, experienced by 14% of Epts treated with SAC and 27.6% of Epts treated with PBC). In multivariate analysis, age was the only factor associated with lower use of PBC (OR 0.67, $p < 0.001$), while ECOG performance status (PS)>0 (OR 0.38, $p = 0.03$) and hospitalization before progression (OR 0.19, $p < 0.001$) were associated to < 4PBC. Notably, in multivariate analysis, PS > 0 (HR 2.19, $p < 0.001$), liver metastases at baseline (HR 3.28, $p < 0.001$) and hospitalization for any cause (HR 3.00, $p < 0.001$) predicted shorter OS. No difference in OS was observed between SAC and PBC: median OS (mOS) was 7.6 months in both arms (HR 1.17, 95% CI 0.83-1.66, $p = 0.36$ for SAC). Comparing <4PBC to 4PBC we found a significant difference in OS, confirmed by a landmark analysis at 63 days (mOS: 6.9 vs 13.7 months; HR 2.38, 95% CI 1.38-4.07, $p = 0.001$ for <4PBC).

Conclusions: Older age is the only factor predicting lower PBC use. PS > 0 and hospitalization before progression are associated to early PBC discontinuation. PS > 0, hospitalization during 1LT, and liver metastases are associated with worse outcome. Further studies are needed to identify which Epts may have a benefit from PBC.

E26 The effects of LIPUS on ctDNA release in the medium of NSCLC cell lines

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Background: Low Intensity Pulsed Ultrasound (LIPUS) application has been shown to have an encouraging effect in inducing a transient pore formation through cellular membranes. This permeability condition has been demonstrated to be useful in enhancing gene and drug delivery. Nowadays, in the management of NSCLC patients, the use of liquid biopsy has entered the clinical practice. One of the main limits in the analysis of circulating tumor DNA is the low concentration rate of nucleic acids in body fluids. Ultrasound stimulation (US) has been recently demonstrated to be effective for the release of specific circulating tumor biomarkers in many mouse models. We demonstrated the role of US in inducing the release of tumor DNA fragments (rtDNA) in NSCLC without inducing any apoptotic or necrotic event.

Material and methods: EGFR wt and del19 NSCLC cells (A549, HCC827) were cultured in RPMI1640 with 10% FBS, 1% pen/strep at 37 °C and 5% CO_2. The day before the sonication cells were seeded in a 24-well plates (20.000 cells/well HCC827; 10.000 cells/well A549). Each well was exposed at the following sonication protocol: frequencies (650 kHz, 1 MHz); acoustic pressure (250 kPa, 25 kPa); 25% duty cycle with three different exposure time points (1, 3, 7.5 min). After US treatment, the cells were incubated for 24h and then cell viability was performed by Cell Titer-Glo® Luminescent Cell Viability Assay. Each experiment was performed in triplicate.

Results: NSCLC cells have been subjected to sonoporation at different exposure time points as well as ultrasonic acoustic pressures and frequencies. We evaluated the viability cells to exclude the possibility that rtDNA analysis could be affected by apoptotic or necrotic DNA fractions. In fact, after ultrasound exposure no significant reduction of cell viability, in terms of ATP content, has been shown. Moreover, the analysis of DNA fragments content, released in the medium, showed a different behaviour on the basis of EGFR mutational status. Indeed, in EGFR mutated cells the concentration of rtDNA was significantly higher than control cells after performing sonoporation at 250 kPa and 1 MHz . For the EGFR wild type cell line, no variation of ctDNA at different exposure time points and pression has been showed.

Conclusions: the assessment of ctDNA is strongly influenced by its amount. Therefore, US application to enhance the release, is of great interest not only in NSCLC but also for all the "oncogene addicted" cancers.

E27 Thymic epithelial tumors (TETs) and additional tumors: a single Centre experience

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Backgound: the association of TETs and previous or secondary malignancy is frequently reported in literature. A review of several studies reported a variable percentage of additional tumors, ranging from 8 to 30%. Despite different results and methodology, all of these studies showed an increased risk for cancer in patients (pts) with TETs.

Materials and methods: from 1993 to 2017 we retrospectively collected pathological and clinical data about pts with TETs, referred to our Medical Oncology Unit and to the Thoracic Surgery Unit of our institution.

Results: 88 pts were enrolled, 74 (84%) with thymomas and 14 (16%) with thymic carcinomas (TCs). Nineteen of them (20%) experienced previous or secondary tumors, 4 (28%) among TC pts and 15 (16%) among thymoma pts. Most frequent tumors were 6 (7%) skin cancers, 5 (6%) breast cancers and 2 (2%) prostate cancers. Other tumors described were lymphatic chronic leukemia, pleural mesothelioma, kidney cancer, biliary tract cancer and a case of gastrointestinal stromal tumor (GIST). In particular, we report a case of a 68 years old man, with both ileal GIST and thymic carcinoma: the association of these two malignancies has never been reported previously. The patient in September 2010 underwent radical resection for an ileal GIST. The tumor was 6 cm, 5 mitosis x 50 HPF, cKIT exon 11 mutated (V559D), moderate risk sec. Miettinen classification. Post-operative staging excluded distant metastasis but detected a mediastinal mass. In February 2011 he underwent total thymectomy with diagnosis of squamous-cells TC, stage IIB sec. Masaoka, and also received adjuvant mediastinal radiotherapy in May. After three years of adjuvant Imatinib (400 mg/die), the patient started follow-up, resulting negative for relapse until Sep-2015, when abdominal MR detected liver metastasis. After histological confirmation of GIST hepatic metastases, patient resumed Imatinib, with partial response. The patients is still alive and on treatment with Imatinib, maintaining response.

Conclusions: our experience confirm the high frequency of additional tumors associated to TETs according to literature. Moreover, we collect several case of rare tumors in TETs patients. In particular, we focused on a case of concomitant GIST, not previously reported.

E28 Circulating programmed death ligand-1 (PD-L1) in non-small cell lung cancer (NSCLC)

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Background: Since the introduction of immune-checkpoint inhibitors for Non Small Cell Lung Cancer (NSCLC) treatment, the predictive and prognostic value of programmed death ligand-1 (PD-L1) is under investigation. Aim of the present study was to define feasibility of plasma PD-L1 testing and to assess how PD-L1 expression is modified by standard treatment.

Material and methods: PD-L1 expression was evaluated in plasma samples from patients with chemo-naïve NSCLC candidate for systemic first-line therapy, irrespective of histology or any other clinical or biological characteristic. A cohort of healthy volunteers, individuals who are not affected by oncology, autoimmune, metabolic and infectious diseases, was also analyzed for plasma PD-L1 expression (Healthy control Cohort-HC). PD-L1 in plasma samples was evaluated using the Human programmed death ligand-1 (PD-L1/CD274) ELISA kit (CUSABIO, MD, USA).

Results: A total of 56 patients with histologically proven stage IV NSCLC and 16 HC were included. The median age of the patients was 70 years (range 48-85). The majority of patients were male (67.9%), with an Eastern Cooperative Oncology Group (ECOG) performance status score of 1 (55.4%) mainly former smokers (57.1%). The majority of patients received chemotherapy as first line treatment (N = 41, 73.2%), 3 (5.4%) received immunotherapy and 12 (21.4%) received targeted therapies (N EGFR inhibitors= 9, N anti ALK= 3). We first defined the PD-L1 plasma levels in the HC. Median PD-L1 basal level was 37.81 pg/ml (range 9.73-90.21). In patients with NSCLC median PD-L1 plasma level was 42.21 pg/ml (range 12.00-143.49). This difference was not statistically significant ($p = 0.78$). Interestingly, levels of PD-L1 plasma expression significantly increased during the first 3 months of systemic therapy (Wilcoxon test $p = 0.04$). In addition, the 5 patients with high levels of plasma PD-L1 expression had significantly shorter progression free survival (PFS) and overall survival (OS) than individuals with low or no plasma PD-L1 expression (PFS: 1.2 versus 6.4 months, $p = 0.056$; OS: 1.2 versus 9.7 months, $p = 0.003$).

Conclusions: Plasma PD-L1 expression is feasible and high levels of expression could correlate with worst prognosis. Additional studies exploring correlation of plasma with tumor tissue PD-L1 expression are needed.

E29 EGFR status evaluation by liquid biopsy during first-line therapy in advanced NSCLC patients

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Background: Over the past decade, personalized management based on the molecular features of tumours in patients with advanced non small-cell lung cancer (NSCLC) has entered routine clinical practice. The poor performance of many advanced NSCLC patients may limit invasive biopsies. The liquid biopsy is a diagnostic procedure performed on cancer-derived material obtained in blood samples. In this abstract, we will describe our experience with liquid biopsies.

Methods: In the Reggio Emilia Clinical Cancer Centre from March 2016 to December 2016, 42 patients with advanced NSCLC were analyzed that had had or had already started first line therapy. The liquid biopsy was repeated at each imaging response evaluation by thoracic-abdominal compound tomography (CT) scan performed every 3 months. In the liquid biopsy, the mutational status of EGFR was analyzed with real time PCR (KIT cobas EGFR mutation test v2 CE-IVD Roche); in tissue, it was evaluated by pyrosequencing.

Results: 21/42 liquid biopsies were EGFR-mutated (12/21 eson 19 and 9/21 eson 21). In 3/21 (14.3%) cases, the tissue biopsies showed wild type (WT) EGFR. 6 liquid biopsies were also performed at time 0 (diagnosis). All liquid biopsies of EGFR WT remained WT during treatment and imaging evaluation. The median number of liquid biopsy tests for patients was 2 (range 1-3). In 4/21 cases, T790M was performed: 3 cases in both liquid biopsies and tissue, and 1 case in tissue but not in liquid biopsy. TKi therapy was ineffective in this patient with T790M mutation detected in tissue, but not in liquid biopsy. In all patients, the disappearance of the T790M mutation during TKi therapy was related to disease progression. In 11 cases, modification of EGFR mutation status during treatment anticipated CT scan evidence of disease progression (median = three months).

Conclusion: The liquid biopsy is an excellent resource. In our experience the liquid biopsy is the sensitive method of choice during treatment of advanced NSCLC patients. EGFR modification status during TKi therapy showed advanced disease progression.

E30 Malignant pleural mesothelioma multidisciplinary team unit: experience of one high-volume center in Italy

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Background: Malignant pleural mesothelioma (MPM) is a rare disease, although its incidence is still increasing in Italy. Its diagnosis and treatment are challenging, and require the expertise of a multidisciplinary team (MDT). Due to the paucity of current treatment options, inclusion of MPM patients in clinical trials is advisable. MDTs are standard of care for several other cancers.

Material and methods: A weekly mesothelioma MDT meeting was established at our Hospital since January 2017. The core team of MTD is comprised of 4 dedicated medical oncologists, 1 palliative care physician, 2 dedicated radiologists, 1 radiation oncologist, 1 thoracic surgeon, 1 research nurse, and 2 data managers. A pharmacist, a pathologist and a lab biologist are available on call. All MPM patients referred to our Centre are discussed at diagnosis, and during treatment and follow up.

Results: From January 2014 to May 2017, 188 new patients were referred to the Medical Oncology Unit of our Clinic. Of them, 23 were referred since January 2017. Diagnostic and treatment advice was provided for all cases within 2 weeks of referral. Since the starting of MDT meetings 7/23 (30%) cases were subsequently enrolled in a clinical trial, versus 35/165 (21%) in the 2014-2016 period. Additional benefits of MTD included evaluation of all new cases by a palliative care physician since diagnosis, and implementation of modified RECIST criteria for MPM for response assessment and radiological monitoring of each patient (both within clinical trials and in everyday practice).

Conclusion: Mesothelioma MDT meetings are very effective at providing timely diagnostic and therapeutic recommendations. The rate of patient inclusion in clinical trials is improved when a dedicated MDT discusses all referred cases. Patients with MPM should be referred to high-volume Centers with adequate expertise.

E31 EGFR mutational status in determining choice of TKIs or standard chemotherapy for patients with advanced non-small cell lung cancer

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Background: Tyrosine Kinase Inhibitors are important therapeutic resources for Non-Small Cell Lung Cancer (NSCLC) patients (pts) expressing EGFR-activating mutations (EGFR-m). However, pts without EGFR-addicted tumors do not display the same benefit. Nevertheless, Erlotinib can currently be prescribed to NSCLC pts after failure of a first-line treatment regardless of their EGFR status.

Material (patients) and methods: We retrospectively analysed 143 pts diagnosed with advanced NSCLC between 2005 and 2016 and followed in two different Oncology Divisions. Sixty-nine pts presented *EGFR*-m while 74 displayed wild-type (WT) *EGFR*. We initially compared the Progression Free (PFS) and Overall Survival (OS) of the *EGFR*-m population according to it's therapeutic sequence i.e. TKIs as first line followed by chemotherapy at progression versus first line chemotherapy followed by anti-EGFR TKIs in second line. We then analysed the PFS and OS of *EGFR*-wt pts treated with conventional chemotherapy or Erlotinib after failing a standard platinum doublet as first line.

Results: In *EGFR*-m pts median PFS was 11 months in the TKI group and 6 months in those receiving chemotherapy (HR 0.59 CI 95% 0.34-1.04; $p = 0.01$). However, OS was similar in the two arms: 21 months among pts receiving TKIs in first line and 26 months in pts receiving chemotherapy as first line (HR 1.24, CI 95% 0.69-2.22; $p = 0.31$). In the *EGFR*-wt group, median PFS after second line was 5 months in the standard chemotherapy arm and 3 months in the Erlotinib arm (HR 0.76, CI 95% 0.45-1.30; $p = 0.01$). Differences in the two groups were also significant for OS (26 months among pts receiving chemotherapy and 19 months for those receiving Erlotinib in second line HR 0.67, CI 95% 0.40-1.14; p 0.05).

Conclusions: Our study confirms, in an unselected Sicilian population, that *EGFR* mutations are a strong predictor of TKI benefit. Hence, *EGFR*-m pts should receive a TKI as first-line treatment as this was associated with improved PFS, although we observed no differences in OS. Moreover, this study suggests the importance of second line standard chemotherapy in subjects with wild-type *EGFR* since, in this population, TKIs generate inferior responses in terms of both PFS and OS.

E32 Clinical use of immune-checkpoint inhibitors: focus on late immune-related adverse events and pseudoprogression

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Background: Immune-checkpoint inhibitors are changed the treatment's paradigm of Non Small Cell lung cancer in second line setting and for patients with high expression of PD-L1, they play a key role in first-line setting. The immune-based mechanism of action of these drugs determine a spectrum of adverse events called immune-related adverse events (irAEs) and a possibility of atypical response patterns called Pseudoprogression. These treatments require understanding of the management of Immune-related adverse events (irAes) in terms of Incidence and Kinetics of onset and a characterization of atypical response (Pseudoprogression) with Immune-related criteria (irRC).

Materials and methods: Sevent-two patients treated with Nivolumab Monotherapy enrolled in Expanded access program and in Clinical Practice were retrospectively studied. Incidence and Kinetics of onset and resolution of irAES (Cutaneous, gastrointestinal, hepatic, endocrine, renal and pulmonary-effects) were evaluated. Late irAEs were defined as irAEs occurred after 12 weeks to start of therapy. Using irRC Pseudoprogression was identified.

Results: From August 2015 to May 2017 72 pts are treated with Nivolumab and 43 (60%) pts are elegibile for evaluation of response and later toxicities. The median age at NSCLC diagnosis was 66.5 (55-80) years. Twenty-three pts (76.7%) were male. Twenty-five pts (58.1%) were former smokers, 16 pts (37.2%) were current smokers.Squamous NSCLC was the most common histology (22 pts, 52%). Most pts received Nivolumab in Second-line therapy (31, 72,1%) and 9 (21%) in third line therapy. Median Progression Free Survival(PFS) was 7.2 months (1.75-20.5 months) and in 9 (21%) PFS was superior to 12 months. Incidence of Pseudoprogression was very low (3 pts, 7%) and the treatment in 2 of these pts is ongoing. The Skin events was reported in 4 (9%) of pts and in 1(25%) occurred after 40 weeks of treatment. Gastrointestinal events was reported in 11(25%) of pts and in 5(45%) occurred after 12 weeks, 2(40%) of these occurred after 30 weeks. Endocrine events occurred in 5(11%) pts and in 2 (40%) pts occurred after 12 weeks. Pulmonary events occurred in 3(7%) and 1 of these occurred at 37 weeks.

Conclusion: Incidence of atypical response seems a rare events in patients treated whit Nivolumab and seems associated with longer PFS. In our clinical practice the incidence of irAEs is very low but the time to onset is not predictable and some events often occur late.

E33 Docetaxel and ifosfamide as salvage treatment in EGFR, ALK wilde type non small cell lung cancer (NSCLC)

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Background: The current standard regimen for advanced EGFR, ALK wilde type non small cell lung cancer (NSCLC) is cisplatin containing regimen. Docetaxel is active durg, has shown promising activity with improvement in survival and quality of live, therefore it's indicated in second line and in successive lines. Ifosfamide is a broadly active anntitumor agent. Therefore we have determined the antitumor activity (response rate) of docetaxel and ifosfamide in patients with relapsed EGFR and ALK wilde type NSCLC previously treated with cisplatin based- chemotherapy and with other agents in successive lines.

Material (patients) and methods: Eligible patients with histological proven EGFR and ALK wilde type relapsed NSCLC, bidimensional measurable disease, PS < 2 and adequate haematological, hepatic and renal function received Docetaxel 60 mg/mq d1 and Ifosfamide 1500 mg/mq d1-3 with Mesna as rescue, repeated q 21 days as blood count permited, until disease progression or appearance of non-tolerable toxicity. Baseline data, toxicity and activity are available in 22 patients (pts) . Pts with median age 67 years (range 43-80), were treated for a median of 4 cycles (range 1-8 cycles). Sites of metastases were lung, mediastinal lymph nodes, liver, bone and adrenal glands.

Results: Out 22 evaluable patients for response, we obtained 3 partial response, 6 stable disease and 13 disease progression. The median survival was 4 months, the median DFS 2 months. The haematologic toxicity was modeste. Seven pts experienced grade 3-4 neutropenia without fever, 5 pts anemia, three pts experienced thrombocytopenia grade 2 and four pts hypertransaminasemia grade 2 . Additional non-haematologic toxicities experienced include mild nausea/vomiting, alopecia and nail onycholysis.

Conclusion: Combined therapy with docetaxel low dose and ifosfamide has demonstrated preliminary clinical activity in pts with relapsed EGFR and ALK wilde type lung cancer heavily pretreated. Further evaluation of this combination in this setting is warranted.

E34 Analysis of clinical outcomes according to mutation subtype in EGFR-positive advanced non-small cell lung cancer (aNSCLC) patients treated with EGFR Tyrosine Kinases Inhibitors (TKIs) as first line

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Background: The correlation between EGFR mutation subtype and efficacy of TKIs in patients with aNSCLC is uncertain. Therefore, TKIs are used regardless of mutation subtype. However, data of literature suggests better outcomes for patients with exon 19 deletions (19del) in comparison with exon 21 point mutations (L858R).

Methods: Patients with EGFR-positive aNSCLC receiving TKIs as first line treatment were included in the analysis. Mutational status at diagnosis was detected on tumor tissue or on circulating free tumor DNA (cft-DNA). The association between mutation subtype and clinical factors was assessed by Pearson chi square test, while differences in progression free survival (PFS) and overall survival (OS) according to mutation subtype were evaluated by Log-rank test.

Results: Between January 2011 and December 2016 a consecutive series of 39 EGFR-positive patients (all with adenocarcinoma) received a first line TKI: Gefitinib (21 pts), Erlotinib (14 pts) or Afatinib (4 pts). Most of patients, whose median age was 70 years (range 35-84), were female (67%), never smokers (74%) and with stage IV (97%). EGFR mutations were detected on tumor tissue in 37 pts and on cft-DNA in 2 pts. No correlation was found between mutation subtype and site of metastases (lung, lymph nodes, liver, adrenal, bone and brain). After a median follow up of 11.2 mos, the mutation subtype did not influence PFS (median 9.6 mos, 95% CI 3.3— 15.9 for 19del group vs 8.3 mos, 95% CI 6.6 - 9.9 for L858R group) and OS (median 17.4 mos, 95% CI .00 - 34.7 for 19del group vs 18 mos, 95% CI 12.3 - 23.8 for L858R group). Anyway, it is noteworthy that 2-y PFS and OS rates were quite different according to mutation subtype being 24.8% and 36.4% in 19del pts, compared to 0% and 14.8% in L858R pts, respectively.

Conclusions: Our analysis showed that TKIs may be used for treating EGFR-positive lung adenocarcinoma regardless of mutation subtype. Despite the small sample size, the mutation subtype did not correlate with site of metastases, and no statistically significant difference was found in terms of PFS and OS between two mutation subtypes.

E35 Efficacy and safety of immune checkpoint inhibitor nivolumab and radiotherapy combination in advanced NSCLC

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In the last decade the discovery of immune checkpoint inhibitors such as PD-1 inhibitor Nivolumab had revolutionized the treatment of advanced NSCLC. The combination with radiotherapy is of particular interest, due to some preliminary observations reporting additive o synergist effect in some tumors.

The purpose of this study was to retrospectively evaluate the role of radiotherapy on the effect of an immune checkpoint inhibitor (Nivolumab) in terms of activity and toxicity in pretreated locally advanced or metastatic lung cancer patients.

From March 2015 to December 2016, 35 consecutive patients (15 men and 5 women) received Nivolumab for a advanced NSCLC. Fifteen received an hypofractionated radiotherapy as palliative measure, and in these patients Nivolumab was administered at least one week from radiotherapy end.

The median age was 69 years, 23 patients (65.7%) had an ECOG score 0-1. All patients had received, previously at least one systemic regimen, for only 3 (8.6%), nivolumab was a third treatment line. The two groups of treatment (radiotherapy-nivolumab and nivolumab alone) were well matched for baseline characteristics.

At a median follow-up of 7.4 months, the 1-year overall survival rates were 57.8% for patients treated with radiotherapy-Nivolumab and 27.4% for patients treated with Nivolumab alone ($p = 0.043$). The 1 year progression free survival was 57.8% in the radiotherapy-nivolumab group and 20.6% in the Nivolumab alone group ($p = 0.040$). No difference in adverse event was detected.

In conclusion, radiotherapy and Nivolumab can be combined in advanced, pretreated NSCLC patients, with potential benefit in overall survival and progression free survival, without significant increase in acute toxicities. Prospective studies are needed to confirm these results.

E36 Very elderly patients and lung cancer in a tertiary care center: a real life experience

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Background: Elderly patients with non-small cell lung cancer (NSCLC) constitute an important part of oncological practice. The peculiar features of patients with more than 75 years and the clinical pathway of patients with adenocarcinoma (ADC) or squamous cell carcinoma (SCC) have not been completely described.

Patients and methods: Patients with A) histologically/citologically confrimed NSCLC, B) diagnosed in 2015-2016, C) >75 years, D) firstly evaluated in our Center were identified from a local prospective database. Demograpichal, staging and treatment data were collected. Differences among groups were analyzed using Chi-Square Test. Radiological response was classified as partial response (PR), stable disease (SD) and progressive disease (PD) according to RECIST 1.1. criteria. Toxicity was evaluated according to CTCAE version 4.0.

Results: 32 patients were enrolled, 26 with ADC and 6 with SCC.

Mean age was respectively 78,9 and 77,2 years. One third of patients had more than 80 years; 80% had arterial hypertension. Median number of medications tooken daily was 3. In nearly 85% of cases diagnosis came from a histological specimen; 50% of patients had a disease non suitable for surgery or radiotherapy.

The two groups differed in:

Table: E36

Item	ADC (n = 26,%)	SCC (n = 6, %)	*p*
Female,%	42.3	16.7	*.24*
ECOG PS 2-3	17.5	50.0	*.11*
Left lung T	57.6	33.3	*.10*

The features and treatments of patients not suitable for local treatment were:

- **ADC** (15 patients); 3 patients had mutated EGFR (2 del-ex19 e and 1 mut-ex21): 2 received 1st line afatinib with a mean PFS of 7.5 months and 1 patient with G3 rash. Among other 12 patients, 4 did not received any chemotherapy, 5 received 1st line single-agent vinorelbine and 3 platinum-based doublet (all the 3 patients had less than 77 years and ECOG PS 0-1 at diagnosis). Disease control rate (SD+PR) was globally 45% (5/11). Four patients had a treatment delay due to G2-3 toxicity, in 1 case a hospital admission was needed.
- **SCC** (3 patients): 1 patient had mutated EGFR and received off-label 1st line afatinib (with a PFS of 7 months and a PR), 1 patient received 1st line paclitaxel and 1 patient 1st line cisplatin/gemcitabine (with a SD).Two patients had a treatment delay due to G2-3 toxicity.

Conclusions: very elderly patients with NSCLC could be an important part of daily practice; a significant part of them, especially those affectd by ADC are in good general clinical conditions at iagnosis. Also in this population active treatments could be proposed.

E37 Elderly patients with lung cancer: does clinical practice reflect evidence-based medicine? our four-year experience (2013-2016)

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Background: Treatment for elderly patients (EP) with advanced non-small cell lung cancer (NSCLC) comprises single agent of doublet chemotherapy (CT) or tyrosine kinase inhibitors (TKI) for those harboring mutations of the epidermal growth factor receptor or translocation of anaplastic lymphoma kinase (ALK). Clinical studies show that EP(>70) physically fit to receive CT obtain from platinum-based CT similar benefits than younger patients, but with a higher risk of treatment-related toxicities; overall survival (OS) advantage with doublet CT is controversial: a meta-analysis shows an OS benefit with platinum-based doublets (Des Guetz, 2012), while other data show that OS was not significantly improved by platinum-based therapy (Qi, 2012). Single agent (SA) gemcitabine, vinorelbine, taxane are used in fragile or vulnerable patients.

Material and methods, results: We registered in our experience a steady increase in NSCLC cases in EP, who accounted for 47% of all NSCLC cases in 2013, 53% in 2014,

50% in 2015, 54% in 2016. We observed an increase in the percentage of EP diagnosed with advanced stage NSCLC (stage IIIB-IV): 45% of cases in 2013, 48% in 2014, 51% in 2015 and 62% in 2016. Patients' status have been evaluated traditionally only according to the ECOG Performance Status scale, while recently patients have been evaluated more frequently using also the G8 and CGA tool (from only 20% of patients in 2013 to 47% in 2016). The use of G8/CGA evaluation allows oncologists to offer to EP a tailored therapeutic choice, with better results in term of quality of life. Upfront doublet or single agent chemotherapy have been used in 50% and 10% of EP, respectively. SA chemotherapy has been used as second-line treatment in 21% of EP in 2013, with a steady increase up to 60% in 2016. Second-line targeted therapy with TKI, when appropriate, has been given in a progressively higher proportion of NSCLC EP, rising from 3% of patients in 2013 to 11% in 2016. As for the overall NSCLC population, EP benefited from immunotherapy with nivolumab, with 60% of EP receiving the treatment in 2016.

Conclusions: Our experience confirms the therapeutic evidence reported in medical literature for advanced-stage NSCLC EP, an ever growing population. A better evaluation of such patients with appropriate tools (G8/CGA) will translate in safer and more effective treatments, better preservation of quality of life and reduced financial toxicity, both for patients and their caregivers.

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F - SARCOMAS

F1 Rechallenge in GIST progressing to imatinib, sunitinib and regorafenib: An Italian survey

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Background: We retrospectively collected data from metastatic Italian GIST patients treated with imatinib or sunitinib reintroduction after progression to conventional three or four lines of therapy.

Material and methods: 104 eligible advanced GIST patients, previously treated with imatinib, sunitinib and regorafenib, were collected in the present analysis from 6 cancer centres. All patients received all three standard kinase inhibitors. Imatinib dose increase as active second line or 800 mg upfront in exon 9 mutant GIST were allowed. Specific mutations were recorded if available (deletion versus others) and correlated with survival and response according to RECIST 1.1 or CHOI criteria.

Results: Seventy-one patients were evaluable. 63 received Imatinib 400 mg as rechallenge, while 8 patients were treated with sunitinib at personalised dose and schedule according to the physician's choice. Mutational status was available in all patients and in 68 patients details about type of mutation were achievable. The median follow-up was 13 months (range 1-42 months). The median time to progression (TTP) in patients receiving a rechallenge therapy was 5.4 months (95% CI 1.9-13.5) and Overall Survival (OS) was 10.6 months (95% CI 2.8-26.9). Apparently, in this setting a correlation between mutational status and response rate, TTP or OS was not found. On the contrary, considering only exon 11 mutated patients and comparing patients with deletion vs non deleted ones a significant difference was identified both in terms of TTP and OS (respectively, $P = 0.04$ and $P = 0.02$).

Conclusions: Our retrospective data confirm that the rechallenge of imatinib or sunitinib is a reasonable option in advanced GIST patients after failure of previous treatments. As expected, imatinib is the most frequently prescribed option in the Italian real-life setting, demonstrating a TTP and OS longer than those observed in previous studies. Also the prognostic value of the specific type of exon 11 KIT mutations has been confirmed in our series.

F2 Molecular characterization and pharmacological profile of myxofibrosarcoma primary cultures

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Background: Myxofibrosarcoma (MFS) is one of the most common sarcoma of the extremities in adult patients and is characterized by a high propensity for multiple local recurrences. Morphologically, it is a myxoid variant belonging to the heterogeneous group of malignant fibrous histiocytomas (MFH). Distinctive histologic features of MFS may include: myxoid stroma, prominent curvilinear blood vessels and pleomorphic areas. Given its relatively recent recognition as a distinct pathologic entity, the clinical behavior and outcomes for patients with MFS are uncertain, and the efficacy of chemotherapy is still not well documented, no randomized trials to guide treatment protocols. Although MFH molecular and cellular biology has been widely investigated, and a large number of human MFH cell lines are available, only a few number of MFS cell lines have been established. In an effort to improve the current understanding of the molecular biology and treatment outcomes of high grade MFS, we have conducted an analysis on a series of MFS patient-derived primary cultures.

Material and methods: Three primary or recurrence MFS were harvested intraoperatively from patients undergoing resection and the cells were brought into cell culture. The diagnostic impact of CD109 expression was evaluated and we also investigate TGF-ß as a marker of chemoresistance. Moreove the efficacy of different drugs which are currently used, including ifosfamide, epirubicin, ifosfamide in combination with epirubicin or trabectedin for the treatment of soft tissue sarcoma (STS) was assessed.

Results: The results showed an overexpression of CD109 gene in all samples compared to the matched healthy tissues highlighting that CD109 could represent a promising marker for MFS diagnosis and a potential therapeutic target. Furthermore, our findings indicated that TGF-ß could be involved in MFS chemoresistance. Finally, pharmacological analysis confirmed the sensitivity of the cultures to the chemotherapy. In particular the most active regimes were represented by epirubicin alone and in combination with ifosfamide which currently represent the standard treatment for advanced STS patients including MFS.

Conclusions: This work seeks to shed light on this poorly explored disease showing potential markers for diagnosis and drug resistance/sensitivity that would represent the basis for further research aimed to improve the management of MFS patients. Our results need to be confirmed in a larger case series.

F3 Elderly patients and metastatic soft tissue sarcomas (STS): a monoinstitutional experience

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Background: Elderly people represent more than 50% of STS patients, but few data are available in this population and old patients in clinical studies are underrepresented or not included. Aim of this retrospective, monoinstitutional study is to describe the activity and feasibility of first and second line chemotherapy in elderly patients with metastatic STS.

Methods: Patients older than 65, with metastatic STS of the scalp, trunk, girdles and extremities, treated and followed from February 1998 to December 2015 in an Italian referral Center for diagnosis and care of STS were included. Median Overall survival (OS) was the principal end point calculated from the start of chemotherapy to the last date of follow up or death. Response rate and toxicities related to type of administered chemotherapy were the secondary end points.

Results: 134 patients (79 M, 55F) were considered, (65-70 y) 63%, (71- 75y) 25%, (>76 y) 11%. STS histologies: mixoid and round cell liposarcomas (34%), leiomyosarcomas (25%), pleomorphic undifferentiated sarcomas (13%), Angiosarcoma (10%), Mixofibrosarcoma (6%), MPNST (4%), synovial sarcoma (2%), other histologies (6%). All the patients received at least one course of chemotherapy (1-12). Mono CT was the preferred administered schedule (92%of cases). Median OS was 7.3 months; at the time of this analysis only 14 patients were alive (10%). In the first line therapy we recorded 1 CR, 14 PR and 43 SD. In second line therapy no CR, 4 PR, 23 SD. PR were recorded mainly in 65-70y old patients. Bad PS, low score in Comprehensive Geriatric Assesment (CGA), vulnerability, comorbidities, number of metastasis, were negative prognostic factors. No toxic death were recorded, but 12% of the pts were recovered for febrile neutropenia, thrombocitopenia and mucositis.

Conclusions: Our study confirms that elderly patients with metastatic STS is a difficult population to be treated. Only patients less aged, with good PS, good GCA and 0-1 comorbidities can be treated with full dose of drug, generally with mono CT. Chemotherapy in elderly pts doesn't produce a significant improvement in Median Survival and the benefit observed support the routine use of citotoxic treatment in selected good performance status population.

F4 Potential therapeutic combination of beta-blockers and trabectedin in metastatic soft tissue sarcoma and ovarian cancer

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Trabectidin has been approved as single agent for second-line therapy of soft tissue sarcomas (STS) such as liposarcoma (LS) and leiomyosarcoma (LMS) and for the treatment of patients with relapsed, platinum-sensitive ovarian cancer in combination with pegylated liposomal doxorubicin. Clinical evidence revealed that beta-adrenergic receptor antagonists such as propranolol, could increase the effectiveness of vinblastine in the treatment of sarcoma patients. In order to realize tailored therapy toward different histological subtypes of STS and of ovarian cancer, the investigation of ß-adrenergic receptors (ß-ARs) as appropriate targets in a combined treatment with Trabectedin was evaluated. After determining the expression of ß-ARs in ovarian and sarcoma cell lines, we started combining propranolol with Trabectedin. Our results demonstrated that propranolol strongly enhances the response to Trabectedin in both A2780 ovarian cancer cells resistant to carboplatin and in the sensitive cell lines OV2008. The evaluation of the synergism among drugs was assayed both in 2D and in 3D cells models. The analysis of cell cycle showed that Trabectedin blocked the cells in S-phase and the addition of propranolol farther caused the accumulation of cells in both G0/G1 and S-phase. Such effects resulted in a strong induction of apoptosis in the combination compared to single treatment. Notewhorty the efficacy of the combination was maintained in stress inducted condition (10µM norepinephrine-NE). In agreement with cytotoxic results, the combination still induced apoptosis even after NE stimulation. We also tested the therapeutic potential of combining propranolol to Trabectedin in the treatment of sarcoma cells. Both drugs alone were effective in reducing cell proliferation of

LS cells stronger than LMS cells, and also the combination was more cytotoxic in LS cells than LMS cells. Interestingly, the activation with physiological concentration of β-ARs agonist Norepinephrine (NE) 100mM, did not resulted in reduced sensitivity to both propranolol and Trabectedin, while the stress induced concentration of NE 10μM resulted in reduced sensitivity to each single agent in LMS model. In conclusion blockage of β-adrenergic receptors enhances Trabectedin effectiveness, therefore further evaluation of underlying mechanisms of drugs synergism are warranted in order to provide a strong rational for suggesting this combination in the treatment of sarcoma and ovarian cancer patients.

F5 The value of trabectedin in the treatment of soft tissue sarcoma: a monoinstitutional retrospective real-life study

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Background: Soft-tissue sarcomas (STS) are rare tumors, accounting for approximately 1% of all cancers worldwide each year. The treatment of STS is often palliative, although a subset of patients may be cured or have a good disease-free interval. Trabectedine is a novel marine-derived antineoplastic agent that is characterized by multiple potential mechanisms of action combining cytotoxic, targeted, and immunological effects. Now it's to be consider a standard second line in not all subtypes.

Materials and methods: From January 2016 to April 2017 we treated 10 patients with STS metastatic (7 females, mean age 58.5 years, 5 liposarcoma, 1 fibrosarcoma mixoyde, 3 leymiosarcoma, 1 lonely pleural fibrous tumor). All patients were entered in the AIFA registry. Six patients were trated with Trabectedin as second line after faiulure of first line therapy containing anthracyclines. Three patients were treated in the third line and one in the fourth line. One was treated as a first line for heart problem. The dosage was 1,5 mg/m2 every 21 days and was administered a total 54 cycles (media 5,4; range 1-11). All administration was performed using CVC. Every two doses (in accord with AIFA) we proceeded to perform CT revaluation.

Results: Best tumor response by RECIST to the second cycle was:, PR = 5, SD = 3, PD = 2 cases, for an overall response rate (PR+SD) of 80%. A patient died after a few days of treatment for intestinal perforation. Median PFS was 8,3 months (range 1-11). Five patients are alive and two of this are still in treatment. Overall, trabectedine was well tolerated, the most common side effect G4 was thrombocytopenia. In the case of first-line treatment, hyperbilirubinemia and significant hypertransaminasemia occurred which caused the drug to be discontinued.

Conclusions: Trabectedin has consistent activity in all types of STS. It can be positioned after failure of first-line therapy with anthracyclines or in patients unfit for anthracycline-based therapy. This analysis confirms the efficacy of trabectedin in clinical practice (with a third of patients experiencing prolonged disease control). Therefore, trabectedin has become one relevant therapeutic option in metastatic STS, especially in selected histologies.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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G - MELANOMA AND SKIN CANCERS

G1 A phase II trial of dacomitinib in locally advanced unresectable or metastatic skin squamous cell carcinoma

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Background: In recurrent/metastatic skin squamous cell cancer (sSCC) not amenable to radiotherapy (RT) or surgery, chemotherapy (CT) has a palliative intent and limited clinical responses. The role of pan-HER inhibitor dacomitinib in this setting was investigated within an Italian clinical trial.

Methods: Patients (pts) with diagnosis of sSCC not amenable to curative treatments were treated. Oral dacomitinib was started at a dose of 30 mg qd for 15 days, followed by 45 mg qd. Primary endpoint was response rate (RR). Tumor samples were analyzed through Next Generation Sequencing methods (pgm, Ion torrent) using a custom panel targeting 36 genes associated with sSCC.

Results: Forty-two pts (33 M, 9 F; median age 77 years, range 45-92) were treated. ECOG PS was 0 in 58%, 1 in 40% and 2 in 2%. One fifth of the pts had distant metastasis. Most pts (86%) received previous treatments consisting in surgery (86%), RT (50%) and CT (14%). Overall RR was 28% (complete response CR 2%, partial response PR 26%), disease control rate 86%. Median duration of response (DoR) and clinical benefit (DoCB) were 10.3 months (range 0.2-20.5+) and 3.8 months (range 0.2-20.5+), respectively. Median treatment duration was 4 months (range 1-26+). Reason for discontinuation were disease progression in 69%, adverse events (AEs) in 19%, disease-related death in 5%; 3 pts are still on treatment. Median PFS and OS were 6 months (95% CI: 5-9) and 12 months (95% CI 9-NR), respectively. Most pts (93%) had at least one AE, mainly consisting in diarrhea and skin rash (71% each), fatigue (36%) and mucositis (31%). AEs higher than G3 occurred in 36% of pts (diarrhea and skin rash 17% each). Tumor material was available from 7 responding (R: 6 PR, 1 CR) and 15 non-responding (NR: 13SD, 2PD) pts. Frequent TP53 (60%), NOTCH1/2 (60%) and FAT1 (40%) mutations were observed. NR pts showed a higher occurrence of HRAS/BRAF/NRAS mutations (40%) than R ones (28%). Moreover, HER3 (27%) CASP8 (27%), KMT2C (33%) and DCLK1 (27%) mutations were restricted to NR pts.

Conclusions: In sSCC dacomitinib showed activity, similar to what observed with anti-EGFR monoclonal antibody cetuximab and panitumumab (RR 28% and 31%); safety profile was comparable to previous experiences in other cancers. A durable clinical benefit was observed as well. Molecular pt selection could improve therapeutic ratio.

ClinicalTrial.gov: NCT02268747.

G2 Prognostic role of disease extent and lymphocyte-monocyte ratio in advanced melanoma

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Background: One-third of patients (pts) with early melanoma experience a disease recurrence. Previous data showed that pts with advanced melanoma (AM) treated with BRAF and MEK inhibitors with normal lactate dehydrogenase (LDH) concentration and fewer than three organ sites of metastases had better outcome. Furthermore, melanoma has been recognized as one of the most immunogenic malignancies. The lymphocyte-monocyte ratio (LMR) is a simple biomarker of host immune system and inflammation and it was suggested as a prognostic factor in different cancer types.

Patients and methods: We retrospectively analyzed 165 consecutive pts with AM between Jan 2010 and Mar 2016 treated at the Department of Oncology of Udine, Italy. The aim of the study was to evaluate the prognostic role of disease extent and LMR at baseline. Outcome was measured in terms of overall survival (OS).

Results: In our cohort 102 pts (62%) were male, 136 (82%) presented at baseline ECOG PS 0-1; 42 pts (25%) received more than 2 treatment lines. Stage classification was III, M1a, M1b and M1c in 19 (11%), 44 (27%), 18 (11%) and 84 (51%) pts, respectively. BRAF was mutated in 76 (56%) of pts (missing data in 30 pts). Overall, 69 pts (42%) received target therapy (MEK and/or BRAF inhibitors) and 43 (26%) received immunotherapy. At a follow-up of 48 months, 129 pts (78%) were died, the median OS was 13 months. Higher LMR was significantly associated with absence of CNS localization ($p = 0.011$), less than 3 metastatic sites ($p = 0.015$) and normal LDH level ($p = 0.005$). In univariate analysis, PS > 1 (HR 2.67, $p = 0.0022$), number of metastatic sites more than 2 (HR 2.38, $p < 0.0001$), lung (HR 1.97, $p = 0.0004$), liver (HR 2.05, $p = 0.0009$), and CNS localization (HR 1.62, $p = 0.0267$), elevated LDH (HR 3.27, $p < 0.0001$), M1b and M1c stage (HR 2.13, $p = 0.0271$ and HR 3.70, $p < 0.0001$, respectively) were significantly associated with worse OS; on the contrary, high LMR was associated with better OS (HR 0.71, $p = 0.0004$). In multivariate analysis, ECOG PS (HR 7.86, $p = 0.001$), LDH (HR 2.82, $p = 0.004$) and LMR (HR 0.75, $p = 0.030$) were significantly associated with OS.

Conclusions: In our study, LMR seems to be associated with extent of AM and increased risk of mortality. Further investigations are needed to confirm these data.

G3 Brain radiotherapy (RT) and immunotherapy (IT) for metastatic melanoma (MM): a retrospective single institution experience

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Background: Brain metastases (mts) are common in MM and their prognosis is poor, though recent therapeutic advances. Limited preclinical and clinical evidences have suggested a potential immune-modulatory role of RT, which may synergize with IT, and some cases of *abscopal* effect (i.e. response of a distant non-irradiated site) have been described. We aimed to investigate efficacy and toxicity of concomitant or sequential IT and RT in a single Institution experience.

Material and methods: We analyzed data about all pts treated at our Institution between 06/12 and 11/16 with a CI, either antCTLA4 or antiPD1, and brain RT, either stereotactic (ST) or whole brain (WB). Only cases treated with RT within 6 months (mos) before or after IT were eligible, without any other oncologic therapies meanwhile. Progression free and overall survival (PFS and OS, respectively) were estimated according to the Kaplan-Meier method.

Results: 36 pts were identified. IT was administered as 1st line in 21 pts, 2nd line in 22, and 3rd line in 7. 23 pts received antiCTLA4, 13 antiPD1. 18 pts were treated with ST RT, 18 with WB RT. Median PFS from RT was 4 and 2 mos in 1st and 2nd line respectively (p .47), not evaluable in 3rd line due to very few data. No significant differences in PFS between antiCTLA4 and antiPD1 were seen (p .58). Most pts progressed at I evaluation after RT (31%). 14 pts presented extracranial progression (PD), with a median PFS of 12 weeks (range 1-55). Brain PD occurred in 15 cases, with a median PFS of 14 weeks (range 5-56). Median OS from RT was 7 and 4 mos in 1st and 2nd line respectively (p .37), not evaluable in 3rd line for the above mentioned reason. No differences in OS were seen between ST and WB RT (p .15), as well as between antiCTLA4 and antiPD1 (p .89). Neither neurologic adverse events nor worsening in immune-related systemic toxicities were observed.

Conclusions: Despite promising preclinical rationale, synergistic effect of RT and IT does not seem to be confirmed in our experience. No cases of *abscopal* effect were observed and most pts underwent early progression of systemic disease after RT. Overall prognosis of this population was poor, without predictors of benefit from combination of RT and IT. Prospective data are needed to focus on this topic, given the acceptable tolerability of combined treatment.

G4 Metastatic melanoma patients treated with Braf and Mek inhibitors: Patterns of progression. An Italian Melanoma Intergroup study

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Background: Progression patterns data after BRAF +MEK inhibitors (I) could help clinicians in choosing the treatment strategy among the multiple available options in the BRAF v600 melanoma setting. We analysed outcomes in pts treated with BRAF+MEK i to characterize pts with rapid progression.

Methods: In this multicenter retrospective analisis, data were collected from 164 consecutive pts affected by BRAF v600 metastatic melanoma and treated with BRAF+MEK i from February 2012 to April 2017.

Results: 64 patients were enrolled. Baseline LDH was elevated in 68(41%)pts, baseline number of metastatic organs were 1, 2, 3 and more in 52(32%), 52(32%), 29(18%) and 32(19%) pts. BRAF+MEK i administered were dabrafenib+trametinib in 151 pts and vemurafenib+cobimetinib in 13 pts, and they were adiministered in first line in 129(79%)pts. Best response was CR, PR, SD and PD in 27, 87, 17 and 2 pts. On cutoff

date, progression was observed in 104(63%) pts - 60(37%) pts still on treatment. mPFS was 9,83(1-54,7+) months: significant difference in PFS was showed in pts with normal baseline LDH or high LDH (13.2 vs 6.3 months, $p < 0.0001$), and in pts with number of metastatic organs lower or higher then 2 (13,4 vs 7 months, $p < 0.0001$). mOS was 18.3(1-62,5+) months: significant difference in OS was showed in pts with normal baseline LDH or high LDH had (24,7 vs 10 months, $p < 0.0006$), and in pts with number of metastatic organs lower or higher then 2 (25.9 vs 10 months, $p < 0.0003$). Among 104 progressed pts, 72 (69%) pts died, mOS after progression was 2,5 months (0,5-42+ months); Subsequent treatments were administered in 44(42%) pts. Duration of response (DR) was defined as time from BRAF+MEK i best response to progression of disease. Significant difference in OS after BRAF+MEK i progression was observed in pts with DR < 6 months(77 pts) or > 6 months (27 pts) (2 vs 8,3 months, $p < 0.0023$) and in pts with number of metastatic organs after progression lower or higher then 3 (4,5 vs 2 months, $p < 0.022$).

Conclusion: DR and extension of progression during BRAF+MEK I are factors that can be useful to identify pts with lower OS after progression, in addiction to known parameters like LDH and baseline number of metastatic organs.

G5 Analysis of miRNAs and their correlation with early malignat melanoma (MM)

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Background: The incidence of MM progressively increases and today 14 cases/100,000 cases per year are expected in Italy. The screening campaigns led to the identification of many early forms of MM, resulting in increased incidence of the disease, but have not changed mortality. This is possibly related to the identification of MM that would have remained silent. The visit and the dermoscopy are operator-dependent methods and require long experience for their optimal use. Even in the most experienced hands, the sensitivity of these methods does not exceed 85% and 90%, respectively. It would be need to identify new effective screening methods, able to eliminate the existing limits. MM is the skin cancer with the worst prognosis, especially when discovered at advanced stages. Moreover, it would be clinically relevant to identify in advance the melanoma lesions at risk of recurrence.

Subjects and methods: In 2014 we have activated an experimental study to investigate the possible role of miRNAs in MM screening tool. All the subjects screened with dermatoscopy by the "Lega Italiana per la Lotta contro i Tumori" (LILT) are invited to join the study. They underwent a blood sample collection and a panel of 15 miRNAs is analyzed. We selected miRNAs described as markers of MM diagnosis and/or to have well supported roles in its progression.

The primary objective is to compare the level of circulating miRNAs in 100 patients with MM and 100 subjects with non-neoplastic skin pigmented lesions, to evaluate their diagnostic value. The study foresees to enroll 700 subjects, to create a data base, to make a multivariate analysis including selected miRNAs, personal anamnesis and exposition to known risk factors

Results: From September 2014 to December 31 2016, we accrued 633 subjects, with doubt of MM at the screening evaluation. We found 101 MM (16%): 36 in situ MM, 59 infiltrating (20 pT1a, 22 pT1b, 7 pT2a, 2 pT2b, 1 pT3a, 4 pT3b, 2 pT4b, 1 pTXNxM1a), 2 lentigo maligna and 4 multiple MM. At the preliminary analysis miR-199a-5p, miR-122-5p and miR-424-5p represent the most promising candidate biomarkers in terms of diagnostic efficiency in distinguishing between MM patients and healthy subjects.

Conclusions: The study gives preliminary information about the incidence of MM in a population clinically screened. Analysis of selected miRNAs and their role as a diagnostic tools for early MM detection will be presented and correlated with clinical and known risk factors.

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H - GYNAECOLOGICAL TUMOURS

H1 Assessing the risk of pelvic and para-aortic nodal involvement in apparent early-stage ovarian cancer: a predictors- and nomogram-based analyses

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Background: Nodal status is paramount to tailor the need of adjuvant treatments in patients affected by apparent early-stage epithelial ovarian cancer (eEOC). Here, we aimed to estimate the prevalence of nodal involvement according to various disease characteristics in order to assess the prognostic advantages to have nodal dissection in eEOC.

Patients and Methods: Data of consecutive patients undergoing comprehensive staging for eEOC were retrospectively evaluated. Logistic regression and a nomogram-based analysis were used to assess the risk of nodal involvement.

Results: Overall, 377 patients were included. All patients had nodal dissection including pelvic and para-aortic lymphadenectomy in 366 and 370 cases, respectively. Forty-four (11.7%) patients were upstaged due to nodal involvement. Pelvic and para-aortic nodal metastases were observed in 32/366 (8.7%) and 42/370 (11.3%) patients, respectively. Nodal involvement was observed in 46/136 (33.8%), 8/24 (33.3%), 15/94 (15.9%), 4/42 (9.5%) and 1/81 (1.2%) patients with serous, undiffentiated, endometrioid, clear cell, and mucinous histology ($p < 0.001$). Via multivariate analysis, we observed that poor differentiated tumor, (FIGO grade 3), serous histology and bilateral tumors were independently associated with both pelvic and para-aortic nodal involvement ($p < 0.05$). Normograms displaying the risk of nodal involvement in the pelvic and para-aortic areas were build. FIGO grade, serous histology and bilateral tumors are the main characteristics suggesting node positivity. Moreover, we observed that pelvic node involvement was more frequently detected in patients affected by FIGO stage II eEOC.

Conclusions: Our data suggested that FIGO grade 3, serous and bilateral eEOC are at high risk of having disease harboring in the lymph nodes. After receiving external validation, our data will help to identify patients deserving comprehensive retroperitoneal staging.

H2 Phase II study of the safety and efficacy of oral capecitabine in patients with platinum-pretreated advanced or recurrent cervical carcinoma

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Background: Cervical cancer is underrepresented in the gynecological clinical research. The objective of this observational study was to evaluate the activity and the safety of capecitabine in patients with platinum-resistant recurrent cervical carcinoma.

Materials and methods: In this phase II study we enrolled patients with advanced/recurrent cervical carcinoma who have failed a previous platinum-based therapy. All patients signed an informed consent and were treated at the Gynecological Units of the IRCCS National Cancer Institute of Milan (Italy). All patients received a starting dose of oral capecitabine 1250 mg/m2 twice a day continuously from day 1 to day 14 every 21 days. We used RECIST 1.1 criteria to evaluate response to therapy and CTCAE 4.0 to evaluate AE. Progression-free survival (PFS) was defined as time from first capecitabine intake to progressive disease (PD) and overall survival (OS) as time from first capecitabine to cancer-related death. We performed descriptive analysis and Kaplan Meier test using SPSS 20.0.

Results: From Dec 2013 to Jan 2017, 20 patients were enrolled. All patients receive a combination of carboplatin/paclitaxel as first-line therapy for advanced/recurrent disease. Median age at the first capecitabine administration was 56.9 years (range 27-82). After a median follow-up of 14.3 months (range 3-39.6), 2 patients were on treatment, 18 patients experienced a PD with a median PFS of 4.7 months and 16 patients died (median OS 14.4 months). With a median exposure to capecitabine of 4.5 cycles (range 3-15), 5% complete responses, 30% partial responses and 25% stabilization of disease were reported. After capecitabine, 65% of patients received further chemotherapy (median 2 lines, range 0-5). No grade$\geq$3 adverse events (AE) were reported; the most frequent grade$\leq$2 AE were fatigue (55%), hand-foot syndrome (40%) and diarrhea (20%). Overall, 5 patients received a reduced dose of capecitabine (1000 mg/m2 twice a day) due to AE (1 grade 2 diarrhea, 2 grade 2 fatigue and 2 grade 2 hand foot syndrome).

Conclusions: Our study suggests that oral capecitabine should be considered an active and safe treatment in patients with platinum-presistant advanced/recurrent cervical carcinoma.

H3 Is chemotherapy worthwhile in patients with high-risk, lymph node negative, FIGO stage 1, endometrial cancer?

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Background: Until the results of the ENGOT-EN2-DGCG/EORTC 55102 trial will become available, the role of adjuvant chemotherapy (CT) in patients with high-intermediate and high risk, early stage, lymph node negative (LN0), type 1 endometrial cancer is unclear.

Methods: We retrospectively collected patients diagnosed with endometrioid endometrial cancer stage 1a and b (2009 FIGO staging), LN0, and grade 3. We performed descriptive analysis and Kaplan Meier test using SPSS 20.0.

Results: From March 1996 to Oct 2016, 54 consecutive patients were identified and enrolled (46 at the National Cancer Institute of Milan and 8 at the University Hospital of Udine). Median age at diagnosis was 65.4 years (range 34.2-84.9). All patients were documented to be LN negative, 27 patients underwent pelvic lymphadenectomy (PLD), 19 PLD plus lomboaortic (LA), and 8 sentinel lymph nodes biopsy. Overall, 35 patients had lymphovascular space involvement (LVS+) and 11 had not, in 8 pathologic report this data was not reported. After surgery, 33 patients received adjuvant radiotherapy (RT): 21 patients (63.6%) received brachyRT, 8 patients (24.2%) received external RT, 4 patients (12.2%) received both; 13 patients underwent platinum-based adjuvant chemotherapy (CT): 7 only CT, 2 external RT followed by CT and 2 brachyRT followed by CT. To note, among patients who received CT, 84.4% had LVS+. After a median follow up of 51.1 months (range 6-249), 14 patients (25.9%) experienced disease relapse and 12 patients (22.2%) died (9 due to endometrial cancer, 2 breast cancer and 1 pancreatic cancer). Median disease-free survival (DFS) was 19.9 months (range 4.7-157.4). Only 1 patients who underwent CT experienced disease relapse, the relapse rate was 7.7% in CT group versus 31.7% in non-CT group ($P = 0.085$).

Conclusions: According to our study, patients with stage 1a and b, LN0, grade 3 endometrioid endometrial cancer seems to derive a great benefit from adjuvant chemotherapy. This data needs to be further investigated in a large prospective clinical trial.

H4 The impact of chemotherapy-related leukopenia on survival outcomes in locally advanced cervical cancer

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Background: The immune system plays an important role against tumor growth. Accumulating evidence indicates that chemotherapy might influence the activity of resident and recruited immune cells that contrast tumor proliferation. Here, we aimed to investigate the impact of hematologic toxicity and leukopenia in locally advanced cervical cancer patients undergoing neoadjuvant chemotherapy (NACT).

Patients and methods: Data of consecutive patients undergoing platinum-based NACT followed by surgery were collected in order to evaluate the impact of chemotherapy-related toxicity on survival outcomes. Toxicity was graded per the Common Terminology Criteria for Adverse Events (CTCAEv.4.03). Survival outcomes were evaluated using Kaplan-Meir and Cox hazard models.

Results: Overall, 126 patients were included. Among those, 94 (74.6%) patients experienced grade2+ hematologic toxicity; while, grade2+ non-hematologic toxicity occurred in 11 (8.7%) patients. After a median follow-up of 37.1 (inter-quartile range, 12-57.5) months, 21 (16.6%) patients experienced recurrence. Via multivariate analysis, no factor was independently associated with disease-free survival; while a trend toward worse prognosis was observed for patients experiencing grade2+ leukopenia at cycle-3 (HR:3.13 (95%CI: 0.94, 10.3); $p = 0.06$). Similarly, grade2+ leukopenia (HR:9.98 (95%CI: 1.14, 86.6); $p = 0.03$), lymph-node positivity (HR:14.6 (95%CI:1.0, 214.4); $p = 0.05$) and vaginal involvement (HR:5.81 (95%CI:1.43, 23.6); $p = 0.01$) impacted on overall survival, at multivariate analysis. Magnitude of leukopenia correlated with survival ($p < 0.001$).

Conclusions: The present study shows an association between the occurrence of leukopenia and survival outcomes. NACT-related immunosuppression might reduce the response against the tumor, thus promoting cancer progression.

H5 ARIEL4: An international, randomised phase 3 study of rucaparib vs chemotherapy as treatment for BRCA1- or BRCA2-mutated, relapsed ovarian cancer

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Background: Approximately 18% of patients with high-grade ovarian cancer (inclusive of fallopian tube and primary peritoneal cancer) harbour a deleterious germline *BRCA1* or *BRCA2* mutation, and approximately 7% harbour a somatic *BRCA1* or *BRCA2* mutation (Pennington et al. *Clin Cancer Res.* 2014;20:764-75). The poly(ADP-ribose) polymerase (PARP) inhibitor rucaparib is approved in the United States for treatment of patients with deleterious *BRCA* mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with ≥2 chemotherapies. Data comparing PARP inhibitors to standard of care treatment for relapsed ovarian cancer are limited. ARIEL4 (EudraCT 2016-000816-14; NCT02855944) is evaluating rucaparib versus standard of care chemotherapy as treatment for patients with relapsed, high-grade ovarian cancer (regardless of histology) and a deleterious germline or somatic *BRCA1* or *BRCA2* mutation who have received ≥2 prior chemotherapy regimens.

Materials and methods: Patients (n≈345) stratified by progression-free interval after their most recent platinum regimen will be randomised 2:1 to receive rucaparib 600 mg BID or chemotherapy. Patients with platinum-resistant (progressive disease ≥1 to < 6 months after last platinum) or partially platinum-sensitive disease (progressive disease ≥6 to < 12 months after last platinum) will receive rucaparib or weekly paclitaxel; patients with platinum-sensitive disease (progressive disease ≥12 months after last platinum) will receive rucaparib or investigator's choice of platinum-based therapy (single-agent or doublet). Patients receiving chemotherapy may cross over to rucaparib upon radiographic disease progression. The primary endpoint is investigator-assessed progression-free survival (per RECIST version 1.1 criteria). Secondary endpoints include overall survival, investigator-assessed objective response rate per RECIST criteria, objective response rate per RECIST/CA-125 criteria, duration of response, and patient-reported outcomes. Safety will be summarised descriptively using standard adverse event reporting.

Results: ARIEL4 is actively recruiting patients.

Conclusions: Randomised studies such as ARIEL4 are needed to assess the benefit-risk profile of PARP inhibitors versus standard of care as treatment for relapsed, high-grade ovarian cancer.

H6 Retrospective analysis of 77 patients with ovarian cancer undergoing genetic testing for BRCA1 and BRCA2 mutations

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Background: Ovarian cancer (OC) is still a big killer in the field of female neoplastic disease, placing itself fifth as cause of death. In recent years, some genetic mutations have been analyzed within high grade serum OC. BRCA1-BRCA2 genes mutation is the most commonly observed in a proportion of patients with ovarian cancer not necessarily belonging to families expressing such alterations.

Material (patients) and methods: A retrospective cohort of 77 OC patients were selected between 2014-2017. All patients samples were collected with appropriate consents and tested for germline BRCA1 and BRCA2 mutations after genetic counselling at the Department of Medical Genetics unit of University Hospital of Careggi in Florence. Genomic DNA was isolated from blood using FlexiGene DNA Kit.Targeted library preparation of BRCA1 and BRCA2 was performed using hybridization capture probes or multiplex PCR strategies and Illumina sequencing was carried out on the Illumina MiSeq following the manufacturer's instructions. Data analysis, including alignment to the hg19 human reference genome and variant calling was done using GATK or SeqNext software package. All pathogenic germline variants were validated by Sanger sequencing.

Results: Pathogenic mutations in BRCA genes were found in 23 out of 77 (29.9%) high grade malignant epithelial OC: 20 of them were in BRCA1 while 3 in BRCA2. The remaining 54 patients were wild type. Patients, after cytoreductive surgery, had chemotherapy of line I according to the carboplatin-paclitaxel scheme for 6 cycles. All 23 mutated patients, except for a platinum-resistant case (4-month progression time), had platinum sensitivity over 6 months. 16 patients over 20 with BRCA1 and BRCA2 mutations, received a chemotherapy II of line. Of these patients, 13 had a PFS greater than 6 months and 3 patients were resistant platinum. Ca 125 basal marker was positive (range of normality between 0-35) in more than 78.2% of cases, while Ca 125 on relapse was positive in 95.7% of cases.

Conclusions: The differentiation of patients in subgroups related to the presence or absence of BRCA1 and BRCA2 genes and their variants, has allowed to identify in the mutated population a higher platinum sensitivity, also in subsequent lines of therapy and to undertake treatments with innovative molecules for OC such as PARP14-16 inhibitors, that partially modified the prognosis of this neoplasia by increasing the disease-free interval.

H7 First line treatment with carboplatin-paclitaxel-bevacizumab in ovarian cancer: retrospective review of a single institute experience

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Purpose: Carboplatin- Paclitaxel- Bevacizumab has became the standard first line treatment of ovarian cancer (OC) at high risk of progression (IIIB, IIIC, IV). The purpose of this study was to investigate the efficacy and safety of this combination in our first 35 patients (pts) treated with this combination.

Materials and methods: This is a retrospective analysis of 35 consecutive OC pts undergoing carboplatin, paclitaxel and bevacizumab chemotherapy regimen, from February 2013 to January 2017, in Reggio Emilia Clinical Cancer Center.

Results: Thirty- five consecutive pts were included in this analysis who received at least one cycle of the combination. Median patient age was 58 years (range 41-73). Except one patient who had a endometroid G3 tumor, the rest had a papillary serous G3 type. Eight pts had a BRCA mutation (22%), 4 BRCA1 and 4 BRCA2. Eigthy percent were stage IIIC, one patient was stage IIIB and 6 pts (17%) were stage IV. A median of 6 cycles of carboplatin-paclitaxel- bevacizumab was delivered (range 3-10). A median of 18 cycles of bevacizumab in maintenance was delivered (range 3-24). Twelve of them are still in bevacizumab maintenance therapy. Eleven pts received neoadjuvant chemotherapy without bevacizumab with 25% of partial responses, one complete response and one stabile disease. Fifty-seven percent of the pts reached an optimal citoreduction and 43% a suboptimal one. The median progression-free survival was 22,7 months (range 3,97- 48,07) (95% 21,5-23,9 CI) . Median overall survival has not been reached with a median follow up of 45,5 months (95% 42,3-48,8 CI) . Grade 1-4 hematologic toxicity was seen in 33% of the pts, mainly neutropenia G2 (5 pts, 14%) and G3 (3 pts, 8,5%). The most frequent G1-G4 non- hematologic toxicity were: paresthesie 44%, myalgie 25%, constipation 25%, asthenia 25%, arthralgie 16%, nausea 19% and vomiting 14%. Main G3-4 toxicities were neutropenia 11% and astenia 8%. During the bevacizumab maintenance treatment the most frequent toxicities were hypertension (5 pts) 13%, in 2 cases G3 (5,7%), 2 cases of epistaxis G1 (5,7%) and 1pt (2,8%) with periodontal bleeding G1. No bowel perforation were notified.

Conclusion: In conclusion, our study provides encouraging evidence that the use of bevacizumab as part of first-line treatment of patients with ovarian cancer at high risk of progression has demostrated high rates of efficacy comparable with those obtained in clinical trials, without unexpected toxicities.

H8 Prognostic impact of CA15-3 pre-treatment levels in ovarian cancer patients

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Background: In ovarian cancer (OC) patients (pts), CA125 represents the pivotal serum tumor marker with a well established role in diagnosis, response to treatment and follow-up. CA15-3 is a breast cancer-associated antigen also expressed in some ovarian cancer and gynecological malignancies, even if its role is still not well clarified.

The aim of this study is to evaluate the prognostic role of CA15-3 at diagnosis in OC patients.

Patients and methods: OC pts treated in Our Center from 2009 to 2017 were eligible for analysis. We retrospectively collected data regarding histopathological type, treatments, CA125 and CA15-3 levels at diagnosis and during treatment, and BRCA genetic testing results. According to our laboratory CA15-3 cut-off values (greater than 35 U/

ml), patients were divided into a group with high CA 15-3 at diagnosis and a group with normal levels. The two groups were compared with regard to clinical and survival measures, including overall survival (OS) and first-line progression-free survival (PFS). Survival distribution was estimated by the Kaplan–Meier method. The association between categorical variables was tested by Fisher exact test and by Chi-square test.

OS was defined as the interval between the start of chemotherapy to death or last follow-up visit, while first-line PFS was defined as the interval between the first-line chemotherapy and progression.

Results: Out of 72 OC eligible pts, CA 15-3 serum levels at diagnosis were evaluated in 38 pts. Among them, 16 (42%) had elevated CA 15-3 level at diagnosis. Analyzing the prognostic impact of CA15-3, a significant difference in terms of OS was found: OC patients with elevated CA 15-3 at diagnosis showed a worse OS when compared with patients with normal CA 15-3 levels (median OS: 30.9 months vs 65.72 months; HR: 3.0179; 95% ci 1.0346-8.8030; $p = 0.0164$) whereas no difference in terms of first-line PFS was observed. High CA 15-3 levels were not associated with histotype or BRCA mutation status, while a statistically significant correlation was found with higher stage at diagnosis ($p = 0.0124$).

Conclusions: Our data suggest that high CA15-3 levels at diagnosis in OC patients could represent a poor prognostic factor. High CA15-3 levels also seem to be related with an advanced stage at diagnosis. Further prospective and multicentric studies are needed to confirm the prognostic role of CA15-3 in OC patients.

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L - HEAD AND NECK TUMOURS

L1 Different signatures of HPV-related oropharynx cancer (OPC) correlate with patients outcome

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Background: HPV-related OPC patients have different epidemiologic, clinical and outcome behaviors in comparison with hpv-negative opc, having HPV-related OPC patients a 70% of reduction in their risk of death. Smoking exposure and bulky neck nodes are negative prognostic factors, however the reasons of treatment failure are almost unknown in HPV-related OPC. In the last years high-throughput gene expression assays allowed to identify predictive signatures in several tumor types. Our objective is to seek whether exists a predictive signature in HPV-related OPC.

Methods: publicly gene-expression data for HPV-positive OPC were searched by a literature revision, through a systematic search, performed in the following databases: PubMed, ArrayExpress, Embase, and GEO meta-analysis. Only studies with HPV status confirmed by DNA sequencing or qPCR were considered eligible. Patients outcome will be described using Kaplan-Meier curves.

Results: 346 available cases from 11 studies were merged through a meta-analysis approach and 324 gene-sets have been investigated. An unsupervised subtype analysis provided evidence that this dataset can be split in four main clusters (Table 1). The clinical relevance of this classification was tested for its association to overall-survival. Kaplan-Meier analysis demonstrated that Cl3 has the worst behavior, while Cl1 has the better one. The four HPV clusters show remarkable different molecular profiles: the most relevant involved pathways include proliferation and the activation of several immune pathways.

Conclusions: Our analysis demonstrated the existence of a molecular heterogeneity within the HPV-related OPC that correlates with patients outcome. Further analyses to validate our gene expression data are already planned.

Table: L1

	Relevant dysregulated pathway	5-yr OS
Cluster 1	EMT	89%
Cluster 2	Inflammatory Response	54%
Cluster 3	Hypoxia	28.5%
Cluster 4	Proliferation	62.2%

L2 Gene-expression profiles of primary and metastatic lesions in head and neck squamous cell carcinoma

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Background: Mechanisms of tumour spread and the deregulation level exisisting in distant metastatic lesions, in comparison with primary disease, are not fully understood in head and neck squamous cell carcinoma (HNSCC). We would test at molecular level the hypothesis that the development of the metastatic disease is linked to the biologic characteristics of the primary tumour more than to the degree of regional nodes involvement

Matherials and methods: We identified 27 HNSCC patients with available tissues of either primary tumor and distant metastasis (DM). As control, a series of 26 cases without DM was matched according to subsite, HPV status and TN stage. Whole-transcriptome profiling was performed by microarray analysis using the DASL assay and BeadArray Chips (Illumina). To identify expression pattern related to patients with or without DM, we applied sparse Partial Least Square—Discriminant Analysis (sPLS-DA). We analysed the potential biological pathways differentiating primary tumors and metastases through Gene Set Enrichement Analysis (GSEA) and interrogating the Hallmark Gene Set Collection database.

Results: sPLS-DA discloses gene-expression patterns between patients who developed or not DM. sPLS-DA defined a set of genes discriminant for patient's DM status. Starting from those genes, we developed a signature following the Bayesian Compound Covariate Predictive (BCCP) algorithm. A core including 10-genes entered into our model and was able to predict patients who develop DM reaching AUC=0.85. To investigate the biological patterns associated to primary tumors of patients who developed or not DM, functional analysis was performed and the gene expression matrix was deconvoluted in 18x18 metagenes. We identified two networks involving a number of gene-ontology terms enriched in patients without DM, related to inflammation and keratinocyte differentiation. We investigated the genes differentially expressed between the primary tumors and the corresponding metastatic lesions and a total of 258 genes were identified. Functional pathway analysis was performed by GSEA and hallmark database was investigated resulting in 14 gene-sets enriched in metastasis imposing FDR<0.1.

Conclusions: Our analysis of matched HNSCC primary tumours having or not developed DM highlighted a 10-gene signature able to stratify patients whose relevance deserves further validation.

L3 Can the salivary microRNA expression profile help to identify novel biomarkers for oral squamous cell carcinoma detection?

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Background: Oral squamous cell carcinoma (OSCC) is the most frequent malignant tumor of the oral cavity with low survival rate, accounting for more than 95% of all head and neck cancers. Generally, fewer than 50% of patients survives more than 5 years, because this tumor is often detected at a late stage. Since saliva has been shown to be a non-invasive, accessible, and highly efficient diagnostic medium, the analysis of salivary biomarkers may provide an efficient tool for oral cancer early detection. The main aim of our study was to analyze the salivary microRNA expression profile in OSCC patients, in order to investigate the molecular mechanisms and signaling pathways responsible for the development and progression of this tumor.

Materials and methods: Total RNA and miRNAs were isolated using the miRNeasy Mini Kit, and their quality and quantity were assessed using the 2100 Bioanalyzer and spectrophotometer NanoDrop ND-1000. Using a TaqMan Low Density Array A human microRNA microarray analysis, the expression profile of 377 miRNAs was analyzed in saliva of ten OSCC patients and ten healthy individuals. In addition, the expression of specific salivary miRNAs was analyzed in other independent samples from fifteen OSCC patients at different stages of disease, using Real-time PCR analyses.

Results: Microarray analysis showed that a subset of twelve miRNAs, such as let-7g, miR-27a, miR-30b, miR-133a, miR-135b, miR-148b, miR-183, miR-199a-3p, miR-328, miR-361-5p, miR-451 and miR-486-5p, involved in several cancer-related pathways, including TGF-b, PI3K/Akt, Wnt, MAPK signaling, was differentially expressed in saliva of OSCC patients. Among these deregulated salivary miRNAs, eight were found to be up-regulated in their expression and four down-regulated. Finally, expression analysis of hypothetical miRNA gene targets involved in the same cancer-related pathways confirmed the coherence of our results.

Conclusions: Recent findings reported in literature regarding variations in expression of some miRNAs involved in proliferation, metastasis development, and therapy response in OSCC have confirmed the coherence of our results.

L4 Plasticity of PD-L1 expression between nodal metastases and primary tumors in p16 negative squamous cell carcinoma of the oral cavity

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Background: the recent achievements of immunotherapy in many different areas (melanoma, kidney, lung and bladder carcinoma) stimulate the investigation about the action of *check points inhibitors* in other tumors, particularly in case of tumors with an high mutational load, that are potentially responsive to immunotherapy approaches, like p16 negative oral squamous cell carcinoma. Phase III studies are ongoing, and there are also preliminary data about the PD-L1 tissue expression, in correlation with tumor grade and stage. However, investigations concerning the possible up/down regulation of this ligand in primary *vs* nodal metastasis are still largely inadequate.

Material and methods: 16 oral squamous cell carcinoma T2-T4, node positive (N1), p16 negative, moderately differentiated (G2), underwent immunostaining with anti PD-L1 rabbit MoAb SP 142, using a VENTANA BenchMark Ultra platform with

OptiView detection kit. Both primary tumors and nodal metastases were immunostained. Results were evaluated according to Roche PD-L1 (SP142) scoring system. In particular, neoplastic cell immunoreactivity (TC) and immune cells (lymphocytes, macrophages, dendritic cells and granulocytes) intratumoral and peritumoral immunoreactivity (IC) were evaluated. CD3 immunostaing of both primary tumors and nodal metastases were also performed, in order to facilitate the interpretation of the results.

Results: the entire group of 16 cases showed PD-L1 expression in perineoplastic IC, ranging from 1% to 50%, according to the scoring. No significant variations of expression between primary and secondary nodal sites were observed in all cases but one.

Conversely, 10 out of 16 showed no expression of PD-L1 on TC (0%) both in primary tumor and nodal metastasis. The other six cases showed: case 4: T 0%, N 60%; case 5: T 80%, N 5%; case 6: T 70%, N 5%, case 11: T 50%, N 0%; case 13: T 30%, N 10%, case 16: T 40%, N 1%.

Conclusions: in the light of the relevance of PD-L1 expression in term of immunotherapy efficacy in other areas (lung and bladder carcinoma), this documented plasticity (37.5% of cases) might be an interesting information for future trials.

L5 A single institution twenty-year experience of recurrent or metastatic epithelial non glandular sinonasal cancer

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Background: Sinonasal cancers (SC) are rare and heterogeneous tumors, whose natural history depends on histology and stage. Clinical trials (ClinicalTrials.gov: NCT02099175, NCT02099188. AIOM: 2013-000075-33) are ongoing to evaluate the role of multimodal therapies (MMT, consisting in induction chemotherapy -iCT- followed by locoregional therapy) as upfront treatment. Few data about the outcome of relapsed and metastatic disease are available.

Methods: This is a retrospective single institution analysis of patients (pts) treated for epithelial non glandular SC progressing after MMT to gather data about treatment outcome. Overall survival (OS) was measured as the interval from disease relapse to death or follow-up.

Results: Among 106 pts with SC treated at our Center from 1997 to 2016 (median follow-up 26 months -mm-, range 5-192), 50 (48% women) relapsed after MMT. Median age was 53 years (range 16-73). WHO 2005 histotypes were: 36% undifferentiated carcinoma (SNUC), 34% squamous cell carcinoma (SCC) and 30% neuroendocrine cancer (SNEC). Among the 41 pts (82%) with stage IV, only 39% (16/41) had a potentially resectable disease at diagnosis. However surgery was part of the initial curative treatment in 32% of pts. RT was given in 92% of cases. Median time from to first relapse after MMT was 13.5 mm. Median OS was 13 mm: 19 mm in SCC, 16 mm in SNUC and 6 mm in SNEC (p=.34). Relapse occurred as distant metastasis in 40%, as nodal recurrence in 6% and at primary site in 54% of cases. First line salvage treatment was surgery in 38%, CT in 30%, RT in 8%, best supportive care in the remaining pts. Median OS was 31 mm in surgically treated pts and 4.8 mm in those receiving CT ($p < .0001$). Median OS was longer in pts with disease control after iCT than in pts with PD (13.4 vs 1.5 mm, $p = .07$). Median OS was 29.6 mm in pts with CR after definitive treatment, 7.1 mm in those with PR and 3.4 mm in those with PD ($p = .002$). Pts with an objective response to palliative CT had a longer median OS than those with PD (20 vs 4 mm, $p = .002$).

Conclusions: About 50% of locally advanced SC actually experiences a recurrence, within a relatively brief time from treatment start. Factors associated with better outcomes are feasibility of salvage surgery, objective response to prior definitive treatment and response to palliative CT. OS after recurrence is poor, so underlining the need of new treatment approaches in this setting.

L6 Subsite-dependent prognostic impact of age in patients with nasopharyngeal and oropharyngeal cancer

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Backgroud: Outcome results in elderly head and neck cancer (HNC) patients (pts) treated with concurrent chemoradiation are controversial. Comparative effectiveness analyses showed a lack of benefit in multimodal treatment; however, retrospective highly selected series reported older patients to have similar outcome compared to younger ones albeit with high burden of toxicities.

Material and methods: Locally advanced oropharyngeal (OPC) and nasopharyngeal cancer (NPC) pts treated at our institution with concurrent platinum based chemotherapy (CHT) and intensity modulated radiation therapy (IMRT) techniques from 2004 to 2015 were retrospectively evaluated. Overall survival (OS) and Relapse Free Survival (RFS) Kaplan-Meier curves were estimated and compared with the log-rank test; acute toxicity rate >G3 according to Common Toxicity Criteria Adverse Event v4.0 was also analyzed, distinguishing between patients >65 years old (elderly) and ≤65 old. HPV status was recorded in all OPC patients.

Results: 375 pts received IMRT-CHT, 215 in OPC and 160 in NPC cohort. Elderly pts represented 26% and 11% of OPC and NPC pts, respectively. OPC HPV positive cases were similarly represented in older (73% of the cases) and younger pts (66%); HPV positivity maintained a significant prognostic role independently of age and also across different age group. On the contrary, age did not significantly impact on survival in OPC. Five-years RFS was 68% in older versus 76% in younger patients $p = 0.391$; the corresponding figures for OS were 93% versus 87% $p = 0.541$. There was no significant difference in cumulative acute toxicity rate = G3 (39% in elderly vs 36% in younger $p = 0.778$). When analyzed separately, no difference was shown for what concerns dysphagia and mucositis. NPC pts showed a different outcome according to age both in terms of RFS (5-years probabilities 41% in elderly vs 80% in younger pts, $p < 0.001$) and OS (48% vs 90%, $p < 0.001$), which turned out to be a negative prognostic factor in this disease. Also for NPC pts, the two age subgroups did not significantly differ in acute toxicity rate = G3 (56% vs 61%, $p = 0.800$). No different platinum total dose was adopted in OPC and NPC elderly pts.

Conclusion: We observed a subsite-specific impact of age on treatment outcome: older NPC pts showed markedly worse survival than the younger counterparts, while in OPC pts such an effect was inconsistent. HPV status was confirmed to be a positive prognostic factor independently of age.

L7 Skin rash and response to cetuximab treatment: a retrospective single-center analysis

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Background: The standard of care for patients with recurrent/metastatic head and neck squamous cell cancer (R/M HNSCC) not susceptible for surgery or reirradiation is chemotherapy with 5-FU and cisplatin plus cetuximab. Skin rash (SR) is a common adverse event of cetuximab. In patients treated with cetuximab for colorectal cancer there is strong evidence of a better outcome in those who undergo moderate or high grade of SR, and some retrospective data seem to confirm this finding in HNSCC. We report our experience.

Materials and methods: We retrospectively reviewed 107 patients treated with cetuximab for R/M HNSCC from January 2014 to December 2016. Patients were divided in two groups by the grade of SR (G0-1 and G2-4), conforming to Common Terminology Criteria for Adverse Events (CTCAE) v 4.0. Progression-free survival (PFS) was computed as time of progression or death since the date of assessment of recurrent/metastatic disease. Overall response rate (ORR) was computed as the sum of partial and complete responses and evaluated according to RECIST 1.1. PFS and ORR were correlated to the grade of rash.

Results: 67 patients were evaluable for PFS: among them PFS was significantly longer (p 0.0014) in those who underwent a G2-4 rash (9,3 months) vs G0-1 (4,9 months). Hazard Ratio was 2,445 (CI 1.412-4.232). 95 patients were evaluable for ORR: among them G0-1 group had 4,2%, while G2-4 group had 36,8% of ORR.

Conclusions: Our results support data of literature on improved outcome according to the development of skin rash in HNSCC. SR might be considered a predictive marker of response in these patients; nonetheless further *ad hoc* studies would be interesting.

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M - BRAIN TUMOURS

M1 Gender and MGMT methylation in glioblastoma patients: interactions in the PERNO prospective study

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Background: Glioblastoma (GBM) remains an incurable disease. Radiotherapy and temozolomide are the backbone of the treatment. Clinical and molecular factors are essential to define prognosis.

Methods: Data on all new cases of primary brain tumors observed from January 1, 2009, to December 31, 2010, in adults residing within the Emilia-Romagna region were recorded in a prospective registry in the Project of Emilia Romagna on Neuro-Oncology (PERNO). We perform a prospective evaluation about prognostic factors in GBM patients treated with temozolomide concurrent with and adjuvant to radiotherapy.

Results: One hundred sixty-nine GBM patients (median age, 60 years; range 29 − 82) were prospectively evaluated. MGMT methylation status was available in 140 patients. Combining gender and MGMT methylation status we obtained four groups of patients: 36 male pts with methylated MGMT (25.7%), 47 male pts with unmethylated MGMT (33.6%), 32 female pts with methylated MGMT (22.9%), 25 female pts with unmethylated MGMT (17.9%).

Results of univariate analysis are summarized in the table 1.

Overall survival (OS) was significantly different between methylated male and methylated female ($p = 0.028$), methylated male and unmethylated female ($p = 0.031$), unmethylated male and methylated female ($p = 0.002$), methylated female and unmethylated female ($p < 0.001$). In multivariate analysis, gender and MGMT methylation considered together (met female vs met male HR = 0.459; 95% CI 0.242 − 0.827; $p = 0.017$), age (HR 1.025; 95% CI 1.002 − 1.049; $p = 0.032$) and Karnofsky Performance Status (KPS) (HR 0.965; 95% CI 0.948 − 0.982; $p < 0.001$) were significantly correlated with OS.

Conclusions: The median overall survival is consistently higher for female pts with methylated MGMT, treated with temozolomide concurrent with and adjuvant to radiotherapy. When considered simultaneously with MGMT methylation status, gender might impact on clinical outcome and should be considered as a prognostic factor.

Table: M1

	n	mOS	95%CI
methylated male	31	16.3	9.2 -23.4
unmethylated male	41	15.6	11.8 - 19.5
methylated female	26	nr	
unmethylated female	21	17.0	11.8 - 22.2
total	119	17.0	15.2 - 18.9

M2 IDH mutant and 1p19q codeleted low grade gliomas: to treat or not to treat?

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Background: Molecular characterization of low grade gliomas (LGG) is essential for diagnosis and treatment of these diseases. LGG patients (pts) with IDH mutation and 1p19q codeletion (codel) are characterized by a median OS (mOS) longer than 10 years. Thus, the role of treatments and side effects should be carefully evaluated.

Methods: We evaluated LGG pts from our data warehouse (n = 679 pts) who received surgery and had sufficient tissue to assess biomarkers characterization. Pts with gliomatosis were excluded. IDH1/2 assessment was performed on formalin-fixed paraffin-embedded samples by qPCR. In wild type cases we performed NGS. 1p/19 codel analysis was performed by FISH.

Results: 93 consecutive LGG with IDH mutation and codel were included. The median follow up (FU) was 96.1 months. Mean age was 40 yrs (range: 25-66); 8 pts (8.6%) underwent biopsy, 61 pts (65.6%) partial resection, 24 pts (25.8%) complete resection. 84 pts (90.3%) were considered high risk using RTOG criteria (> 40 years and/or incomplete resection). Fifty pts (53.7%) received only FU, 17 pts (18.3%) received chemotherapy (CT), 18 pts (19.4%) received radiotherapy (RT), 8 pts (8.6%) received RT + CT. Median PFS (mPFS) was 59.6 months (95%CI: 41.8-77.4) and was significantly longer in pts who received postsurgical treatments (79.5 months, 95%CI: 66.4-92.7) than pts who received FU (46.3 months, 95%CI: 36.0-56.5; $P = 0.001$). mPFS was 50.8 months (95%CI: 17.4-84.3), 103.6 months (95%CI: 11.7-195.6) and 120.2 months (95%CI: 40.5-199.8) in pts treated with CT alone, RT alone and RT + CT, respectively. Multivariate analysis showed that receiving a post-surgical treatment ($P < 0.001$), and the extent of resection ($P = 0.043$) were significantly correlated with PFS.

Conclusions: Our study evaluated the role of treatments in LGG pts assessed with NGS and FISH. Post-surgical treatments are crucial to extend PFS in pts with IDH mutation and codel. The choice of post-surgical treatments seems to have a role, being CT alone less effective than RT and RT+CT. Longer FU is needed to provide information about OS.

M3 The role of clinical and molecular characteristics in low grade gliomas

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Background: - Low grade gliomas (LGGs) are rare tumors. Molecular characterization has been recently integrated into diagnostic workup of low grade gliomas (LGG) defining specific prognostic features. Moreover, clinical factors, such as age and the extent of resection have a prognostic role in LGG. Here we report a comprehensive analysis on clinical and molecular features impacting on outcome in a large cohort of LGG.

Methods: We evaluated adult LGG patients (pts) which occurred from 1991 to 2015, who received surgery and had sufficient tissue to assess molecular biomarkers characterization. We assessed the status of IDH mutation (using PCR or NGS) 1p19q codeletion (FISH), MGMT methylation (detected with PCR).

Results: 213 consecutive LGG were included. The median age was 38 (range:18−69). Median follow up was 98.3 months, 25 pts (11.7%) underwent biopsy, 124 pts (58.2%) subtotal resection, 64 pts (30%) grosstotal resection. According to RTOG criteria 37pts (17.4%) were low-risk (<40 years with complete resection), and 176 (82.6%) were high-risk. IDH1/2 mutation was found in 93% of pts. 1p/19q codeletion was found in 50.8% of pts, MGMT methylation in 65.3% of pts. Median progression free survival (PFS) was 47.8 months. Median survival was 211.0 months (95%CI: 185.7-236.3) and 164.0 months (95%CI: 123.0-205.0) in low risk and high risk patients patients. Significant factors in univariate analysis are listed in the table. Multivariate analysis showed that PFS was influenced by extent of resection ($P < 0.001$), IDH mutation ($P < 0.001$) and treatment. IDH mutation ($P < 0.001$) and extent of resection ($P = 0.029$) were significantly correlated with overall survival in multivariate analysis.

Conclusions: The definition of LGG outcome is complex. Both clinical and molecular factors are needed to determine prognosis and treatment strategies.

Table: M3

Variable	OS (months)	P	PFS (months)	P
IDH mutation	187.2 vs 32.2	0.001	50.8 vs 16.5	<0.001
1p19q codeletion	189.4 vs 164.0	0.015	57.1 vs 41.1	0.031
MGMT methylation	211.0 vs 148.7	0.013	56.0 vs 44.3	0.024
Surgery (complete vs biopsy)	211.0 vs 83.0	0.038	52.9 vs 40.0	0.011

M4 Worsening of quality of life (QoL), cognitive functions (CF) and psychological status (PSY) can predict radiologic progressive disease (RPD) in glioblastoma (GBM) patients (PTS) treated with radiation therapy (RT) and temozolomide (TMZ): a mono-institutional prospective study

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Background: Almost all of GBM PTS treated with RT and TMZ relapse during and after treatment. We performed a prospective study to assess if deterioration of QoL, CF and PSY is a predictor of RPD.

Methods: PTS with newly histologically diagnosed GBM treated with RT and TMZ as first-line therapy and KPS>60 were enrolled. PTS received TMZ for 12 cycles of until unacceptable toxicity or progressive disease. All questionnaires were given to PTS for self-assessment before performing MRI. Macdonald criteria were used for radiological evaluation. We assessed QoL, CF and PSY before starting treatment, at the end of RT and every 3 months until 9 months after the end of RT using EORTC-C30, BN-20, MMSE and HADS questionnaires. Brain MRI were performed at the same times.

Results: At our oncological center, Veneto Institute of Oncology, between January 2013 and December 2015, we prospectively enrolled 111 consecutive PTS; median age was 59; 69 PTS were male and 36 PTS aged ≥65. PTS showing a RPD reported lower physical functioning ($p = 0.018$), minor role function ($p = 0.0007$) and a lower global health status ($p = 0.01$) than patients without RPD. In addition, they reported greater uncertainty in the future ($p = 0.007$), increased drowsiness ($p = 0.013$), increased itchy skin ($p = 0.005$) and greater weakness in the legs ($p = 0.027$) compared with PTS without RPD. PTS with RPD resulted more anxious ($p = 0.0021$) and depressed ($p = 0.0001$) than the other PTS. The two groups significantly differed in the CF ($p = 0.0007$) especially, after 1 and 6 months after RT reporting worse results in the MMSE for PTS with RPD.

Conclusions: Worsening of QoL, CF and PSY can predict RPD in GBM PTS treated with RT and TMZ

M5 The role of treatments in IDH mutant molecular astrocytomas

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Background: Low grade glioma (LGG) is a heterogeneous disease. Recently, the 2016 WHO classification of brain tumors has underlined the role of genetic and molecular features. Molecular astrocytomas have been defined as grade II tumors with IDH mutation and without 1p19q codeletion.

Methods: We evaluated 213 consecutive patients with LGG who received surgery or biopsy and had adequate tissue to assess molecular characterization. IDH mutations were assessed by immunohistochemistry (IHC) and next generation sequencing (NGS) in IHC negative cases, MGMT methylation status was assessed by polymerase chain reaction (PCR) and 1p19q deletion was assessed by fluorescence in situ hybridation (FISH).

Results: 198 patients (93.0%) showed IDH-mutation. Ninety patients (49.2%) were 1p19q non codeleted (molecular astrocytomas). The median follow up was 98.3 months. Median age was 36 (range: 18-69), 11 patients (12.2%) underwent biopsy, 48 (53.3%) patients subtotal resection and 31 (34.4%) patients total resection. According to RTOG criteria, 68 patients (75.6%) were considered high risk (> 40 years and/or incomplete resection), and 22 patients (24.4%) were considered low risk (< 40 years and/or complete resection). 59 patients (65.5%) did not receive any post-surgical treatment, but only follow-up, 31 patients (34.4%) received post-surgical treatments: 20 (22.2%) received radiotherapy (RT), 7 (7.8%) received chemotherapy (CT), 4 (4.4%) received CT+RT. Median progression-free survival (PFS) was 44.3 months. Significant differences in PFS were observed between treated and untreated patients (64.8 vs 35.7 months $p = 0.004$) and treated with RT versus follow-up (60.0 vs 35.7 months $p = 0.004$). Multivariate analysis confirmed the treatment after surgery as an independent prognostic factor (HR 0.456, $p = 0.005$). Median overall survival (OS) was 164.0 months. At time of analysis no significant differences in OS were available.

Conclusions: Post-surgical treatment after resection of IDH mutant molecular astrocytomas is an independent prognostic factor. A longer follow-up is needed for worthy results in terms of OS.

M6 Suspicious for recurrent low and high grade glioma and indeterminate MRI: the role of 18F-DOPA PET/CT

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Background: The aim of present study was to assess the role of 18F-FDOPA PET/CT in patients who had a suspicious for recurrent low and high grade glioma but with an indeterminate MRI.

Materials and methods: From a monocentric database, we retrospectively analyzed 21 patients (median age: 60 yrs; 19-80) who underwent 18F- DOPA PET/CT for the restaging of low and high grade glioma. All PET/CT images were re-examined by two nuclear medicine physicians. Both visual and semiquantitative analysis was used for the interpretation of images. At visual analysis, PET/CT was defined as positive in case of a DOPA uptake in the lesion (identified by MRI) higher than controlateral striatum uptake. For the semiquantitative analysis, the ratios between SUVmax of the lesion and SUVmax of the striatum (T/S)/normal brain tissue (T/B) equal to 1 and 2 respectively were used. Clinical reassessment consisted of standard evaluation including MRI and assessment of neurological symptoms. The agreement between visual and semiquantitative analysis was obtained by k statistical analysis. Diagnostic performance was calculated by standard methods.

Results: Six patients had a low grade glioma and 14 a high grade. At visual analysis, 15 (75%) patients had a positive PET/CT result, in particular 4 with a low grade glioma and 11 with a high grade (67% and 79%, respectively). Based on semiquantitative analysis, 14 (70%) and 14 (70%) patients had a positive PET/CT, respectively for T/S and T/B. The agreement between visual and semiquantitative analysis was 88% ($p < 0.001$). In accordance with clinical reassessment available in 13 patients, 10 subjects had recurrence of disease. Sensitivity, specificity, positive and negative predictive value of PET/CT based on visual and semiquantitative analysis were 90%, 100%, 100% and 75% versus 80%, 100%, 100% and 60%, respectively.

Conclusions: In patients with suspicious for recurrent low and high grade glioma, DOPA PET/CT has a high sensitivity and specificity. Therefore, in case of indeterminate MRI, DOPA PET can anticipate the presence of recurrent disease useful for the treatment planning.

M7 18F-sodium fluoride (18F-NaF) PET/CT scan for the assessment of brain metastases (BMs)

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Background: ^{18}F-NaF does not distribute to normal brain but it can be uptaken by BMs. This data suggests that it can cross the blood-tumor barrier (BTB). However, whether the ^{18}F-NaF uptake is reflective of BTB permeability, possibly indicating the entity of drugs penetration into BMs and therefore representing a predictive tool of response, is still unknown. We did the present study with the aim to investigate the potential predictive and/or prognostic role of the ^{18}F-NaF uptake by BMs.

Patients and methods: From November 2014 to July 2016, 28 patients (pts) with MRI-documented BMs from different solid tumors (13 lung, 9 breast, 4 genitourinary, 2 other primaries) were enrolled in the study and underwent ^{18}F-NaF PET/CT scan using a 40-minute dynamic acquisition protocol. Area under the curve (AUC) of SUVmean was calculated for BMs (AUC^{BM}) and for internal carotid artery (AUC^{ICA}). We used the AUC^{BM}/AUC^{ICA} ratio (BM/ICA ratio) for estimating ^{18}F-NaF penetration of BMs. The median value of BM/ICA ratio was established as the cut-off, with a value higher than the cut-off indicating high ^{18}F-NaFpenetration. Pts received investigator-choice treatment for BMs and response was assessed by brain MRI according to RECIST criteria.

Results: ^{18}F-NaF PET/CT scan identified 75 out of the 130 BMs with a diameter $\geq$ 5 mm (i.e. PET spatial resolution) detected with MRI with a sensitivity of 0.58 and a positive predictive value of 1.0. A patient with only 1 BM less than 5 mm had a negative ^{18}F-NaF PET/CT scan. Among 27 evaluable pts, 11 pts had 1 BM, 8 pts 2-3 BMs and 9 pts $\geq$ 3 BMs. The BM/ICA ratio cut-off was 0.53. As treatment for BMs, 4 pts received chemotherapy alone, 10 radiotherapy alone, 1 surgery alone and 12 had a multi-modal treatment. There was no significant difference in terms of RR, PFS or OS according to BM/ICA ratio.

Conclusions: To our knowledge, this is the first study of ^{18}F-NaF PET/TC scan for the assessment of BMs. BM/ICA ratio indicating ^{18}F-NaF penetration of BTB was not predictive nor prognostic in pts with BMs. However, pts enrolled in this study were widely heterogeneous in terms of primary tumor, number of BMs and treatment, and such heterogeneity could have affected the results.

M8 Concomitant versus sequential Fotemustine and Bevacizumab in recurrent malignant gliomas: treatment response and survival outcomes in a retrospective analysis

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Background: Despite the standard therapy of newly-diagnosed maglignant gliomas (MGs), recurrence rate remains high (~90%) and the treatment of recurrent MGs is still a clinical challenge. Nitrosoureas, mainly fotemustine (FTM), have been employed in monotherapy or in combination with other agents, including bevacizumab (BEV).

Materials and methods: We performed a retrospective analysis of 26 recurrent MGs patients (20 Glioblastoma multiforme and 6 Anaplasic gliomas) treated with concomitant or sequential FTM and BEV (cFTM/BEV and sFTM/BEV respectively) as second-line therapy after first-line with radio-chemotherapy as Stupp protocol. Efficacy was evaluated as median progression free survival (mPFS) and overall survival (mOS) with best response to MRI assessment (complete/partial response − CR, RP − and disease control rate − DCR). Subgroup analyses according to MGMT status were performed.

Results: Patients treated with the combination of FTM and BEV, both as concomitant and sequential scheme, had a mPFS of 9 months and a mOS of 11 months. Patients treated with cFTM/BEV (n = 13) experienced longer mPFS (8 vs 5 months; p = 0.2) and mOS (12 vs 6 months; p = 0.2) compared to sFTM/BEV patients (n = 13). PFS at 6 months was of 31% for sFTM/BEV and 62% for cFTM/BEV while PFS at 1 year was of 15% and 23% respectively. OS at 1 year was of 23% for both groups. With sFTM/BEV, RP was observed in 38% of patients with a DCR of 62%. With cFTM/BEV one CR (8%) and 9 RP (69%) were assessed with a DCR of 85%. Methylated MGMT patients (n = 12) had longer mPFS (11 vs 6 months; p = 0.2) and mOS (15 vs 6 months; p = 0.1) compared to unmethylated patients (n = 7) independently of type of treatment. Methylated patients treated with cFTM/BEV (n = 4) experienced longer mPFS (8 vs 5 months) and mOS (p = 0.08) compared to methylated patients treated with sFTM/BEV (n = 8).

Conclusion: In recurrent MGs the concomitant association FTM/BEV provide a survival and response benefit compared to sequential therapy FTM/BEV. Methylated patients experienced longer survival outcomes with the concomitant scheme of FTM/BEV.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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N - NEUROENDOCRINE TUMOURS

N1 Prognostic relevance of VEGF, VEGFR, IGF and IGFR immunohistochemical expression in gastroenteropancreatic neuroendocrine tumors

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Background: angiogenesis represents a peculiar trait of gastroenteropancreatic neuroendocrine tumors (GEP-NETs). We aimed to analyze the immunohistochemical expression of angiogenic markers on tumor tissue and their potential prognostic role in GEP-NETs.

Methods: we selected 28 patients with available material (excluding biopsies and small samples). The immunohistochemical evaluation involved the use of 6 monoclonal antibodies: anti-VEGF, Flt-1, Flk-1, Flt-4, IGF-1 and IGF-1R.

Results: Median age was 60 (range 29-79), 24 cases (85%) were pancreatic NETs and 17 patients were male. Statistical analysis revealed a significant correlation between low-positive VEGF immunostaining (1+) and DFS compared to higher positivity (2+ and 3+) ($p = 0.0301$ HR: 0.2291); furthermore, subjects with a higher percentage of positive cells (more than 50%) showed a trend towards worse DFS ($p = 0.2681$; HR: 0.4433). Our analysis also showed a trend towards worse DFS in patients with immunohistochemical positivity for IGF-1R regardless of the intensity ($p = 0.1151$; HR: 0.3274). Finally, patients were stratified in two subgroups according to the presence of all the immunohistochemical staining with negative prognostic value identifying a group 5 patients (17.9%) with median DSF of 9.2 months compared to 46.0 months in the remaining population ($p = 0.0093$; HR: 0.1763).

Conclusions: Our results suggest that specific immunohistochemical characteristics might influence the aggressiveness of GEP-NETs identifying a specific subgroup characterized by poor prognosis. These results should be validated prospectively in order to better stratify patients with GEP-NETs in order to offer a more personalized therapy improving outcomes and quality of life.

N2 Retrospective analysis of the therapeutic efficacy of platinum/etoposide schedules in the treatment of advanced poor differentiated neuroendocrine carcinomas of the lung

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Background: Neuroendocrine carcinomas (NEC) of the lung are usually associated with a dismal prognosis. Few studies evaluated the impact of platinum/etoposide combination in NEC, including those of lung origin. However, little advances have been made in the last few decades and it is still unclear whether the outcome of such patients (pts) has been improved. The aim of our study was to evaluate the outcome of pts with advanced NEC of the lung treated at two Italian institutions with a platinum/etoposide combination.

Patients and methods: We retrospectively evaluated 68 consecutive pts with histological-confirmed advanced/metastatic neuroendocrine carcinomas of the lung treated with platinum/etoposide chemotherapy between September 2006 and December 2016. We collected clinic-pathologic characteristics, treatments, and outcome of all pts. Statistical differences were considered significant with a p value < 0.05.

Results: We included in the present study 68 pts with pulmonary NEC (82% SCLC; 18% LCNEC). Median age was 67 years (range 45-80 years), 81% were male and 19% were female, ECOG PS was 0-2 in 97% of pts and 3 in 3%. Stage distribution at diagnosis: stage IV 91%, stage III 9%. Symptoms at diagnosis were present in 63/68 pts, including cough (25%), tumor pain (35%), dyspnea (36.5%). Cisplatin/etoposide was used in 50% of pts, and carboplatin/etoposide was used in 50% of pts. Median number of chemotherapy cycles were 4 (range 1-8). 18% of pts required a dose reduction. Major toxicities in evaluable pts were as follows: hematological 70.5%, gastrointestinal 26.5%, and fatigue 18%. ORR was 39% (5% CR), DCR was 73%. Pts receiving a second line therapy after progression were 44%. Fifteen percent of pts were still alive at the time of the present analysis. Median PFS with platinum/etoposide was 5.0 months (mos) (range 1-70). Median OS was 9.0 mos (range 1-70). Median PFS and OS did not differ between cisplatin and carboplatin groups ($p = 0.192$ and $p = 0.191$, respectively).

Conclusions: Data presented here confirm the poor outcome of pts with lung NEC in a large retrospective cohort confirming the results of previous reports in a similar population. Moreover, our data did not evidence any significant difference in terms of efficacy. These data suggest that cisplatin- and carboplatin-based chemotherapy at the moment remain the standard of therapy for advanced lung NEC, but novel therapeutic strategies should be pursued.

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P - PREVENTION, SCREENING AND FOLLOW-UP

P1 Sharing long term follow-up of breast cancer survivors with family physician: a province of Lecco experience

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Background: Breast cancer (BC) is commonly diagnosed at early stage and more than 80% of patients (pts) are long-term survivors. Most cancer society guidelines recommend a non-intensive follow-up, that, after 5 years from diagnosis, consists of annual medical history, physical examination and surveillance mammogram. The role of family physician in the management of BC follow-up is still under discussion.

Material and methods: Since 2013, we have launched a shared BC survivor follow up program involving family physicians working in the Province of Lecco. Pts with diagnosis of early BC have been referred to their family physician to continue surveillance with annual physical examination and mammogram at the completion of adjuvant treatment and after at least 5 years of follow-up, if no clinical evidence of disease recurrence was present. In case of suspicious disease recurrence, a direct access to our oncology unit has been offered.

Results: From May 2013 to March 2017, 643 women have been enrolled in our program. All pts were disease free (as per clinical assessment), had completed adjuvant treatment and at least 5 years of follow-up at the time of enrollment. 11% of pts had ductal carcinoma in situ, 66% invasive ductal carcinoma, 7% invasive lobular carcinoma and 16% other histologic subtypes. 11% was hormonal receptor negative and 7% was HER2 positive. 44% was G2 and 34% G3. 25% received chemotherapy followed by hormonal treatment, 9% received adjuvant chemotherapy alone and 61% received hormonal treatment alone. Median follow up time was 8 years (range 5-23 years). 10/643 (1,6%) pts experienced BC recurrence: 3 had distant metastasis, 4 unilateral breast recurrence and 3 contralateral. Those with local recurrence underwent breast surgery followed by adjuvant chemotherapy in 1 case, chemotherapy and hormonal treatment in 1 and hormonal treatment alone in 5. Pts with distant metastasis are still alive and currently on treatment (1 with chemotherapy, 2 with hormonal treatment).

Conclusion: This preliminary analysis has shown the feasibility of our program with a significant number of pts referred to their family physicians, reducing the need for specialist follow-up. Only a small proportion of pts experienced subsequent relapse requiring reassessment by the treating oncologist. Further analysis is planned to define the adherence to the shared follow-up.

P2 Post-survey data about "I do not smoke it", smoking prevention campaign addressed to schools

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Introduction: According to *Il fumo in Italia* (DOXA-Italian Institute of Health survey, 2016), most smokers try their first cigarette in the range from age 15 to age 17 (56.8%). The main reason why people start smoking is emulation (60.7%). There is the need to strengthen the work of the healthcare professionals in preventive care about cigarette smoke. Considering these, WALCE (Women Against Lung Cancer in Europe), since 2011, promotes "I do not smoke it – We shall try to see things clearly in the smoky speeches", an information campaign on damages of smoking, aimed at 9-11 year-old pupils in Primary schools.

Materials and methods: After the administration of a questionnaire and the use of the educational kit we asked to some teachers to administer a post-survey to pupils, in the 2015-2016 school year. We analyzed 253 surveys: 76 questionnaires from 9 years-old Primary school pupils; 137 from 10 years-old Primary school pupils; 40 from 11 years-old Lower Secondary school pupils. Surveys were filled in by 130 male (51.38%) and 123 female pupils (48.62%), in schools of 3 different Italian regions (Piemonte, Veneto and Puglia).

Results: 81% of pupils believes that this type of intervention is useful as prevention action, 8.7% thinks that cigarette smoke only harms those who smoke, 1.6% thinks that smoking improves performance in sports and 9.5% thinks it can help to lose weight. Answers to the question "*In your opinion, is it possible to quit smoking?*" are encouraging: 77% responded "*Yes*", 21.3% "*No*". Analyzing in the different classes the reasons why people start smoking: "*to be cool*", with percentages of 60.5%, 76.6% and 82.5%, in the fourth, firth grade of Primary school and in the first grade of Lower Secondary school, respectively. Other reasons reported in high percentages were: "*to imitate adults*" and "*to feel accepted*". When asked, "*What do you think is more dangerous for you?*", "*smoking a cigarette*" was the most answered response.

Conclusions: Several health education studies have shown that prevention programs addressed to school are more effective if conducted by the teachers. It is known that young people, especially during the adolescence, try to put in practice behaviors that allow them to affirm their identity and build a network of social and affective relationships. For this reason, health promotion and behavioral prevention activities, implemented in schools and at home by families are crucial to avoid to endanger the well-being of tomorrow's adults.

P3 Genetic counseling for BRCA1/BRCA2 testing

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Backgroung: Increasing evidence supports the benefit of identifying BRCA1/2 mutations in Hereditary Breast and Ovarian Cancer (HBOC) either for implementing prevention strategies and for the recent availability of target therapies.

Material and methods: From May 2013, a Multi-disciplinary Counseling (medical oncologist, genetist, psycologist) for HBOC has been undertaken in our Department. Screening for select individuals to be tested is carried out through a multistep process by collecting a detailed personal and family history, drawing the family tree and determining the genetic risk. The BRCA1/2 genes were analyzed by DNA-Sequencing and by Multiplex ligation-dependent probe amplification. From May 2013 to April 2017 a total of 251 patients (pts) and 99 healthy individuals have been seen. The 251 cancer pts were: 187 Breast (BC):178 women+9 males, 36 Ovarian (OC), 16 Colon (CC), 6 Thyroid (TC), 3 Uterine (UC), 1 Gastric (GC), 1 Pancreatic, 1 Lung (LC). Eighteen of the 187 pts with BC had another tumor: 6 OC, 6 TC, 2 UC, 1 NHL, 1 HL, 1 LC, 1 CC. One of the 16 pts with CC had a Prostate cancer (PC) too. One triple tumor was studied: PC + GC + TC.

Results: BRCA1 pathogenic variants (BRCA1+) were detected in 10.3% (26/251) of pts: 14 women BC, 8 OC, 1 TC, 1 CC. Two more pts had a double tumor (BC+OC). BRCA2 pathogenic variants (BRCA2+) were detected in 7.1% (18/251) of pts: 12 women BC, 1 male BC, 3 OC. Two more women had a double tumor: BC + LC, BC + TC. A total of 19 BRCA1+ and BRCA2+ families were studied: BRCA1+ and BRCA2+ were seen in 10 and 11 healthy individuals, respectively. Prophylactic bilateral mastectomy (PM) + bilateral salpingo-oophorectomy (SO) were performed in a healthy woman BRCA1+ during a single operative session. PM was performed in a CC BRCA1+ and in a OC BRCA2+. The SO was performed in 2 BC: 1 BRCA1+ and 1 BRCA2+.

Conclusions: Clinical testing for mutations in BRCA1/2 remains the most prominent example of the use of human genetic variation to prevent cancer and reduce disease risk. The goal of pre-test genetic counseling is to ensure the patients having sufficient information to make a decision about being tested. On the other hand, at results disclosure, during post-test genetic counseling, individuals can learn their results along with information about cancer risks and surgical and medical management options. In our opinion, the clinical BRCA1/2 testing programs should include pre- and post-test genetic counseling.

P4 Hypercoagulable state as marker of occult cancer in healthy blood donors: data from HYPERCAN Prospective Study

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Background: HYPERCAN is an ongoing prospective Italian, multicenter, observational study structured in two sub-projects that involve non-cancer and cancer subjects. Aim of this part is to establish whether the persistence of a hypercoagulable state in healthy subjects as detected by laboratory thrombosis markers, may predict for an increased risk to develop cancer.

Material and methods: Healthy Italian blood donors from Bergamo and Milan areas are enrolled and followed-up for 5 years for the occurrence of cancer. Blood donors are periodically screened for serological, biochemical and clinical parameters, and tested for viral infections. We plan to enroll 10,000 donors of both gender, age range 35-65, in 5 years. Whole blood is collected at the enrollment and after 6-12 months. Clinical data (BMI, current drugs, comorbidities), hematological and biochemical parameters are

collected. In addition, subjects are asked to fill in a questionnaire about their lifestyle. Identification of all malignant tumors is carried out every 6 months.

Results: Between April 2012 and April 2017, 7,328 blood donors (71% males; median age 48 yrs) have been recruited. Most of the donors had biochemical and hematological parameters into the normal range. The analysis reveals that 57% of the donors were not smokers, 15% regular smokers, 28% ex-smokers; 49% of them were moderate alcohol consumers (=2 drink/die). At now, after a median follow-up of 2.8 years, we recorded a total of 50 cancer cases (35M/15F). The most frequent tumor type in male donors is prostate (27.0%), followed by colorectal (16.2%) and thyroid (10.8%) cancers, while in females, the most frequent is breast cancer (41.6%). Both in males and females the most frequent tumor is the same compared to the general population in Bergamo and Milan area. Interestingly, we observed that the occurrence of tumor correlate with educational status ($p < 0.05$). According to hematological parameters, tumor cases had significantly lower red blood cell counts and higher values of glycemia and cholesterol compared to healthy population ($p < 0.05$).

Conclusions: The enrollment of healthy donors and follow-up is ongoing, as well as the identification of new cancer cases. Next, according to the original plan, samples from 3 matched cancer-free donors for each cancer−case donor will be analyzed in parallel for hypercoagulation markers.

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P5 Occurrence of ultrasound-detected symptomatic and asymptomatic central vein catheter-related thrombosis in pediatric oncology patients

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Background: Pediatric oncology patients are more likely to develop venous thromboembolic events CVC−related, but the incidence of CVC-related thrombosis (CRT) is still under debate. First objective of this perspective monocentric study is to investigate the incidence of symptomatic and asymptomatic CRT using Doppler Ultrasound and evaluate the possible risk factors linked to this pathology.

Methods: This study was performed on all paediatric patients with cancer, aged< 18, requiring CVC implantation for chemotherapy infusion, from October 2015 to December 2016 in Istituto Nazionale Tumori of Milan. All patients underwent US examination at 15, 30 and 90 days after implantation.

Results: A total of 114 medium - long term CVC were inserted into 104 patients (median age; range: 9.5; 0.4-17 years). Patients have been followed up for an average of 269 (range: 11-503) days. Incidence of asymptomatic CRT was 0.11 (0.03-0.33) events for 1000 catheter-days. Only three cases of thrombosis were identified with Doppler Ultrasound screening. In no patient symptomatic DVT occurred. The only common risk factor in these cases was the presence of a previous catheter-related infection (p value= 0.0018).

Conclusion: Despite the high risk of CRT associated with the considered sample, the incidence of symptomatic and asymptomatic thrombosis in our patients is very low, especially when compared to other studies. Following these results, the role of US surveillance for the prevention of CRT could be revaluated, perhaps limiting it to patients with previous CVC-related complications. Possible limitations of this study are the limited number of patients and the limited follow up.

P6 Observational case-control study about the adherence to the Mediterranean diet in elderly oncological patients in Salento

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Background: Mediterranean Diet (MD) is the only alimentary model that could prevent degenerative chronic disease and cancer. We analyzed the alimentary habits of elderly oncological patients (pts), compared to healthy elderly pts, to evaluate the correlation between the adherence to MD and cancer development, due to the high incidence of tumor in Salento.

Matherials (patients) and methods: 293 (155 males, 138 females) oncological pts (=70 years) were enrolled in the Oncology Unit of Vito Fazzi Hospital in Lecce and 135 elderly pts (=70 years) without cancer diagnosis. Predimed test was used to evaluate the alimentary habits and to define the adherence to MD, using 14 questions (score 0-14). A value =7 was estimated as low adherence, 8-9 as median adherence, =10 as high adherence. Oncological pts showed the subsequent diagnosis: lung, prostate, breast, urinary tract, gastric, colorectal cancer.

Results: The main fat sauce in diet is extra-virgin olive oil (98% of pts). 37% of pts eat almost 2 times/die vegatables and 50% almost 3 times/die fruit. 71% of pts eat less that 1 time/die red meat, hamburger and sausages and 86% eat less than 1 time/die butter, margarine or cooking cream. During a week, 43% of pts drink > 7 glasses of red wine, 22% eat 3 times legumes and 15% eat fish more than 3 times. 44% eat less han 3 times/week cakes and 34% eat dried fruit. 59% eat white meal and 90% eat more than 2 times/week vegatables, pasta or rice. Low adherence to MD is showed for oncological pts and healthy pts in 46% and 15% respectively, median adherence 25% and 48%, high adherence 28% and 36%.

Conclusions: In healthy pts a higher adherence to MD was observed and they eat more vegetables, fruit and red wine, compared to oncological pts. Both pts groups eat low quantity of fish and legumes. Pts with urinary tract cancer shows a diet rich of vegetables (more than 2 times every day): this could be related to the ingestion of pesticides used in farming. Gastric cancer pts showed a low use of onion and garlic, so an protective role in development of this disease is confirmed (as previously demonstrated in literature). Healthy women drink more red wine than breast cancer pts: red wine polyphenols could prevent the breast cancer disease. The results of this study suggests that could be a relationship between the adherence to MD and the incidence of tumor, but further studies, in a several number of pts, are necessary to confirm this hipothesys.

P7 The follow-up and lifestyle (FUCSAM project). Oncology Network of Piemonte and Valle d'Aosta: update 2017

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Background: Lifestyle factors can benefit not only the quality of life of cancer survivors, but also overall survival, and decrease the risk of recurrence from cancer. Integrating life-style support into standardised models of aftercare for cancer survivors is a challanging purpuse.

The FUCSAM project (osservational study) aims to assess the impact of an intervention designed to change the lifestyle of patients in follow-up after treatment of colorectal and breast cancer followed by different Interdisciplinary Groups and Care.

Material and methods: Eligible patients: diagnosis of breast or colorectal cancer (histologically confirmed), at first follow-up after surgery and adjuvant medical therapy (if indicated), free of disease, able to walk and with informed consent. Data detected: personal, therapies, comorbility, stage at diagnosis, anthropometric, clinical and bioumoral parameters, adherence to programs on lifestyle, changes carried out by local Patients Associations. All patients were handed information brochures and recommended adherence to specific programs, if any. The collection of information has been replicated at subsequent follow-up visit.

Results: Until now 19 local hospitals have joined the FUCSAM project after of the ethics committee approval. Patients enrolled are **1615** (304 colorectal cancer, 1311 breast cancer) and 78% are < 70 years old. Among 1265 women in the mammography screening age group (50-69 yrs) 352 (28%) had the diagnosis through the locale screening program, while among 289 subjects in the colorectal cancer screening age group (58-70 yrs) 42 (15%) subjects were diagnosed through the organized programme.

Information brochures were delivered to 95% of the patients in the study.

Conclusions: Although at the beginning, the first study results show that the introduction of lifestyle recommendations within the follow-up protocols is feasible. After diagnosis of cancer, people are more inclined to consider the relationship between their behavior and the effects on health. To encourage the adoption and maintenance over time of new habits, the Oncology Network of Piemonte and Valle d'Aosta will plan to provide practical guidance for the realization of the desired changes.

P8 Breast cancer secondary prevention: get fit to feel healthy

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Background: Healthy lifestyle, including caloric restriction, balanced diet and physical activity, is important in primary and secondary prevention of breast cancer (BC). It is known that Mediterranean diet reduces metabolic syndrome and insulin resistance that are associated with increased risk of BC onset and recurrence. Physical activity decreases BMI, blood concentrations of testosterone, estrogens, insulin, its resistance and strengthens anti-inflammatory pathways against tumor cells.

The aim of our study was to evaluate the clinical impact of healthy lifestyle promoted by a project named "Lifestyle Programme" created in our Centre.

Patients and methods: 67 women with BC who underwent primary surgery in our Centre were enrolled between January 2014 and July 2016. We included the ones who had high risk of recurrence due to BMI ≥25, increased levels of testosterone and/or insulin or metabolic syndrome and we evaluated them every six months after first assessment. The project involved oncologist (performing oncologic anamnesis, laboratory exams and HADS score for anxiety and depression), dietician (performing

nutritional anamnesis and providing an hypocaloric diet) and physiatrist (questioning about ordinary physical activity, applying 6 minutes walking test, brief fatigue inventory test and Borg respiratory and muscular score and providing a personalized physical activity program). All collected data were analyzed by Chi-square test assuming statistical significance at $p < 0.05$.

Results: Most of BC had positive hormonal receptors (Luminal phenotype 85.1%) and high proliferative index (62.7% with Mib-1 >20%); 55.2% of patients were in stage I. We observed a statistically significant reduction of BMI, body weight and waist circumference between every single evaluation. These results are associated with a significant reduction of glycemic ($p = 0.0405$) and insulin levels ($p < 0.0001$) in the first six months of observation. Total HAD score and the specific one for anxiety were significantly reduced during the first six months of observation ($p < 0.0001$ and $p < 0.0064$). 72% of patients increased their physical activity levels in the first six months of observation and 20% of them referred a clinical benefit regarding arthralgia ($p = 0.4459$).

Conclusions: BC in overweight women have aggressive features despite early stage. These data demonstrate that healthy lifestyle can reduce risk factors implied in disease recurrence and assure psychological benefit improving quality of life.

P9 Three-monthly dynamic evaluation of CEA and CA15-3 and 18-FDG PET vs usual practice in the follow-up of early breast cancer patients: a prospective, multicenter, randomized trial (KRONOS – Patient-Oriented New Surveillance-Study Italy)

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Background: Current guidelines for breast cancer (BC) surveillance in asymptomatic patients (pts) recommend only annual mammography and periodical physical examination. These recommendations arise from trials conducted in the 1980's: since then our knowledge on breast cancer biology, diagnosis of metastases and treatment has deeply improved. The aim of this prospective randomized trial is to verify if the serial measurement of CEA and CA15-3 followed by 18-FDG PET can anticipate the diagnosis of BC recurrence compared to control arm by estimation of the difference of restricted mean survival time (RMST) between the two arms. If the end-point will be met a subsequent extension trial will investigate the impact of the earlier diagnosis of distant metastases on survival.

Methods: Pts diagnosed with stage I-III BC, who underwent adequate surgery are eligible. Special histologies and low-risk cases according to St. Gallen criteria are excluded. The study includes pts at the beginning of the follow-up after the conclusion of primary treatment (cohort 1), and pts that have concluded without relapse the first 5 years of follow-up (cohort 2). Eligible pts will be randomized in a 1:1 ratio to follow-up according to local practice (control arm) or to three-monthly serial dosing of CEA and CA15-3 and subsequent 18 FDG-PET only in case of an increase of CEA and/or CA 15.3 greater than a critical difference compared to baseline (experimental arm). The following stratification factors will be used: node negative *vs* positive, HER2 negative *vs* positive, ER positive *vs* negative. Eight-hundred pts will be enrolled over 3 years. For such a calculation, we made the assumption of a 20% baseline 5-year incidence of relapse. The target reduction of three months in RMST implies a median time of diagnostic anticipation, conditional on having BC recurrence, of 10 months. The follow-up will continue until 10 years from surgery. Since 23rd October 2014 625 pts have been enrolled. The present trial was approved by the Ethical Committee of each participating centre and is registered on clinicaltrials.gov (NCT02261389).

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R - PSYCHOLOGICAL AND PSYCHOSOCIAL ASPECTS

R1 The effect of loneliness on cancer mortality

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Background: Convergent findings indicate the need of broadening the vision of cancer beyond known prognostic factors, as many variables of different nature equally affect the course of disease. Loneliness has been found to be associated with various health outcomes, but its relationship with cancer remains unclear. Here we aimed to investigate the specific effect of loneliness and other demographic, psychological, and clinical variables on cancer mortality and to validate the Italian UCLA Loneliness Scale in cancer patients.

Methods: This descriptive and correlational study was conducted at the Veneto Institute of Oncology in Padua. 400 cancer patients undergoing chemotherapy from 01/2014 to 06/2015 were enrolled. The sample was stratified by sex and age (4 groups, 40-80 y). We collected demographic, clinical (site and stage of cancer, type of chemotherapy, death date), and psychosocial [self-esteem (RSE), perceived social support (MSPSS), social interaction anxiety (SIAS), personality (EPQR), and depression (BDI)] data.

Results GLM analyses: loneliness was higher in women than men ($F(1,398) = 7.5$, $p = .006$) and it linearly increased with age ($F(1,398) = 10.9$, $p = .001$). Loneliness was also influenced by marital status ($F(3,396) = 2.9$, $p = .037$), cohabitant offspring ($F(1,398) = 7$, $p = .008$), and educational level ($F(3,396) = 4.7$, $p = .003$), but not by clinical variables (all ps > .05). Correlation analyses: loneliness was inversely related to RSE ($r = -.51$), MSPSS ($r = -.52$), and extroversion ($r = -.32$), and directly related to SIAS ($r = .46$), neuroticism ($r = .43$), and BDI ($r = .44$). More importantly, a hierarchical binomial logistic regression revealed that patients' mortality was reliably predicted by gender, stage of cancer at diagnosis, time from diagnosis to UCLA collection, BDI, and UCLA (HL? $2(8) = 3.53$, $p = .90$). In particular, high BDI predicted higher mortality (Wald = 11.6, $p < .001$); surprisingly, after controlling for BDI and other effects, high loneliness predicted lower mortality (Wald = 7, $p = .008$).

Conclusion: Our results are in line with prior research. Importantly, the present results also reveal a surprising association between loneliness and mortality risk after partialling out the impact of sex, age group, cancer stage, time since diagnosis and, especially, depression.

R2 Evaluating depression in elderly patients with cancer

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Background: Depression is one of the most common psychiatric disorders in elderly people, especially among oncologic patients, yet it often goes unrecognized. Performing a comprehensive geriatric assessment (CGA) is recommended to identify medical, psychosocial, and functional limitations of a frail older person. The aim of the present study was to assess associations between depressive symptoms and other variables of CGA in a population of elderly oncologic patients.

Patients and methods: We considered all patients who underwent a CGA in the Geriatric Clinic of Trieste Maggiore Hospital over 2 years on request of the oncologist. We registered age, sex, cancer type and evaluated functional, cognitive, nutritional, comorbidity and affective status respectively through ADL (Activities of Daily Living), IADL (Instrumental Activities of Daily Living), MNA (Mini Nutritional Assessment), CIRS (Cumulative Illness Rating Scale), MMSE (Mini Mental State Examination) and GDS (Geriatric Depression Scale). First we identified associations between the presence of depressive symptoms (i.e. GDS>5) and CGA variables through Wilcoxon's non parametric test; then we used a generalized linear model to test independence. Finally we evaluated the ability of two screening tools that are commonly used to detect frailty among elderly oncologic patients to identify depressive symptoms (G8 screening tool and Vulnerable Elderly Survey 13).

Results: 147 patients completed CGA. Of these 39 (26.5%) had significant depressive symptoms. Worse functional, nutritional, cognitive and comorbidity status was significantly associated ($p < 0.05$) with depressed mood, but only nutritional status was an independent predictor. G8 screening tool and VES 13 had a sensitivity and specificity respectively of 92, 22% and 54, 72%.

Conclusions: Our study confirmed that among elderly patients with cancer depression is associated with cognitive, nutritional and functional decline and greater comorbidity burden. The significant association with MNA highlights the vicious circle between malnutrition and depression. Given its high sensitivity, G8 screening tool could be a useful instrument to identify as soon as possible this condition with use of specific assessment scales.

R3 Music intervention during chemotherapy infusion reduces anxiety in oncological patients

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Background: Oncological patients frequently react to cancer diagnosis and treatments, including chemotherapy, by developing disturbing emotional symptoms such as anxiety. Anxiety for chemotherapy may induce anticipatory side effects, such as emesis and fatigue. Music is considered a common "complementary therapy" in various clinical settings (i.e. surgery, radiation therapy and chemotherapy) able to reduce anxiety, lessen treatment side effects, improve mood, and enhance pain management. Moreover, music may have a beneficial effect on heart and respiratory rate and blood pressure. The present study was aimed to investigate the effects of music intervention upon some physiological and psychological parameters, especially anxiety, in cancer patients during chemotherapy administration.

Methods: Between October 2015 and May 2016 a quasi-experimental study was conducted on a total of 100 patients at the Medical Oncology Unit of the Tor Vergata Clinical Center. Patients were randomly assigned to one of the following: 1) music intervention group (n = 50) and 2) control group (n = 50).

Procedure: Patients were asked to respond to some self-reported questionnaires (State-Trait Anxiety Inventory, Visual Analog Scale for Pain intensity) and physiological parameters were registered (blood pressure, heart rate, respiratory rate). Pre- and post-test data were thus collected. Measurements on the experimental group were recorded twice: prior to T0 and after music medicine intervention, which was characterized by passive listening to pre-recorded music for a period of 45 minutes (T1) during chemotherapy administration. Measurements on the control group were also recorded twice at the same time points, but without music.

Results: Statistically significant differences were observed in mean change of State-Trait Anxiety Inventory scores between the music and the control group (F 9.55; $p = 0.003$). Although significant decreases were observed in heart rate ($p = 0.027$), no significant differences were seen as regards blood pressure, respiratory rate or pain perception.

Conclusion: Music intervention during chemotherapy administration decreased the state of anxiety levels and heart rate in oncological patients, showing that a simple environmental intervention can promote psychological well being and quality of life improvement.

Acknowledgement: this study was carried out within the PhD program in Experimental Medicine and Systems (XXIX cycle, Medical Oncology Course)

R4 Risk and protective factors for the construction of prenatal attachment in women with oncological diagnosis during pregnancy: an exploratory observational study

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Background: Prenatal attachment begins with the mental representation of the foetus and develops with the construction of an emotional bond between the mother and her unborn baby. The quality of prenatal attachment has an important influence both on the neuropsychological and emotional development of the child and subsequently on the mother-child interaction. Although only a few studies have been carried out on the psychological aspects of oncologic diagnosis during pregnancy (Vandenbroucke et al., 2016) it is possible to consider it "a challenge" for the construction of this bond (Attril, 2012) since it is linked to a loss or weakening of those factors that are necessary for women to deal posirively with gestation. The aim of this study is to investigate possible risk and protective factors associated to prenatal attachment in women with oncological diagnosis during pregnancy.

Material, patients and methods: At present, 10 mothers with oncological diagnosis (9 with diagnosis of breast cancer, one with hepatic PEComa) have been enrolled. Recruiting took place at the European Institute of Oncology and ASST Bergamo Est. Prior informed consent, women filled out questionnaires to investigate the quality and intensity of prenatal attachment, affective states such as depression, confusion and fatigue, perceived social support and the role that pregnancy has on their lives.

Results: Preliminary correlational analyses showed a negative correlation between the intensity of prenatal attachment and negative affective states, particularly depression (r = - .846, p = .344), confusion (r = - 871, p = .024) and fatigue (r = .947, p = .004). Moreover, a positive correlation between maternal attachment quality and perceived support by their partner (r = .804, p = .016) was found. Finally, the more pregnancy is perceived as a turning point in their life, the better the quality of prenatal attachment (r = .926, p = .016).

Conclusions: These preliminary data indicate that in addition to providing medical support to these patients it will be important to consider their experiences, their psychological adaptation to pregnancy as well as the perceived social support. It will be necessary to implement research in this direction, considering possible intervening variables, in order to structure targeted interventions aimed at supporting parenthood in the prenatal and postnatal period.

R5 Evaluation OF psychological aspects of taking care cancer patients: a multicentre study on a sample of caregivers

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Every day about a thousand people receive a cancer diagnosis (AIOM,AIRTUM,2016).The cancer is one of the disease that most of all represent a serious danger for the human life and arises as one of the most stressful and traumatic events with witch who is hit must deal with.When a pathology hits a person, immediately the whole family and all his internal and external relations are involved.The family is the first relational network and the first subjective dimension of the individual, indeed, when a member is hit from an oncologic pathology, the whole family "lives" the disease and this could play a determinant role on how the illness is faced and lived.The oncological disease forces the family to face an incredibly amount of stress or changes on daily activities.Supporting caregivers so they can deal with their relatives' cancerous condition is useful to improve both patient care and collaboration with medical teams.

San Raffaele Hospital's Clinical and Health Psychology Service, developed a study to make a psychological evaluation of who attend the patient during course of the disease.This multicentre study is in line with the intervention model "action research".In a sample of 201 caregivers (mean age=51.46;sd=14.92) (M = 72;W=129) Short Form Health Survey (SF-36), Zarit Burden Interview (ZBI), Coping Orientation Problems Experienced (COPE), Experience Close Relationship (ECR) were administered to evaluate respectively Quality of Life, perceived emotional Burden (B), Coping styles and Attachment styles. The sample takes care his/her partner (P) (n = 85), parent(PA) (n = 68), son/daughter (SD) (n = 7), brother/sister (BS) (n = 19), or others (O) (n = 22).

Preliminary results show a main effect of type of relationship between caregiver and patient for "Mental Health Index"(MHI) ($F(4,191)=4.150;p<.003$).In particular P (m = 35.28; sd = 1.38) and PA (m = 36.25;sd=1.53) reported worse levels of MHI than O (m = 45.23;sd=2.68). MHI and Anxiety attachment style average were significantly correlated($r=-.522,p<.05$).Furthermore a main effect of type of relationship between caregiver and patient was found for B ($F(4,190)=4.091;p<.003$). Specifically P reported higher levels of B (m = 23.31;sd.=1.39) than O(m = 14.24;sd.=2.78). P, PA, SD reported mild or moderate levels of Burden.

On the basis of the results, the relationship is a relevant element in the experience of caregiving. The final aim is increasing the knowledge about specific oncological caregivers' needs, in order to improving psychological interventions.

R6 Evaluation of QoL as a predictor of chemotherapy-induced toxicity

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Background: The increased number of quality of life (QoL) studies in the oncology setting highlighted the negative effects of chemotherapy administration, including toxicity, on health-related (HR) QoL during or after treatment. However, the predictive value of pre-treatment HRQoL assessment on the subsequent occurrence of chemotherapy-related side effects, has never been tested. The present study aimed to investigate whether baseline patients' perception of well-being, as HRQoL index, could influence both subject perception of chemotherapy-induced side effects and objectively measured parameters of toxicity.

Methods: A total of 110 cancer patients (41% male, mean age 62 ± 10.49 years) treated at the Medical Oncology Unit of the Tor Vergata Clinical Center, were enrolled. Primary tumors were gastrointestinal (53%), breast (32%), head/neck/lung (10%), uro-gynecological (5%). The following self-reported questionnaires were administered before chemotherapy start: 1) the National Comprehensive Cancer Network Distress Thermometer (NCCN-DT) and 2) the EORTC QLQ-C30. Chemotherapy-related toxicity was recorded in medical records according to NCI-CTC v4.0 criteria. Data were analyzed using MedCalc statistical software. The predictors of side effects toxicity were assessed using logistic regression analysis. Primary endpoint was overall toxicity incidence grade 0-2 vs. grade 3-4. The following variables were analyzed: age, sex, primary tumors, Karnofsky Performance Status, Global Health Status (GHS) and Distress. The effect size of predictors was estimated using adjusted odds ratio (OR) with 95% CI. A p-value lower than 0.05 was considered as statistically significant for all tests.

Results: GHS values were stratified in three categories, low (0-25), medium (26-49) and high (50-100) levels of QoL. Patient distribution according to GHS levels were 7.3% in the low, 13.6% in the medium and 79.1% in the high QoL category. In the whole population, age, sex and GHS were found significantly associated to chemotherapy-induced toxicity at the univariate analysis (p = 0.01, p = 0.02, p = 0.03, respectively). However, at multivariate analysis GHS was the only independentpredictor of the occurrence of chemotherapy-related side effects (AOR: 2.78, 95% CI: 1.01-7.62; p = 0.04), particularly of grade 3-4 toxicity.

Conclusions: Pre-chemotherapy evaluation of health-related QoL parameters, might represent a useful tool to predict common chemotherapy-related side effects occurrence.

R7 Unmet needs in Head and Neck (H&N) cancer patients: unmet needs, emotional disorders and pain

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Background: few is known about head and neck (H&N) patients (pts)' unmet needs (UNs) and about their association with debilitating symptomatologies that worse quality of life (QoL), adherence to treatments and prognosis. Caregivers (cgs)' recognition of pts' needs is much less assessed. The aim of the research was to investigate the main H&N pts' UNs and their possible link with pain, anxiety, depression and distress. Besides, the study conducted an investigation on cgs', nurses (nrs)' and oncologist (onc)'s capacity of understanding pts' needs, as regards five macro-areas: psychological (PsA), communicative (CmA), physical (PhA), social/health care (ShA) and sexuality (SxA).

Methods: we surveyed 100 H&N pts during the active phase of chemotherapeutical treatment; 59 cgs, 6 nrs and 1 onc. The instruments used were: Hospital Anxiety and Depression Scale (HADS), Distress Thermometer (DT), a survey on somatic and emotional symptoms (sx) perceived by pts in the last 24 hours and Supportive Care Needs Survey-short Form (SCNS-SF34).

Results: UNs in PsA were associated with somatic and emotional sx ($c^2=10.213,p<.01$); UNs in CmA with pain ($c^2=5.260,p<.05$); UNs in PhA with pain ($c^2=9.962,p<.01$) and somatic and emotional sx ($c^2=6.760,p<.01$); UNs in ShA with distress ($c^2=4.459,p<.05$), anxious symptomatology ($c^2=4.071,p<.05$) and pain ($c^2=14.733,p<.01$); UNs in SxA with anxious symptomatology ($c^2=7.328,p<.01$) and pain ($c^2=4.833,p<.05$). Worry about the future was associated with distress ($c^2=5.929,p<.05$) and anxious symptomatology ($c^2=17.189,p<.01$); incapacity of doing usual things with distress ($c^2=6.540,p<.05$), pain ($c^2=7.366,p<.01$) and anxious symptomatology ($c^2=4.854,p<.05$); concerns about the worries of people close to patient with pain ($c^2=12.953,p<.01$) and depressive symptomatology ($c^2=4.529,p<.05$); lack of energy with pain ($c^2=22.335,p<.01$); fears about cancer spreading with anxious symptomatology ($c^2=12.815,p<.01$); feelings about death and dying with anxious ($c^2=6.451,p<.05$) and depressive symptomatology ($c^2=5.317,p<.05$). As regards cgs, nrs and onc just cgs detected the presence of pts' UNs in the PsA, in the PhA and in the SxA. There were many missing in the SxA regarding nrs' and onc's answers.

Conclusions: Several UNs can negatively impact the H&N pts' QoL. The awareness of such association between somatic, emotional and social aspects of pts' dissatisfaction can steer health team to a more focused clinical intervention.

R8 Linkage project: specific training of a linguistic-cultural mediator for the management of Chinese cancer patients resident in Italy within healthcare facilities

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Background: Population resident in Italy coming from the People's Republic of China is one of the largest foreign communities in our country. Literature shows that the admission to health services for foreign patients is characterized by a low-quality standards, mainly due to communication problems. To overcome the language barrier for the chinese community, the professional profile of the linguistic-cultural mediator (LCM) becomes essential. We collected data of chinese patients referring to our Institution after the creation of a linguistic-cultural mediation service desk (LCMD).

Patients and methods: Chinese cancer patients referring to the LCMD set up at Istituto Nazionale Tumori of Milan (INT) between July 2016 and April 2017 were evaluated. The LCMD guarantees the presence of a LCM who supports Chinese patients during the admission to the hospital and/or diagnostic assessment, offering a service of counseling to healthcare professionals and to the patient and his/her family. General practitioners located in specific neighborhoods of Milan were provided with chinese language brochures and posters in order to expand this service to the broader chinese community. The linkage project was supported by an AIOM grant.

Results: From July 2016 to May 2017, 42 chinese cancer patients referred to the LCMD. The distribution of the population based on the main characteristics is summarized in table 1. Overall 33 patients (78.6%), out of 42 Chinese cancer patients accepted and underwent treatment proposed by the physicians while 9 (21.43%) didn't follow the indications. 26 out of these 33 subjects started a treatment at INT (78.8%), while the remaining 21.2% followed the treatments indicated at other hospitals.

Table: R8. Main characteristics of Chinese cancer patients who referred to the LCMD

Age (years)	*Median 50* Pts (N=)	*Range (1-76)* %
Sex		
Male	26	62
Female	16	38
Tumor type		
Breast Cancer	*8*	*19.05*
Cervical Cancer	*4*	*9.52*
HCC	*4*	*9.52*
CNS Cancer	*4*	*9.52*
Gastric Cancer	*4*	*9.52*
Other	*18*	*42.86*
Metastasis status at diagnosis		
M+	14	33,3
M0	28	66,7
Type of treatment at diagnosis		
Surgery	11	26,2
Medical	10	23,8
Surgery+Medical	14	33,3
Unknown	7	16,7

Conclusions: After only 10 months from the beginning of the LINKAGE PROJECT, our findings showed a positive impact on qualitative standards regarding the access to healthcare services and the patient-caregiver interaction by Chinese cancer patients. Data showed that the vast majority (80%) of Chinese cancer patients referring to our LCMD accept to receive a treatment at INT.

R9 Psychological resources and strengths in adults living with lung cancer. A pilot study

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Background: Lung cancer is widely diffused and associated with high levels of mortality. Due to its impact on people's functionality, it can significantly affect subjective well-being, everyday life and future planning. However, even a person with lung cancer may rely on some personal resources that can promote his/her adaptation and reorganize his/her life positively. Our aim is to have a deeper knowledge about which are the most relevant resources in this critical context. It could be particularly relevant to patients, by recognizing which are the strengths they can refer to, and to all care process. Resilience, optimism, hope, future orientation, courage and life satisfaction have been explored.

Methods: We proposed a test battery (Pro.spera, Designing My Future, Resilience Scale for Adults, Courage Measure, Satisfaction With Life Scale) to 26 patients with lung cancer from Camposampiero and Cittadella D.H.O. (69,23% men; mean age=67,42). We analysed the degree to which patients identify them: if they represent recognized resources, strengths, or vulnerability areas (Table 1). Then we identified any specificity in relation to the stages of the disease (14 patients under TKI or Chemotherapy; 12 under control) and the age of patients (16 patients <70; 13 ≥ 70).

Results: Most recognized strengths are Courage, Social Resources and Family Cohesion (Table 1). Vulnerability areas are, like expected, Optimism, Hope and Future planning. Anyway, over the 50% of participants recognize the presence of resources for all dimensions investigated. Using the Mann-Withney statistic, however, no significant differences emerge between different therapeutic conditions or different ages ($p>.05$).

Conclusion: Results show that the elements of positivity are greater than those of vulnerability. Medical staff can better understand which dimensions help to cope and maintain good levels of compliance in patients with lung cancer, also in older ones. It seems useful to enhance them and increase vulnerability areas. Future studies are suggested.

Table: R9

DIMENSIONS	VULNERABILITY	RESOURCES	STRENGHTS
	People who recognize themselves in these 3 areas. Values expressed in %		
Hope Pro.spera	24	**64**	12
Optimism Pro.spera	28	**72**	-
Future orientation DMF	12,5	**58**	29,5
Courage	-	38,5	**61,5**
Life Satisfaction	16	**84**	-
Resilience DMF	29	**50**	21
Resilience RSA	4	**58**	38
Perception of Self RSA	1	**65**	23
Planned Future RSA	27	**58**	15
Structured Style RSA	15	**70**	15
Social Competence RSA	19	**62**	19
Family Cohesion RSA	12	**50**	38
Social Resources RSA	-	**62**	38

R10 The thermometer of distress in oncology

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Background: Routine screening for distress is today recognized as a standard of care in oncology practice, given the high incidence and the high negative impact on quality of life. It is demonstrated that a quickly identification of distress may led to prompt treatment and consequently to a better adherence to the oncologic plan.

Methods: Our principal aims were identify factors associated with distress and propose a simple and acceptable method to measure distress and unmet needs of oncologic patients. At the first visit, a brief interview with a psychologist and the Distress Thermometer were given to all new patients submitted to our Unit. A score of 5 or more was considered for a risk of distress and patients were than referred to the psychologist for taking charge. After six months, the Distress Thermometer was proposed again to search a variation in its score.

Results: From January to May 2016 we screened for distress 106 new oncologic patients. At the baseline evaluation, a score of 5 or more was discovered in 54 patients. Of these, after the psychological support six month later, the score was equal or increased in 9% of patients, respectively; in the remaining patients, the reduction of score was of 5 or more point in a 34% of cases. Taken the whole population, at the second evaluation, the score appeared equal in a 13.2% of cases while it was increased in 24.5% of patients. The main reason for this evidence, was the poor acceptance of the disease. In every case, we did not find a correlation between the score and other factors such as sex, age, schooling, and social and work situation.

Conclusions: Using a brief interview and a simple instrument such as the Distress Thermometer, our psychologists were able to individuate distress very quickly. This allowed us to perform fast intervention thus improving the quality of life and adherence to the oncologic treatment. Moreover, repeating the test after six month we were able to identify another subgroup of patients at risk for distress at the end of the oncologic journey.

R11 Role of Theatre as Psychological Support in Cancer Patient

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Background: The application of expressive forms of art in oncology is considered an integral part of patient care and the theatre seems to be a powerful resource for training, personal growth and rehabilitation. At the Medical Oncology Department of "S.G. Moscati" Hospital in Avellino, within a humanization program of cancer care a rehabilitation project of theatre therapy for cancer patients has been carried out for 8 years. The project has been designed in a holistic view of the complex and multidimensional care.

Methods: All cancer patients with at least 1-year of life expectation referred at the Division of Medical Oncology, have been selected for inclusion. Enrolled patients are identified by the psycho-oncologists with clinical and motivational interviews. The first

phase is characterized by the selection of potentially eligible patients. After the interviews, the selected patients complete a registration form and receive the MAC entry-questionnaire. The second phase involves the formation of the group and the 'start-up of the workshops. It uses pre-expressive techniques and post-expressive techniques. All the activities are characterized by the group mode. Is very important the presence of men in the group.

Results: Quantitative Analysis: As the therapy theater experience of our U.O. came in 2016 to the 'eighth edition of the project it has been decided to make an assessment of half of the course and evaluate the analysis results for the fourth edition. The sample consists of 10 women with an average age of 52 (Minimum age 36 - maximum age 68), of which 9 were suffering from breast cancer and an ovarian cancer and 3 males of average age of 46, of a 30-year boy with a testicular cancer and two others of 50 and 59 respectively with seminoma testicular with colon carcinoma. All patients gave their Informed Consent before starting the theatre therapy activities.

Qualitative Analysis: From semi.-structured interview analysis of patients who participated in the theater therapy it emerges that participation to these forms of art, leads to a quality of life improvement, but also to the acceptance of the disease and medical treatment.

Conclusion: From the analysis of the results of the experience of the year 2013, which is in the middle of our path, a substantial improvement in the style of adaptation to patient disease who took part in the theater therapy emerges and, in particular, this result appears to be more evident after the final performance.

R12 Incidence of alcoholism among cancer patients undergoing active treatment

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Background: Substance abuse was frequently underdiagnosed among patients in oncologic treatment and palliative care. Alcoholism occurs in approximately 8% of the general population, being more frequent among hospitalized patients (approximately up to 20%). It has been described as a poor prognostic factor for cancer symptoms management. Previous studies focusing on frequency of alcoholism in advanced cancer patients admitted to palliative care unit in Italy detected this condition for only a minority of patients (4%). Aim of our study is to determine the incidence of alcoholism among patients with advanced cancer admitted to two Oncology Units for active cancer treatment, using a simple and validated assessment instrument.

Methods: We present an unplanned interim analysis of a prospective cohort study. From August 2015, all consecutive eligible patients completed the Cut down, Annoyed, Guilty, Eye-opener (CAGE) questionnaire. Baseline symptom assessment and quality of life were also evaluated by Edmonton Symptom Assessment System (ESAS) and EORTC-QLQ-C30 questionnaires. Demographic data, cancer disease and extension features, disease-oriented treatment and all medical information were collected. Performance Status was evaluated according to Karnofsky (KPS).

Results: In total, 117 patients were evaluated. The mean age was 63.3 (SD 12) years and 66 (56.4%) were males. The mean KPS was 68.3 (SD 16). Lung and Gastrointestinal cancers were the majority. The mean ESAS was 25 (SD 14.8) points and the mean BMI was 24.5 (DS 4.). The CAGE score resulted positive in twelve patients (10.3%). In this population, the mean age was 61.7 (SD 11.1), the mean KPS was 69.2 (SD 16.2). Furthermore, the mean ESAS was 18.3 (SD 13.7) and the mean BMI was 24 (SD 5.2) points.

Conclusions: First preliminary data prove that alcoholism is highly prevalent and underdiagnosed among patients undergoing active cancer treatment, compared with other studies in palliative and home care settings reported in the literature. Independent of diagnosis and performance status, CAGE-positive patients are more likely to be male, as described by other studies. Other demographic data from this subgroup are equally represented.

R13 "I have a cancer, I am ill, it's Sunday, my oncologist is not here, I am despairing." How a telephone call can resolve a great difficulty of cancer patients

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Background: Cancer is a multifaceted illness that includes physical as well as psychosocial challenges. The ability to cope effectively with cancer is heavily influenced by psychosocial challenges, such as distress. For patients, unresolved distress is associated with anxiety, adjustment, and depressive disorders. In order to reduce the patient's and caregiver's distress, avoiding referral to the Emergency Department (ED) for non-urgent conditions and to supply the patient and needs, we have performed a procedure to listen to the patient needs through a phone call.

Methods: The family members are told that they will be able to contact the Oncology Unit (OU) by telephone regarding problems. During the weekend and when the outpatient clinic is closed, the nurse on call of the OU will answer to phone call, and then the needs of the patient is registered on a specific form. If the nurse can solve the problem, the patient is provided with all the information needed and the form is filled in; if the problem requires the consultation of an oncologist, the nurse notifies the doctor on call. When paged by phone, the doctor on call may decide whether to give telephone advice to the patient or to the caregiver in order to handle the problem at home, to arrange an urgent hospitalisation or to send the patient to the ER.

Results: Between January and March 2017, 55 calls from 44 patients were registered in the OU. The main problems were related to gastroenterology symptoms (18,18%), pain (16,36%), fever (14,55%) and hypo/hyperglycaemia (10,91%). 61,82% of the calls ended with the resolution of the problem simply thanks to telephone advice; in 27,257% of the cases, the patient went to the ED, and in 3,64% of the cases, the patient went directly to the OU. The resolution of the problem was carried out by telling the patient to take medications or to change therapy (32.73%), advising the patient go to the ED (14.55%), to the OU (1.82%) or giving simple advice on how to handle the problem (10.91%).

Conclusions: The possibility of receiving immediate support is useful for both the patient and caregiver, who feel protected and supported during the entire course of the disease. Through a phone call, the healthcare staff can intervene on symptoms before they become unmanageable and manage the problems and the possible changes, such as additional calls to the oncologist before the next visit, unscheduled visits, visits to the ED and hospitalisations.

R14 Music and its influence on affectivity and relationships in oncologic and hematologic patients

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Background: Cancer mortality has decreased in the last 10 years, but surviving oncohematologic patologies does not relate necessarily to a good quality of life: several studies have demonstrated that symptoms like anxiety, depression, stress can persist after recovery, and the impact of the disease on familiar, sexual, working relationships is very strong. According to the American Music Therapy Association, Music Therapy is the clinical and evidence- based use of music by credentialed professionals to address physical, emotional, cognitive, and social needs of individuals; it can find application in many clincal contests. Considering the previous problems, it can be effective also for neoplastic patients.

Methods: Objective of this qualitative study was to evaluate changes on affectivity and relationships in a sample of oncohematologic patients who took part in 12 Music Therapy group sessions. Being adults (age $>$ 18) and participating at least in 7 sessions were the only inclusion criteria. After consent to participation and to the use of personal data, 7 patients were interviewed on themes like quality of life, coping, relationships with relatives and health workers. To better indentify changes during sessions, questions were divided in 3 areas: pre, intra and post Music Therapy treatment. Interviews were recorded, transcribed and finally analyzed with a phenomenological approach: 3 researchers read interviews, underlining words and sentences considered relevant, then they compared what was highlighted by each one. Products of the comparison were put together, creating and developing common themes.

Results: Seven common themes were identified: knowing the diagnosis and its consequences; loneliness; the experiences during Music Therapy sessions; the role of the therapist; the relationship with the other members of the group and relatives; metaphors to describe the sessions; the redesign of life.

Conclusions: Thanks to Music Therapy, patients have increased self awareness and have found coping techniques to deal with their disease and its outcomes. Music enhanced relationships especially between patients who took part to the sessions with their caregivers; also the relationships among participants and between them and the Music therapist were strongly positive. It is desirable that health workers apprise patients of these treatments, in order to make therapeutic offer more complete.

R15 Evaluation psychological distress in elderly cancer patients

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Background: Comorbidities and disabilities coexist in elderly cancer patients (age = 70 years old). Depression and anxiety are also common and they can lead to weight loss, fatigue, affecting the perception of their own quality of life, the compliance with therapies and perhaps the outcome. AIM: our mono-institutional experience has evaluated elderly cancer patients using both geriatric multidisciplinary assessment and the psychological distress parameter.

Methods: Inclusion criteria: age $\geq$ 70; any cancer disease; hospitalized in a Medical Oncology Department. From January 2017 to March 2017, we enrolled in the study 40 patients (pts) whose demographic features were: male/female 21/19; median age: 74.5 years. All pts underwent a psychological interview to investigate specific areas: cognitive

impairment; living alone; history of psychiatric disorder; alimentary behavior; sleep/wake; rhythm; family/community supports; awareness about their diagnosis.

Scales: Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL). ADL are activities in which people engage on a day-to-day basis. These are everyday personal care activities that are fundamental to caring for oneself and maintaining independence; IADL are activities related to independent living and are valuable for evaluating persons with early-stage disease, both to assess the level of disease and to determine the person's ability to care for himself or herself. Psychometric tools used: The Distress Thermometer (DT). PRELIMINARY RESULTS. Among the patients (pts), 28 cases (70%) showed a significative Distress (cutt off = 4). Twenty seven pts (76,5%) reffered sleeping sickness and 18 pts (45%) have feeding problems. Twenty of the pts (50%) are autonomy; 14 pts (35%) are partially autonomy and 6 pts (15%) are no autonomy.

Conclusions: The most of the patients showed significative distress levels, suggesting the need of process an assessment multidisciplinary form. The mentioned form would be attached to the Medical Records and would be filled by any professionals in contact with the patient with the aim of providing a summary of the geriatric score scales. The use of the geriatric information contained in the form will help to improve the therapeutic strategy.

R16 Image and self-esteem: a photo-therapy program to improve body image, increase self-awareness and the expression of emotions in breast cancer patients. A pilot study

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Background: Conventional breast cancer therapies often provoke consistent changes in patients' image than can negatively impact their self-perception and social relationships. Photo-therapy consists in the use of personal snapshots, magazine pictures and photos taken by others, under an expert therapist guide to reduce painful psychologic symptoms, facilitate the process of change, improve body image, self-consciousness and encourage the manifestation of emotions, better than words alone.

Methods: In **Photo-*langage*** each patient chooses one of a set of images that represents her, to introduce herself to the group and to increase emotional awareness; **Photo-*collage*** consists in cutting and pasting images on a individual poster to explore cancer-related experiences and to recognize changes; in **Photo-dialogue** patients select a photo, on a set, that represents how they perceive their body in order to create an individual story; **Self-portrait** consists in comparing pictures of the patients taken by themselves with those taken by other people, to understand how they perceive themselves and how they are seen by others. Basic Self Esteem scale (SE), Positive and Negative Affect Scale (PANAS), FACIT Fatigue scale, NRS pain score, Distress Thermometer (DT), and two anxiety/depression tests (HADS and STAI-Y) were administrated at the beginning and end of the course.

Results: From 12/2016 to 03/2017 6 breast cancer patients, median age 54 (47-72), attended 16 weekly sessions of Photo-therapy, 5 of them in adjuvant hormonal therapy after surgery and chemotherapy, 1 in chemotherapy for advanced disease. Before Photo-therapy, Basic Self-Esteem was >75 percentiles in 1/6 cases; after the course 3/5 pts, who returned final test, scored >75 percentiles. Median PANAS-positive score showed an increase (from 23.7 to 27.3 points) and PANAS-negative a decrease (from 18.5 to 16.8). Fatigue, pain, anxiety, depression and distress evaluations did not show any change.

Conclusions: This pilot study of an image-based therapy suggests possible advantages of this technique in breast cancer patients to improve self-esteem and emotions. Larger studies are recommended.

R17 Dignity Therapy: a new psychoterapeutic approach for people facing advanced disease

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Background: The fear of loss of dignity is a recurring concern among oncological patients, especially in the advanced stage of illness, for those who are in advanced stage of their disease. Chochinov has made the model of Dignity Therapy (DT) used primarily with people who were terminally ill. It consists of a short-term psychotherapy intervention that includes 3 major issues: physical aspects related to the disease and symptoms; existential/spiritual based on the patient's life history; social relationships linked to the quality of the relationship between the patient, practitioners and family members. The DT is a multi-dimensional psychosocial intervention for patient-centered care and it depends on experiences of generativity and the pursuit of purpose and meaning. It invites patients to discuss issues that matter most or that they would (most) want mainly to remember.

Methods: Since 2016 we applied to 4 patients the DT in the perspective of simultaneous care with metastatic disease, in psychological therapy and still in chemotherapy. We are using the Italian validate version of semi-structured interview. The intervention takes place in 3-4 meetings, lasting 1 hour each, after informed consent. The interview uses 10 core questions and the responses are used to create a written legacy document to family members. The DT session is audio-recorded, transcribed, edited and given back to the patient. Content includes lifetime events that are most significant in the life of the patient, who can later personalize adding photos, images, titles or more.

Results: Because the our small sample, we do not have a statistically relevant data, but we have noticed that the common themes that emerge in patients mainly concern the attributed value to the affections and the family and the experiences that have contributed to building their identity. The introduction of topics such as dignity, searching for meaning, has proved to be a valuable tool for the development of the true meaning of one's life, despite the changes in the disease. Moreover, in some cases, it has contributed to allowing the person to find a way of self-reliance in relation to loved ones.

Conclusion: In our experience, DT showed to be a new promising therapeutic intervention for suffering and distress at the end of life. The literature review finds robust evidence for DT's overwhelming acceptability, rare for any medical intervention, especially in psychosocial-spiritual care.

R18 Cancer as family disease

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Background: Cancer disease doesn't only affect the patient, but also his family. Many studies show that caregivers have to deal with multiple difficulties, developing psychological reactions such as anger, anxiety, depression, fatigue, that is *caregiver burden.* These evidences have led us to believe that the family is an integral part of taking care process, and it's need to be supported in turn to provide adequate support to his loved one.

Material (patients) and methods: In our Oncological Department Day Hospital, sited in Fivizzano (Institute Tuscany Tumor ITT) we have been thinking of widening the psychological support, already provided to patients, also to families. So they can meet psychologist that evaluates caregiver burden with clinical interview and *Caregiver Burden Inventory(CBI)*, a multiple choice self-administration questionnaire composed of 24 items, 5 sub-scales, each of which measures a type of burden:reductions in personal time (Time-Dependence Burden, *T/Dep-B*), failure of hopes and expectations (Developmental Burden, *Dev-B*), physical stress (*Phys-B*), work and family conflicts (Social Burden, *Soc-B*), negative feelings towards patient (Emotional Burden, *Emot-B*). Score range is 0-4 for each item, 0-20 for each dimension, whereas total score is between 0-100. 57 caregivers (38 women,19 men) have agreed to answer to CBI in an outpatient setting, while waiting for their family members to visit or therapies. The median age of the caregiver was 55.93 (range 33-77), while that of the patients 73.40 (range 45-86).

Results: CBI total score varies between 0 and 62 (M 20.93), with highest scores respectively for T/dep-B (M 7.07, range 0-18), Dev-B (M 6.25, range 0-20) and Phys-B (M 4.75, range 0-16) while the lower ones for Soc-B (M 1.81, range 0-10) and Emot-B (M 1.05, range 0-10).

Conclusions: CBI results show the most subjective burden in time required by caregiving, the sense of failure of hopes and expectations and perception of fatigue and health problems, while role conflicts and feelings towards the patient have lower scores. We have not provided detailed quantitative data because the research is still ongoing and sample of caregivers is too small to be able to make inferences of any kind. Starting from these data, specifically the dimension of psychological burden(Dev-B), the opportunity to avail of a psychological support is given to families, to improve their psychological well-being, patient relationship, and coping strategies of this Family Disease.

R19 Screening of distress in hospitalized patients: the experience of medical oncology department

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Background: Despite the numerous studies on the topic and the clear guidelines that recommend routine distress assessment in cancer patients, this psychological parameter is often not recognized or debated at all. The aim of our study is to determine whether the Distress Thermometer (DT), used in each patient's hospitalization, may favor a more targeted takeover of the patient's real needs and faster monitoring of the symptoms in the various stages of illness.

Methods: We analyzed 371[57.7% male, 42.3% female] patients (pts) between 23 and 91 (median 63.2) years old who completed DT during hospitalization through the cooperation of suitably trained and motivated nurses. They almost represent the total population of pts taken over in a 10-month period by the oncology department of ASST Sette Laghi of Varese. These pts are randomly characterized by heterogenety of tumors and staging of disease. The ANOVA (ANalysis Of VAriance) method was used for data analysis to test the differences between scores at TD (0-10) and the presence/absence of other problems or disturbances (39-item) in the last week.

Results: 49.6% of pts show TD scores between 6 and 10 (11% = 10). ANOVA (One-way) shows significant differences between DT scores averages in different type of

tumors. Sarcoma, ENT (ear, nose, and throat), Melanoma and Breast are the pathologies that show greater levels of distress. However, this assessment does not show differences between subjects in early diagnosis and patients with recurrence. Female pts show DT average scores significantly higher. In addition, some sources of emotional, relational, or physical discomfort better explain the high values of DT.

Conclusions: The results, moreover higher than those reported in literature, confirm the validity and sensitivity of DT measurement in hospital admissions. From a clinical point of view, the choice to further re-evaluate (clinical psychological interview) all pts with distress $\geq$8 (27%) reiterates the relevance to assign a stable psycho-oncologist figure to each oncology department. This is the challenge we are launching for the foreseeable future.

R20 Cancer care for migrant patients: the value of a dedicated service

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Background: In developed countries, including Italy, the immigrant population with cancer is growing and wide disparities in cancer prevention and treatment have been demonstrated between migrants and native populations. Here we report preliminary data of a project aimed to create a dedicated service for immigrants affected by cancer in order to reduce health disparities in this subgroup of patients (pts) by implementing the right and access to healthcare as an opportunity for integration and social inclusion.

Patients and methods: In September 2016, a specific service for migrant oncology pts consisting of a dedicated outpatient clinic was started at our Medical Oncology Unit. From then, any foreign born accessing our hospital with a suspicion or with a diagnosis of cancer was referred to our dedicated clinic. This project is supported by AIOM.

Results: From September 1st 2016 to April 30th 2017 a total of 72 pts (20 male and 52 female) accessed our dedicated service. Most pts (66 pts) were from Less Developed Countries (Eastern Europe, Africa, Asia, Central/Southern America), whereas a minority of them (6 pts) was from Developed Countries (United Kingdom, France, Australia, Japan). 52 pts were managed in the outpatient clinic whereas 20 needed hospitalization. The most common diagnosis was breast cancer (36 pts), followed by gastrointestinal (9 pts), genitourinary (8 pts), gynecologic (8 pts), lung (6 pts), head and neck (3 pts), skin (1 pt), and hematologic cancer (1 pt). 53 pts underwent curative surgery, 37 received radiotherapy, (29 in adjuvant/neo-adjuvant setting, 3 with curative intent, 5 in palliative setting), 46 received chemotherapy (27 in adjuvant/neo-adjuvant setting, 3 with curative intent, 16 in metastatic setting) 24 received endocrine therapy (20 in adjuvant setting, 4 in metastatic setting), 10 received best supportive care. Most patients reported that financial, social, and logistical support would help them to comply with the diagnostic-therapeutic pathway.

Conclusions: These preliminary results showing high attendance of migrant cancer pts at our clinic suggest that a dedicated service could provide migrants greater access to cancer care. Further multidisciplinary interventions directed to psychologic and social needs of these pts should be implemented, in order to ensure that each migrant have a full access to high-quality health care, without discrimination on the basis of nationality, religion, gender or race.

R21 Preliminary data for assessing the impact of psychological stress on the development of primitive tumors or relapses of disease

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Background: The relationship between psychological and immune systems in the development of chronic inflammatory and cancerous diseases has been already hypothesized. In particular, the presence of strong emotional stress has been considered as a cause for development of neoplasms such as breast cancer, melanoma, and gastrointestinal tumors. What is still unknown is how stress of nervous origin can influence the chain of molecular events leading to cell proliferation, leading primarily to the development of tumors and, subsequently, the occurrence of relapses. The present study aimed to investigate risk factors for early onset of primary cancer or cancer relapse, that are strictly related to lifestyle and psychological stress.

Methods: Between January and September 2017, we provided a questionnaire to 100 patients followed at the University Hospital in Cagliari and San Marcellino Hospital in Muravera, regardless of tumor histology, disease stage, and ongoing therapy. The questionnaire was focused on hystological diagnosis, onset time, relapse time, and the quality of life reported over the last three years. The surprising news is that 94% of patients reported the presence of a highly stressful/painful event in the three years prior to diagnosis, whether they were in adjuvant therapy or after relapse of the disease: altogether 46% of patients reported a strong psychological stress due to family mourning (29%) or serious illness (17%) in a close relative (parent, brother/sister, son/daughter); 15% reported a heavy emotional burden caused by work stress (incompatibility with leader or colleagues) and 10% reported family problems caused by economic reasons related to inheritance.

Conclusions: Although psychological stress is difficult to assess, this preliminary analysis suggests the need for a wider study with a control arm to confirm our hypothesis and, if so, to identify clinical and instrumental parameters that allow us to customize the control of subjects potentially at risk of relapse.

R22 Cancer, emotions, and cinema: a preliminary study about the changes experienced by oncological patients

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The event of cancer can be considered among the most feared ones due to its emotive impact and the nuances of meanings that the term carries with itself.This explains why its diagnosis has a strong influence and why the various approaches to the oncological disease—starting with the biopsychosocial model- unanimously agree on affirming that said impact happens not solely on the physical level,but also social and above all emotional ones.Cancer diagnosis affects the patient's sensitivity and it is has been often the goal of several researches to determine the changes that it implies.One of the most recent methods proposed makes use of mediation techniques thanks to the application of a *medium*, such as photographs, images, or — the *medium* par excellence — cinema.In fact cinema represents an important form of entertainment and communication but it also could have a therapeutic and preventive function on mental health.

This preliminary study took place at HSR Clinical and Health Psychology Service in Milan.It is projected to extend such research towards a wider multi-centric perspective.12 oncological patients (M = 33%;F=67%;mean-age=61.25±9.14)affected (n = 6;50%)or recovered (n = 6;50%)underwent a qualitative interview on their disease history, emotions and the use of cinema during illness. Different percentages with respect to the different tumor sites were observed, including:breast (33%), bowel (8%), ocular (8%), foot sarcoma (8%), biliary tract (8%), brain (17%)and lung(17%).Software *Nvivo* was used to analyse the frequency of the occurrence of various key words in patients' speech during the interview, in order to describe their willingness to speak-also in quantitative terms-about the themes that are crucial of this research.

Preliminary results show that people who recovered from the disease talk easily and more thoroughly about "suffering"(0.07% of total amount of words vs 0% one of people affected by cancer) and "disease"(1,13% vs 1,08%).On the contrary, people still affected by cancer talk more thoroughly about "change"(0.36% vs 0.16%),"film"(0.82% vs 0.53%),"violence"(0.56% vs 0.30%),"death"(0.04% vs 0.03%),"emotions"(0.39% vs 0.25%),"oncology"(0.52% vs 0.24%).

On the basis of these results, it is therefore maintained that an inquiry, using cinema as *medium*, would provide multi-level information on the transformations that the cancer experience inevitably entails.It could be then possible to design several action researches which would involve both individuals and groups.

R23 Photography as a therapeutic tool to re-elaborate "cancer" experience

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Background: In the project of Humanization of Oncology Care, the development of a therapeutic photography program can be a catalyst for therapeutic communication, improving the quality of life, self awareness, exploration of memories, feelings and emotions in oncologic patients in follow up care after cancer treatments.

Material (patients) and methods: In 2016 a two months therapeutic photography course was performed at the Medical Oncology of the A.O Papardo di Messina, using the language and various photographic techniques as a tool for reworking the oncology experience and sharing experiences. Meetings and practical workshops were developed by a psychotherapist and an expert of multimedia communication.

Results: 8 women in follow-up after breast cancer treatment, with a median age of 47.3 years (range 38-58), performed experimental activities, in weekly group labs for a total of 5 meetings each of 180 minutes. The achievement of specific therapeutic goals has been evaluated and monitored by the provision of ad hoc quality questionnaires. 90% of patients said that reviewing and narrating through photographic images has allowed to recapture parts of themselves, improving the acceptation of cancer experience.

Conclusions: The climate and strong supportive power of group experience and the use of photography as a sharing tool have activated of dynamics and the elaboration of

important emotional experiences related to the memory of the disease and the need to rebuild daily life.

R24 Patient relationship training in an integrated perspective: guidelines for psychological intervention

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The world of Oncology is now facing new challenges in the need for multidisciplinary work.Our work aims to identify a model to improve the skills of each professional in an integrated perspective.Training is an area of psychology that in recent years has had more attention by the clinicians, for its implications on Care and Health Promotion.The group is an elective tool for this job, as it works as a natural container that expresses aspects of the worker identity through coping and identification mechanisms.The specificity of the techniques used established a link and became contact facilitators with the primitive expression of emotion. The matters encountered dealt with both the relationship with cancer and terminally ill patients, and with the management of internal team dynamics.To identify the Training model, the contributions of all the professionals have been fundamental, in particular of oncologists, psychologists, psychotherapists, nurses and coordinators.

25 health workers[3 males(12%),22 females(88%);mean age:43.55, SD = 8.36](years of service M = 19.13;SD=8.68)were enrolled at the Department of Medical Oncology at "Presidio Ospedaliero"of Saronno, ASST Valle Olona, Italy.Nurses were tested three times with (A)Maslach Burnout Inventory, (B)Coping Inventory for Stressful Situations and (C)SF-36.Cronbach's alphas ranged from 0.58 to 0.91.8 health workers didn't want to change work, 15 thought about that and 2 reported the intention of changing.11 health workers reported the desire to be moved to other department(D).

Preliminary results show a significant main effect of the possibility of changing work for "vitality" of SF-36[$F(1,22)=4.571;p=.022$].Furthermore a significant main effect of the desire to be moved to other department was found for "Emotional Exhaustion"(EE)[$F(1,22)=5.634;p=.027$].D(m = 19.27; SD = 8.90)reported more EE than who didn't want moved to other department(m = 11.69;SD=6.74). D showed moderate levels of EE.Results evidence statistically significant association between years of service and "Personal Accomplishment" of MBI[$\beta=.453;p=.034;F(1,21)=5.157$].

The team of highly specialised oncologists, nurses, healthcare assistants, radiotherapists, psychologists and head nurses has to work together towards the development and care of a relational ability for interaction in a group.Results of this study could permit better understand psychological aspects of taking care oncological patient, in order to improve relationships trough different member of the group.

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S - SIMULTANEOUS CARE

S1 Simultaneous Care clinic: a three-year monoinstitutional experience

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Background: Early palliative care has been shown to improve outcomes in patients (pts) with advanced cancer such as quality of life, mood, end-of-life care. In accordance with American Society of Clinical Oncology (ASCO) and AIOM recommendations of implementing palliative care early in the course of illness for pts with metastatic cancer along with active cancer treatment a Simultaneous Care Clinic (SCC) was set up at Istituto Oncologico Veneto (IOV) in Padova since 2014.

Methods: Data of pts referred to the SCC at IOV from March 2014 to November 2016 were retrieved from a prospectively maintained database. Data collected included cancer type, status of disease, performance status, ongoing oncological treatment, psychological evaluation, social evaluation, nutritional evaluation. Collected data included activation of home territorial services and/or Palliative Care services, use of other health services after a first visit and place of death.

Results: 533 pts were evaluated by a multidisciplinary team (oncologist, palliativist, nutritionist, psychologist, radiation therapist, nurse, case manager). Overall symptom burden was low with baseline symptom scores (ESAS) highest for fatigue, lack of appetite and depression. Nutritional evaluation revealed 224 pts (42%) with nutritional problems, the most frequent being weight loss (n = 121). Some form of psychological distress was present in 185 pts (35%). Social issues were present in 26 pts (5%) and were dealt with activation of social services (n = 9) or volunteer territorial services (n = 8). Patients deemed in need of home care services after the first access to the SCC were 177 (33%) and for these a formal request for Home Care services activation was sent to the Local Health Territorial Unit (Distretto ULSS). After the first visit 141 patients referred to Emergency Room for intervening problems with median time of 41 days. Globally 290 pts (54%) died with 53% of deaths occurring at home. The median time from first visit in the SCC to death was 85 days. For pts who were receiving active oncological treatment at the time of first visit, median time from first-visit in the SCC and death was 126 days. We are also evaluating a score for priority for access to SCC.

Conclusion: Early integrated SC may be most effective if targeted to the specific needs of each patient population.

S2 Nutritional Counseling with or without Systematic Use of Oral Nutritional Supplements in Head and Neck Cancer Patients Undergoing Radiotherapy

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Background. The benefit of systematic use of oral nutritional supplements (ONS) in addition to nutritional counseling in head and neck cancer (HNC) patients undergoing radiotherapy (RT) has not still been properly assessed.

Methods. In a single-center, randomized, pragmatic, parallel-group controlled trial (ClinicalTrials.gov: NCT02055833; February 2014 - August 2016), 159 newly diagnosed HNC patients suitable for to RT regardless of previous surgery and induction chemotherapy were randomly assigned to nutritional counseling in combination with omega-3 enriched ONS (N = 78) or without ONS (N = 81) from the start of RT and continuing for up to 3 months after its end.

The primary endpoint was the change in body weight at the end of RT. Secondary endpoints included changes in protein-calorie intake, muscle strength, body composition and quality of life (EORTC-QLQ-C30) over the study time points and anti-cancer treatment tolerance.

Results. In patients in whom all the variables could be assessed, counseling plus ONS (N = 67) resulted in smaller loss of body weight than nutritional counseling alone (N = 69; mean difference, 1.6 kg [95%CI, 0.5 to 2.7]; P = 0.006). Imputation of missing outcomes provided consistent findings. In the ONS-supplemented group, higher protein-calorie intake and improvement in quality of life over time were also observed (P < 0.001 for all). The use of ONS reduced the need for changes in scheduled anti-cancer treatments (i.e. for RT and/or systemic treatment dose reduction or complete suspension, HR = 0.40 [95%CI, 0.18 to 0.91], P = 0.029). Nine patients reported gastrointestinal intolerance to ONS.

Conclusions. In HNC patients undergoing RT or RT plus systemic treatment, and receiving nutritional counseling, weight loss could not be completely prevented, but the use of ONS resulted in better weight maintenance, increased protein-calorie intake, improved quality of life and was associated with better anti-cancer treatment tolerance.

S3 Quality of end of life care in patients with pancreatic cancer receiving systematic versus on-demand early palliative care at diagnosis: a secondary outcome analysis from a randomized controlled trial

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Background: The main goal of palliative care (PC) is to improve the quality of life of patients and their families facing life-threatening illness, with a special attention to achieve high quality end of life (QoEOL) care. Here we report about caregiver perceived quality of care in the last week of life, a secondary outcomes from a randomized controlled trial comparing systematic versus on-demand early palliative care (SPC vs ODPC) in patients with pancreatic cancer.

Methods: Informal caregivers of patients enrolled in the main study (NCT01996540) and died within the period 31.10.2013 to 31.12.2016, were eligible for this mortality follow-back survey. Six to twelve months after patients' death, bereaved caregivers were contacted to ask for informed consent to study participation. Accepting caregivers were interviewed over the telephone by a trained psychologist. The summary scales of the Toolkit of Instruments to Measure End-of- Life Care, namely patient and family information, respect for patient treatment preferences, symptom control, death with dignity, family emotional support and global QoEOL, were used for assessments. Scale scores are reported on a range from 0 (worst) to 100 (best end-of-life care). Student t-tests for independent samples were used to compare SPC vs ODPC pts on the questionnaire scale scores.

Results: 118 patients were eligible for the present survey. For 71 of them (58%) it was possible to contact the main caregiver, who accepted to be interviewed in 65 cases (54%). Interviewed caregivers were most often females (65%), with a mean age of 57 years. Respondents were more often partner (51%) or son/daughther (33%) of the decedent. Percentages of patients dying with EOL PC were the majority in both SPC and ODPC groups (72% and 60%). Global QoEOL care was fairly good in both groups (84.6 vs 85.6, group difference -0.9 p = 0.8). Similarly, other scale scores were rather high (all average scores above 80, but family emotional support which scored 74) and the comparison of the two groups did not show any treatment effect (all groups differences not statistically significant and ranging from -1 to 3.4).

Conclusions: While the main study results shows a benefit of SPC vs ODPC during the first 3 months from diagnosis of pancreatic cancer, the fairly high QoEOL scores found for both groups suggest that the management of EOL care is relatively uniform and good in this patient population.

S4 Integration of Palliative and Oncology Care in patients with lung and other thoracic cancer: referral criteria and clinical care pathways

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Background. Recent evidences showed that early integration of palliative care in oncology have a positive impact on patients' quality of life, quality of care and costs. However there is no consensus on outpatient referral criteria. Based on the experience of the collaboration between the Palliative care Outpatient Clinic (POC) and the Thoracic Medical Oncology outpatient Clinic (TMOC) of the Fondazione IRCCS Istituto Nazionale dei Tumori of Milan, the aim of this study was to identify timing and factors associated to POC referral by the oncologist, and to describe the subsequent clinical care pathway of these patients.

Material (patients) and methods. This observational retrospective study included all patients with lung cancer seen for the first time at TMOC between Jan. 01, 2014 and Dec. 31, 2014. Patients were followed-up till death or till Dec. 31, 2015. Clinical and demographic patients' data were collected from the electronic patient records form. Univariate and multivariate Cox regression models were used to evaluate the association between time to POC referral and performance status, disease stage and presence of symptoms at inclusion. Results are reported as percentages, interquartile range (IQR), hazard ratios (HRs) and 95% confidence intervals (95%CI).

Results. 229 patients were eligible for the study. 98 of them (43%; 95% IC 36%-49%) were referred to the POC with a median time interval of referral of 30 days (IQR 4-188 days). 80/98 patients continued to receive anticancer therapy and palliative care

simultaneously. Univariable analysis showed that HR of being referred to POC is significantly higher for patients with worse performance status (HR = 4.5), more advanced disease stage (HR = 3.1), and presence of pain (HR = 4.9), dyspnea (HR = 2.5) and cough (HR = 2.2). The multivariable model confirmed independent prognostic value for ECOG PS, disease stage and pain. On Dec. 31, 2015, 25/98 patients were still alive, 65/98 had died and 8 patients were lost at follow up. Among patients who died, 19 (29%) were admitted to the hospital in the last 30 days of life, 56 (86%) did not receive chemotherapy in the last 30 days of life, 40 (61%) died with hospice or home care service.

Conclusions. Our results suggest to consider symptom burden, ECOG PS, disease stage among the screening criteria for referral to palliative care in patients with lung cancer.

S5 Simultaneous Home Care project for frail advanced cancer patients: a model of integration between no profit and Public Health System

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Backround: Despite widespread evidence reported in literature and attention by Health System, limited research exists evaluating principles and effectiveness of cancer patients-centered home care management according on patients' needs rather than on prognosis. Our Simultaneous Home Care (SHC) pivotal project represents both an opportunity for those advanced cancer patients who may benefit from chemo so far but present physical and social problems coming to day hospital and a model of integration between "no profit" and Public Health System.

Methods: The Oncology Department of ASST-Settelaghi Varese with the support of Varese per l'Oncologia, a non-profit organization, a grant from Regione Lombardia and according to the general practitioners, has conducted from May 2014 to April 2017 a pilot project of a SHC, a dedicated home-based service for frail advanced cancer patients. We included patients with advanced disease, treated with oral or subcutaneously biological agents and zoledronic acid, with limiting day-hospital access co-morbidities and at least six months life expectancy. Home care was provided by a high qualified team including three oncologist with expertise in palliative care, four nurses, a psychologist and a physiotherapist; home care was available 12 hours a day and included an on call oncologist every day of the year.

Results: a total of 115 patients, median age 72 years (range 38- 84), affected by advanced solid tumors or hematological malignancies were enrolled. All of them had metastatic disease and received both supportive care and anticancer treatment as outpatients. 95% received a cancer therapy. The median length of simultaneous care was 155 days (range 7-825). A total of 187 (range 169-198) nursing and 148 (range 142-155) medical visit were performed a year, with an average of 1.4 and 1.8 visit a month respectively. The median number of in-line patients were 20 (range 17-23). Hospitalization occurred in 18.4%. Blood transfusions at home was delivered in 2 patients and paracentesis in 8. One third of them died at home.

Conclusions: Our experience within SHC shows that the integration of supportive care and cancer treatment in home setting is effective. Hospitalization rate is lower than other studies. If confirmed in prospective pharmaco-economics studies, our data suggest that SHC provides high quality of assistance to frail. Integration with no profit was successful. Model can be replicated in other settings.

S6 Efficacy of neurokinin-1 receptor antagonists in the prevention of Chemotherapy-Induced Nausea and Vomiting (CINV) in patients receiving carboplatin-based chemotherapy: a systematic review and meta-analysis

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Background: Carboplatin was traditionally included among moderately emetogenic chemotherapy (MEC). According to 2016 guidelines of Multinational Association of Supportive Care in Cancer (MASCC) for chemotherapy-induced nausea and vomiting (CINV), a combination of a NK1 receptor antagonist (RA), dexamethasone and a 5-HT3 RA is recommended to prevent carboplatin-induced emesis, with moderate level of confidence and not unanimous consensus. Our aim was to perform a literature-based meta-analysis of all randomized trials (RCTs) evaluating the addition of a NK1 RA in the prevention of emesis for patients treated with carboplatin-based chemotherapy.

Methods: A systematic review of articles published or presented at major meetings was performed in January 2017. RCTs comparing NK1 RA + dexamethasone + 5-HT3 RA vs. dexamethasone + 5-HT3 RA in patients receiving first cycle of carboplatin-based CT were included. Primary outcome was complete response (CR), defined as no emesis and no use of rescue medication. CR was measured in day 1 (acute phase), days 2-5 (delayed phase) and days 1-5 (overall period). A random effects model was applied.

Results: 9 trials were potentially eligible (7 aprepitant, 1 fosaprepitant, 1 rolapitant): 6 were RCTs including patients receiving carboplatin, and 3 were subgroup analyses of patients receiving carboplatin within RCTs including various MEC. Data of CR were available in 8 trials (1598 patients). The addition of NK1 was associated with a significant improvement in CR during acute phase (94.5% with NK1 RA vs 90.1% with control, Odds Ratio 1.75, 95%CI 1.19-2.59, p = 0.005), during delayed phase (76.4% with NK1RA vs 61.7% with control, Odds Ratio 2.04, 95%CI 1.64-2.55, p < 0.0001) and during the overall period (75.3% with NK1RA vs 60.4% with control, Odds Ratio 2.04, 95%CI 1.64-2.54, p < 0.0001). There was no significant heterogeneity among trials. Sensitivity analyses, performed excluding subgroup analyses and excluding open-label trials, produced similar results.

Conclusions: In patients receiving carboplatin-based chemotherapy, triple therapy with NK1 RA, 5-HT3 RA and dexamethasone is associated with a statistically significant and clinically relevant improvement in CR, compared to 5-HT-3 RA plus dexamethasone. An individual patient data meta-analysis could help to identify patients who are likely to obtain the higher improvement from the addition of NK1 RA.

S7 Medication-Related Osteonecrosis of JAW (MR-ONJ) After Bisphosphonates, Denosumab and other Drugs in Advanced Cancer Patients: Recent Experience Data from Rete Oncologica Piemonte – Valle D'aosta (North-Western Italy Cancer Network)

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Background: Data concerning incidence of Osteonecrosis of Jaws (ONJ) are scarce. As an almost unique experience, since 2005 a multidisciplinary study group collected data of ONJ cases in patients receiving Bisphosphonates (BP) due to metastatic bone disease in oncology and hematology centers of a regional network, and followed in the main dental care and maxillofacial surgery centers of the area. By December 2008, 221 cases were registered (*Fusco et al, ISRN Oncology 2013*); the number of new ONJ cases per year in cancer and myeloma patients increased since 2004 until 2006 and then reduced (till to 21 cases on 2008). Several possible reasons of this "up and down" trend (shift from pamidronate to zoledronic acid; increase of ONJ awareness; diffusion of preventive dental measures; late modifications of BP prescriptions) were hypothesized.

In recent years, literature data showed increasing numbers of ONJ cases after denosumab or after other drugs (bevacizumab, sunitinib, etc), so that the new term Medication Related – ONJ (MRONJ) was introduced. Consequently, we decided to repeat the survey to verify the time trend in advanced cancer and myeloma patients.

Patients and methods: We asked for new ONJ cases observed between January 2009 and March 2016. We identified cases after cross-checking reports from medical oncology, haematology, and oral care centers to avoid double count.

Results: We received partial data about 335 cancer patients: 72% were female and 28% male; primary neoplasm was: breast cancer 153 (46%), myeloma 78 (23%), prostate cancer 42 (13%), lung 17 (5%), renal cell 11 (3%), and other types of cancer or not specified 34 (10%). The median number of new cases per year was 39 (range 30-49) in years 2009-2015. Local visits to collect complete data of all cases (duration and doses of therapy; concomitant treatments and diseases; oral health risk factors) are ongoing.

Conclusions: Preliminary data show an unexpected increase of new ONJ cases per year, in spite of measures prescribed to reduce the ONJ risk (dental visit and oral care before antiresorptive treatment). Possible reasons include: introduction of denosumab treatment in bone metastatic patients; larger use of biological agents potentially inducing ONJ; longer survival of some subsets of cancer patients (eg, lung and renal cell cancer, etc);); higher risk from antiseporptive plus antiangiogenic drugs.

The collection of full clinical data is warranted to explore these suggestions.

S8 The tailored nutritional counseling in early cancer patients

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Background: The benefits of a nutritional support in patients diagnosed with metastatic cancer is well recognized. Evidences suggest that nutritional care should be an integrated part of the global oncology care of the patients, especially during chemotherapy administration.Therefore, the aim of the current study was to examine the clinical impact of a tailored nutritional counseling on patients during adjuvant or neo-adjuvant chemotherapy.

Methods: Patients diagnosed with early stages cancer were included before starting adjuvant or neoadjuvant treatment. After informed consent was obtained anthropometric parameters (see Table) were recorded at baseline (T0) nutritional visit. A personalized diet prescription was delivered and patient revaluation at 3 weeks (T1), 3 months (T2) and 6-months (T3), was scheduled. Data were analyzed by non-parametric statistical analysis by applying Student's test (for paired data) with a SPSS 15.0 software.

Results: Within a six-month period, 10 patients (7 women and 3 men; mean age 61.5 ± 10.3 years) followed at the Medical Oncology Unit of the Tor Vergata Clinical Center, were considered evaluable for the present study. Statistically significant improvements in strength (F), resistance, muscle mass (MM), left arm circumference (AC), phase angle, control of symptoms (nausea anddysphagia); Functional Assessment of Chronic Illness Therapy Trial Outcome Index (FACIT-TOI); Functional Assessment of Anorexia/Cachexia Therapy (FAACT) and Quality of Life (QoL) (EORTC scale) were reported (see Table).

Conclusion: This study provides suggestive evidence of a favorable effect of a tailored nutritional counseling during chemotherapy.

Acknowledgement: this study was carried out within the PhD program in Experimental Medicine and Systems (XXIX cycle, Medical Oncology Course).

Table: S8

Variable	T0/T1	T1/T2	T2/T3	T0/T3	T1/T3
Performance data					
F max (Kg)	0.01*	0.00*	0.01*	0.03*	-
Resistance (s)	0.01*	0.01*	0.01*	0.01*	-
FFM (Kg)	0.73	0.15	0.09	0.20	-
MM (Kg)	0.23	0.04*	0.00*	0.17	-
Anthropometric data					
Right AC	0.68	0.18	0.08	0.20	-
Left AC	0.86	0.01*	0.01*	0.29	-
Gastrointestinal symptoms					
Nausea	-	-	-	.	0.03*
Disgeusia	-	-	-	-	0.24
Dysphagia	-	-	-	-	0.04*
FACIT-D TOI	-	-	-	-	0.01*
FAACT-TOI	-	-	-	-	0.02*
Wellness					
Phase angle	0.08	0.06	0.03*	0.01*	-
FACIT-fatigue	-	-	-	-	0.06
EORTC	-	0.00*	0.03*	-	0.00*

*statistically significant; FFM: fat free mass

S9 Sunitinb, hypertension and renal function: a monocentric experience

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Background: sunitinib and other antiangiogenetics (AAG) have been shown to significantly increase blood pressure (BP). AAG-related hypertension (AAG-HTN) may be defined as a new diagnosed HTN or worsening of a pre-existing one. If not correctly managed it may lead to major cardiovascular (CV) events (i.e. acute coronary syndrome and stroke) and to AAG withdrawal. Preservation of renal function may be crucial for both AAG and antihypertensive treatments.

Patients and Methods: between 1st March 2012 and 1st May 2017, at Treviglio Hospital (Italy) all patients (pts) receiving sunitinib underwent a basal multidisciplinary evaluation. BP and renal function (estimated glomerular filtration rate [e-GFR], and basal 24h microalbuminuria) were monitored before, during and after sunitinib treatment.

Results: 20 pts (median age 63.5yrs, range 49-83, male/female=15/5) were evaluated, all being affected by renal cancer (clear cell=16; papillary=3, poorly differentiated=1), 2 pts had also colo-rectal adenocarcinoma. All pts but 3 underwent radical nephrectomy. Basal e-GFR was >89 ml/min*1.73mq in 3pts, 60 to 89 in 10, <60 in 6 (not available in 1); basal 24-h microalbuminuria (evaluable in 10pts) was normal in 2 pts, 30-300mg/24h in 7 (median=45mg/24h), and > 300 in 1. Evaluation at 6 months and at the end of sunitinib showed stable (6pts) or improved (5pts) e-GFR, 6 months worsen with subsequent improvement in 2pts, and worsened e-GFR in 7(35%). Overall 65% of pts had stable or improved e-GFR. Eleven pts had a pre-existing diagnosis of HTN(55%), 5 of them requiring an adjustment of antihypertensive therapy before sunitinib because of uncontrolled HTN. Importantly, a new diagnosis of HTN before sunitinib was done in 4pts(20%). After sunitinib initiation, AAG-HTN was observed in 14(70%). HTN control was obtained in 12 out of 13 evaluable pts(92%). All classes of antihypertensive drugs were used, but all pts received an inhibitor of the renin-angiotensin-aldosterone system (RAAS). The number of drugs/patient to control AAG-HTN, was 1(N = 2), 2-3(N = 6), 4-5(N = 5).

Conclusions: The high rate of HTN diagnosed before sunitinib introduction (20%) and that of AAG-HTN (70%) suggest the crucial role of a careful multidisciplinary basal evaluation of pts. Renal function should be carefully monitored, but in most of pts e-GFR is stable or even improved. These results suggest that sunitinib and RAAS inhibitors may be used safely, thus resulting in a better management and outcome of pts.

S10 Baseline characteristics of cancer Patients demanding integrative oncology (IO) support. The experience of Nuova Oncologia Integrata (NOI), an Italian non-profit organization

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Background: A part of cancer patients (pts) ask for IO.We assess their basal traits to justify their need to integrate conventional cancer therapy.

Methods: Nuova Oncologia Integrata (NOI) allows pts to choose mind-body support without having to depend upon economic factors.At entry, each pt recieves 8 validated tests addressing basic self-esteem(BSE), anxiety/depression(HADS, STAI-Y), distress (DT), pain, fatigue(FACIT), pos/neg emotions(PANAS) and a self-reported measure of health(SF36)

Results: From 10/2016 to 4/2017,79 pts asked for mind-body programs.Males(M) 8/79 (10,1%);females(F) 71(89.9%).Median ageM: 68(42-82), F:59(32-80).43.7% of F were 50-59 years old;50% of M 70-79 years old 60 pts(76%)completed tests,15 pts(19%)returned incomplete tests Primary tumor:64 pts(81%)breast, other 19%(thyroid 2, prostate 1, lung 1, lymphoma 2, brain 1, gastrointestinal 5 and gynecological 3) HADS-A:no-anxiety 41 pts(56.9%), slight 15(20.8%), moderate 14(19,4%), severe 2 (2.8%).Anxiety any grade: F45.5%, M16.7%;moderate/severe anxiety: F22.7%, M16.7% State-trait(S-T) anxiety (STAI-Y).Clinically relevant:54.7%;pts T/Spos:50%;T-neg/S-pos:5.4%;T/Sneg:37%.Per age (cut-off:age 65):73.9% S/Tpos pts (<65) vs 10.7% (>65) HADS-D:no-depression 52 pts(72.2%), slight 13(18.1%), moderate 6(8,3%), severe 1 (1.4%).Depression any grade:27.8%;moderate/severe:9.7%.No differences by sex. Pain:absent 15.8%;slight 19.7%;moderate 43.4%;considerable 19.7%;severe 1.3% DT:no-distress 9.3%, slight 21.3%, moderate 40%, severe 29.3% FACIT:no-fatigue 4.1%, slight 59.7%, moderate 30,5%, considerable 5.5%, severe 0% PANAS:equivalent pos-emotions F vs M(median pos-score 26 vs 27); neg-emotions F>M (median neg-score 20 vs 11.5) BSE:15 pts(18,9%) scored >75 percentile.Low score mostly seen in age 40-60 SF36:22.8% feels worse than general population, namely physical role (39,2%), emotional role (30.4%), social activities (27.9%).In >80%, physical/mental activity, pain, vitality, is in the normal range

Conclusions: Cancer pts in IO programs are comparable to the general population of same sex/age in vitality and physical/mental activity, but perception of physical/emotional role and social activities are worse.Anxiety is more prevalent than depression, particularly in younger/females.Women have neg emotions twice as much as men.Moderate pain is common.Fatigue is generally light;distress is common.A low Self-Esteem is seen in pts 50-60 year old.Knowing the basal traits of cancer pts seeking support can guide IO organizations.

S11 High cumulative anthracycline dose without cardiac toxicity: a study on outlier patients

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Background: Cardiac toxicity is a well known dose dependent side effect of anthracyclines. We aimed to explore the clinical characteristics of those patients who in spite of very high cumulative doses of anthracyclines did not develop cardiotoxicity.

Patients and methods: We searched the database of our medical oncology unit to identify patients who received =900mg/m^2 of epirubicine (considered as the threshold dose) irrespectively of primary cancer site or treatment line, undergoing to regular cardiac monitoring by echocardiography and without any evidence of cardiac toxicity.

Results: We identified 10 patients with a high cumulative dose of anthracyclines who did not show cardiac toxicity (F/M ratio 9/1, median age 58 [range 49-71yrs]). All but two patients (one metastatic sarcoma and one advanced epatocellular carcinoma) were affected by a metastatic breast cancer. Patients received weekly epirubicin as last resort active treatment for heavily pretreated disease. Treatment resulted in in long-term disease control so leading to higher than usual cumulative dose. Four out of 10 pts previously received epirubicin as part of adjuvant treatment. The median total dose was 1600mg (range 1350-2220mg). We searched for a clinical or pharmacological protective profile associated to the lack of cardiac toxicity in these patients. Only two patients were treated with a cardioprotective agent (one β-blocker and one RAAS inhibitors). Interestingly, the main difference with respect to the patients who developed myocardial dysfunction was the fact that all patients who did not develop cardiac toxicity concomitantly received long-term opioids for pain control (median morfine dose 60mg/die [range 20-160mg/die]).

Conclusions: Our preliminary clinical data could support the preclinical evidence of a cardioprotective effect of morfine against anthracycline cardiotoxicity thus providing a rationale for a prospective observational clinical study on a larger population.

S12 Role of Anaplus HP in prevention of chemotherapy-induced peripheral neuropathy (CIPN) in patients affected by breast cancer treated with taxane-based adjuvant chemotherapy

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Background: Peripheral neuropathy is one of the main side effects of chemotherapy, especially taxane-based, greatly impairing patients' quality of life and often leading to dose delay, dose reduction or treatment discontinuation. Incidence of CIPN is 1-12%. Taxanes may induce sensory neuropathy with paresthesia and neuralgia, as they cause blockage of axonal microtubules and peripheral demyelination. Anaplus HP is a dietary supplement based on L-acetylcarnitine, N-acetyl-L-cysteine, inositol and α-lipoic acid, used to prevent and treat CIPN. This study was to evaluate the role of Anaplus HP in prevention of CIPN in patients affected by breast cancer treated with taxane-based adjuvant chemotherapy.

Patients and methods: Since September 2015 to January 2016, we administered 2 capsules per day of Anaplus HP to 25 patients affected by breast cancer treated with taxane-based adjuvant chemotherapy. Average age of enrolled patients was 60 ys (range 39-75 ys). 16 patients were undergone to 4 cycles of EC chemotherapy, followed by 12 weekly cycles of paclitaxel; the remaining 9 patients were undergone to 3 cycles of FEC chemotherapy, followed by 3 cycles of docetaxel, administered every three weeks. The 12 Her-2 + tumors were also treated with trastuzumab for one year. We evaluated incidence and severity of CIPN by administering patients the EORTC-QLQ-CIPN20 survey at the beginning of taxane treatment, after each cycle of chemotherapy with docetaxel or after each cycle of three paclitaxel weekly doses, and finally three and six months after the end of taxane treatment. Neurotoxicity was recorded according to CTC-NCI 3.0.

Results: 3 patients (12%) treated with weekly paclitaxel showed G1-G2 paresthesia of the lower limbs. Paresthesia appeared between eighth and eleventh cycle of paclitaxel, resulted in no delays, no dose reductions, no additional therapies required and disappeared within three months after the end of chemotherapy. The remaining 22 patients (88%) didn't exhibit the typical symptoms of taxane-induced peripheral neuropathy (pain, numbness, paresthesia).

Conclusions: Although enrolled patients are few, our experience highlighted the efficacy of Anaplus HP as prophylaxis of taxane-induced peripheral neuropathy in patients undergone to adjuvant chemotherapy for breast cancer. Because of small sample size and the absence of a control arm further randomized studies are needed to better assess the impact of Anaplus HP on CIPN.

S13 Micetrin to prevent chemotherapy-induced nausea and fatigue in adjuvant treatment of breast cancer

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Background: Chemotherapy of neoplastic disease often causes many side effects. Among these, we should consider fatigue and nausea that, thanks to the new antiemetic therapies, rarely results in vomiting. A high incidence of fatigue and nausea is observed among patients affected by breast cancer treated with anthracycline-, taxane- and alkylating-based adjuvant chemotherapy. Micetrin is a nutritional supplement consisting of fungi(Lentinula edodes, Ganoderma lucidum, Grifola frondosa), C vitamin, magnesium bisglycinate and superoxide dismutase, which can be used to mitigate the side effects of adjuvant chemotherapy in breast cancer, due to its antioxidant and immunomodulatory properties. This study was to evaluate the role of Micetrin in the prevention of nausea and fatigue in patients affected by breast cancer treated with adjuvant chemotherapy.

Patients and Methods: since February 2015 to April 2016, we enrolled 30 patients with stage II and III breast cancer treated with adjuvant chemotherapy. They received 4 cycles of EC chemotherapy every 21 days, followed by 12 weekly cycles of paclitaxel. Patients with Her-2 + breast cancer were treated with trastuzumab. We administered Micetrin (1 sachet per day) to 15 patients from 2 days before the beginning of adjuvant chemotherapy until a month after last dose of chemotherapy. The remaining 15 patients received only supportive care. To evaluate nausea and fatigue, we administered enrolled patients EORTC QLQ-C30 survey (Version 3.0) at the beginning, during (after three months) and at the end of adjuvant chemotherapy. Nausea and fatigue were assessed according to the criteria CTACE (version 4.0).

Results: Average age of the patients enrolled in Micetrin arm was 55 years (33-72), in the control arm was 51 years (32-70). Nausea was less frequent in Micetrin than control arm (nausea G1 20% vs 33%, nausea G2 0% vs 7%). Fatigue was less frequent and severe in Micetrin than control arm (fatigue G1 47% vs 33%, fatigue G2 33% vs 60%). Micetrin was well tolerated with no significant side effects.

Conclusions: Micetrin has proven to be able to help traditional supportive care in the prevention of side effects of adjuvant chemotherapy in breast cancer, especially nausea and fatigue.

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T - MISCELLANEA

T1 Thrombin generation (TG) and D-dimer levels for the identification of cancer patients at higher VTE risk enrolled in the HYPERCAN study

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Background: Identification of cancer outpatients who might benefit from primary thromboprophylaxis is still actually a major challenge for cancer patient management. A promising approach is the stratification of patients according to their risk of thrombosis, applying risk assessment models that include clinical parameters and biomarkers. Aim of this study is to assess whether in a cohort of newly diagnosed metastatic non-small cell-lung, gastric, colorectal and breast cancer patients, enrolled in the ongoing HYPERCAN study (Thromb.Res. 2014), the measurement thrombin generation assay (TG), fibrinogen, and D-dimer, may be predictive of VTE and may help physician in the better treatment of cancer patients.

Methods: As of September 2016, overall 739 patients with metastatic cancer have been enrolled. Blood samples of patients are collected at enrollment (before starting chemotherapy treatment), after 3 and 6 chemotherapy cycles, and at end of treatment, or earlier if VTE occurrence or cancer disease progression. We measured TG, fibrinogen, and D-dimer levels at enrollment from the first 433 patients (NSCL= 50.1%, gastric= 11.5%, colorectal= 20.6%, breast= 17.8%). TG was measured by the Calibrated automated thrombogram (CAT assay, STAGO, France) at 1pM TF and results expressed as Peak of thrombin; fibrinogen and D-dimer were measured by commercial assays (Q.F.A. Thrombin; D-dimer HS; Werfen, Italy).

Results: In our group of patients, VTE incidence is 25%. At enrollment, patients have Peak, fibrinogen and D-Dimer levels significantly greater than those of healthy subjects ($p < 0.01$). Pre-chemotherapy levels of D-dimer $\geq$493 ng/ml or Peak $\geq$407 nM are associated with increased VTE rates ($p < 0.05$). Differently, fibrinogen levels are not associated with an increased VTE risk. Khorana score fails to identify HYPERCAN patients at higher risk of VTE. We tried to modify the Khorana score adding D-dimer and Peak, assigning 1 point to each biomarker over the cut-off value. Integration of the Khorana score with these biomarkers allowed us to identify those patients at higher VTE risk.

Conclusions: This study supports the hypothesis that measurement of plasma coagulation markers can improve the identification of cancer subjects at high VTE risk. These subjects may probably be best candidate for primary thromboprophylaxis.

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T2 Thrombin generation for prediction of early cancer recurrence in breast cancer patients undergoing post-surgical adjuvant therapy: data from the prospective HYPERCAN study

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Background: Screening for breast cancer has greatly increased early diagnoses, leading to anticipated cancer treatments by surgery and systemic adjuvant chemotherapy (SAC) and reducing the risk of disease recurrence (DR). However, local relapses and distant metastasis may occur in 2-7% and 20% of resected patients, respectively, in the 10 years following surgery. In this setting, the identification of high-risk patients who might most benefit from more aggressive therapy is fundamental. Aim of this study is to evaluate whether some hemostatic biomarkers may be prognostic of early (first two years) disease recurrence (EDR) in a group of breast cancer patients undergoing post-surgical SAC.

Methods: Plasma samples from 690 limited-resected breast cancer patients (10M/680F), enrolled in the Italian, prospective, multicenter HYPERCAN study, were obtained at enrollment before starting SAC and after 1, and 2 years follow-up. Samples were tested for fibrinogen, D-dimer, and thrombin generation (TG). Clinical data and information regarding surgery, cancer subtype, and treatment were recorded. DR was routinely monitored by imaging during post-treatment surveillance.

Results: At enrollment, fibrinogen levels were in the normal range (316±87 mg/dl), while D-dimer and endogenous thrombin potential (ETP) were increased (respectively 257±353 ng/ml and 1680±377 nM*min) compared to a control group of healthy subjects. During follow-up, D-dimer significantly diminished over time, while no modifications occurred in the other biomarkers. After 2 years follow-up, 5.7% of patients presented with EDR. Kaplan-Meier analysis revealed that an ETP value $\geq$1670 nM*min at enrollment was an independent risk factor for EDR (HR = 3.65; 95% CI 1.60-8.34; $p < 0.01$). Differently, EDR was not associated with fibrinogen and D-dimer levels. A risk assessment score for the identification of breast cancer patients at higher risk of EDR has been created using ETP, hemoglobin level and triple-negative subtype variables, that were found to be independent risk factor of EDR in multivariate analysis.

Conclusion: We showed, for the first time, the prognostic significance of measuring pre-chemotherapy TG levels on the risk of EDR in resected breast cancer patients. After a proper validation, this biomarker could be a candidate to tailor a risk-adapted adjuvant treatment.

Project funded by AIRC "5xMILLE" n. 12237 grant from the "Italian Association for Cancer Research (AIRC)".

T3 Increased frequency of acute reactions to iodinated contrast media after anti-CTLA-4 immunomodulating antibodies in cancer patients

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Background: The aim of this study was to investigate whether cancer immunotherapy, in particular with immune checkpoint inhibitors, increased the incidence of allergy-like immediate adverse reactions to iodinated contrast media (ICM) with respect to "standard" cancer chemotherapy or targeted therapy.

Methods: We retrospectively evaluated the incidence of contrast-enhanced computed tomography (CECT)-related immediate adverse reactions (ARs) in cancer patients undergoing treatment. Using an institutional radiological database (Elefante, Agfa), we identified all consecutive cancer patients who performed at least one CECT after starting any medical cancer treatment at our institute between January 1, 2006 and December 31, 2014. All patients were outpatients and with a performance status of 0-1 by ECOG scale. Each ICM-related AR was classified according to the American College of Radiology Manual on Contrast Media, version 10.1 as "allergy-like" or "physiologic" and graded as mild, moderate, or severe.

Results: The final database included 3,521 patients who underwent first- or second-line systemic treatment for metastatic disease and were re-evaluated at the end of treatment with CECT. Fifty-nine of the 3521 patients received ipilimumab (Ipi), 75 received cytokines (Cy), and the remaining 3,387 received non-immunologic agents (CHT). The mean number of CT scans performed before the index CT scan did not significantly differ between groups ($p = 0.190$). Overall, 71 (2%) patients developed ICM-ARs. The distribution of events among the groups was: 11.9% of reactions in Ipi patients (7/59), 5.3% in ts (4/75), and 1.8% in the CHT ones (60/3,387) with a $p < 0.001$ that indicates a significant statistically difference between treatment groups and reactions number. All the ARs registered in the Ipi and Cy groups were allergy-like reactions, while 10% of the ARs observed in the CHT group were of the physiologic type (6/60).

Conclusions: Our data show that immunological cancer treatments, Ipi in particular, considerably increase the risk of developing CECT-related immediate adverse reactions with respect to non-immunologic agents. Although these findings now need to be validated in larger prospective studies, they serve as a "wake-up call" to radiologists to closely monitor patients who have previously received cancer immunotherapy with anti- CTLA 4-antibodies when using ICM in order to reduce the risk of potentially severe immediate adverse reactions.

T4 New rules for clinical trials: who will play the game?

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Background: The recent legislation on clinical trials, as the Italian Determination 809/2015 about Phase 1 studies and the European Regulation 536/2014, definitively imposes the transition from a "physician addicted" research to the acknowledgment of specific skills, such as those of clinical research coordinators (CRCs) and research nurses.

However, the national collective health contracts allow the employment of these professionals only through atypical contracts that, due to "jobs act", will soon be banned, causing a large professional vacuum. Before the deadline extension granted by Government, we decided to map how much the problem was widespread among the CRCs.

Methods: In November 2016 an anonymous web survey has been addressed to CRCs from Gruppo Italiano Data Manager. The survey, preceded by a brief written description of the aims, was composed by 7 items focused on the problem of the imminent expiration of contracts.

Results: 231 CRCs completed the survey, with a prevalence of participants from Emilia Romagna (22%), Piemonte (13%), Lombardia (12.5%) and Veneto (10%). The majority of respondents (78%) worked through an atypical contract, while few can count on more stable type of employment (7.4% fixed term contract and 14.6% open-ended one). The most virtuous region is Emilia Romagna (37.5% of the open-ended contracts), followed by Piemonte (21.9%) and Lombardia (18.8%). The 67.5% of respondents will be affected by the jobs act problem, with multiple contract expiration timing: 32% from January to April 2017; 23% from May to August 2017; 23% from September to December 2017; 17.3% from Jan 18; 4.7% unknown. Interestingly, about 50 CRCs were unwilling to participate in the survey, now demoralized from the age-issue of the lack of professional recognition.

Conclusions: The recent extension granted by our Government has only postponed a problem that should be quickly resolved. Where a such large number of CRCs will remain unfilled, it would create a vacuum of skilled work force that can hardly be covered by physicians. Whereas these numbers are understated and the problem also affects another big ghost of clinical research (research nurses), in the absence of a permanent solution, Italy is unlikely to meet the quality standards imposed by Europe. This will be reflected in a loss of appealing to the pharmaceutical market but mostly in a slump of therapeutic options for patients.

T5 The pre-emptive screening of multiple polymorphisms in gene-encoding dihydropyrimidine dehydrogenase (DPD) improve prevention of toxicity on patients candidate for fluoropyrimidine based-chemotherapy. An experience of the Reggio Emilia Cancer Center

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Background: Fluorouracil is one of the most used anti-tumor chemotherapeutic agents in oncology and dihydropyrimidine dehydrogenase (DPD) plays a key role in the metabolism of this drug . In patients with DPD deficiency the use of standard dose of fluorouracil can produce life-threatening toxicities. Deleterious polymorphisms in gene-encoding DPD (*DPYD*) may results in the severe reduction of DPD enzymatic activity. DPYD*2A (IVS14 + 1G > A) is the most common single-nucleotide polymorphism (SNP) associated with critical DPD deficiency. At present, most of the evidence supports screening for at least 3 SNPs (DPYD*2A, c.2846 A > T, c.1679T > G). The aim of this study is to confirm that the detection of additional polymorphisms of DPYD could enhance prevention of fluoropyrimidine toxicity.

Methods: In 2011, we began to screen DPYD*2A in patients candidate for fluoropyrimidine based-chemotherapy. As the first step of the evaluation, we selected all cases of DPYD*2A wild type, from 2011 to 2013, who developed CTC-NCI-V.3 toxicity ≥ G3. In these patients, we researched the other 3 SNPs (c.2846 A > T, c.1679T > G, c.2194G > A). Mutational status was analysed with real Time PCR.

Results: From 2011 to 2016 we pre-emptively screened DPD deficiency in 1,863 patients. Thirty two subjects (1.6%) were carriers of the DPYD*2A mutation. As the first step of the evaluation, 917 subjects were assessed from 2011 to 2013. Of these 917 wild type cases, 127 presented toxicities ≥ G3. In this subgroup, 24 patients (19%) proved to be mutated for the other SNPs of DPYP, as reported in the Table.

Table: T5

SNPs	No. of pts	%
c.2846 A > T	1	0.79
c.1679T > G	2	1.57
c.2194C > A	21	16.53
Total	24	18.89

Conclusions: Preliminary data show that in 24 (19%) of 127 patients who presented severe toxicity which was not correlated with DPYD*2A, we found other polymorphisms of gene encoding DPD. Out of the 3 SNPs evaluated, c.2194 G > A proved to be the most frequent, although it is the polymorphism that is least known and least studied. Such results suggest that the evaluation of additional polymorphisms could enhance the prevention of fluoropyrimidine toxicity. The results are expected to be clarified further in the second step, which is ongoing.

T6 Final results from CAMEO-PRO study: complementary and alternative medicine in oncology. physicians inform oncological patients

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Background: The role of Complementary and Alternative Medicine (CAM) in oncology is heavily debated. It is estimated that about half of cancer patients use at least one form of CAM in their life but there is a strong unwillingness of patients in talking about CAM with their oncologist. Primary aim of this study was to inform patients about CAM, focusing on their supposed benefits, toxicities and interactions with conventional therapeutic agents. The study also explored patient's perception about CAM and ascertained the level of CAM its use among cancer patients of an Italian academic hospital.

Methods: From April 2016 to April 2017, the observational pilot trial "CAMEO-PRO" prospectively enrolled 239 cancer patients that were invited to attend a tutorial about CAM at the Department of oncology, University Hospital of Udine, Italy. Before and after the informative session, patients were asked to fill a questionnaire reporting their knowledge and opinion about CAM .

Results: Overall, 163 (70%) women and 70 (30%) men were enrolled. Median age was 61 years. At study entry, 168 (72%) patients declared they had never been interested to this topic previously; 24 patients (11%) revealed the use of a type of alternative therapy and 58 (28%) revealed the use of complementary therapy. In total, 139 (55.2%) patients attended the informative session. Table 1 shows the percentage of response and the opinion's change about CAM before and after the tutorial. All patients that participate to the session reported that the session was moderately (16%) or very (83%) helpful.

Table: T6

	Strongly disagree %		Slightly agree %		Moderately agree %		Strongly agree %		P
	before	after	before	after	before	after	before	after	
I clearly know the difference between alternative and complementary medicine	24.1	5.3	27.6	4.4	33.9	25.8	14.2	64.2	<.0001
Alternative medicine is a valid alternative to conventional medicine	34.5	67.2	41.6	26.5	20.35	5.3	3.5	0.9	<.0001
Even if alternative medicine does not work, it does not do damage	25.9	63.3	35.7	25.9	29.4	8.0	8.9	2.7	<.0001
Alternative medicine can be dangerous	10.2	3.4	17.6	5.6	51.8	25.6	20.4	65.7	<.0001
Use of alternative medicine can hinder a correct therapeutic path	10.6	1.8	25.7	4.4	38.9	36.3	24.8	57.5	<.0001
I would do or I do use CAM	28.8	52.9	27.9	19.2	28.8	18.3	14.4	9.62	.003

Conclusions: Informative sessions seem to have an impact on patients' perceptions and opinions about CAM.

T7 Economic burden of cancer: a population-based cost analysis

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Background: Cancer poses a substantial economic burden on health care systems." Cost-of-illness" analysis allows for a comprehensive estimation of the costs of cancer care and for the identification of relative costs of specific subgroups of diseases, informing future decisions for governmental budgets allocation.

Methods: We ran a population-based cost analysis in the Forlì-Cesena province (396.696 inhabitants) in 2016, using a government perspective (direct health care resources only). We considered 6 subgroups of cancers, using the International Classification of Diseases, 10th rev.: hematologic, gastrointestinal, breast, urogynecological, thoracic, rare tumours and others. We included five categories of services: inpatient, outpatient, emergency, and end-of-life care, drugs. We used National and Regional official charges for the valuation of care settings. For drugs, we used the national pharmaceutical formulary by AIFA. We estimated per capita (PC) cost by dividing the total cost for cancer subgroup for the total number of residents in the Forlì-Cesena Province.

Results: Total costs equaled to more than 98 million euro. Among cancers subgroups, hematology absorbed the largest share (28%, 70,6 €PC costs), followed by gastrointestinal (20%, €49,6 PC costs). Thoracic accounted for 12% of total costs, but per patient costs were the highest (€19.349). Lowest per patient costs were in breast. Cost absorption is uneven referring to health care services, too: eg. gastrointestinal cancer absorbs about 30% of total inpatient care cost compare to only 8% for breast, which however accounts for 30% of total outpatient care whereas thoracic only 8%.

Conclusions: Our analysis sets the basis for better understanding total costs in cancer care and resource allocation among cancer subgroups and care settings. Benchmarking is feasible for the use of administrative databases.

T8 Genetic Factors Associated with Platinum Toxicity: A Preliminary Study

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Background: Platinum-based doublets are the standard chemotherapy for lung cancer. The identification of markers associated with drug-toxicity may improve the success of the treatment. Single nucleotide polymorphisms (SNPs) mapping into the genes involved in platinum transport or detoxification may explain occurrence of toxicities. In this study, we evaluated the role of 4 SNPs in predicting the onset of adverse events for lung cancer patients receiving cisplatin or carboplatin.

Methods: Eighty-two patients affected by non-small-cell and small-cell lung cancer treated with cisplatin- or carboplatin-based chemotherapy (st. II-IV) were enrolled. Before genetic analysis, patients signed a written informed consent. DNA was extracted from peripheral blood samples and genotypes were determined by Real-Time PCR. We selected and analyzed 4 SNPs: ABCC2 -24C>T/rs717620, ABCG2 c.421C>A/rs2231142, ABCB1 c.3435C>T/rs1045642 and GSTP1 c.313A>G/rs1695. Patient characteristics and genotypes were retrospectively correlated with haematological, gastrointestinal, renal and global toxicity as recorded by Common Terminology Criteria for Adverse Event (CTCAE) v4.03.

Results: Variant alleles were present in 18.3% of patients for ABCC2 -24C>T, 8.5% for ABCG2 c.421C>A, 53% for ABCB1 c.3435C>T and 34.8% for GSTP1 c.313A>G. Heterozygous "CT" at ABCB1 c.3435 were significantly associated with both global (OR = 0.23; 95% CI 0.07-075; p = 0.02) and haematological (OR = 0.20; 95% CI 0.05-0.69; p = 0.01) toxicity. Similar results were observed by genetic dominant model (CT+TT vs CC) for global (OR = 0.33; 95% CI 0.11-0.96; p = 0.04) and haematological (OR = 0.26; 95% CI 0.09-0.79; p = 0.02) toxicity. No other significant associations were observed.

Conclusions: This study reveals that ABCB1 c.3435C> T polymorphism influences platinum toxicity. Variant "T" allele seems to exert a protective effect on the development of toxicities. Further epigenetic regulation studies are needed to validate and shed more light on this association.

T9 The role of the clinical risk group classification system in the management of oncologic patients in need of high complexity of care. A pilot study in the local health unit "USL Umbria 2"

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Background: Complex oncologic patients require high standards of care, multidisciplinary approach and great resources. The aim of our study is to evaluate the capability of the 3M Clinical Risk Group (3M CRG) system in identifying and managing this specific type of population.

Patients and methods: The study was conducted on a cohort of oncologic patients in need of highly complex care provided by six districts in the Umbria 2 Local Health Unit (USL) during 2013. This cohort of patients was identified through the 3M Clinical Risk Grouping Software by using individual demographic, morbidity and pharmaceutical information retrieved from administrative data (e.g. inpatient, outpatient, drug). The same system (CRG) stratified the population from nine mutually exclusive health status up to 1080 risk groups. Both the analysis of the healthcare provided and the analysis of costs entailed were computed in all the six districts.

Results: In 2013, USL Umbria 2 provided health care to 2682 patients (0.7% of the total population; 11% of the total health care expenditure) assigned by 3M CRG to the health status 8 (dominant and metastatic malignancies) and 5 severity of illness. The patients were predominantly males (51.52%) and belonging to 55-74 years age group (47.76%). 97.95% of the cohort was hospitalized. In all the six districts, the largest amount of resources was provided for inpatient care. Terni district had the largest number of patients with health status 8 (33.89%). Orvieto district recorded the highest healthcare cost (€17978.7).

Conclusions: Our study confirmed CRG as a useful system to identify different high-need population and manage complex oncologic patients by assessing their needs and adjusting interventions and resources. The CRG system combines inpatient data with information from territorial services. For this reason it can be a useful tool for epidemiological analysis, governance of therapeutic-diagnostic pathways and continuity of healthcare in sync with "Italian plan of the chronicity".

Table: T7

	ALL	Hematology	Breast	Gastrointest	Uro-Gyn	Thoracic	Rare, Others
Patients (n°)	**11.931**	**4.388**	**2.759**	**1.849**	**1.457**	**600**	**877**
Inpat. Care*	34.107	8.341	2.721	10.142	5.604	3.901	3.395
Drugs*	26.864	10.624	5.496	2.444	3.238	2.753	2.308
Outpat. Care*	17.889	3.955	5.381	2.623	2.578	1.672	1.677
End-of-life care*	18.722	4.802	1.707	4.328	2.407	3.220	2.257
EmerG. Care*	764	286	98	153	91	69	64
Total (€)*	**98.348**	**28.010**	**15.404**	**19.692**	**13.920**	**11.617**	**9.702**
Resident Popul. 396.696							
Per Capita Costs	**€247,9**	**€70,6**	**€38,8**	**€49,6**	**€35,1**	**€29,3**	**€24,5**
%	100%	28%	16%	20%	14%	12%	10%
PER PATIENT COSTS	**€8.243**	**€6.383**	**€5.583**	**€10.650**	**€9.553**	**€19.349**	**€11.067**

(*costs in thousands of €)

T10 Osteonecrosis of jaw (ONJ) after antiresorptive treatment (bisphosphonates, denosumab) of cancer-treatment induced bone loss (CTIBL): a negligible risk?

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Background: CTIBL is a concern for breast and prostate cancer patients (pts). Treatments proposed for prevention and/or treatment of CTIBL include: oral alendronate (70 mg/week); oral risedronate (35 mg/week); iv ibandronate (3 mg q3months); oral ibandronate (150 mg monthly); biannual iv zoledronic acid (4 mg q6months); yearly iv zoledronic acid (5 mg q12months); sc denosumab (60 mg q6months). All these agents showed possible induction of ONJ, described by some Authors as "rare" (1/1.000-1/10.000, according to WHO) or "very rare" (<1/10.000). Actually, evaluations about the individual ONJ risk are uncertain, due to bias in old trials (unknown ONJ; short-term follow-up; etc) and in recent trials (very restricted ONJ definition; limited observation time). Vice versa, real life ONJ cases after bisphosphonate (BP) and/or denosumab treatment in osteoporosis pts are not so rare (even if probably underdiagnosed), exceeding the ONJ cases in metastatic cancer pts in some countries (eg, Korea). Since 2005 a multidisciplinary study group collected data of cases of ONJ in pts treated with BP in oncology and hematology centers of a regional network (Piemonte—Valle d'Aosta), and among pts followed in the main dental care and maxillofacial surgery centers of the area. Between 2004 and December 2008, out of 241 total ONJ registered cases, 20 pts (8.3%) had ONJ diagnosis after BP therapy of bone disease different from bone metastases or myeloma (i.e., osteoporosis, osteopenia, Rheumatoid Arthritis, Paget's disease, etc.) (*Fusco et al, ISRN Oncology 2013*).

Patients and methods: The survey was repeated, asking for ONJ cases observed between January 2009 and March 2016. We identified cases after cross-checking reports from medical oncology, haematology, and oral care centers to avoid double count and to integrate data.

Results: We received partial data about 440 cases: 335 advanced cancer pts (76%) and 105 pts treated for other diseases (24%). The median number of cases per year was clearly increased in years 2009-2015, especially in osteoporosis patients. Local visits to collect complete data of all cases (duration and doses of therapy; concomitant treatments and diseases; oral health risk factors) are ongoing.

Conclusion: Preliminary data show increase of ONJ cases in pts receiving BP or denosumab for osteoporosis. The cancer patients receiving antiresorptive drugs to treat or prevent CTIBL need oral care measures to reduce the ONJ risk.

T11 Safety and metabolic effects of the fasting mimicking diet in cancer patients

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Background: Preclinical studies have shown that a plant-based, low-calorie, low-protein, low-carbohydrate diet, also known as fasting mimicking diet (FMD), modifies systemic metabolism and displays significant antitumor effects. Nonetheless, no clinical data are available yet. In this study, we explored the safety and metabolic modifications of the FMD in cancer pts.

Methods: We prospectively evaluated cancer pts who followed a 5-days FMD (700 Kcal on day 1 and 300 kCal on days 2-5) every 21-28 days. Inclusion criteria were: pts with any cancer type (except for small cell lung cancer), stage and concomitant antitumor therapy. Main exclusion criteria were: BMI $< 20\ kg/m^2$, recent unintentional weight loss >5%, insulin-dependent diabetes and severe comorbidities,. Before and at the end of the FMD, we collected blood and urine samples to measure changes in metabolites and growth factors. We show data of FMD safety and metabolic effects at the end of the first cycle.

Results: We recruited 29 pts from November 2016 to April 2017. 20 had metastatic disease, and 27 received concomitant anticancer treatment. Breast (12), lung (3), prostate (3) and pancreatic (3) cancer were the most represented tumors. All pts completed at least one cycle of FMD. Based on the analysis of diet diaries, compliance to the diet was good, with only minor deviations (±10%) in the quantitative intake of permitted aliments. 79% of pts reported G1-G2 AEs, in particular fatigue (72%) and headache (10%), more likely to be related to the diet. One patient experienced G2 symptomatic hypoglycemia that required sucrose intake. No G3-G4 toxicities were observed. Relative weight loss during the first cycle was 4.65% (range 2.5-6.5%). The FMD reduced median glycemia by 15.6%, IGF-1 blood levels by 27% and insulin levels by 32%, while median triglyceride, total cholesterol and uric acid levels increased by 31.5%, 11% and 80%, respectively; finally, we observed an increase of average urine ketone body levels from 0.38 mg/dl (range 0-10) to 62 mg/dl (range 20-100).

Conclusions: Our interim analysis suggests that the proposed FMD scheme is safe and significantly modifies systemic metabolism in a heterogeneous population of cancer pts.

T12 The impact of social factors on oncology: The experience of the Reggio Emilia Clinical Cancer Center

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Background: After treatment for the acute phase of the disease, patients(depending on clinical condition)can be transferred to other sub-acute wards, discharged to home or released to local care facilities.This process is frequently hampered by social problems.The aim of this study is to highlight non-clinical factors that reduce the capability of the oncology wards.

Methods: We analyzed 265 clinical hospital records in our department.We assessed nationality, age, diagnosis, causes of admission, length of hospital stay and reasons for delayed discharge, if any.

Results: From October 2016 to April 2017, we authorized 265 hospitalizations for a total of 2665 days(d)of stay and a median of 10.07d. 239(90%)were EU citizens and 26(10%)non-EU.Of these,171(65%)were useful for initiating or continuing active oncological treatment,33(12%)for managing toxicity during cancer therapy,33(12%)for dealing with clinical deterioration and 28(11%)for performing diagnostic tests.In 31 cases(12%),we observed delayed discharge resulting in an average increase in stay of 7.35d.This translated into a median prolongation of 0.9d for all hospitalizations, corresponding to a total of 228d(9%)for non-clinical needs.The average length of stay of non-EU citizens was 11.4d, while that of EU nationals was 9.9d.The average delay in discharge was greater for non-EU citizens(2.5d)than for those in the EU(0.7d).The delays were caused by waiting for relocation to local care facilities(LCF 34%), inadequate support of caregivers(ISC 31%)(virtually all due to the lack of a suitable home), waiting for home medical devices(HMD 22%)and transfer to other departments(13%).

Conclusions: The above analysis revealed an acute care department that is burdened by social problems, the complexity of providing external care to patients and the impact of these factors on the cost effectiveness of health care, especially for non-EU inpatients.The data suggests the need to strengthen assistance on the local level and to identify caregivers and possible assistance-related social difficulties as early as possible.

Table: T12

Total days of hospitalization	2665
Median age(y)	60(22-88)
Nationality(%)	239 EU(90)
	26 non-EU(10)
Major non-EU nationaties(%)	Ukraine(27)
	Ghana(19)
	Morocco(15)
	Georgia(12)
Most frequent diagnoses(%)	Soft tissue sarcomas(14)
	NSLC(13)
	colorectal(11)
	breast(10)
Average length of all hospitalizations(d)	10.1(EU:9.9-non-EU:11.4)
Average delay in discharge(d)	0.9(EU:0.7-non-EU:2.5)
Total days for non-clinical needs	228
Average waiting time(d)	LCF(7)
	HMD(6)
	ISC(9)

T13 Blood stream infection in cancer patients—device management and epidemiology: the BSIDE study

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Background: Cancer patients are at a high risk of sepsis, and infection management is a major issue in this setting.

Methods: We retrospectively analyzed 55 consecutive cancer patients diagnosed with primary blood stream infection (BSI), according to CDC/NSHN Surveillance Definitions, at University Hospital of Udine from June 2013 to December 2016.

Patients' characteristics were collected at the hospital admission. Statistical descriptive analyses were performed on the whole population. Kaplan-Meier estimator and Log-Rank test were performed for survival analysis among patients with a central line (CL).

Results: The study population consisted of 52 patients (3 patients were lost on follow-up): 20 (38%) women and 32 (62%) men, median age 68 years. The most represented sites of the primary tumor were lung (21%), pancreas (17%) and stomach (15%); 85% of the patients had stage IV disease and, overall, 37 (52%) were on active anticancer treatment. ECOG PS was distributed as follows: 0 (4%), 1 (40%), 2 (52%), 3 (4%). 47 (90%) patients had a CL, 23 (44%) carried an infuse-a-port, 19 (37%) a peripherally inserted central catheter, 5 a central venous catheter. S. Epidermidis was the most frequent microorganism involved in the infection (36%), followed by S.Aureus (19%). Multi Drug Resistant pathogens represented the 23% of the microorganisms. In the 58% of the infections antibiotic therapy was shifted after knowing the blood culture results, in the other cases the empiric therapy was confirmed. Nineteen (40%) patients removed the CL after the antibiotic therapy has been started, 21 (45%) retained the CL. For 7 patients the management of the device was not known. Percentage of patients alive at 30 days after diagnosis was higher in the group who had the CL removed: 17 (89%) patients vs 11 (52%) (OR: 7.1 p = 0.0078). After the resolution of the infection, considering the whole population, 19 patients (37%) received further active cancer treatment.

Conclusion: The study suggests a survival advantage for cancer patients who removed the CL after the BSI, compared with those that retained the device. Further investigations are needed to confirm these findings and contribute in improving the management of sepsis in the oncologic context.

T14 The continuing training program of oncology network of Piemonte and Valle d'Aosta: a model for improving the management of oncologic patients

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Background: One of the goals of Oncologic Networks is to organize training courses for operators involved in the diagnostic and therapeutic pathways of cancer patients, in order to update everyone of them about innovations introduced every year.

Methods: We yearly plan a training offer, both as residential and "on field" education, allowing to earn credits within the "continuos medical education program". These courses have the dual purpose of technical-scientific updating and of raising relational and communicative skills.

Results: During 2017 the Oncology Network of Piemonte e Valle d'Aosta has organized 31 residential courses: 7 dedicated to medical doctors, 10 to nurses, 5 to district directors and territorial nurses, 2 to biomedical lab technician, 7 to psycho-oncologist, administrative employees and social assistants. Reguarding "on field education", 32 courses have been conducted, carachterized by 5 lessons/year and 20 CME credits: 18 for cancer-site specific groups, including 2 for hematologists, 5 for groups engaged in trasversal topics such as cardiooncology, support therapies, late toxicities, geriatric oncology and palliative care, 1 for nurses and 1 for hospital pharmacists.

Moreover, 8 study groups composed of pathologists have been formed to allow clinical cases discussions and to enhance diagnostic uniformity. 108 recommandations and 17 consensus documents have been drafted during the last 5 years, and they are entirely published on Oncology Network web site (www.reteoncologica.it). Since 2016, P.I.C.O. System has been applied to draw up consensus documents.

Conclusions: Continuous medical education is an effective and basic tool to enhance operators' knowledge. It allows to decrease mistakes and time and money waste, to improve and uniformate clinical assistance; training enables operators to acquire high innovative value interventions and to recognizetheir limits. Patients benefit by CME programs, and their negative experiences can reduce.

T15 Can the use of clinical decision support system (CDSS) affect the number of adverse drug reaction (ADR) reports in the oncological patient? A preliminary evaluation of the status quo in Reggio Emilia Oncological Center (CORE) and future perspectives

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Introduction: The new legislation (DMS 4/30/2015) reaffirmed the obligation to report suspected adverse drug and vaccine reactions promptly and set strict time limits within which healthcare operators are required to report to the local network and agency. An internet site (www.vigifarmaco.it) was developed (AIFA n.519 10/7/16).

Objective: Monitoring of ADRs is a challenging research issue. Our belief is that there is little attention and information about this subject. We evaluate the state of reporting ADR in both oncologic and non-oncologic settings.

Methods: On 5/22/2017 we collected the data from a survey sent to 400 medical doctors in our Hospital, by e-mail on 5/11/2017. The survey included 8 questions in Italian language: age, sex, department, number of total ADR reports in 2016, number of ADR reports due to oncological drugs in 2016, number of ADR reports due to biological oncological drugs in 2016, the kind of reactions to report on and the knowledge of www.vigifarmaco.it site.

Results: 165 doctors completed the survey (41%), of whom 39 in the oncological departments (24%); 88 female (53.7%) and 76 male (46.3%); the most represented age range was from 31 to 40 (n = 63 41.2%). The number of reports/year was 0 (75.8%),1(8.7%), 2-5 (10.5%), 6-10(3.1%), 11-15(1.9%), 16-20(0%), >20 (0%); the number of reports/year for oncologic drugs was 0 (88.1%), 1 (5.6%), 2-5 (4.4%), 6-10 (1.9%), >11 (0%); the number of reports/year for biological oncologic drugs was 0 (93.6%),1-10(6.4%), >10(0%). No difference in the oncological or general doctors group. To the question "What kind of reactions are to be reported?" the right answer "mild and severe, known and unknown" was chosen by 38%, only "if severe" by 41.7% and only "if unknown" by 20.3%. 80.1% do not know the official site, 13.9% knows it but do not use it, only 6% knows and uses it.

Conclusion: Despite a strong commitment to awareness and information of doctors, adherence to ADRs is unacceptably low; doctors do not know the criteria for sending reports and are not up to date on new tools created to encourage the delivery of ADRs. It is essential to develop a simple and automated tool that will enable doctors to send all ADRs reports. Our next step will be to set up an instrument with these characteristics and to study its impact in clinical practice.

T16 Clinical trials and risk-based approach: reality or Utopia?

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Background: During the past 20 years, the increased complexity of Clinical Research generated new challenges to trials oversight. There is a growing consensus that a risk-based approach, focused on risks to the most critical data elements and processes needed to achieve study objectives, is better than 100% data verification during on-site visits (OSV) to ensure good quality and subject protection. Moreover, several authors have suggested that some data anomalies may be more readily revealed through centralized monitoring techniques than by OSV. These evidences have led in 2013 to a Food and Drug Administration (FDA) guidance document which encourages Sponsors to implement centralized monitoring in lieu of 100% OSV. We explore the actual extent of the risk-based monitoring approach implementation in Italy.

Methods: A review of all sponsors visits (from site selection to close out) received in a single institution in 2016 and in the 1st quarter of 2017 was done. The type and number of remote visits were analyzed. This review was subsequently expanded to other 13 Italian Oncology Units with a load of more than 50 studies per year.

Results: In 2016 in a total of 246 working days, 169 Sponsor Visits were received (mean of 84.5 visits for each data manager);11.8% were performed remotely. This trend is confirmed in the 1st quarter of 2017: 12.3% of remote visits on a total of 65 sponsor visits in 84 working days. The still high number of OSV forces the study staff to plan, sometimes, 2 OSV per day (10 times in 2016 and 5 in 2017) or to associate 1 remote and 1 OSV in the same day (5 times in 2016 and 4 in 2017). The low proportion of remote visits seems to be confirmed by data from other Centers. In the 23% of sites the sponsors performed over 20% of remote visits, while in almost the 40% a range from 10 to 20% is performed and <10% in the other 38.5% sites. The type of remote visit is mainly performed by no-profit sponsors (about 80%).

Conclusions: Despite FDA's recommendations, our data suggest that Sponsors seem to prefer OSV approach to clinical trials oversight. This trend, coupled with the Italian scenario in which the Study Coordinator is a profession not recognized by the Institutions, poses the Centers to a high job overload. Considering that a monitoring visit lasts approximately 6 hours, the time to devote to data entry drastically decreases endangering the foreseen deadlines and the quality of the study conduction.

T17 Adjuvant treatment in elderly cancer patients: a multicenter real-life experience

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Background: Elderly cancer patients are frequently underrepresented in clinical trials. Therefore standardized approaches to treat these subjects lack. Survival is further limited in elderly patients, who are often unable to tolerate aggressive regimens. Purpose of our work is to describe the patterns of care of elderly cancer patients as well as reporting resulting survival outcomes in a multicenter real-life experience.

Methods: We conducted a retrospective analysis of 358 consecutive patients aged ≥75 years with nonmetastatic cancer who received an adjuvant treatment at Sant'Andrea Hospital in Rome and San Camillo de Lellis Hospital in Rieti.

Results: Median age at diagnosis was 77 years. At the histological breast (65.6%) and colorectal (22.3%) cancer were the most represented ones. Comorbidities emerged in 80% of patients not resulting in a significant correlation with disease free survival (DFS) [Hazard ratio (HR), 1.1; (95% confidence interval [CI], 0.72-1.71); p = 0.63]. We didn't report any association between increased age and adverse events on chemotherapy. Risk analysis for DFS showed that female gender (HR,0.53; 95% CI, 0.37-0.78; p = 0.001) and a better performance status (PS) according to ECOG scale (PS1 vs PS0: HR,1.60; 95% CI, 1.08-2.34; p = 0.02 and PS2 vs PS0: HR, 3.31; 95% CI, 1.32-8.28; p = 0.01) had a significant lower risk for replace or death. Increased age (HR, 1.1; 95% CI, 1.07-1.16; p < 0.0001) and colorectal (CR) cancer (HR, 2.39;95%CI, 1.58-3.59; p < 0.0001) were associated with a shorter DFS.

Conclusions: This real-life multicenter experience identified four (gender, PS, age, CR histology) prognostic factors among elderly patients who received an adjuvant treatment. Prospective trials are necessary to select and customize chemotherapy in this group of patients.

T18 Preventive dose reduction of capecitabine in elderly population

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Background: Nowadays life expectancy is longer than a few decades ago and entails an increase in elderly population, defined as people over the age of 65. Since old age is a well known risk factor for developing neoplasia, in the future we can expect an increase in elderly cancer patients, a different population as far as the pharmacodynamic and pharmacokinetic processes are

concerned. The objective of this retrospective, mono-institutional study is to compare the efficacy and tolerability of the oral drug capecitabine among patients over 75 years compared to the reported data in literature.

Patients and methods: 117 pts older than 75 years treated with capecitabine as monotherapy (67% of patients) or in combination with other anti tumor drugs (33%) from 2006 to 2016 were evaluated. Colon, breast and stomach cancers were the most represented tumors (76%, 13% and 11% respectively); 58% were stage IV. All therapeutic regimens (adjuvant and advanced stage treatments) containing capecitabine were considered. A dose reduction of 25% of capecitabine was preventively applied at the beginning of the treatment.

Results: In this series, the median age was 80 years, ECOG PS 0-1. The median number of comorbidities was 2,8. DCR, PFS and OS were evaluated and compared to randomized trials in literature. DCR in this study was much lower (48% vs. 67,2%), but PFS and OS were not different (PFS: 5 vs. 5,7 months. OS: 11 vs. 13 months). Adverse Drug Reactions (ADR) were evaluated to assess tolerability. 3% of our patients had hematological ADR (grade III) and 24% of them non-hematological ADR (including diarrhea, asthenia, mucositis of grade III). In literature ADR are much more frequently reported (13% of hematological and 43% of non-hematological ADR).

Conclusions: Capecitabine is an oral anti tumor drug largely used in a variety of diffuse cancers (colon-rectum, stomach, breast). Elderly patients, with their physiologically altered metabolism processes, represent a current and future challenge in the treatment of a part of population increasing over time. In this study we found that a preventive 25% dose reduction of capecitabine reduces ADR, but at the same time it implies a reduction in efficacy. Further prospective studies are needed to understand if this reduced efficacy is due to physiological alterations peculiar of the elderly patients or to the numerous associated comorbidities, and if combination therapy is safer than monotherapy in this subset of patients.

T19 Internet in oncology: a new way to improve communication and information?

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Background: Cancer patients and their families are always looking for more information about prognosis and treatment. In recent years the Internet has become the main source of medical information but little is known about its impact on the oncologic patients and relatives and if it can change the patient-physician relationship.

Methods: After the clinical visit either for active chemotherapy or for follow-up, physician or nurses invited patients (with an oral informed consent) to complete a ten-minutes written questionnaire regarding their use of the Internet to seek medical information. Each questionnaire was coded with a consecutive identification number so as to ensure privacy. The questionnaire consisted of seven questions investigating other than demographic data, possibility of Internet access, type of information obtained online, its accuracy and usefulness, its impact on patient-physician relationship and any other sources of information.

Results: Over a period of four months, 200 questionnaires were distributed to 77 men and 123 women, with a mean age over seventeen years. A 60% of our patients declared the use of the Internet, more often in order to cope better with the disease and know more about the disease and therapeutic options. An eighty-seven percent of the patients indicated the need for greater clarity and security as the main reasons for search in the Internet. Only tirthy-six percent of the patients discussed the information with the healthcare providers and this was a way to feel better. The main reason to not discuss the Use of the Internet was the fear of a negative reaction form the oncologist. Obviously the use of the Internet was related with a younger age and higher schooling.

Conclusion: Oncologic patients and carers increasingly often use the Internet for searching medical information since it appears help to cope better with the disease. Discussing these information with the healthcare provider may improve the patient-physician relationship. Future efforts are needed to improve the quality and accuracy of Internet information and to provide a guide to patients in searching and interpretation of such information. Physicians should help patients to clarify the misunderstandings that arise from search on the Internet. Since the outcome of a patient might be influenced by the accuracy and quality of the information, today "the prescription" of websites to search medical information could become a commonplace.

T20 Implementation of the International Myeloma Working Group reccomendations on renal impairment in multiple myeloma patients in routine clinical practice

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Background: Renal impairment (RI), is one of the most common complications of multiple myeloma (MM), and it is associated with an increased risk of early death. The incidence of RI at MM diagnosis ranges from 20% to 50%, while its comparison occurred in 60% MM patients (pts). In this scenario tempestive diagnosis of RI in MM pts and exclusion of possible alternative causes of RI are essential.We applied the diagnostic algorithmproposed by the International Myeloma Working Group in pts admittedto our Hospital for RI (with known and unknown MM, or suspected cast nephropathy, CN), in order to verify the possible positive impact of this diagnostic workflow on MM-related RI management.

Patients and methods: We collected data of adult pts, with known or unknown MM, with or withouth monoclonal component (MC). We performed complete blood analysis, with eGFR (CKD-EPI and MDRD methods), serum and urine electrolites, bicarbonatemia, serum and urine immunofixation, fraction 3 and 4 of complement, crioglobulinemia, HbA1c, arterial gas analysis, evaluation of urine rate every 6 hours, daily urine collection. We investigated eventual nephrotoxic concomitant therapies, clinical parameters and objectives signs of RI (edema, symptomatic disionia). In the second day of hospitalization we tested protein electrophoresis on serum and urine, chest X-ray, ultrasonography of abdomen, ecocardiography and electrocardiography. In the third day we evaluated results of previous exams and we decided, if necessary, eventual biopsies (bone marrow in unknown MM pts, renalin suspected CNpts, umbilical fat for amyloidosis).

Results: From March to December 2016 we admitted 89 pts with RI and MC (51 F, 38 M, 41-83 yrs range), 25 are knownMM pts with newly diagnosed RI. Among RI cases, we diagnosed 22 de novo MM, 26 diabetes related RI, 5 amyloidosis, 11 other causes. We obtained diagnosis of RI within 4 days, both in known and in de novo MM pts.

Conclusions: The implementation of the International Myeloma Working Group Reccomendations on RIin a routine clinical practice confirmed its feasibility and utility in the optimal workout of MM pts, with a positive impact on reduced hospitalization, uncessary dyalisis and steroids overtreatment.

T21 The evolution of palliative care from the oncology patient to the chronic illness

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Introduction: Law 38/2010 marked an important turning point in palliative care ensuring access to "patients whose basic illness, characterized by unstoppable evolution and a poor prognosis, no longer responds to specific treatments". This has led to extend the concept of palliative care to areas that are not strictly oncological, for example patients with chronic diseases that need an intervention by a palliative care team.

Purpose of the study: To evaluate the number of patients hospitalized in hospice over the year 2015, 2016 and the first 4 months of 2017 with a terminal situation for non-oncological disease. The data collected will be compared to evaluate if there was a change in the number of non-cancer patients hospitalized in Hospice during the three years comparing.

Methods: In a retrospective study, non-oncologic patients hospitalized in hospice have been assessed for a period between January 2015 and April 2017. For each year, the percentage of non-cancer patients hospitalized was compared to the total number of hospitalizations to appraise if there's any change in the hospital admissions.

Results: 160 patients were hospitalized in 2015, 22 (13.7%) non-oncologic (10 dementia/Alzheimer's disease, 4 heart disease, 3 Parkinson's disease, 3 liver cirrhosis, 1 SLA, 1 pulmonary fibrosis), in 2016 176 patients, 30 (17%) non-oncologic

(18 dementia/Alzheimer's disease, 7 heart disease, 3 SLA, 1 multiple sclerosis, 1 kidney disease). In the first 4 months of 2017 47 patients, 14 (29.7%) non-oncologic (9 dementia/Alzheimer's, 2 heart disease, 2 liver cirrhosis, 1 SLA).

Conclusions: The number of patients admitted for a terminal condition because non-oncological disease has been increasing in our hospice over the years considered to demonstrate that there is a change in palliative care with increasing sensitivity and attention to final stages of the patients regardless of their pathology. A desired and desirable change to further increase, in order to give the needed treatment in a palliative home care course or in a protected environment such as Hospice to all terminal patents. In particular the most common non-oncologic illness with a higher percentage were dementia/Alzheimer's and heart disease. Specifically dementia/Alzheimer's were 45.4% in 2015, 60% in 2016, 64.2%, while heart disease in 2016 was 18.2%, 23.3% in 2016.

T22 Association between the development of autoimmune hypothyroidism and objective response to nivolumab: report of two cases

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The use of checkpoint inhibitors has been rapidly growing, despite the relative lack of predictive factors. Their toxicity includes a spectrum of autoimmune disorders, thyroid dysfunctions being one of the commonest. Correlation between autoimmune thyroiditis and antitumor immunity has been well demonstrated in experimental models and the development of autoimmune hypothyroidism has been postulated to be predictive of objective tumor response in patients treated by high-dose IL-2.

Immune-related thyroid dysfunctions have been reported in as many as 20% of cancer patients treated by checkpoint inhibitors, but until now no clear relationship between thyroid disorders and tumor regression has been described. We hereby describe two cases in which the appearance of autoimmune hypothyroidism heralded radiographic response to nivolumab. 1) A 75-year-old woman with metastatic renal cell carcinoma progressing on sunitinib with massive left pleural effusion and multiple lung metastases started i.v. nivolumab 3 mg/kg q2w. Three months later a CT scan showed complete resolution of pleural effusion and almost complete disappearance of lung metastases. Concurrently, measurement of serum TSH showed values > 75 mcIU/ml with FT4 0.3 ng/dl (normal range 0.8-1.7). Anti-TPO autoantibodies were > 1000 IU/ml (range 0-6). Treatment with levo-tiroxine ensued with progressive titration to assure normal thyroid function. Nivolumab was continued and the patient is in vgPR 12 months after beginning treatment.

2) A 69-year-old man with stage IIIB squamous cell lung cancer progressing after induction platinum-based chemotherapy and during mediastinal RT began i.v. nivolumab 3 mg/kg q2w. After a minor response at first evaluation, he presented with peripheral and periorbital edema, profound asthenia and somnolence. TSH serum levels were > 75 mcIU/ml, FT4 was < 0.3 ng/dl, anti-TPO antibodies were > 1000 IU/ml and anti-TG were 130 IU/ml (range 0-6). Levo-tiroxine was immediately started with rapid clinical improvement. A subsequent CT scan showed PR. The patient is continuing nivolumab, thyroid function is balanced and clinical signs of toxicity have completely resolved.

The parallel development of autoimmune thyroiditis and tumor response upon nivolumab suggests a shared mechanism of antigen recognition and deserves to be elucidated to identify possible predictive factors of anti-PD1 activity.

T23 Access of the oncologic patients to the emergency room of the local hospital during the three-year period 2014–2016

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Background: The aim of this study is to highlight through the access of the oncologic patients to the emergency room of the local hospital the health and socio-assistance criticalities present in the territory that affect this category of patients and to identify potential solutions to mitigate the level.

Patients and methods: For this purpose, during the three-year period 2014-2016, we examined the total number of patients arriving in the Emergency Room, including the number of cancer patients, distributed by age and sex, the number of oncologic patients given to their home, those hospitalized, the reasons for the hospitalization and the facilities where they were hospitalize.

Table: T23

ACCESS total	96.961	oncologic pts hospitalized in: - internal medicine	25
Total of admission	15.587	- pneumology	7
Total of oncologic patients (pts)	356	- other departments	15
oncologic pts resigned at home	30	- oncology total:	241
oncologic pts sent in hospice	11	males	133
oncologic pts who refudes hospitalization	17	females	108
oncologic pts who voluntarily left the emergency room	10		

Reasons for Hospitalization:

Blood Dyscrasias	35	Dyspnea	25
Neurological Symptoms	34	Cachexia	25
Pleural Effusion/Ascites	33	Intestinal Symptoms	18
Pain	31	Jaundice	12
Fever	28	Other	10

Distribution By age group/numberof pts

45-50	13	**71-80**	73
51-60	25	**81-85**	20
61-70	101	**>85**	9

Conclusions: The Admission of oncologic patients to emergency care continues to be a health problem. Our survey shows: 1. Patients with potentially manageable home illness access the emergency room; 2. Need to provide adequate information to patients about the different health options (hospital, territory, home care, hospice); 3. Improve treatment procedures against pain; 4. Increase efforts for better therapeutic continuity.

T24 Nutritional counseling

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The growing scientific evidence on links between lifestyle and cancer incidence as well as the recommendations that research institutes like WCRF (World Cancer Research Fund International) and AICR (American Institute for Cancer Research) have compiled guided us in organizing an outpatient nutritional counseling for cancer patients. Nutritional counseling is done by a biologist specializing in science of nutrition and dietitian. At the first meeting we collect the medical history and lifestyle with emphasis on eating habits and of physical activity, we evaluate the BMI (Body Mass index) and waist circumference. Bearing in mind the recommendations of the WCRF and AICR we give specific guidance for:

- introduce or increase consumption of whole grains, advising preparation methods
- increased consumption of vegetables especially for those vegetables at a higher content of protective nutrients, advising the methods best suited to preserve the nutrients in the culinary preparations
- encourage a regular consumption of seasonal fruit-enter or increase consumption of vegetables as a source of vegetable protein
- insert the bluefish 1-3 times weekly
- insert the nuts according to individual requirements
- limit consumption of red meat and dairy products, avoid sausages
- limit the simple sugars and high caloric density foods
- avoid sugary drinks
- limit your intake of salt.

We recommend physical activity adapted to play regularly.

Meetings are scheduled monthly or quarterly revaluation nutrition to make sure the objectives of change in eating habits, assessment of BMI and waist circumference. We enrolled 54 patients; the 46% have made at least one control. Patients are very interested and cooperating. Among the overweight patients on 15% of controls has reduced the BMI of at least 1 point, the 90% of patients who presented to the checks introduced whole grain or low-profiles, the 70% legumes and fish at least 2 times a week. The food education project also foresees the organisation of themed group activities to help patients to greater awareness in food choices.

T25 Oncogeriatric assessment of older patients with cancer in the ASL Cuneo 2

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Introduction: The number of oncologic elderly patients has increased with global aging Close collaboration between oncologists and geriatricians becomes necessary to evaluate the health status and the residual reserves of old patient, to provide adequate approach and therapy.The G8 screening has been specifically developed and validated to screen for frailties and identifies patients who may benefit Multidimensional Geriatric Assessment (MGA). G8 consists of 8 items concerning nutritional status, body mass index, motor skills, psychological status, number of medications, and self-perception of health.The score ranges from 17 (not at all impaired) to 0 (heavily impaired). A score lower or equal to 14 requires MGA.

Methods: The Outpatient Oncogeriatric Service of the ASL Cn2 started in January 2017. If the G8 screening results are lower or equal to 14, the patient is sent to our Service and a MGA is carried out.

Results: We evaluated 25 patients (11 women and 14 males). Average age was 83 years (range 75-96).The G8 average score was 10.7; 8 patients had urological cancer, 7 patients had colon cancer, 4 had breast cancer, 4 had lung cancer, 1 had pancreatic cancer, and 1 had vulvar cancer. 11 patients had metastasis when evaluated in our outpatient.The 44% of patients knew their health status, 28% had partial consciousness and 28% had no awareness of cancer. After our evaluation 19 patients resulted less frail: 13 received conventional therapy and 6 had personalized protocols, whereas 6 patients were sent to palliative care because too frail.

Conclusions: Our initial experience points out that multidisciplinary approach in the elderly is important in detects frailty and leads to tailored oncology treatments. Cognitive impairment, the advanced stage of cancer and inadequate social situation are the factors that most influenced us in deciding not to treat the patient (Table 1).

Table: T25. Patients' characteristics

	Less frail N = 19	Frail N = 6	p
Average age (range)	82 (76-96)	84(75-93)	0.30
G8 (±SD)	11 (± 2.9)	9 (± 2.2)	0.59
ADL	1 (± 1.8)	1.8 (± 1.8)	0.62
IADL	9.4 (± 4.3	5.5 (± 3.6)	0.56
SPMSQ	1 (± 3.2)	3 (± 4.0)	0.00
BMI	25.1 (± 3.6)	21.0 (± 2.1)	0.09
CIRS-G	5.4 (± 2.9)	5.0 (± 2.9)	0.71
Metastasis (%)	42	68	0.53
Illness awareness (% total)	46	50	0.54
Social situation (% co-caregiver)	61	17	0.05

T26 Surgery and the elderly: when an apparent overtreatment becomes safe and effective

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Background: There are unique issues to consider when caring for an older with cancer. Since older patients with cancer are under-represented in clinical trials, there are less evidence-based data to guide the treatment. The challenge of managing older patients is to assess whether the expected benefits of treatment are superior to the risk in peoples with decreased life expectancy and tolerance to stress.

Methods: Our approach for identification of fit patients match the comprehensive geriatric assessment with a multidisciplinary evaluation of older patients. At the roundtable there were the oncologist and the surgeon, a radiologist, internist with expertise in pulmonology, geriatrician, anesthesiologist with expertise in nutrition, psychologist, physiatrist, oncologic nurse, the general practitioner and caregiver of the specific patient, social worker. Starting from a careful analysis of medical history, physical examination, biochemical and instrumental exams the team proceeded applying the comprehensive geriatric assessment and balancing risks and benefits of all possible therapeutic options; the final decision was made taking into account the opinion of general practitioner and caregiver. Thereafter, the decision-making process was completed through a discussion with the patient in order to explain the risk-to-benefit ratio of surgery and to better understand wishes, hopes and unmet needs.

Results: In the last year we were able to identify as fit, forty-five very old oncologic patients. Whit an aggressive surgical approach all the patients are free of disease and their quality of life is ameliorated. Notably, for six patients the surgical approach was firstly excluded for age and tumor burden as evidenced on Computed Tomography at another oncologic hospital with high surgical volumes. After our re-evaluation, all six patients were deemed as fit and surgery was radical for all. The length of hospital stay was of three days for two of them, seven days for other three; for a patient with nutritional problem, the total parenteral nutritional support was prolonged for ten days.

Conclusions: Aging and increased life expectancy mean that cancer in the older is becoming an increasingly common problem. Proper selection of patients is mandatory to administering effective and safe oncologic treatment. Advanced age alone should not preclude an effective cancer option that could improve quality of life or extend survival.

T27 LibroBluApp: a mobile app to improve cancer care

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Background: Libro Blu was born in 2012 as an effort to coordinate Oncology practice in our institution and consisted of recommendations deriving from Italian and international guidelines. After its first publication, periodic updates were made until 2015, when a major revision took place, involving also consultants from many fields other than Oncology in order to also improve supportive care. Our next goal was developing a mobile app to make consultation easier and to share this tool with physicians from other institutions.

Methods: After the 2015 revision, Libro Blu was updated, with the inclusion of new recommendations based on new scientific evidence; it was also submitted for review by a number of Italian oncologists from other institutions. The mobile app development, based on the updated version of Libro Blu, has been realized, with an unconditioned support from Eli Lilly, by Medica Editoria e Diffusione Scientifica, a company involved in medical publishing and education.

Results: Since its debut in 2015, the new version of Libro Blu received a positive feedback from physicians in our institution; the review from other Italian oncologists ensured its adherence to good clinical practice. The mobile app development resulted in LibroBluApp, a mobile app for iOS devices (both iPhone and iPad are supported), that was finally released for download in April 2017. A version for Android devices is currently being developed and will soon be released.

Conclusions: Libro Blu was our first effort to establish a common standard of care in Oncology practice in our institution. The development of the LibroBluApp has made consultation easier and will allow to share this tool with oncologists and physicians from other institutions (in this regard, Eli Lilly Medical Information will contribute writing to 1680 Italian oncologists). The mobile app will be periodically updated with emerging scientific evidence and upon the approval of new treatments. We think that LibroBluApp will be a useful tool to coordinate Oncology practice, ensuring up-to-date information, and this is of particular relevance at this moment, in which Oncology is facing rapid innovations.

T28 CREAM study: Clinical correlation between immunotherapy-RElated colitis And intestinal Microbiote in metastatic patients

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Background: Today it's well known that the composition of intestinal flora is able to influence the development of inflammatory gastrointestinal diseases, even though the association of inflammatory diseases with specific intestinal microbes is still unknown, because the inflammation itself and its treatment can change the composition of the microbiota. Surely some bacterial species are essential to maintain the mucosal

physiological tolerance, although species such as Bacteroides, Clostridium and Faecalibacterium can induce the up-regulation of T-cells and stimulate the production of anti-inflammatory cytokines. Innovative therapies such as Ipilimumab, Nivolumab and Pembrolizumab, a monoclonal anti-CTLA-4 antibody and inhibitors of the PD-1 receptor, respectively, are particularly involved in the up-regulation of lymphocyte system: among their side effects, the most relevant are those immune-mediated such as hypophysitis, thyroiditis and colitis. In particular this last one usually occurs within 16 weeks from the start of treatment: about one third of patients develop intestinal inflammation (of any grade) as a result of dysregulation of the immune system of the intestinal mucosa. Therefore, the high incidence of colitis in patients treated with immunotherapy offers the possibility to characterize the intestinal microbiota before the development of immune-mediated inflammation.

Trial design: Our study is a single-center observational study of clinical and biological parameters prospectively stratified. Specifically, we collect from patients eligible for immunotherapy a blood sample to analize serum cytokines levels and a sample of fecal material at baseline and at least after 3 administrations of treatment: actually we enrolled 12 out of 40 planned patients; we suppose to complete the enrollment in approximatively 4 months. According to preliminary data already published in the literature, we expect to find an alteration of the intestinal microbiota in metastatic treated with immunotherapy. Once we'll identify the presence of an alteration of the microbiota, we want to assess whether there is any correlation with the patient's clinical outcome.

T29 Cost-effectiveness of a cancer diagnosis on frail elderly cancer patients

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Background: Elderly patients admitted to the hospital with a suspect of cancer are often offered a complete diagnostic. However some of them are not referred to an oncologic department. We analyzed the variables that could potentially have interfered with this decision.

Patients and methods: Electronic charts of older patients with an admittance or discharge diagnosis of cancer were analyzed. The inclusion criteria were as follow: age older than 70 years old; hospitalization at the medical area department (including Oncology, internal medicine, Nephrology, Pneumatology, hepatology and neurology); at least a cancer diagnosis in the dismissing codes. For every patient we had: type of hospitalization, polypharmacy, comorbidities, oncologic diagnostics, status of disease (metastatic or not) and destination after discharge. The end points were as follows: find a frailty profile for older patients, explore the elements that infulence the approach to oncological department or not, the role of a cancer diagnosis in this type of patients.

Results: 838 patients were included in the analysis, 721 (86%) with cancer as main oncological diagnosis and 117 with another non oncological disease as main diagnosis at the dismissal. 461 (55%) were metastatic, 648 (77,3%) patients received some form of cancer diagnosis. Of these 243 (37%) were referred to an oncological department. 154 out of patients were adimitted to the hospital with an oncological diagnosis 85,8% and 44% of patients had cardiovascular and metabolic comorbidities respectively. In the logistic regression, male sex (p 0,001, OR 1,68), metastatic disease (p 0,0001 OR 1,79), number of comorbidities and a complete oncological diagnostic e (p 0,001 OR 0,88 e 0,38 respectively) were the parameters significantly associated with an oncological course after dismissal.

Conclusions: More than 70% of patients received some form of oncological diagnosis (complete or partial) and among them only 37% had an oncological route after dismissal. Some efforts should be done to improve the identification of those patients that have to be excluded from a oncological diagnosis. This approach could be helpful to reduce costs and distress for patients that are not able to receive cancer treatment.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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U - MANAGEMENT OF CANCER PAIN

U1 Breakthrough-pain likelihood scoring system in cancer patients

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Aim of investigation: Breakthrough cancer pain (BTP) shows variable prevalence in different clinical settings[1]. BTP diagnostic tools with demonstrated reliability, validation and prognostic capability are lacking[2]. Samolsky Dekel validated a diagnostic/prognostic tool, the IQ-BTP, for BTP likelihood ('High', 'Intermediate' or 'Low') recognition among chronic pain (CP) patients[3]. Using IQ-BTP scoring system and the Naive Bayes classifier[4] we evaluated its performance on correct classification of BTP in cancer patients with CP.

Material and methods: Patients competent with Italian language, age>18ys and cancer CP treated by strong opioids were included. Using the IQ-BTP we assess potential presence of BTP and its characteristics. Then, we computed, for each selected predictor, the score for each likelihood level. We repeat the questionnaire once a month (±10 days) for each patients for 3 times. The developed BTP-likelihood scoring system, is being used in a national multicenter impact study (n = 400 patients). We report the preliminary results of our first 33 recruited patients.

Results: Baseline patients characteristics are listed in table 1. Potential-BTP was found in 36% (n = 12) of patients. In 75% (n = 9) of them, potential-BTP was present in 2 or more visits. The likelihood for BTP diagnosis was 'high' in 25% (n = 3), 'intermediate' in 50% (n = 6) and, 'low' 83% (n = 10) of patients. BTP was predictable in 54% of cases. Only patients with high potential or recurrent intermediate likelihood-BTP level in two or more visits received rapid onset opioids.

Conclusions: The IQ-BTP scoring system may enable, in cancer patients, the detection of potential-BTP and its likelihood with significant relevance to BTP correct management.

Table: U1. Baseline characteristics of patients (n = 33)

Characteristics	N (%)
Mean age, 69 years (range: 49-89)	
Gender	
Male	16
Female	17
Median Karnofsky index score 60 (range: 40-100)	
Place of assessment	
Outpatients	22 (67)
Home care	11 (33)
Primary tumor site	
Pancreas	8 (25)
Lung/mesothelioma	5 (15)
Urogenital	5 (15)
Breast	6 (18)
Gastrointestinal	5 (15)
Others	4 (12)
Care setting	
Palliative Care	13 (39)
Oncology	20 (61)
Therapy in the last 3 months	
Chemotherapy	18 (55)
Radiotherapy	7 (21)
Others	4 (12)
None	11 (33)

U2 BTcP: Retrospective study on integrated hospital care between palliative care clinical and oncologist

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Background: Breakthrough Cancer Pain (BTcP) is distinguished in idiopathic or spontaneous, accidental or procedural. Prevalence of BtcP reported in literature is 40-80%.Presence of BTcP has a negative impact on the quality of life and is a prognostic factor of *hard to treat pain* . Diagnosis and therapy of chronic pain and its exacerbations are fundamental aspects of the patient's care pathway. In recent years, several studies have demonstrated how effective is simultaneous care approach of palliative care in oncology. We undertook a retrospective study regarding simultaneous care experience in Oncology Day Hospital (ODH), in presence of Palliative Care (PC) clinician, with attention to diagnosis, characterization and treatment of BTcP.

Material and methods: Patients who have performed PC visit in ODH setting, have been recruited from 1 January 2017 to 30 April 2017. Data were analyzed consulting patient's clinical folders and reporting the following variables: demographics, pathology, therapy, ECOG-Performance Status, features of chronic pain and BtcP and specific therapies prescribed.

Results: 36 patients who performed at least 3 progressive PC-visits(F = 16, M = 20, mean age 67.4, ECOG average 1.3) have been observed. The primary cancer origin was different (9 pancreas, 7 colon, 5 prostate, 3 lungs, 3 breast, 3 ovaries/uterus, 2 liver/bile ducts, 2 bladder/ureter and 1 pleura, 1 sarcoma). All presented metastases. 25 were undergoing chemotherapy. The baseline pain had an average of NRS=2.5 (range 0-7), Pain Relief (PR) at the third assessment was of 60% average. Basic therapy, intended as the equivalent dose of oral morphine, was mean=72.4 mg/day with a proportional dose increase of 78.6% during the 3 evaluations. 21 patients referred exacerbation of basic pain: the median values of NRS were: idiopathic NRS=0.5; incident NRS=1.7; procedural NRS=0.1. Among these, 4 patients presented BTCP and underwent treatment with Rapid Onset Opioids, resulting in an median relieving pain of 24.5%.

Conclusions: The full results of the study will be presented at the meeting and will include ongoing data over a 8 months period. The impact of the disease stage, ECOG and metastases number related to the presence and intensity of baseline pain and BTcP will be evaluated . Correlation between pain tp adjustment and the presence/intensity of BTcP will be assessed as well.

U3 Fentanyl pectin nasal spray for breakthrough cancer pain treatment: a single center experience

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Background: Breakthrough cancer pain (BTCP) is defined as a temporary exacerbation of algic symptomatology occurring in patients with controlled chronic cancer pain. Tipically BTCP arises with rapid onset, high intensity and has an average duration of 30 minutes. From 64% to 89% of patients with chronic cancer pain have episodes of BTCP and most episodes are unpredictable. Episodes of BTCP are usually treated with short-acting opioid analgesics. Fentanyl, an highly liposoluble opioid molecule, showed efficacy and feasibility in treatment of BTCP in different formulations, including transmucosal and nasal administration. Intranasal fentanyl was reported to be often preferred by patients because of easy spray delivery of the drug and it seemed to be more helpful than transmucosal one in patients with oral mucosal disorders. In our center we studied compliance and satisfaction of patients treated with fentanyl pectin nasal spray for BTCP.

Material (patients) and methods: We retrospectively studied 48 patients attending our Oncology Unit from May 2014 to April 2017. They were affected by various types of tumors (mainly gastrointestinal and non-small cell lung cancer) and they were already taking maintenance opioid therapy for chronic cancer pain. They received fentanyl pectin nasal spray 100 mcg or 400 mcg for BTCP episodes. Patients were asked to report the effect of intranasal fentanyl on pain intensity according to numerous rating scale (NRS), the action time, the grade of satisfaction (from 0 to 5) and how many times they fentanyl pectin nasal spray in relation to BTCP episodes.

Results: Most patients obtained a significative reduction of pain intensity with intranasal fentanyl: 70% (33) had a reduction of 7-8 points according to NRS scale, 31% (15) had a reduction of 2-3 points in NRS. 50% (24) showed pain relief within 5-10 minutes after administration, 44% (21) within 15 minutes. 67% of patients reported a grade of satisfaction from 5 to 3, with feasibility and efficacy as the most frequent referred reason. 90% of patients used fentanyl nasal spray for most episodes of BTCP obtaining an improvement of daily life quality.

Conclusions: Our patients showed high compliance towards fentanyl pectin nasal spray, thanks to its ease use and the quick release from breakthrough cancer pain, which had also a good impact on quality of life.

U4 "At home without pain": a national project on real time pain monitoring system in advanced cancer patients assisted at home by the ANT Foundation

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Background: The ANT Foundation is implementing a cloud computer platform (Vitaever®) developed by Nethical srl, for the clinical monitoring of cancer patients at home. Within this, the national project "at home without pain" was launched in 2015 with the aim of achieving an optimal pain control in the assisted patients. The purpose of the present study is to evaluate, for the first time, the efficiency reached by the system and the information supplied on the efficacy and appropriateness of the analgesic treatment use in the year 2016.

Methods: The project envisages that doctors working in the 20 ANT Home Care Hospitals (HCH), record pain presence and intensity at each home visit in the Vitaever® platform via the personal smartphone. Pain intensity was assessed by the NRS scale and the ANT scale (physician' assessment according to the class of analgesic drugs used). In this way a database is continuously updated and real-time information on the prevalence, intensity and evolution of the symptom in individual patients, individual HCHs and in the whole case can be obtained. The present analysis is based on three indicators: 1) actual efficiency achieved (percentage of visits with NRS reported), 2) effectiveness (difference between the first and the last NRS score) and 3) appropriateness (difference in the percentage of patients taking strong opiates between the first and the last ANT scale score). Indicators 2 and 3 were evaluated only in HCHs with $>75\%$ efficiency and in deceased patients.

Results: In the course of 2016, 6607 new cancer patients were enrolled in the 20 ANT HCHs. The median age was 76, the median KPS 50, the main primary tumor sites were GI (33%), Lung (20%) Breast and Gyn (19%). Five out of 20 HCHs had an optimal efficiency rating (indicator 1). Patients evaluated for indicators 2 and 3 were 945. In these, pain was significantly reduced at the last evaluation (mean NRS from 3.1 to 2.4 and from 5.7 to 3.3 when initial NRS ≥ 4) ($P = 0.01$). At the same time, there was a reduction by almost 35% of patients with severe pain (NRS 7-10). The percentage of patients taking opiates shifted from 44% at the first home visit to 66% at the end of the assistance.

Conclusions: This innovative project is able to provide reliable information on the efficiency of the real time home-based pain surveillance system and on the effectiveness of analgesic treatments. This first analysis indicates the need to optimize the physician's participation.

U5 Long-lasting strategy of pain management: the "comitato ospedale senza dolore"

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Background: The pain's evaluation and treatment are relevant for the management of hospitalized patients (pts). From 2010 in our hospital "Comitato Ospedale senza dolore" acts with the aims of correctly evaluate and treat pain, above all when the patients experienced a chronic illness, like oncological disease. To achieve this purpose the Committee coordinated training program for nurses and physicians. In a previous analysis for pain survey from 2012 to 2014, we observed a good level of satisfaction about pain treatment, pain management and informations obtained in both Medical and Surgical Department (Dept). The aim of our study was to evaluate if this program continue to obtain a good level of satisfaction in particularly in Medical Dept where the older age pts and the kind of chronic disease request a major attention from operators to evaluate and treat pain. At discharge all patients fill in a customer satisfaction questionnaire; some of items concern the pain management.

Patients and methods: From January 2012 to December 2016 a questionnaire of customer satisfaction was delivered at discharge: 6 items abut pain evaluation were measured. The results were pooled into 5 years. 9340 questionnaires were filled: 2700 (28,9%) in Medical Dept. The items considered are shown in the Table. For each question the patient gives a score from 1 to 10, that is "at all" to "a lot". For the first and second item the score is the pain intensity.

Results: In the Table we show the median score for the six items considered, pooled in 5 years for Medical Dept.

Conclusions: The "Comitato Ospedale senza dolore" program reached in all patients considered in Medical Dept a reduction of pain score from admission to discharge (reduction pain score over two points for exception of 2014). In all patients there is a good level of satisfaction about pain treatment, pain management and informations obtained, and this result was maintained along five years. We think that is necessary a periodically re-train for nurses and physicians to maintain high the sensibility for this problem.

Table: U5

Year	pain score at admission	pain score at discharge	pain reduction after treatment	information about pain treatment during hospitalization	patients satisfaction about pain management	information about pain management at home
2012	5,12	3,06	7,37	7,87	7,86	8,50
2013	5,06	2,80	7,24	7,66	7,79	8,60
2014	4,62	2,77	6,93	7,68	7,81	8,30
2015	5,08	3,05	7,11	7,81	7,83	8,48
2016	4,79	2,77	7,23	7,76	7,77	8,55

U6 Prophylactic use of antiemetics for prevention of opioid-induced nausea and vomiting: a web based online survey among Italian experts on supportive care in cancer

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Background: Antiemetics are being used both for the treatment and prophylaxis of opioid-induced nausea and vomiting (OINV) in clinical practice, despite the lack of evidence for the prophylactic benefit. Studies among Japanese physicians trained in cancer pain management demonstrated over 80% prescribe antiemetics, with neuroleptic antipsychotics (prochlorperazine 88%) as the most commonly prescribed drugs. The objective of this study was to evaluate the practice among Italian experts on supportive care in cancer of the prophylactic use of antiemetics when starting opioids prescription for OINV prevention.

Material and methods: From January to March 2017, we carried out a web-based cross sectional national survey. The survey was created with the GoogleDocs™ online surveys maker (https://docs.google.com). All invited participants received e-mail with the 12-items electronic questionnaire that was only accessible through a direct link. The questionnaire assessed the physicians' practice and beliefs regarding the prophylactic antiemetics prescription when they start opioids in patients with cancer pain (7 items) and other demographics data (5 items). According to the exploratory intent of the survey, we did not predefine any formal statistical hypothesis or sample size.

Results: 112/256 responded to the electronic questionnaire (ORR 43.7%): 54 medical oncologists, 16 anesthesiologists, 11 radiation/clinical oncologists, 5 internists, 2 geriatrics, 1 infectivologist, 1 general surgeon. 22 physicians declared no formal medical specialization. Responders were geographically evenly distributed among Italian areas and came from palliative care units (61), community hospitals (21), education hospitals (20) and comprehensive cancer centers (10). 45% prescribed prophylactic antiemetics at the beginning of opioid prescription, and the most commonly prescribed drug for this purpose were prokinetics such as metoclopramide and domperidone (84%), followed by 5-HT3 antagonists (8%), neuroleptic antipsychotics (6%), corticosteroids (2%). Among physicians who prescribed prophylactic antiemetics, 41 (82%) also prescribed antiemetics (prokinetics as well) for use as treatment at the occurrence of OINV.

Conclusion: Italian physicians do not commonly prescribe prophylactic antiemetics for OINV. Unlike previous reported evidences, dopamine antagonists resulted the most commonly prescribed drugs. Prospective clinical trials are necessary to evaluate the real efficacy of this practice.

U7 Manipulative scar treatment and ostheopatic manipulative treatment for pain, shoulder motion and quality of life in post-mastectomy pain syndrome (PMPS). A randomized clinical trial

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Background: PMPS affects about 25% of breast cancer survivors. Drugs, sometimes ineffective, carry risks of adverse events.

Purpose: This study assesses the effect of Manipulative Scar Treatment (MST), with/without Osteopathic Manipulative Treatment (OMT), on pain, shoulder range of motion in external rotation (ROM-RE), distress and Quality of Life (QoL).

Methods: Upon informed consent, 18 (mean age 52.88, SD 10.92) PMPS patients, attending oncologic follow-up, were randomized during 5 weekly sessions of treatment MST+OMT (9 patients) vs MST-alone (9 patients). Pain quality/intensity was assessed with *Short-form McGill Pain Questionnaire* (SF-MPQ) and *Douleur Neuropatique-4* (DN-4); Distress with *Distress Thermometer* (DT); QoL with *36-Item-Short-Form Health Survey* (*SF-36*); ROM-RE of the shoulder with an universal goniometer. Data were collected before the 1st(T0),3rd(T2),5th(T4) sessions, and monthly thereafter (F1,F2). Wilcoxon, Paired *t* test, Mann-Whitney test and Two-sample t-test were used for statistical analysis.

Results: 18 patients attended the entire schedule until F1 and 17 patients until F2. Both group MST+OMT and MST improved their condition concerning pain intensity at T4, F1 and F2 vs T0: SF-MPQ overall score at F2 vs T0 decreased in group MST+OMT (mean change -5.88, SD 3.72; $P = 0.009$) and MST (-5.62, SD 5.31; $P = 0.020$); SF-MPQ Visual-analogue scale at T2 vs T0 decreased in group MST+OMT (-25.33, SD 14.43; $P = 0.007$) and MST (-28.25, SD 21.49; $P = 0.017$). DN-4 score decreased at F2 vs T0 in group MST+OMT (-2.33, SD 1.58; $P = 0.008$) and MST (-2.12, SD 3.35; $P = 0.11$). DT score improved in F2 vs T0 in group MST+OMT: (-3.77, SD 2.65; $P = 0.007$) and MST (-2, SD 2.13; $P = 0.040$). ROM-RE significantly improved in MST+OMT at all intervals (F2 vs T0: +10.55, SD 5.72; $P < 0.001$), but not in MST. QoL by SF-36 improved at F2 vs T0 in group MST+OMT, with significant differences in physical functioning (+11.11, SD 9.27; $P = 0.016$), pain (+23.66, SD 16.79; $P = 0.011$), social functioning (+24.88, SD 19.77; $P = 0.017$), emotional role (+37.11, SD 38.88; $P = 0.026$) and emotional well-being (+12.44, SD 15.15; $P = 0.008$), while group MST showed no significant change in all scales, at all intervals. Between-group differences at F1 vs T0 were observed in general health ($P = 0.037$), energy/fatigue ($P = 0.002$), emotional role ($P = 0.007$).

Conclusions: Our results suggest a reduction in pain and distress in all patients, with/without OMT, maintained at 2 months, and an additional improvement in range-of-motion and QoL in MST+OMT group. A larger study is required to confirm these results.

U8 Procedural pain: acknowledgement of the issue by palliative care professionals

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An optimal pain control is a constant challenge for palliative care professionals. As with all treatment and medical assistance processes, palliative care patients can undergo potentially painful procedures. Procedural pain is therefore a form of breakthrough pain that should be averted and treated adequately in order to improve the quality of life of terminally ill patients.

Detection and control of procedural pain can be effectively achieved only if medical operatives have the necessary training. In order to assess the knowledge and awareness of this issue, palliative care workers of the home care and residential care staff of our Hospice were given a specific questionnaire to complete.

27 doctors and 36 nurses were interviewed. 96% of doctors and 90% of nurses indicated knowledge of the definition of procedural pain. Among doctors, 85% state that they prescribe a medication for intense breakthrough pain, although only 65% of nurses claim to be able to find them amongst available prescriptions. For both operative categories, procedural pain affect the quality of life of patients, but only 68% of nurses and 77% of doctors interviewed ordinarily detect it. The procedure most commonly believed to be a source of procedural pain is mobilisation, followed by medication. Overall, operatives think that in 84% of the situations, procedural pain is appropriately managed in their own setting.

Our results show evidence of high levels of awareness about procedural pain by palliative care professionals. However, this does not seem to be reflected in its systematic detection al the bedside nor in a regular prescription of appropriate medication to control it, which results in a sub-optimal management of this type of breakthrough pain. Although the majority of the operatives apply their theoretical training to their medical practice, an increasing appreciation of the importance of procedural pain remains an important goal to improve these results, which will be compared to the findings of a targeted survey shortly to be conducted among patients.

U9 Odynophagia and dysphagia,: clinical experiences and cancer pain integrated management

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Background: Most patients experience pain in swallowing during cytotoxic treatments and radiotherapy, worsing Cancer Related Cachexia. Transdermal fentanyl can provide effective pain relief. An effective pain treatment should include a fixed medication and breakthrough medication with an appropriate dose and schedule for each. Odynophagia should be considered breakthrough pain to be treated with appropriate breakthrough medication dosing. Increasing evidence, supports to adequate pain control in patients with cancer related dysphagia/odynophagia, to avoid malnutrition and cachexia. Most pain/palliative care specialists and oncologists worldwide are well aware to adequately treat the pain, but it was yet established that half of cancer patients have insufficient pain control. The goal of pain control in any patient with cancer should be to optimize the patient's comfort and function.

Methods: Clinically, 103 Patients with cancer pain and cancer-related dysphagia/odynophagia we followed. Everyone was treated with analgesic opioids at a stable dose equivalent to 60 mg oral morphine to control background pain using transdermal administration to control background pain. It is considered a convenient method of continuous administration of opioid drugs in situations requiring alternative routes to the oral route. This is possible with fentanyl, as it has physical-chemical characteristics suitable for transdermal administration. We measured the BTCP using algorithm.We used Fentanyl pectin nasal spray (FPNS) 100 mcg per 2 at Btcp .11 patients had opioid induced constipation, 13 developed cachexia. Furthermore, we corrected the cachexia and improved the BMI, using dietetic foods for special purposes. We used naloxegol in the treatment of opioid-induced constipation.

Results: Fentanyl is a rational approach to odynophagia. A wide range of assessment tools for dysphagia were identified. Increasing BMI is very important, as fentanyl is a lipophilic drug. Preventive administrations of breakthrough pain medication a half hour before eating may improve swallow function . We have performed frequent monitoring, using NRS scale. Patient assumed no more than 3 doses per day at main meals.

Conclusions: To promote effective and total pain control, it is strictly necessary to identify patients with odynophagia and dysphagia for avoiding malnutrition, dehydration and cachexia. Correct integrated management of cancer pain improves Quality of Life in this pool of cancer's patient.

U10 Management of breakthrough cancer pain in patients with oral mucositis

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Background: Oral mucositis, which typically appears with erythematous and ulcerative lesions of the oral mucosa, is a common affection in cancer patients as a consequence of chemotherapy or radiotherapy or cancer itself. It can compromise nutritional status and quality of life, being a cause of pain, especially during swallowing and inhibiting proper feeding. Furthermore, inflammatory state of oral mucosa can negatively affect absorption of therapy, especially analgesic drugs, causing insufficient efficacy. So alternative administration routes need to be investigated to control algic symptomatology. Intranasal fentanyl formulation is recommended for breakthrough cancer pain (BTCP), it provides fast pain relief and it may be a valid treatment option for these patients, in particular the assumption immediately before meals can allow a better feeding. We investigated efficacy of fentanyl pectin nasal spray in a subset of patients with oral mucositis and its impact on quality of life.

Material (patients) and methods: We retrospectively studied 31 patients attending our Oncology Unit from August 2015 to April 2017, with many tumor sites, with oral mucositis and non controlled BTCP, treated with fentanyl pectin nasal spray 100 mcg/D or 400 mcg/D, assumed during the BTCP episodes and before meals. We asked the patients to report the effect of fentanyl pectin nasal spray on pain intensity (using NRS scale) and on feeding (0 = no improvement 1 = slight improvement 2 = good improvement). We asked if the use of fentanyl pectin nasal spray had effects on quality's life too (0=NO 1=YES).

Results: 58% of patients (18) had a pain reduction of 2-3 point of NRS scale, 25% (8) had a pain reduction of only 1 point, 17% didn't have benefits (5). 65% (20) of patients had a slight or good improvement of feeding. 68% of patients report positive effects on their life's quality.

Conclusions: Fentanyl pectin nasal spray led to better pain control in patients with oral mucositis; its administration before meals, allowing improved feeding and provided a better quality of life.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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V - ONCOLOGY NURSING

V1* Observational study on the effectiveness of the Dragon Boat in reducing the risk of incidence of lymphedema in women with breast cancer

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Introduction: In women with breast cancer undergoing sentinel node biopsy and axillary lymph node dissection, the ipsilateral upper extremity lymphedema is one of the most disabling complications. The gold standard for the treatment of this condition is physiotherapy, called complete decongestant therapy, but also constant exercise is an important element of prevention. The Dragon Boat, a very popular rowing activity, has been reported to be of clinical benefit and improve quality of life in some studies . However, given that studies lacked to demonstrate the effectiveness of this Dragon boat in reducing the incidence of lymphedema, this study's objective was created to precisely assess this influence in women with lymphedema, as well as the impact on quality of life and on the possible predictors of this condition.

Materials and methods: Observational study of two groups: women who participate in the Dragon Boat activity for at least six months and women who practice different physical activities both biweekly. For the collection of epidemiological and clinical data a questionnaire constructed ad hoc was used for the assessment of QoL the EORTC QLQ-C30, a and a tape measure was used for the local measurement of lymphedema. Data were collected at the Hospital Physiotherapy Institutes of Rome (IFO) and the lake of Castel Gandolfo (RM) from June to October 2016, upon approval from the Central Ethics Committee IFO. A comparison of categorical variables with the Chi-square test and statistical significance with $p < 0.05$ through the software Statistical Package for the Social Sciences (SPSS), version 19.0 was used.

Results: The sample consisted of 100 women, equally divided between the two groups. The presence of lymphedema was detected mainly in the group of women who did not practice the Dragon Boat (26% vs 4%), confirmed by measuring limbs before and after exercise. From the data obtained through the Questionnaire EORTC QLQ C-30, it is clear, moreover, how the Group of the Dragon Boat present a better quality of life ($p < 0.0001$), a reduced presence of fatigue ($p = 0.02$), insomnia ($p = 0.001$), pain ($p = 0.003$), and dyspnea ($p = 0.03$ in women who practice the Dragon Boat that ultimately have a lower BMI and a more balanced lifestyle.

Conclusions: Practicing Dragon Boat reduces the risk of onset of lymphedema and improves QoL. The possible predictive factors: high BMI, reduced physical activity and high protein diet, rich in carbohydrates and fats.

V2* Efficacy of cryotherapy in paclitaxel-induced nail toxicity: Final results from a Phase II Clinical Study

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Background: Taxanes are cytotoxic agents that induce nail toxicity, including severe effects such as pain and discomfort. Cryotherapy, causing temporary vasoconstriction, is a successful approach in preventing nail toxicity. However, so far, few studies, have described cryotherapy and its effects on nails.

Materials and methods: We conducted a phase II clinical study to investigate the efficacy of cryotherapy in preventing nail toxicity in breast cancer patients treated with paclitaxel. The study, conducted in a Multidisciplinary Day Hospital at CRO Aviano from October 2015 to September 2016, was planned to enroll 62 women to estimate a 40% to 25% reduction in nail toxicity ($a = 0.05$; $b = 0.20$). The study included women diagnosed with breast cancer, with no previously nail disease, treated with weekly chemotherapy containing hourly paclitaxel for the first time for 3 cycles. Specifically excluded were women with Raynoud's syndrome and those previously treated with taxanes. Participants worn frozen gloves (temperature: -5 °C to 0 °C) on hands and feet during drug infusion for a total of 70 minutes. Nails condition was assessed weekly by trained nurses. Nail changes, including pain, were evaluated using CTCAE 4.03 grades and through photographs.

Results: G2-G3 nail toxicity was reported in 13 women (21.0%, 95% confidence interval – CI: 11.7-33.2), which was significantly lower than the expected 40% ($p = 0.002$). Nail toxicity was more frequent in women aged ≥50 years (31.0%, 95% CI:15.3-50.8) than in younger ones (12.1%, 95% CI: 3.4-28.2). Onycholysis was the most frequent nail toxicity (10 patients, 16.1%) with a 56-day median time of occurrence. Subungual hematoma was observed in 6 patients (9.7%; median occurrence time: 56 days) whereas onychomadesis was observed in only 1 patient after 63 days. Other G1 toxicities were observed: nail yellowing in 41 women (66.1%, 95% CI: 53.0-77.7); Beau's lines in 27 women (43.6%, 95% CI: 31.0-56.7); leukonychia in 2 women (3.2%, 95% CI: 0.4-11.2). Pain was reported by 25 women (40.3%, 95% CI: 28.1-52.5) – of whom 15 (24.2%) with pain ≥4 – and it was more frequently reported by women with age ≥50 years than younger ones (55.2% vs. 27.3%, $p = 0.033$).

Conclusion: Final results confirm the efficacy of cryotherapy in reducing G2-G3 nail toxicity associated with paclitaxel, providing evidence for a new tool in care management. Feasibility of cryotherapy was confirmed by good compliance and by patients' satisfaction.

V3* Italian translation of a nursing instructor helping the patient to treat oral antineoplastic medicine: the MOATT

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Introduction: In recent years, the introduction of oral therapeutic formulations has contributed to making oncologic patients responsible, in the first place, for the assumption and management of the therapeutic plan. This "empowerment" required reflects the need for better information to manage side effects and favor adherence to therapeutic treatment. The nurse appears to be the figure mainly involved in the therapeutic education of patients, so they need more and more tools to guide them in favoring the correct intake of prescription drugs. Among those encouraging/guiding therapeutic education about taking oral antineoplastic drugs is the Mascc Oral Agent Teaching Tool (MOATT), created by the Multinational Association of Supportive Care in Cancer (MASCC), consists of four sections and is present in 16 different languages ??with the exception Italian.

Objective: To translate the MOATT into Italian.

Method: A forward-backward translation was performed following the guidelines provided by Beaton et al for transcultural adaptation of self-report questionnaires. The stages of the translation process were: authorization request, forward translation (two translators with good knowledge of both languages), creation of a new version and backward translation (concluded with the approval of the MASCC).

Discussion: The main issues arisen in the individual translation phase are largely dependent on the presence of Anglo-Saxon terms in Italian which provide more than one translation. It was useful in this regard to resort to a comparison between the translators, which made it possible to reach t a unique choice of Italian terms best suited to replace the original ones, as well as to the cultural adaptation that will ensure the optimal use of the instrument in clinical practice.

Conclusion: The Mascul Oral Agent Teaching Tool from 2015 is available in Italian and can also be consulted through the official website: http://www.mascc.org/assets/Guidelines-Tools/moatt_italian_2015.pdf. This version can become a valid means of patient support and a tool for simplifying nursing educative work, useful in achieving a form of empowerment-based therapeutic education and therefore aimed at self-management of the disease and especially treatment.

V4* Development and psychometric testing of a measure of perception of care dependency in cancer patients

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Background: The number of patients with comorbidities and cancer-related disabilities is expected to increase in the near future. Care dependency is central to nursing and can be associated with suffering, humiliation, but also with positive balances and personal developments. Understanding the patients' perception of care dependency enables nurses to better meet the patient's needs. No instrument is available to evaluate patient' perceptions about their dependency experience.

Material and methods: This study is part of an ongoing project aimed to develop and validate an instrument to measure the patient's perception of nursing care, in particular the patient's basic emotions anger, guilt, shame and sadness. The project follows the European Statistical System' Guidelines for Instrument Development including five steps: conceptualization, questionnaire design, pre-field and field testing, final validation. Conceptualisation implied the formation of concepts from a meta-synthesis and

qualitative studies on cancer patients with dependence that were operationalized into indicators. Questionnaire design involved a panel of clinical nurses, psychologists and experts in questionnaire design who met to identify the wording and structure of the questionnaire draft. Pre-field testing encompassed evaluation of the questionnaire content validity by clinical nurses' and its revision by questionnaire design experts. Field test aimed at improving the questionnaire was conducted by clinical psychologists and nurse researchers using observational and cognitive interviews, behaviour coding scheme and respondent debriefing. Retrospective think aloud, retrospective probing, verbal paraphrasing and evaluating the response latency were used as cognitive interview methods.

Results: From an initial pool of 63 items questionnaire design produced a 25-item draft. We enrolled 13 patients for pre-field test and 12 patients for field test. After pre-field and field test the wording of several items, the questionnaire layout and the answers' structure were modified to increase clarity and 6 items were removed producing a 19-item tool.

Conclusions: The final questionnaire is being validated in a multicentre study. This study will provide oncology nurses with an instrument based on patients' accounts, valid and reliable to assess the patient' perceptions of care dependency, enabling them to better meet the dependent patient' needs through personalized quality care.

V5* The predictive role of toxicity induced by chemotherapy: systematic review on relationship between toxicity and effectiveness

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Background: The toxicity of chemotherapy is the major problem for the continuity of treatments. Despite this, they may be used as a guide to treatment response as demonstrated by various studies in the literature. The purpose of the review is to deepen the relationship between the side effects and the effectiveness of chemotherapy in order to improve the management.

Material and methods: We have been performed several literature research by the following internet databases: PubMed, The Cochrane Library and Toxnet, Biomed Central, Trip Liberating the literature. The research was performed linking search headings: "correlation toxicity and efficacy chemotherapy", "toxicity markers correlation", "body markers and oncology toxicity", "prognostic toxicity and chemotherapy". The correlation between toxicity and survival was evaluated according to the PFS and OS. We have applied the following filters: human species and 5 years.

Inclusion criteria: Our research was not limited by study design or outcomes. We have been included full-text and abstract, until January 2017. We have included patients with all types of tumor and toxicity, both adult and pediatric, subjected to every type of chemo.

Exclusion criteria: We have been excluded all articles not written in English or Italian language. For the fulfilment of this review it has been possible to formulate the question with Pico model.

Table: V5

PATIENT	Patients with chemotherapy-related toxicity
INTERVENTION	/
COMPARISON	Patient without chemotherapy-related toxicity
OUTCOME	Best response to treatment

Results: For review we were found 33 articles, but only 21 meet the inclusion criteria (for a total of 6537 patients). The review supports the hypothesis that there is a correlation between toxicity such as hand-foot syndrome, rash, hypoalbuminaemia, myelosuppression, proteinuria and the effectiveness of the treatment. There was no correlation between treatment efficacy and hypertension, cachexia, nausea and vomiting. Furthermore, in a few trials, the correlation between the degree of toxicity and the best therapeutic response has been demonstrated.

Conclusions: Although there are studies in the literature, it is necessary to deepen with works of greater statistical value and sampling; identifying efficacy classes based on the degree of toxicity. It is also necessary to identify time-related landmarks that predict the efficacy of treatment, promote continuity and improve nursing management of side effects.

V6 Exploring the nutrition nursing's care surrounding terminally ill patient. A scoping review

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Background: Eating and drinking have a deep symbolism in all societies because they are necessary to sustain life [Bryon, 2008]. They are among the most fundamental physiological human needs [Maslow 1943, Henderson, 1958]. Many patients with long-term conditions experience symptoms that reduce appetite, impair nutrient utilization and restrict their ability to obtain, consume and enjoy food. For them eat and drink is very difficult to do, while for healthcare providers is pivotal to restore and maintain a good state of nutrition and hydration through different interventions [Holmes, 2010].The use of artificial nutrition and hydration for terminally ill is made possible through diverse site such as enteral or parenteral. Define the nutritional care planning is a healthcare professionals' responsibility. Physicians are considered th primary responsible for decision-making and for prescription of initiating artificial food or fluid; nurses are usually the main responsible to provide nutritional care essentially through practical activities but that they are no integrated in a deeper way

Aim: To find the nursing involvement in artificial nutrition and hydration of palliative care and understand what are their competences and professionals' provisions on it.

Method: The Arksey and O'Malley five steps approach of scoping review revised by Levac and colleagues. The research was conducted in Italy with an evaluation of the literature in an international perspective, to not exclude the different perspectives of this phenomenon Three nursing students and two experts nursing professors in palliative and hospice care, formed the research team. After this the meaning was mapped by creating the main categories.

Results: Twenty-five articles were identified by database searching, five by screening reference lists and five directly by the journals. The main categories found were related to: ethics, decision making, clinical aspects and education where nurses act in conjunction with other health professionals.

Conclusion: Still confusion and not great clarity exists on nutrition and hydration in palliative care. Nurses have a great importance in such fragile context. It is demonstrated not just relying on their practical activities or clinical skills but also from their role and position in the planning and support to the decision-making process of the artificial nutrition and hydration process.

V7 Observational study on dietary habits and quality of life in patients with colorectal cancer

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Introduction: Colon cancer is the second leading cause of cancer death in Western countries after lung cancer and male breast cancer. Numerous studies report the effectiveness of a healthy diet in reducing the risk of developing colon cancer or its recurrence. Although the literature provides us with some indications of the most appropriate foods to be used to reduce the risk of developing the cancer or its recurrence, there are not many scientific studies that allow us to understand whether the quality of life of people diagnosed with carcinoma of the Colon can improve by following healthy eating habits. By virtue of this, the objective of this study was to observe the eating habits and quality of life in patients with colorectal cancer.

Materials and methods: Observational study on a sample with age >18 years and diagnosis of colorectal cancer at the Oncology Clinic of an IRCCS in Rome. For the collection of socio-demographic and clinical data (including anthropometric data, blood type and eating habits), an ad hoc questionnaire was used, while EORTC QLQ-C30 was used for QoL (Version 3.0). The data were then analyzed using the SPSS (version 9.0) program and represented by tables describing the frequency of the variables under consideration.

Results: 69 patients with a median age of 62 years were recruited, mainly married, with a low average medical title, with a BMI (Body Mass Index) 25 and a predominantly type A blood type 36%. The sample included many animal based foods, especially chicken meat (77.1%), beef (73.2%) and raw ham (77.6%) but not dairy (15.8%) or fish (20.3%), and few food of origin Vegetable (27.4%). Drinking sparkling beverages (1.3%) and alcohol (12.3%) is also limited. Despite the presence of some disorders, such as insomnia (43.5%), abdominal swelling (55.5%) and anxiety (37.4%), the QoL of the sample being tested is average (57.6).

Conclusion: The study found that patients with colorectal cancer did not follow a balanced diet regime. It is therefore necessary to raise the awareness of patients to take on foods that can reduce the disturbance and bring quality of life to higher levels.

V8 Distress in the hospitalized oncological patient: a study observation

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Background: Distress is an unpleasant emotional experience of a psychological, social, and/or spiritual nature that may interfere with the ability to cope with the disease. This phenomenon appears to be very common in cancer patients, especially during hospitalization, and is therefore considered to be the sixth vital parameter in oncology. The literature also reports a significant association between distress and patient compliance on the therapeutic plan. It is therefore important for the nurse to constantly monitor patient distress during hospitalization. In practice, the NCCN Guidelines provide an algorithm for identifying it with an analogue visual scale, known as the Distress

Thermometer (DT), with a score ranging between 0 to 10. A result greater than 5 requires counseling with a psycho-oncologist: therefore its early detection is fundamental.

Objective: To evaluate distress in hospitalized cancer patients.

Materials and methods: A quantitative descriptive study was used. Patient enrollment took place at an IRCCS in Rome between February and April 2016. Inclusion criteria included age>18 years and hospital hospitalization for an oncology pathology. Cognitive impaired patients who could prevent active participation in the study were excluded. A data-demographic, clinical dataset and the distress thermometer (DT) were used for data collection. On the collected data, a descriptive analysis and an association of categorical variables (statistical significance with $p < 0.005$) were performed with the Chicago Statistical Package for Social Science (SPSS) program 19.

Results: The sample consists of 77 patients, predominantly women (53%) with medium-high level of education (70%). The average distress score was 5.79. The most present emotions experienced were fear (51%), nervousness (55%) and worry (70%). Individuals in the high age group have a lower level of child-related distress (p 0.0056) and work (p. 0.016), despite being the most depressed (p. 0.0065) and with the following Physical problems: constipation (p. 0.017), urinary disorders (p. 0.09), tingling of hands and feet (p. 0.007). Patients with a medium to low cultural level experienced significant disorders such as swelling and diarrhea (p. 0.034).

Conclusion: Hospitalized patients requiring counseling with a psycho-oncologist, had scores higher than 5. DTs should be used by nursing staff in clinical practice focusing on significant problems present in the patient's therapeutic pathway.

V9 Nutritional status in elderly cancer patients: Prospective observational study

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Background: The cancer impact on nutritional status of the affected persons. Weight loss is usually severe, precocious and related in frequency and extent, with the disease stage. The most commons weight loss related cancers are pancreatic and gastric. Malnutrition is associated with increased incidence of adverse drug-related reactions, reduced response to therapy and poor prognosis. An inadequate nutritional status in cancer patients, is a frequent problem over 65 years old. Despite this evidence, the attention to weight loss and consequences remains largely insufficient. The aims of this study are to assess the prevalence of malnutrition in a sample of elderly cancer patients in the Hospital of Novara and, if necessary, to porpose a tool for the evaluation and monitoring of the condition during hospitalization.

Material and methods: A prospective observational study was carried out between April the 1st and December the 30th 2016. Inclusion criteria were: older 65 years, affected by cancer and agreement to participate in the study. It was used the MNA questionnaire property of Nestlè Nutrition Institutes. Data analysis by Microsoft Excel 2010.

Results: The used tool showed 44% of malnourished patients and, 50% of potentially malnourished. These results are in line with the literature findings, showing high prevalence of malnourished cancer patients, while no studies were found that consider potentially malnourished patients. However, if we consider potentially malnourished patients, we are almost at the totality of the enrolled sample. It would been useful to stratify the sample for kind of cancer as the consulted studies show very variable prevalence depending of cancer-affected district. This stratification was not possible for the smallness of the sample.

Conclusions: There is a high prevalence of malnutrition in elderly cancer patients. Cancer and its chemotherapy may favour this condition that negatively impacts on the treatments outcome. Attention to weight loss and negative impact on prognosis of elderly cancer patients remains largely inadequate. In Italy, malnutrition prevalence data are missing in the elderly cancer patients and, the few available data refer to types of non homogeneous patients in different stage of illness and treatment. In the clinical setting, th use of detection tool suche as the MNA, could be encouraged to allow timely intervention to provide adequate nutritional support, prevent further deterioration and improve patient'safety.

V10 Intensive mucositis management in head and neck cancer patients treated with concomitant chemo-radiotherapy: the pivotal role of the nurse

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Background: Treatment-induced oral mucositis affects 90% of head and neck cancer patients undergoing concomitant chemo-radiotherapy (CHT-RT) leading to a impairment in food intake in up to 50%-70% of the cases. This translates in significant weigh loss, dehydration, renal failure and prolonged hospitalization, hampering the completion of treatment plans. We considered that an early and continuous toxicity monitoring could provide better outcomes.

Methods: Since May 2016, all patients diagnosed with locally advanced squamous carcinoma of head and neck candidate to CHT-RT treatment were included to our study. The nurse performed her first evaluation concomitantly to the first visit with the oncologist. Oral cavity, skin and nutritional screening, social and family background were assessed. During CT-RT, the toxicity assessment was performed three times a week: the nurse detected body weight, oral mucosal and skin hydration status, oral pain and dysphagia. The nurse was in close contact with patients and their caregivers, the oncologist and the nutritional team, as medical/nutritional measures were undertaken with her input.

Results: 13 patients were included in our analysis: five received CT-RT after surgery, eight as an exclusive treatment. Weekly Cetuximab, weekly Cisplatin (CDDP) 40 mg/m2, high-dose q3w CDDP 100 mg/m2 were administered concomitantly to RT in three, seven and three patients, respectively. All the patients completed the programmed treatment plan. 12 patients had minimal weight loss (<5%) during the treatment, with significant weight loss observed in only one case, associated to early disease progression. One patient required hospitalization because of the lack of familiar and social environment; we moreover recorded a death due to massive pulmonary embolism. The median cumulative dose of weekly CDDP was 220 mg/m2; the three patients treated with high-dose CDDP received a total of 300 mg/m2 as planned; Cetuximab was administered without interruption. The scheduled program of RT was accomplished in all cases.

Conclusions: Our design is based on the early nurse involvement; this allows a multidimensional and early identification of patients with major risk of developing treatment complications. The early and continuous nursing monitoring entails an efficient toxicity management in this high-risk population, whose final results are treatment completion in all patients, prevention of severe adverse events and a low rate of hospitalizations.

V11 Efficacy and patient acceptability of the DigniCaP ScalpCooler to prevent hair loss in breast cancer patients receiving adjuvant chemotherapy

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Background: Alopecia is a common and distressing adverse effect in breast cancer (BC) patients (pts) receiving adjuvant chemotherapy. The aim of the study was to assess the effectiveness and safety of this device to prevent chemotherapy-induced alopecia in early breast cancer patients (EBCP) receiving adjuvant treatment. The quality of life of pts was also evaluated.

Patients and methods: From January to December 2016, a sensor-controlled scalp cooling system (DigniCap: Sysmex Europe GmbH, Norderstedt, Germany) was proposed to a consecutive group of EBCP submitted to adjuvant chemotherapy at the Breast Unit of Spedali Civili Hospital of Brescia. Degree of hair loss was assessed by two nurse using Dean's alopecia scale by digital photographs at baseline and each chemotherapy cycle. EORTC QLQ-C30 questionnaire and self-reported visual analogical scale (VAS) of symptoms (anxiety, tone of mood, fatigue, nausea, well-being, activity) were collected at baseline and after the first two cycles of chemotherapy.

Results: 70 pts were enrolled and 49 (70%) completed the chemotherapy plan and were evaluable. Median age was 51 years, 8 pts (16%) received neoadjuvant and 41 pts (84%) adjuvant chemotherapy, 21 (43%) were treated with 4 cycle of chemotherapy (TC, EC or paclitaxel alone), and 28 (57%) with sequential chemotherapy with antracycline and taxane +- trastuzumab. Fifteen pts (30%) stopped the treatment because of loss of hair in 9 pts, for headache in 4 pts and for other problems in 2 pts.

At the end of chemotherapy, 13 pts (27%) had no loss of hair (Dean score 0), 25 pts (51%) had a minimal loss of hair (Dean score 1), 9 pts (18%) had a 50% hair loss (Dean score 2), 2 pts (4%) had a 75% hair loss (Dean score 3). No pts reported hair loss more than 75% (Dean score 4). There wasn't a significant difference between mean score value of QLQ-C30 at baseline and after chemotherapy and between the groups with and without hair loss. VAS documented an increase of fatigue and decrease of anxiety from baseline to final evaluation. The side effects presented with the use of DigniCap were the following: headache in 32% of pts and cold feeling in 57% of pts.

Conclusion: Scalp cooling with cold caps appears to be effective in preventing CIA among the majority of women undergoing treatment chemotherapy. The quality of life did not change in scalp-cooled patients.

Acknowledgments: a thank you to the ESA association that donated Dignicap to Oncology Department.

V12 Prospective qualitative study on the emotional experience of the patient undergoing radical prostatectomy

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Background: In Italy, prostate cancer is currently the most frequent cancer in humans from the age of 50 onwards. To date, prostatectomy is the only treatment used for localized prostate cancer that has shown a reduction in overall mortality and that is tumor-specific, as

well as a reduction in the risk of metastasis and local disease progression, albeit related to complications and physical deficits which are reflected directly on the couple's relationship and on the sexual sphere associated with it. Exploring the perceptions and experiences of men with prostate cancer undergoing this type of intervention is therefore of particular relevance today as it can encourage nurses to improve their approach to disease and improve the quality of assistance. Given the scarcity of qualitative studies, the aim was to investigate the patient's quality of life when undergoing radical prostatectomy.

Methods: A hermeneutical phenomenological prospective study was performed on patients >18 years of age, with prostatic carcinoma undergoing radical prostatectomy at the Oncology Urology Clinic of the National Regulatory Tumor Institute of Rome at 6 And 12 months of follow-up. A semi-structured interview was conducted to investigate the patients' experience. The analysis was guided by the Van Manen approach that brings the experiences to four existential foundations, namely: spatiality, corporality, temporality and relationality.

Results: Ten patients were included, with a mean age of 67 years and a prevalently medium-high (67.3%) study. The main spatial results indicate that patients need accurate information regarding their PSA before procedures are performed. With regard to corporality, distress and concerns about incontinence and changes within the sexual sphere emerge. The waiting period leading up to intervention is the main aspect of temporality that causes anxiety and stress. The theme of feeling comforted by the presence of others is the relationship that men with prostate cancer maintain with family members, friends, and healthcare workers.

Conclusions: The study showed that the quality of life of patients with prostate cancer significantly decreased after radical surgery. It is necessary to encourage patients to describe the history of their diagnosis and illness to understand their needs, establish more solid helpful relationships, and improve nursing care.

V13 Clinical results of the effectiveness of verbal versus written and verbal information about nausea and vomiting in patients receiving chemotherapy

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Background: The incidence of nausea during chemotherapy (37%-70%) is mainly related to the emetogenic potential of chemotherapeutic drugs associated with the individual variations of each patient. Chemotherapy-induced nausea and vomiting (CINV) is difficult to control because of several potential reasons: subjectivity of the symptom, limited understanding of physiopathology, lack of validated instruments, inefficient record of this event from patients, failure of nurses to assess its impact on patients' life. Empowerment of patients in the identification of CINV and in its reporting will be helpful to improve therapy adherence; nurses may play a role in this context. Despite the great number of studies investigating the efficacy of different antiemetic drugs in reducing CINV, no study focused on patients' educational program through written information about CINV.

Material and methods: We will conduct a phase III randomized clinical trial to investigate the efficacy of written and oral information (experimental arm) versus oral information alone (control arm) about CINV, in patients undergoing chemotherapy. The study, will be conducted in a Multidisciplinary Day Hospital at CRO Aviano from September 2017 to April 2018. Overall 384 patients are needed (192 per arm) to estimate a reduction of CINV from 60% to 45% ($a = 0.05$; $b = 0.20$). The study will include all patients undergoing chemotherapy for first time, with no previously psychiatric disease, neurologic disease e visually impaired. Specific exclusion criteria includes: life expectation <6 months; low compliance with interview. An information brochure and verbal information about nausea and vomiting will be provided to patients in the experimental arm, whereas, only oral information will be provided to patients in the control arm. All information will be provided by trained nurses. All patient will be evaluated after first chemotherapy cycle according to the criteria of CTCAE 4.03 and with two questionary: FLIE Questionary and Hamilton Anxiety Rating Scale.

Results: Study results is expected to demonstrate the efficacy of oral and written information versus oral information in reducing CINV in patients treated with chemotherapy (-15%). We also expect a reduction of anxiety and a increased level of compliance to chemotherapy.

Conclusion: A standard brochure about CINV may be introduced in nursing practices to make progress in clinical practice, improving the quality of life of patients undergoing chemotherapy.

V14 Role and competence of oncology nurse: a narrative review

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Background: In recent years there has been a steady increase in tumor incidence, due to screening and early diagnosis, which have led to a decrease in mortality rates and the chronic disease of oncology. It goes without saying that this change determines the need for the sick person and his/her family to receive, in addition to clinical and health information, indications also for social and nursing care and, if necessary, psychological assistance. These skills are beyond the sphere of knowledge of the "clinical-generic" nurse and fall into those of a nurse's specializing in oncology. Today in Italy, there is no real training course for the oncological nurse (ON), which becomes subordinate to the structure in which it operates and the will of the practitioner to search for new knowledge and new techniques of care.

Objective: To carry out a literature review in order to identify the competencies and roles of the ON in the different realities.

Methods: The research was conducted by consulting PubMed, Scopus and Kinahl with no restrictions related to the kind of publication, in a time span that includes the last 5 years. The keywords used are derived from the following string made with Mesh: ("Nurses"[Mesh] OR "Nurse Practitioners"[Mesh] OR "Nurse Clinicians"[Mesh] OR "Nurse Specialists"[Mesh] OR "Nurse's Role"[Mesh]) AND ("Oncology Nursing"[Mesh]) OR "Cancer Care Facilities"[Mesh]) OR "Neoplasms/nursing"[Mesh]) AND (("Professional Competence"[Mesh] OR "Clinical Competence"[Mesh]) OR "Nurse's Role"[Mesh]).

Outcomes: 16 studies were included, of which 8 were general ONs, 2 in the care of breast and lung cancer patients, respectively, 3 ON in the geriatric field, 1 specialized in prostate cancer and 2 Advanced clinical nurse. The analysis highlighted the importance of the ON figure as a benchmark for the patient, the need to provide patient-centered care and the use of a strictly evidence-based approach where the practitioner manages the patient through the therapeutic alliance, therapeutic communication, the involvement of caregivers in the welfare process and the territorial assistance services; Working in multidisciplinary teams, favoring adherence to diagnostic and therapeutic treatment.

Conclusions: The studies analyzed reflect the importance of having a specialized figure in the field of oncology, able to accompany the patient throughout the clinical, bureaucratic, social and psychological traits that characterize this disease.

V15 Effectiveness of cryotherapy in prevention and control of chemotherapy-induced oral mucositis

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Background: Mucositis is an inflammatory process that affects the oral mucosa. It's estimated to occur in approximately 40% of patients undergoing chemotherapy and almost 100% of those treated by radiation for head and neck cancer. It's a dose-limiting side effect of the cancer treatment. It can be expensive and sometimes hospitalization is request. It cause pain, eating difficulty, increased use of total parental nutrition (TPN), a rise of infection risk, much more opioid use and more days of hospitalization. Many interventions have been proposed to prevent or treat mucositis, such as topical antimicrobials, marrow stimulating cytokines, vitamins, propolis, laser therapy and cryotherapy. Some studies indicate the efficacy of oral cryotherapy in reducing mucositis severity. The effect was attribuited to the local vasoconstriction and decreased blood flow to the oral mucosa, thus preventing the damage by cytotoxic chemotherapy in the oral mucosa. The aim of this review is to highlights the best evidence about the effectiveness of cryotherapy in prevention and control of chemotherapy-induced oral mucositis.

Material & methods: Articles in the scientific literature were reviewed if published between January 2000 and September 2016. Searches were conducted using Pubmed, CINAHL and EMBASE databases. The search terms included were: Neoplasm, Stomatitis, Cryotherapy, Drug therapy; co-related by the boolean operators AND and OR. 64 records were analyzed according to inclusion and exclusion criteria and 5 records were included in the review. For critical evaluation it was used CASP checklist for RCT.

Results: Five RCT published between 2005 & 2011were included in the review for a total of 447 participants, consisting of adults with onco-hematological disease underwent chemotherapy. For each of the included studies, sample characteristics, variables, results and conclusions were analyzed. In four studies, the use of ice cubes reduce significantly chemotherapy induced oral mucositis. Only one study affirm that the incidence of severe oral mucositis (G3 - G4) was comparable in the two groups.

Conclusions: Currently there are not sufficient evidencies to affirm effectiveness of cryotherapy in the prevention and control of chemotherapy incuced stomatitis. The use of ice cubes is not associated with side effect of relevance. It has a good safety and a low risk for cancer patients. Further studies are needed to know this treatment more in a deep and targeted manner.

V16 ISOLA15: A multicenter study to assess the perception of protective isolation in cancer patients receiving hematopoietic stem cell transplantation

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Background: Haematopoietic stem cell transplantation (HCST) patients become immunosuppressed after chemotherapy. In order to control the infection risk, they

usually receive hospital care in protective isolation until neutrophil recovery. This means for the patient staying alone in a germ-free room with positive pressure and having limited contact with the outside world and with loved ones. However, isolation-related loneliness might increase patient suffering. Thus, the aim of this study was to develop and psychometrically test a self-report questionnaire to assess the patient's perception of protective isolation.

Material and methods: We developed 28 items according to three dimensions emerged in a metasynthesis: Suffering, Relating to oneself, and Missing the relationship with others. Item selection was performed through focus group, comparison with the findings of two phenomenological studies, and content validity with 22 experts. A total of 17 items yielded an adequate content validity index (CVI). The CVI of the questionnaire was 0.88. Cognitive interviews with 5 patients were used to verify face validity. A validation study was conducted in 10 Italian centres. Participants included 123 adult patients receiving autologous (55%) or allogeneic (45%) HSCT in protective isolation. Patients completed the questionnaires between 7 and 9 days post-transplant. Dimensionality was tested through Exploratory factor analysis (EFA).

Results: The scale yielded adequate psychometric properties, with the exception of 3 items, which were eliminated. The EFA yielded a three-factor solution explaining 49% of the variance. The more patients felt supported by nurses, the less they suffered because of isolation, as they were more able to relate to themselves in a positive way (Table 1).

Conclusions: Nurses can help patients live their isolation with greater serenity and mitigate their suffering. Risk factors for a negative isolation experience should be taken into account in order to avoid unnecessary patient suffering. Future studies should test the psychometric properties of the questionnaire through confirmatory factor analysis and verify its trans-cultural validity.

Table: V16. Correlation matrix (n = 123)

	Mean (SD)	1	2	3	4
1) Suffering	2.6 (0.9)	(0.90)			
2) Relating to oneself	3.1 (0.8)	-.150	(0.60)		
3) Missing the relationship with others	3.0 (1.0)	.644**	-.043	(0.80)	
4) Support from nurses	6.4 (0.7)	-.197*	.291**	-.049	(0.80)

*p <.05; **p<.001; [1), 2), 3)] range=1-5; [4)] range=1-7

V17 When nursing becomes transdisciplinary: promoting health in cancer experience, a collaboration between nurses and professional educators at an oncology center

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Receiving a diagnosis of cancer and bearing the heavy side effects of oncological therapies has a significant impact on the psychosocial condition of the patient and his/her family members. Psychic pain often does not allow them to express important subjective needs besides those of a strictly physiological nature, with severe effects on the quality of life, sense of self-efficacy and, more generally, health.

In the Oncology Complex of Hospital S.G. Bosco in Turin, the close collaboration of nurses with other professional figures (oncologists, psychologists, social workers) has enabled them to implement their ability to intercept the unexpressed needs of users and to promote innovative projects for that purpose.

Since 2016, this oncological center has hosted training sessions for students of the Degree Course in Professional Education of the University of Turin.

For two days a week trainee educators, under the supervision of a psychologist and a nurse, spend some time in company of patients when they are given chemotherapy, listening to their stories of life and illness.

Throughthe drawing of periodic reports on these interactions, it has been possible to intercept certain needs in the experience of cancer that not always are expressed and therefore satisfied.

Among these: the needs of membership, esteem and self-realization.

These needs are met when the educator shows to the patient, that when listening to him, he is worthy of being appreciated and understood not only by him, but also by family members and roommates.

Recognizing fragility and positively reinforcing the resources that the educator feels active in the interaction with the patient, can implement his sense of autoefficacy, encouraging a more active participation in the context of his meaningful relationships and the care process.

This experience opens up to interesting perspectives of integration between nurses and professional educators, in the direction of protecting the health of cancer patients and their families, retirning subjective value to the "life they lived" during the course of cancer and care.

V18 Sleep and hematopoietic stem cell transplantation: a pilot study with sleep questionnaire in the intensive care unit

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Introduction: Over 50% of the patients have trouble sleeping before hematopoietic stem cell transplantation (HSCT), 82% during hospitalization and 43% after the resignation, prevalence rates much higher than the general population. Sleeping less than 300 minutes per night increases the risk of mortality by 4 times.

Aim: Change the rating scale "Sleep in The ICU Questionnaire" used in ICUs for patients undergoing HSCT.

Materials and methods: The administration of the questionnaire: May/September 2016. The average time of administration for each individual patient is 15 minutes. The interviews were carried out 33, but the number of questionnaires that have been analysed are 30. The interviews were carried out in adult Bone Marrow Transplantation Unit, Hematology, Hematology Clinic of some Hospitals in Northern Italy.

Results: Questionnaires administered to 30 patients (17 men, 13 women). considered most bothersome symptoms: waking at night to go to the bathroom (43.30% of respondents rated this disorder with 10 points and 13% with a score of 9) consequence of liquid doses required for the type of transplantation; followed by the alarm of the infusion pump with the 16.7% that said a disorder equal to 10 and 20%, equal to 9. Degree of sleepiness: increases to half of the period of hospitalization and decreases for more than half of patients close to resignation. On a scale where 1 is unable to stay awake and 10 corresponds to fully alert and awake, judgment 10 was given by 36.70% for the first night in the ward, from 0.00% to half of the period and from 6.66% towards the end the period of hospitalization. Since, however, point out that the median between the middle and end of the period of stay is the same. The median of sleep quality during hospitalization is equal to 5, with 0% results equal to 1 (which is very bad) and the 3:30% equal to 0.

Conclusions: Patients have provided many ideas for further and more detailed analysis. Some survey items seemed to them unnecessary or wasteful while other fundamental deserving of further study to eliminate noise. In addition to reducing the hassles and noise that lead to continuous nocturnal awakenings, during service with this patient, we should also focus on decreasing anxiety and stress and the increase of activities based on the strength and the will of patients can stimulate it by reducing the feeling of isolation and boredom that impact negatively on the need for sleep and rest.

V19 Narrative review of quality of life in survivors of colorectal cancer

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Introduction: The quality of life of survivors of colorectal cancer after five years of diagnosis, seems to have a slow deterioration, due to the emergence of long-term symptoms in particular in the population of survivors with ostomy.

Aims: Investigate and identify the variables that affect the overall quality of life.

Material and methods: PICO method. Databases: Pubmed, Scopus, Cochrane, CINAHL, Johanna Brigss Institute (JBI), a journal: Journal of Advanced Nursing. Search terms: surveys and questionnaires, colorectal cancer survivors, long-term survivors, quality of life, patient continuity of care questionnaire, perception, social, continuity of patient care. Inclusion criteria were age ≥18 years, survivors of colorectal cancer, finished chemo/radio therapy, ostomy vs. no permanent ostomy, questionnaires that investigated the QoL, articles published in the last 10 years. Exclusion criteria: articles absent in the national catalog, items that only take in the studio men or only women survived to the CRC. Evaluation of the quality of the articles: STROBE, PEDro, PRISMA statement.

Results: Focus identified: socio-demographic variables, physical health status variables, clinical, psychosocial variables, sexual dysfunction associated with demographic, medical and psychosocial aspects in stoma care.

Conclusions: The oncology nurses are essential in all phases of cancer care but their role in caring for the survivors is unclear. The identified focus, must be taken into account by the nurses from taking charge of the patient and be re-evaluated at each follow-up in order to identify actual problems and potential in order to improve their quality of life.

V20 Dietary habits in women with breast cancer in treatment with endocrine therapy: a review of letterature

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Background: Breast cancer is the most frequently diagnosed tumor and the leading cause of cancer-related deaths in women around the world. Approximately, 60-75% of women diagnosed with breast cancer have a positive pathway to the estrogen and

progesterone receptor, for which treatment is selected with Tamoxifene or Aromatase Inhibitors orally for 5-10 years. One of the side effects associated with these drugs, which mostly affects the female sex, is weight gain. This condition, if associated with unhealthy food styles, can also cause an increase in cancer-related morbidity and mortality. Nevertheless, the correlation between eating habits and the response to hormonal treatments still remains an unexplored area today. The aim of this narrative review is to describe the studies in literature on dietary habits in women with breast cancer in endocrine treatment.

Method: A narrative review of literature on online databases was performed with: PubMed, CINHAL, Scopus. The proposed Mesh string on PubMed, from which the free words used in the second phase are then identified, is: ((“Breast Neoplasms”[Mesh]) AND “Antineoplastic Agents, Hormonal”[Mesh]) AND (“Diet, Food, and Nutrition”[Mesh] OR “diet therapy”[Subheading]). All the studies published in English between 2006 and 2016 included studies on adult humans.

Results: Out off the 229 items identified, 10 items of interest were added to the eligibility criteria. These articles include: three systematic reviews, five cohort studies, one case-control study, and one related to creating guidelines. The most investigated elements are soy, coffee, alcoholic beverages, and lifestyle-related factors.

Conclusions: Given the limited number of studies and the ineffectiveness of the results, it cannot be established with certainty whether there is a real association between the intake of particular foods and the response to the treatment. For the future, it is recommended to repeat the review by expanding the number of databases consulted and leading a multicenter observational study to assess dietary habits and the quality of life of endocrine-treating breast cancer patients.

V21 Cancer related fatigue in adults, adolescents and children. Literature review

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Introduction: Subjective feeling of persistent fatigue that undermines the quality of life. Exhaustion reduced physical and mental failure not relieved by rest. Increased from Radio Therapy to 90% and Chemo Therapy to 80%. Factors associated: therapies; anaemia; cachexia; metabolic and endocrinology disorders; sleep; emotical distress; inactivity; lung, heart, kidney, neuromuscular diseases; pain; infections. For research nurses it is a symptoms with slight effects of exhaustion to unbearable fatigues in daily activities. It appears in cancer in adult and pediatric patients where it less studied. The pediatric patient presents peculiarities both for oncology and that for pediatrics: age, cognitive and emotional development. The nurses wil assist both infant totally dependent on their parents and sexually mature teenagers.

Aim: Search in literature similarities and differences in the description, evaluation and treatment in children and adolescent than in adults and welfare peculiarities in the non pharmacological treatment of fatigue.

Material and methods: Consulted database: Cinahl, PubMed, Medline. Sources with a high lelevel of evidence, supplementary reviews, mate-analysis, review Cochrane and nursing journal in English.

Conclusions: The fatigue is a common symptoms, with different manifestations for associated factors, type of tumor and/or treatment as well as for the characteristics of each individual. Patients perceive it with different intensity and frequency of daily activities. If recognized it is treatable and controllable but very often is recurs even in drug treatments and persists for a long period. It manifests independently by other symptoms in adults and childhood. The fatigue requires multidisciplinary holistic care. A review of studies of adults and adolescents shows a need futher research to relative lack of indications of tertment in childhood.

V22 Potential contribution of the study nurse to colorectal cancer (CRC) translational research

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Background: Translational research aiming at the identification of prognostic and predictive markers is a fundamental area of modern oncology. In the field of CRC many appealing translational results derived from no profit/independent research. A tight cooperation between different professional figures, such as study nurses, clinicians, study coordinators, technicians and molecular biologists is needed. A dedicated CRC study nurse is able to understand the needs and interact with patients and health/laboratory personnel improving daily translational research. In Italy, scattered examples of study nurses committed to a specific disease are available. Our experience is presented in this work.

Material and methods: CRC study nurse is involved in the direct assistance of patients with specific focus on organizational and logistics aspects related to clinical trials, including patients’ monitoring, administration of surveys, training about protocols and biological samples collection for clinical and research purposes. Biological samples collection requires careful handling in terms of timing, processing, labeling, storage and delivery to other research centers or to the local laboratory.

Results: Since 2010 to 2016, 1319 patients with diagnosis of metastatic CRC were referred to Medical Oncology 1 – Veneto Institute of Oncology IRCCS; among them 956 received treatment or follow up and 400 were enrolled in at least 1 clinical trial. Every day 25-45 CRC patients are referred to our center for visits or chemotherapies. The study nurse checks records and prepares a flowchart of required procedures. In the last year, 116 patients received 1-line and 110 subsequent-line treatments in clinical trial settings and underwent to blood samples collection at specific time-points. A comprehensive database of the collected biologic material was built. “Baseline” and “at progression’s time” biological samples are available for 213 and 72 patients, respectively. For each patient, amounts (blood, plasma and serum), processing method, date and time of collection are recorded.

Conclusions: The involvement of a CRC dedicated study nurse simplifies the procedures required to enroll patients in clinical trials and is fundamental to maintain standard quality and to carefully address methods of biological samples collection leading to an overall improvement of patient care. Moreover it is crucial to conduct retrospective/prospective research programs in connection with the daily clinical practice.

V23 Breast unit and caring, gordon nursing model and NNN taxonomies: the nursing care planning from efficacy in trials to effectiveness in clinical practice

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Background: The *Breast Unit*, regulated by international guidelines, is a new opportunity to cure and to care that allows women with breast cancer to deal with their illness supported by a *Multidisciplinary Team*.

The complexity of this disease requires adopting the bio-psycho-social-spiritual paradigm, typical of Caring, focused on “taking care *of the person*” rather than focusing only on illness treatment.

Materials and methods: In this study 10 women with breast cancer in Trieste’s Breast Unit were enrolled and “*Gordon Nursing Model*” has been used. NANDA-I connections with NOC and NIC support Diagnostic Reasoning. NANDA-I defines the *person’s health problems* of exclusive nursing competence; the NOC Taxonomy defines the relative health *outcomes* shared with the person and the NIC Taxonomy defines the Nursing *Interventions*.

Results: The main Dysfunctional Patterns found were the “Coping and Stress Tolerance” and the “Self-Perception and Self-Concept”.

For the first pattern, the NANDA-I diagnosis was “Ineffective Coping (00069)”, the NOC identified was “Coping (1302)”, while the NIC was “Coping Enhancement (5230)”.

For the second pattern the NANDA-I Diagnosis was “Disturbed Body Image (00118)”; NOC: “Body image (1200)”; NIC: “Body Image Enhancement (5220)”.

Conclusions: This study shows the importance and the effectiveness of having a tool with solid scientific background that allows a complete Assessment. The Gordon Model turns out to be “*complete*” (it investigates the person in its totality), “*fast*” (it reduces the assessment time) and with a “*high scientific value*” (it uses the NNN Taxonomies that allow a wide variety of choices, to make research and to compare results on an international scale).

V24 Shiatsu in oncology: a treatment of healing processes’ activation. Observational study

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Nowadays, Alternative and Complementary Medicines (CAM) is increasingly used on cancer patients, holistic approach seems to be the most functional and satisfying. In 2006, the American Nurses Association (ANA) officially recognized Holistic Nursing as a specialty area of nursing practice. For holistic nurses, healing is a dynamic process

focused on caring body-mind-spirit in a complex, taking care of the whole person. *Shiatsu* is a complementary mind-body treatment; it can be considered like a psycho-physical help during oncology disease. It could also be considered as a resource for well being, relaxation, and life quality improvement

The aim of this observational study is describe *shiatsu* effects in cancer patients and connection between this treatment and improvement on psychophysical well-being and quality of life (QoL).

The study involved 21 oncological patients of Day Hospital. These patients voluntarily took part in *shiatsu* treatment offered by an association that works in prevention and rehabilitation area. The study participants answered a questionnaire and EORTC-QLQ C-30 to respectively evaluate *shiatsu* effects on psychophysical well-being and QoL sensed.

Shiatsu treatment improved health perceptions in patients, 65% of attendees declared that *shiatsu* activated changes in perception of themselves and their body. 85% showed psychophysical relaxation and the 75% felt general well-being. Subjective perception of fatigue decreased (-35%), like emesis (-35%), anxiety (-20%), depression (-15%); also paraestesias decreased, sleep quality and perception of energy of body and mind increased. The relationship between *shiatsu* professional and patient is rest on trust (95% of cases) because patients declared to feel embrace and well-liked from the *shiatsu* professional. 45% of sample adopted a well-being oriented life style during and after *shiatsu* treatment. The 75% of sample felt benefits days after treatment end. 65% of attendees adopted at least one CAM in the past and during the study 50% was adopting at least one type of CAM.

Shiatsu is an holistic treatment which shows multidimensional effects for well-being on the whole person. It could be considered a treatment that activate healing process, it could be integrated in the medical oncology care.

V25 Massage therapy and quality of life of cancer patient in palliative care: literature review

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Introduction: The object of assistance to cancer patient, bearers of overall suffering, is to take care of the whole person, to ensure quality of life and accompany a peaceful death. Physical contact, extraordinary means of communication, goes beyond words, it allows you to heard and be heard, reassure and demonstrate emotional participation.

Aim: Identify techniques and approaches complementary, such as massage therapy, and assess whether, with the traditional therapy, can improve the comfort of the person with advanced oncologic disease, treating it as a whole. Reference is made to concept of total pain not only physical suffering but also psychological, social and spiritual.

Material and methods: We have consulted databases which PudMed and Cinahl, analysing 98 articles. There wan been included, oncologic patients with advance cancer, age < 18, in palliative cancer centre, hospice or

home and patients who received therapeutic massage techniques, excluding other types such as: Reiki, therapeutic touching. Articles published before 2000 were exclude. Finally, for the literature review 13 articles have been considered.

Results: The articles assess the effectiveness of massage therapy on the physical al psychological symptoms. There has been reduction in pain, anxiety, depression and stress. Significant evidence of an increase in the feeling of relaxation and tranquillity. The treatment improved the state of health of the person and it was useful to find inner peace.

Conclusions: Because in the literature are not documented adverse events related to massage therapy, it is considered and economic tool, non-invasive, easy to access and reach good levels of effectiveness, facilitating and establishment of an empathetic relationship. The evidence found allows the nurse to expand the knowledge and training for taking charge in personal care that is more holistic and improve the quality of life.

V26 Narrative Medicine: from words ..... to actions

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Background: "Narrative Medicine" (NM), also known as "Narration-based Medicine" (NBM), can be considered as a clinical-care intervention method that makes possible to define a personalized care pathway; furthermore, it allows all healthcare professionals to develop and improve their empathic, reflexive, listening ability with the purpose of taking care of the person, as well as cure the disease.

The nurse, responsible for the care process, all along is intended to take care of the person and, for education, to consider it as a whole. For nurses, thinking about their action is a duty, not only about technical and organizational aspects (based on the use of valid scientific instruments), but also about relationship and communication with the patient.

Here we report a direct professional experience in the NM field, based on the reading of a book written by the husband of a patient we have taken care for eleven years.

Methods: The book "Mentre aspetto vivo"(While I wait live) tells how despite a terrible illness, judged "incurable" since diagnosis, one can live a life defined "a fantastic adventure" and testifies how, even with the knowledge that "cancer" has arrived and is scary, you may be unwilling to spend life waiting for the worst. The book, gave by the author, was read voluntarily by some nurses who took care of the lady. This has led to professional considerations resulting in improvement actions.

Results: This NM experience has brought several results in our clinical practice. Firstly, the awareness of how written words give voice and dignity to the sick people who are the protagonists of the care process (empowerment). Secondly, the recognition by the health team of the value of NM, so that health professional can optimally assist the patient in her/his history of illness. Finally, this experience allowed the realization of an organizational model aimed at creating moments of communication with patients.

Conclusion: NM helps those who live a disease experience to rebuild the new identity that ensues and allows the health team to know aspects of the quality of patients' and caregivers' life that cannot be evaluated with quantitative instruments, but only through their testimonies. The relationship, based on dialogue and narration requires proper training and should be integrated with Evidence-Based Medicine, to make clinical-care decisions more complete, personalized and effective.

V27 "Cure alopecia": results on the first period of use of the Dignicup system in the AORMN

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Preventing hair loss during chemotherapy has always been the goal of the oncologist's nursing, physician and the patient who has to undergo this treatment.

Chemotherapy-induced alopecia, although reversible, is one of the most impacting psychological effects in treatment patients, but the woman's patient has an impact, if possible, even greater. Psychosocial implications and alteration of the body image may affect the acceptance of chemotherapy treatment. (Kome et al, 2013, The Oncologist).

Since 1970, various cooling systems have been used to prevent hair loss but with poor results and a high discomfort for the patient. Thanks to the improvement of technology, DigniLife is now used routinely in several centers of excellence in Italy and Europe; Is today the only scalp cooling tool to have been approved by FDA in December 2015.

This work want to verify the results obtained during the first period of use of the Dignicup system, in the AORMN Oncology Department (Hospital S. Croce); since from September 15, 2016 to May 15, 2017, no. 40 women who have undergone this treatment. The corporate protocol envisages the selection of all patients who have been diagnosed with breast cancer (No. 34) or gynecological cancer (No. 6 cases) who will have to undergo chemotherapy; To date, 24 patients have completed treatment.

The first results showed the following alopecia data:

Treatment was positive in 81.2% of cases where hair loss was modest (G1 = 2 women, G2 = 7 women, G3 = 3 women); while in 18.8% of the cases the treatment failed (G4 = 2 women, G5 = 1 woman), but they continued treatment until the end of the therapy

Among patients who have suspended the treatment:

4 patients with hair loss (G4)

1 patient for change therapy

1 patient for cold cough failure

1 patients for cold intolerance + hair loss (G4)

1 patients per intervention

Our partial experience shows that an effective cooling of the scalp and the use of a technologically advanced device such as Dignicup, favoring women in treatment: better collaboration between nurses and patients, better acceptance of chemotherapy, acceptance of Its own body image that tends to not change, the maintenance of its daily and social activities

It is clear from the reported data that patients have achieved satisfactory results; The percentage of patients leaving treatment does not give up on a tool that keeps patients more confidence in themselves and in their own image.

V28 A try to positively influence the quality of life of patients undergoing stem cell transplantation in protective isolation with the use of a tablet

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Backgorund: Patients with Multiple Myeloma who undergo autologous stem cell transplantation (HSCT) are often hospitalized in protective isolation in a single room.They cannot leave it and just one visitor can visit them for a short time.This situation might negatively affect their QoL.It was hypothesised that the use of a tablet during their hospital stay in isolation could improve their QoL by reducing the distance with the external world and increasing their activities in the isolation room.

Material and methods: This was a pre-post study with two patient groups.A total of 8 patients completed the FACT-BMT questionnaire at admission and at discharge.Among these,3 participants were provided with a tablet with Internet during all the hospitalization.The tablet had a lot of applications to communicate with the external world, to listen music, to play games and other. Their primary informal caregivers($n = 6$) completed the Hospital Anxiety and Depression Scale at admission and discharge to evaluate a change in anxiety and depression.

Results: At discharge patients who used the tablet showed an improvement in the Social/Family Well-Being and their Physical/Social/Relational Limitations remained stable.The QoL of patients without a tablet worsened in these aspects.In particular patients with tablet referred to feel close like before to their caregivers, to feel closer than before to their friends and less far than before from people.They also reported that the tablet helped them to maintain a visual contact with the external world in an active way during the isolation.They used mostly applications to communicate, to read news and to play games.Although the tablet did not show a positive effect on caregivers'anxiety and depression, they believed that the experience was positive because the tablet facilitated the relationship with the external world and family virtual contact.

Conclusions: Since protective isolation can worsen patients'QoL, nurses should help patients to find effective strategies to spend their time in a positive way and to reduce the isolation burden.

Table: V28

Well-Being	TABLET (n = 3)		NO TABLET (n = 5)	
	T0	T1	T0	T1
Physical	23 (1.73)	11.6 (6.65)	16.8 (9.80)	13.8 (6.72)
Social/Family	18.3 (6.42)	19.6 (5.50)	20.32 (2.16)	17.33 (3)
Emotional	19.3 (1.15)	18.6 (3.05)	18.25 (3.42)	17.75 (4.57)
Functional	15.6 (6.65)	9.6 (4.16)	13.5 (6.06)	7.25 (2.87)
Bone Marrow Transplant Subscale	28.3 (4.72)	19.3 (3.78)	27.25 (9.05)	20.75 (6.60)
Physical/Social/ Relational Limitations	41.3 (8.32)	41 (4.35)	43.98 (5.07)	38.79 (4.02)

V29 "Feel beautiful to feel alive"

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Background: On March 8, 2016, the first Pink Day has been held at the Pink Room of the Department of Medical Oncology of our institution. The Pink Room is a literally pink ambulatory, involving internal hospital specialists and external professionals, who provides their professional skills free of charge to help women during anti-cancer treatments. The aim of the project is to help women recapture the physical image and psychological identity through complementary pathways to oncological therapies.

Materials and methods: A questionnaire investigating what is the perception of the body image as well as the unmet needs of the patients was administered to all the consecutive patients admitted to the Pink Room. The first part of the questionnaire included both personal data and medical data, while in the second part there were questions exploring the body image both before and after the illness and the unmet needs.

Results: The study included 86 patients with a median of 56 years of age. From the questionnaire, the following data emerged:

1. 96.2% of women who benefited the Pink Room are Italian;
2. 54.7% are married, 17% are nubile, 7.5% are divorced, 3.8% are cohabiting;
3. 39.6% have a high school diploma, 34% have a university degree and 26.4% have a lower or elementary secondary school license;
4. 47.2% declare to have a job, 32.1% are retired, 11.3% are unemployed and 9.4% are housewives;
5. 58.5% is in a post-menopausal state and 41.5% is in pre-menopausal state;
6. 62.3% have a diagnosis of breast cancer, 20.8% a gastrointestinal tumor, 5.7% an ovarian cancer and 1.9% a lung cancer;
7. 29.3% has required aesthetic advice, 20.3% breast cancer counseling, 12.2% hair styling and yoga counseling, 7.3% dermatological and nutritional advice, 6.5% psychological counseling, 2.4% endocrinological advice and 0.8% a plastic surgery consultancy;
8. 100% of women feel less physically attractive after the illness and the treatments.

Conclusion: As Jane Cook, breast cancer survivor, once said "breast cancer change you and the change can be beautiful". The pink room has the main goal of returning the patient's self-confidence, respect and love to one's own body. Aesthetic treatments, in a field like oncology, become true complementary therapies to the medical ones: "feel beautiful to feel alive" and to deal with the difficulties of the disease.

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See you at the

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President of the Congress
Stefania Gori

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