

# IGCS 2023

## Annual Global Meeting

# SEOUL

### **IGCS 2023 Abstracts: ePosters**

Registered delegates will have access to all submitted ePosters via the IGCS 2023 mobile application, IGCS 360 Educational Portal and the ePoster Stations onsite at the meeting venue.

Poster presenters were given the option to submit an audio file with a short presentation together with their ePosters. Submitted audio files will be available together with their ePosters within the ePoster Stations onsite and the IGCS 360 Educational Portal.

EP001 / #255

Topic: *AS01. Basic/Translational Science*

## **KNOCKDOWN OF E-CADHERIN EXPRESSION PROMOTE CERVICAL CANCER PROGRESSION THROUGH EGFR SIGNALING PATHWAY.**

Gwan Hee Han<sup>1</sup>, Hee Yun<sup>2</sup>, Sunghoon Kim<sup>2</sup>, Hanbyoul Cho<sup>2</sup>, Jae-Hoon Kim<sup>2</sup>

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**Introduction:** The expression of E-cadherin, a crucial cell adhesion molecule, plays a significant role in the progression of various malignancy. However, the role of E-cadherin in cervical cancer has not been elucidated yet. Therefore, we aimed to investigate the expression of E-cadherin in cervical cancer patients and its association with the pERK signaling pathway.

**Methods:** Immunohistochemical analyze E-cadherin and pERK were performed using tissue microarray of cervical cancers and normal cervical epithelial tissues and clinicopathologic variables were analyzed. Also the functional studies with cervical cancer cell lines were evaluated.

**Results:** The expression of E-cadherin was significantly reduced from normal to cancer, and associated with FIGO stage. Furthermore, E-cadherin expression was negatively correlated with pERK expression in cervical cancers. The Kaplan-Meier plots demonstrated that E-cadherin lowexpression was associated with poor DFS and OS, and pERK, overexpression was significantly associated with poor DFS and OS. The DFS and OS with expression of low E-cadherin/high pERK was compared with patients with others which revealed a significant difference in DFS and OS. The Cox proportional hazards model revealed that a low E-cadherin/high pERK expression was an independent prognostic factor with respect to overall survival (HR=8.48 [95% CI, 3.36 – 21.37, p<0.01]. In cervical cancer cell lines, the knock down of E-cadherins promoted proliferation in cervical cancer cells and loss of E-cadherin led to EGFR mobility, which may stimulate EGFR dimerization and further boost its activation.

**Conclusion/Implications:** Low expression of E-cadherin or combined with pERK is an indicator of poor prognosis in cervical cancer, suggesting their potential utility as prognostic test in clinical assessment.

EP002 / #234

Topic: *AS01. Basic/Translational Science*

## **RESULTS OF CLINICAL RESEARCH (PRUM-IBIO STUDY): ESTABLISHMENT OF PROGNOSTIC BIOMARKERS FOR UTERINE MESENCHYMAL TUMORS**

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**Introduction:** Benign uterine leiomyoma (U.LMA) and malignant uterine leiomyosarcoma (U.LMS), which are both uterine mesenchymal tumors, are distinguished by the number of cells with mitotic activity. However, uterine mesenchymal tumors contain tumor cells with various cell morphologies; therefore, making a diagnosis, including differentiation between benign tumors and malignant tumors, is difficult. For example, cotyledonary dissecting leiomyoma (CDL) or uterine smooth muscle tumors of uncertain malignant potential (STUMPs), etc. are a group of uterine mesenchymal tumors for which performing a differential diagnosis is challenging. A standardized classification system for uterine mesenchymal tumors has not yet been established. Furthermore, definitive preoperative imaging techniques or hematological examinations for the potential inclusion of CDL or STUMP in the differential diagnosis have not been defined.

**Methods:** We have been carrying out multicenter clinical research to establish life prognostic markers for uterine mesenchymal tumors.

**Results:** Our clinical research showed that there is correlation between biomarker expression and mitotic rate or tumor recurrence. The candidate factors of immunohistochemical biomarkers can effectively help determine the malignant potential of CDL or STUMPs in patients who wish to become pregnant in the future.

**Conclusion/Implications:** The establishment of gene expression profiles or detection of pathogenic variants by employing next-generation molecular techniques can aid in disease prediction, diagnosis, treatment, and prognosis. Here, we describe the problems in diagnosing uterine mesenchymal tumors along with the results of the latest our clinical research.

EP003 / #550

Topic: *AS01. Basic/Translational Science*

## **EFFICACY OF COMBINATION CHEMOTHERAPY AND THIRD-GENERATION ONCOLYTIC HERPES VIRUS THERAPY FOR CERVICAL CANCER**

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**Introduction:** Radiotherapy and chemotherapy are the most common treatments for advanced or recurrent cervical cancer, but the prognosis is poor. We have investigated viral therapy with triple mutant herpes simplex virus (T-01) in a mouse model of cervical cancer as a novel therapeutic approach. However, its antitumor effect is not sufficiently effective. In this study, we examined whether the combination of viral therapy and anticancer agents could enhance the antitumor effect.

**Methods:** A mouse-derived immortalized cell line TC-1 with HPV16 E6/E7 as tumor antigen was inoculated subcutaneously into the back of C57BL/6 mice to generate cervical cancer model mice. cisplatin (CDDP), etoposide (ETP), fluorouracil (5-FU) from in vitro results, irinotecan (CPT-11), and cyclophosphamide (CPA) were administered to model mice, and anticancer agents that showed antitumor effects were combined with T-01. The combination therapy was evaluated as enhancing the antitumor effect when it exceeded the antitumor effect of viral therapy and chemotherapy.

**Results:** The CPT-11, ETP, and 5-FU combination with T-01 groups showed no enhancement of antitumor effect. In contrast, the CDDP and CPA combination with T-01 group showed significant tumor growth inhibition compared to the chemotherapy and T-01 groups. Although there was no significant difference in survival rates between the chemotherapy and T-01 groups, no mice died during the observation period in either treatment group.

**Conclusion/Implications:** The combination of CDDP or CPA and viral therapy exceeded the tumor growth inhibitory effect of viral therapy and chemotherapy, and we concluded that the combination of the two therapies enhanced the anti-tumor effect.

EP005 / #1379

Topic: *AS01. Basic/Translational Science*

## **HIGH-THROUGHPUT VIABLE CIRCULATING TUMOR CELL ISOLATION USING TAPERED-SLIT MEMBRANE FILTER BASED CHIPSETS IN DIFFERENTIAL DIAGNOSIS OF OVARIAN TUMORS**

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**Introduction:** Circulating tumor cells (CTCs) have received enormous attention as a novel biomarker in various malignant diseases. The aim of this study was to evaluate CTC detection using tapered-slit membrane filter based chipsets in differential diagnosis of ovarian tumors.

**Methods:** A total of 230 preoperative women with an indeterminate ovarian tumor were prospectively enrolled. Seven patients diagnosed with other primary origin and 20 patients sampled after neoadjuvant chemotherapy were excluded from the analysis. Sensitivity, specificity, accuracy, and area under the receiver operating characteristic curve (AUC-ROC) of CTC detecting chipsets were analyzed according to postoperative pathologic results respectively.

**Results:** 81 (39.9%) benign tumors, 32 (15.8%) borderline tumors, and 90 (44.3%) ovarian cancers were pathologically confirmed. CTC detecting chipsets had sensitivity, specificity, accuracy, and AUC-ROC of 75.6%, 58.0%, 67.3%, and 0.655 (95% confidence interval [CI], 0.570-0.740) for differentiating ovarian cancer from benign ovarian tumor. Sensitivity, specificity, accuracy, and AUC-ROC for detecting ovarian cancer from borderline tumor were 75.6%, 50.0%, 68.9%, and 0.622 (0.505-0.739), respectively. In addition, sensitivity, specificity, accuracy, and AUC-ROC were 68.9%, 58.0%, 64.5%, and 0.622 (0.540-0.703) for differentiating borderline and malignant ovarian tumor from benign tumor. Sensitivity, specificity, accuracy, and AUC-ROC for detecting ovarian cancer from benign to borderline tumor were 75.6%, 55.8%, 64.5%, 0.645 (0.567-0.723), respectively.

**Conclusion/Implications:** Our study suggests that preoperative high-throughput viable CTC isolation using tapered-slit membrane filter based chipsets could have a potential role in differentiating ovarian malignancy from benign and/or borderline tumors.

EP006 / #881

Topic: *AS01. Basic/Translational Science*

## **DIFFERENTIAL GENE EXPRESSIONS IN ENDOMETRIAL CANCER CELLS WITH ACQUIRED CISPLATIN RESISTANCE**

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**Introduction:** To identify differentially expressed genes (DEGs) and signaling pathways in cisplatin-resistant endometrial cancer (EC) cells.

**Methods:** Cisplatin-resistant endometrial cancer cells were established through continuous treatment of endometrial cancer cells (RL95-2 and Ishikawa) with gradually escalating doses of cisplatin. RNA-seq was performed on both original and cisplatin-resistant EC cells to evaluate DEGs. Gene-set enrichment analysis (GSEA) was also performed to find biologic processes or pathways in relation to cisplatin resistance.

**Results:** Common hallmark gene sets enriched in both cisplatin-resistant RL95-2 and Ishikawa include inflammatory response, epithelial-mesenchymal transition, and KRAS signaling\_up. Common DEGs include EMP3, CD70, and SERPINE1 in the inflammatory response gene set; LAMA2, BDNF, OXTR, CDH2, VIM, MATN3, ABI3BP, EDIL3, EMP3, CXCL1, SERPINE1, and IL32 in the epithelial-mesenchymal transition gene set; PTPRR, MMD, and KCNN4 in the KRAS signaling\_up gene set.

**Conclusion/Implications:** We identified DEGs and several pathways enriched in cisplatin-resistant EC cells as potential therapeutic targets of cisplatin resistance, which need further validation.

EP007 / #793

Topic: *AS01. Basic/Translational Science*

## **THE MECHANISM THAT AFFECTS CELL DEATHS FOR TUMOR SUPPRESSION GENE-PTEN BY EZH2 ACTIVITY IN A CERVICAL CANCER CELL LINE(HELA-R) WITH RADIATION-TREATMENT RESISTANCE**

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**Introduction:** To determine the mechanism affecting cell deaths for tumor suppression gene-PTEN by targeting EZH2 activity as a therapeutic strategy against EGFR inhibitor resistance in the EGFR-Mutant cervical cancer cell line with radiation-treatment resistance

**Methods:** We investigated the mechanism affecting cell deaths for tumor suppression gene-PTEN by targeting EZH2 activity as a therapeutic strategy against EGFR inhibitor resistance in the EGFR-Mutant cervical cancer cell line with radiation-treatment resistance. Epidermal growth factor receptor (EGFR) expression is expressed in various types of tumors, including cervical cancer, in an increased state than normal tissue.

**Results:** EGFR was expressed in the human cervical cancer cell line (Hela cell line) and cervical cancer radiation-resistant cell line (Hela-R cell line), and it was observed that the Hela cell line disappeared by drug-reacting EGFR inhibitor (Apatinib), but the Hela-R cell line did not die. Therefore, it can be inferred that HeLa-R cell lines generally have pathways other than EGFR-related signaling cascades (e.g., PI3K/Akt, STAT, and MAPK), which have become interesting in EGFR/PI3K/PTEN/AKT signaling pathways, which serve as PTEN tumor suppressors. The role of the PTEN gene in the carcinogenesis of cervical cancer is not well known. PIP3 generated by activation of PI3K is converted from PIP3 to PIP2 again by PTEN and SHIP, thus inhibiting the signaling pathway activated by PIP3.

**Conclusion/Implications:** In this study, PTEN and EZH2 can be observed in cervical cancer tissues with radiation resistance. Therefore, the Inhibitor of EZH2 ultimately provides clues about the new chemotherapy's role in palliative cervical cancer patients with radiation resistance.

EP008 / #896

Topic: *AS01. Basic/Translational Science*

## TRANSCRIPTOME ANALYSIS OF HERV-K ENV KNOCKOUT OVARIAN CANCER CELL LINES

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**Introduction:** Human endogenous retroviruses (HERVs) are suggested to be involved in the development of certain diseases, especially cancers. In pancreatic cancer cells, shRNA-mediated downregulation of HERV-K env RNA decreases cell proliferation and tumor growth through the RAS-ERK-RSK pathway; in colorectal cancer, CRISPR-Cas9 knockout (KO) of the HERV-K env gene affects tumorigenic characteristics through the nupr-1 gene.

**Methods:** To elucidate the function of HERV-K Env protein in cancers, HERV-K env gene was knocked out using CRISPR-Cas9 in ovarian cancer cell lines SKOV3 and OVCAR3. Tumorigenic features like cell proliferation, migration, and invasion were analyzed, as well as related protein expression via western blotting. Gene expression patterns were evaluated using next-generation mRNA sequencing and gene ontology and pathway analyses.

**Results:** After HERV-K env gene KO, RNA and protein expression significantly decreased, and tumorigenic features like cell proliferation, migration, and invasion significantly reduced. RB protein expression significantly increased in HERV-K env KO SKOV3 cells, while phospho-RB protein decreased in OVCAR3 cells. Transcriptome analysis showed significant differences in 37 DEGs out of 4,325 DEGs. SKOV3 cells had 31 upregulated and 32 downregulated DEGs, mainly related to RNA splicing, aging, and angiogenesis genes. OVCAR3 cells had 226 upregulated and 1,464 downregulated DEGs, mainly related to RNA splicing and aging genes.

**Conclusion/Implications:** The results of this study showed that HERV-K env gene KO affects cell proliferation, invasion, and migration of ovarian cells through RB and Cyclin B1 proteins, but the specific regulation pattern can differ by cell line.



EP010 / #59

Topic: *AS01. Basic/Translational Science*

## **INSUFFICIENT SERUM APOLIPOPROTEIN A1 IMPAIRS ANTITUMOR RESPONSE OF CD8<sup>+</sup> T CELL VIA HIF-1A-GLYCOLYSIS PATHWAY**

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**Introduction:** The immunosuppressive microenvironment plays an important role in the occurrence and development of tumors. Studies have shown that ApoA1 insufficiency is closely related to tumor development, but the underlying mechanisms are not well understood.

**Methods:** Serum lipids in endometrial cancer and ovarian cancer patients were compared. Then tumor models in ApoA1 transgenic mice, and in vitro experiments were used to identify the immunomodulatory roles and potential mechanisms of ApoA1 on CD8<sup>+</sup> T cells.

**Results:** Serum ApoA1 significantly decreased among the lipid parameters in patients with endometrial cancer and ovarian cancer compared to healthy controls. In endometrial cancer tissues, compared to ApoA1 sufficiency group, ApoA1 insufficiency group showed an immunosuppressive state, manifested as increased CD163<sup>+</sup> macrophages and decreased CD8<sup>+</sup> T cell infiltration. Consistently, tumor-bearing A1KO mice also showed impaired tumor-infiltrating CD8<sup>+</sup> T cell infiltration and function. Further CD8<sup>+</sup> T cell depletion experiments confirmed that CD8<sup>+</sup> T cells were required for the antitumor activity of ApoA1. In vitro, ApoA1 peptide L-4F can directly potentiate the antitumor activity of CD8<sup>+</sup> T cells via HIF-1 $\alpha$ -mediated glycolysis pathway. Mechanistically, we found that ApoA1 reduced the ubiquitination degradation pathway of HIF-1 $\alpha$  by down-regulating FIH1, further maintain the stability of HIF-1 $\alpha$  protein and signaling activation. Lastly, tumor-bearing A1TG mice showed significant sensitivity to anti-PD-1 therapy, with retarded tumor growth and increased tumor necrosis.

**Conclusion/Implications:** Our data demonstrated the critical roles of ApoA1 in remodeling immune microenvironment and enhancing CD8<sup>+</sup> T cell immune functions via HIF-1 $\alpha$ -mediated glycolysis, which supports the clinical investigation for a combination of ApoA1 supplementation and anti-PD-1 therapy in tumors.

EP011 / #717

**Topic:** AS01. *Basic/Translational Science*

## **PREDICTION OF CHEMOTHERAPY RESPONSE WITH LIQUID BIOPSY OF BODY FLUID FROM PATIENTS WITH GYNECOLOGIC CANCER**

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**Introduction:** Organoids are three-dimensional in vitro culture systems. This model has been shown to be superior to conventional two-dimensional cell culture in recapitulating functionality, architecture, and genomic features of tissues seen in vivo. Patients with gynecologic cancers, especially with refractory disease status, may experience the accumulation of malignant effusion fluids. In this study, accumulated body fluids were analyzed to predict chemotherapy response by using organoids culture systems.

**Methods:** We obtained tumor specimens in the form of multicellular spheroids present in malignant effusion fluids. We developed organoid growth of tumor cells and used them as a platform for empirical drug sensitivity testing. Body fluid samples (either ascites or pleural effusion) from 44 patients with gynecologic cancers were collected. Multicellular spheroids were recovered and subjected to culture conditions designed to support organoid growth. Drug sensitivity testing with various chemotherapeutic agents was performed on these specimens.

**Results:** Our model demonstrated organoids formed within days of primary culture. Established organoid lines showed patient-tumor dependent morphology and disease characteristics, recapitulating the features of patient-specific malignant cells. Drug sensitivity testing identified several agents with therapeutic potential and these results displayed patient-specific sensitivity to different chemotherapeutic agents.

**Conclusion/Implications:** Establishment of organoid culture of multicellular spheroids from gynecologic malignant effusions can be used as a platform for empirical drug sensitivity testing. These models may be helpful in screening new or existing therapeutic agents prior to individualized treatment options.

EP012 / #719

**Topic:** AS01. *Basic/Translational Science*

## **GENOME-WIDE CELL-FREE DNA ANALYSIS ALGORITHMS FOR EARLY DETECTION AND PREDICTION OF PROGNOSIS OF OVARIAN CANCER**

Joseph Noh<sup>1</sup>, Yoo Young Lee<sup>1</sup>, Chel Hun Choi<sup>2</sup>, Tae-Joong Kim<sup>2</sup>, Byoung Gie Kim<sup>3</sup>, Lee Jeong-Won<sup>4</sup>  
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**Introduction:** The purpose of the present study was to develop artificial intelligent (AI) algorithms for analyzing genome-wide cell-free DNA (cfDNA) for early detection and prediction of prognosis of epithelial ovarian cancer.

**Methods:** Whole blood samples from epithelial ovarian cancer patients (n=120) stored in a biobank were used to develop AI algorithms for genome-wide analysis of cfDNA. Convolutional neural network (CNN) and multilayer perception (MLP) deep learning methods were used for algorithm development. Another batch of whole blood samples from the patients who were newly-diagnosed with ovarian tumor (both benign and malignant) were prospectively collected and run through the developed algorithms. Sensitivity and specificity of the developed algorithms in differentiating malignant tumors from benign tumors were explored.

**Results:** A total of 219 whole blood samples from the patients who were newly-diagnosed with ovarian tumor were run through the algorithms and the probability scores of malignancy were calculated. The probability scores calculated by the analysis of DNA fragmentation size, patterns of sequence of end motif, regional mutation types and their density were found to be significantly higher in cancer patients than those with benign tumors. Furthermore, these scores became increasingly higher as the extent of disease assessed by the FIGO staging system increased. This machine-learning model incorporating genome-wide cfDNA analysis had sensitivities of detection at 92% at 98% specificity, with an overall area under the curve value of 0.99.

**Conclusion/Implications:** The use of AI algorithms for analyzing cfDNA yielded high diagnostic accuracy for epithelial ovarian cancer demonstrating the potential value of precision oncology based on whole-genome analysis.

EP013 / #1522

Topic: *AS01. Basic/Translational Science*

## **OU MC DECRESCENDO PHENOMENON AS A COMPONENT OF PHYSICAL ACTIVITY FOR CANCER PREVENTION**

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**Introduction:** The causal relationship between physical activity and anti-cancer effect are not proved by the current studies. Ou MC decrescendo phenomenon treatment (OuDPt) as a component of physical activity, shows an anti-cancer effect.

**Methods:** We review the anti-cancer effects of the Ou decrescendo phenomenon treatment (OuDPt) in the context of physical activity and human body anatomical axes (HBAAAs).

**Results:** OuDPt showed to induce apoptosis and regression of uterine endometrial cancer, suppression of ovarian and pancreatic cancer growth, regression of early suspicious pancreatic cancer, enhancement of chemotherapy effect of pancreatic cancer and stop of cancer-related bleeding.

**Conclusion/Implications:** However, such anti-cancer effect by OuDPt shows insufficient efficacy for advanced cancer in long term treatment. Nonetheless, the anti-cancer effect by OuDPt may be availed for cancer prevention. Further study is warranted. Reference: 1. Ou MC et al. Cancer Symposium: Hallmarks of Cancer. Seattle, WA, USA, 2019, P1.11. 2. Ou MC et al. 2nd JCA-AACR precision cancer medicine international conference. Kyoto, Japan, 2023, 5-4. 3. Ou MC et al. APJCP, 2023;24(8) (in press).

EP014 / #682

**Topic:** AS01. Basic/Translational Science

## **EFFECT OF DECITABINE COMBINED WITH BELOTECAN ON T-CELL MEDIATED IMMUNITY IN OVARIAN CANCER**

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**Introduction:** We evaluated the effect of decitabine on T-cell mediated immunity in ovarian cancer cell lines when combined with topoisomerase I inhibitors

**Methods:** We selected five human (ES2, OV90, SKOV3, TOV21G, TOV112D) and one mouse ovarian cancer lines (ID8). After we selected belotecan after comparison of the cytotoxic effect with topotecan, we determined the concentration of decitabine not showing the additive cytotoxic effect when combined with belotecan. We administered decitabine of 0.25 mg/kg six times every two days, followed by belotecan of 0.17 mg/kg five times daily eight weeks after we inoculated ID8 cells in the subcutaneous layer of C57BL/6, and then evaluated T-cell immunity in the spleen and tumor cells with expressions of PD-1 and CTLA4.

**Results:** The cytotoxic effect of belotecan was superior to that of topotecan in the six cell lines, and mRNA expressions of PD-L1, TNF, IL6 and TFG $\beta$  were increased in ES2, SKOV3, TOV21G and TOV112D cell lines. Moreover, the low concentration of decitabine did not show the additive cytotoxic effect when combined with belotecan, whereas decitabine increased apoptosis by belotecan synergically in the five human ovarian cancer cell lines. Even though PD-1 and CTLA4 were not increased in the allograft C57BL/6 mouse by ID8, CD3+CD8+T cells were increased after administration of belotecan and decitabine in the spleen and tumor cells.

**Conclusion/Implications:** Even though decitabine dose not increase expressions of PD-1 and CTLA4 as targets of immune checkpoint inhibitors, it may increase CD3+CD8+T cells in the spleen and ovarian cancer cells when combined with belotecan.

EP015 / #747

Topic: *AS01. Basic/Translational Science*

## **PROGNOSTIC IMPACT OF CD73 EXPRESSION IN EPITHELIAL OVARIAN CANCER**

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**Introduction:** CD73 (ecto-5'-nucleotidase) is a membrane-bound enzyme crucial in adenosine generation. The adenosine pathway plays a critical role in immunosuppressive tumor-microenvironment (TME). The purpose of the study was to evaluate CD73 expression in TME, and its association with clinicopathological features to better understand the role of CD73-adenosine pathway in epithelial ovarian cancer (EOC).

**Methods:** A total of 48 patients (treatment-naïve, n=35; recurrent, n=13) with epithelial ovarian cancer were enrolled in the current study. For each patient, a retrospective review of medical records was conducted. Immunohistochemical staining for CD73 was performed using paraffin embedded tissue block. CD73 expression level were graded on a scale of 0 to 3.

**Results:** Median age was 59 years (range 38-84 years), and the majority of the patients presented with high-grade serous carcinoma (HGSC, 85.4%) and stage III-IV disease (89.6%) at diagnosis. Among the treatment-naïve patients, 17.1% of patients (n=6) showed low CD73 expression (grade 1), whereas 60.0 % of patients (n=21) showed high CD73 expression (grade 2/3). All of the BRCA1/2-mutated tumors were high CD73 (n=7), whereas 20% of BRCA1/2-non-mutated tumors (n=5) were low CD73 expression. The CD73 high group showed better PFS compared to the CD73 low group (median PFS 20.1 versus 11.9 months, P=0.043). Among the recurrent patients, 84.6% of patients (n=11) showed high CD73 expression (All HGSC [n=10] were high; all clear cell carcinoma [n=2] were low).

**Conclusion/Implications:** Our study suggests that higher CD73 expression is associated with favorable survival outcomes in EOC. Further studies are needed to explore the role of CD73 in EOC.

EP016 / #819

Topic: *AS01. Basic/Translational Science*

## ORGANOIDS AS PRE-CLINICAL MODELS TO ASSESS THE EFFICACY OF HEATED INTRAPERITONEAL CHEMOTHERAPY IN MUCINOUS OVARIAN CANCER

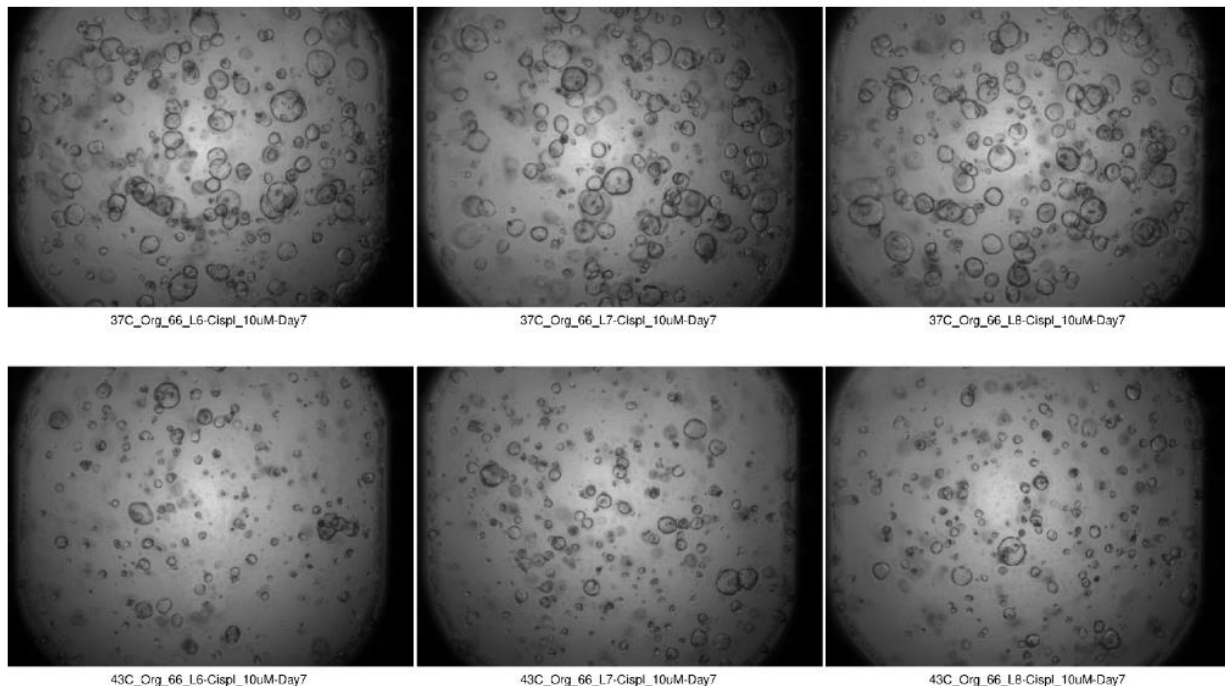
Niveditha Rajadevan<sup>1,2</sup>, Suad Abdirahman<sup>1</sup>, Olivia Craig<sup>1</sup>, Xiang Li<sup>1</sup>, Sumitra Ananda<sup>3</sup>, Orla McNally<sup>2,4,5</sup>, Kylie Gorringe<sup>1</sup>

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**Introduction:** Mucinous ovarian cancer (MOC) is a rare subtype of epithelial ovarian cancer (EOC) comprising <5% of cases. Despite its rarity MOC contributes significantly to the poor outcomes seen with EOC due to its inherent resistance to platinum-based chemotherapy regimens. Heated intraperitoneal chemotherapy (HIPEC), where a single dose of heated chemotherapy is given at surgery, has gained traction in recent years following benefits seen in high grade serous ovarian carcinoma and colorectal carcinoma. Data on the use of HIPEC in MOC remains limited.

**Methods:** Following the development of successful MOC organoid models, we undertook drug screening with eight chemotherapy agents often used in HIPEC. To simulate HIPEC conditions, we incubated our organoid models at 43C for 120 minutes following addition of the chemotherapy agent. Drug response was evaluated using CellTiter-Glo and Brightfield imaging.

### Results:



In the HIPEC model, platinum-based chemotherapy appears to have a cytostatic effect on MOC organoids in comparison to normothermic conditions. Variable responses were seen to gemcitabine,

mitomycin C and 5FU with the addition of heat having no therapeutic effect. Strongest response was seen to irinotecan with the addition of heat again having no additional effect.

**Conclusion/Implications:** Utilising organoids to assess HIPEC chemotherapy regimens in MOC provides a unique opportunity to assess drug response. HIPEC appears to improve response to platinum-based chemotherapy in MOC organoids whilst having little additional benefit with other agents. Going forward we aim to assess further combination chemotherapy regimens and to correlate results with genetic and gene expression characteristics to further understand treatment response.



## INSIGHTS FROM OVARIAN CANCER PATIENTS' RAPID AUTOPSY SHED LIGHT ON MECHANISMS OF CD4<sup>+</sup> T CELL-MEDIATED PRE-METASTATIC NICHE FORMATION THROUGH THE STAT3 AXIS

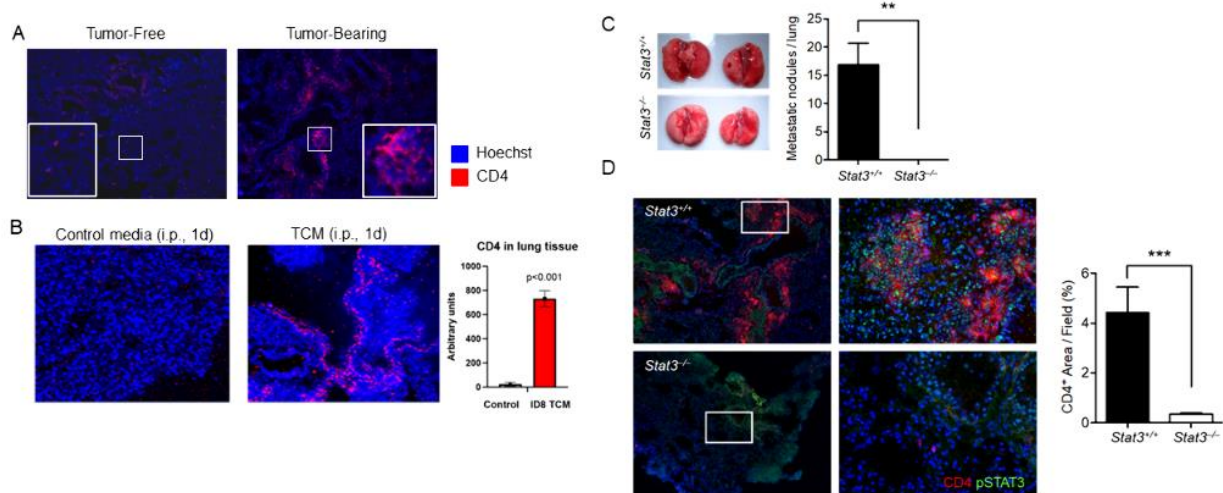
Antons Martincuks<sup>1</sup>, Rosemary Senguttuvan<sup>2</sup>, Maciej Kujawski<sup>1</sup>, Saul Priceman<sup>1</sup>, Eliza Barragan<sup>3</sup>, Kena Ihle<sup>3</sup>, Ernest Han<sup>2</sup>, Jeff Lin<sup>2</sup>, Lorna Rodriguez-Rodriguez<sup>2</sup>, Hua Yu<sup>1</sup>, Mihae Song<sup>2</sup>

<sup>1</sup>City of Hope, Immuno-oncology, Duarte, United States of America, <sup>2</sup>City of Hope, Gynecologic Oncology, Duarte, United States of America, <sup>3</sup>City of Hope, Precision Medicine, Duarte, United States of America

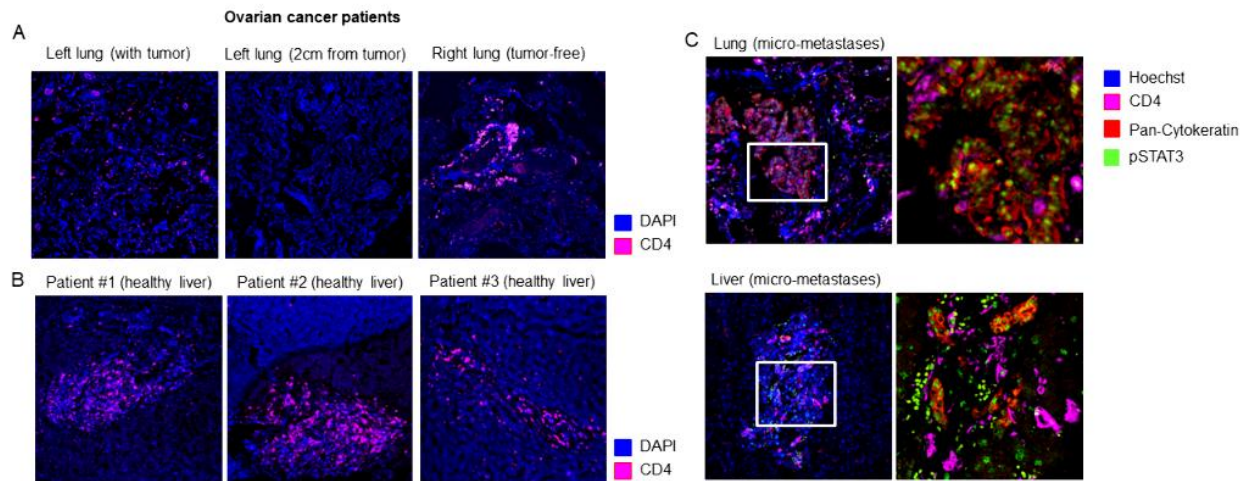
**Introduction:** Whether adaptive immune cells are required for the formation of pre-metastatic niches critical for tumor metastasis remains unknown. Prior research indicates that Signal transducer and activator of transcription 3 (STAT3) contributes to the accumulation and function of innate immune cells in these niches. This study investigates whether CD4<sup>+</sup> T cells can directly condition future metastatic sites and if STAT3 is necessary for CD4<sup>+</sup> T cell-mediated niche formation.

**Methods:** We evaluated CD4<sup>+</sup> T cell infiltration in non-metastatic lung regions of mice and examined the role of STAT3 signaling using CD4Cre-Stat3<sup>Fllox</sup> transgenic mice lacking functional Stat3 in T cells. Clinical correlations in ovarian cancer patients' disease-free lung and liver tissue sites from rapid autopsy tissue collection were also analyzed.

### Results:



**Figure 1. CD4<sup>+</sup> T cells accumulate to form pre-metastatic niches in the lung and Stat3 ablation in T cells reduces pre-metastatic niche formation and tumor metastasis.** **A.** In contrast to tumor-free mice (top left panel), non-metastatic regions in the lungs of C57BL/6 mice bearing MB49 bladder carcinomas are highly infiltrated by CD4<sup>+</sup> T cells (top right panel). Frozen lung tissues analyzed by immunofluorescence, CD4: red; Hoechst 33342: blue. **B.** TCM derived from ID8 ovarian tumor cell lines induce CD4<sup>+</sup> T cell infiltration in the lung as early as 24hr post i.v. injection, as compared to control media, shown by immunofluorescence staining and quantification of CD4<sup>+</sup> T cells. Data are shown as averages  $\pm$  SEM. **C.** Metastatic nodules were not detectable (ND) in MB49 tumor-bearing CD4-Stat3<sup>-/-</sup> mice in comparison to Stat3<sup>+/+</sup> mice with similar primary tumor size. Representative images of lung-associated tumor nodules and quantification per lung, n = 8 - 9 mice per group. Data are shown as averages  $\pm$  SEM. **D.** Non-metastatic regions of lungs of CD4-Stat3<sup>-/-</sup> mice bearing MB49 tumors are significantly less infiltrated by CD4<sup>+</sup> T cells in contrast to CD4-Stat3<sup>+/+</sup> mice. The majority of CD4<sup>+</sup> T cells in Stat3<sup>+/+</sup> mice showed Stat3 activation. Representative staining of CD4<sup>+</sup> T cells (red) and p-Stat3 (green) in the lung and CD4 quantification, right panel; n = 10 analyzed tissue regions per group. Data are shown as averages  $\pm$  SEM.



**Figure 2. CD4<sup>+</sup> T cells accumulate in tumor-free lung and liver tissues of ovarian cancer patients. p-STAT3 positive CD4<sup>+</sup> T cells accumulate around p-STAT3-expressing micro-metastases** **A.** In contrast to tumor and tumor proximal regions, distal non-metastatic regions in the lungs of ovarian cancer patients are highly infiltrated by CD4<sup>+</sup> T cells. **B.** Non-metastatic regions of ovarian cancer livers are highly infiltrated by CD4<sup>+</sup> T cells as well. FFPE lung and liver tissues from Rapid Autopsy program were analyzed by immunofluorescence, CD4: magenta; Hoechst 33342: blue. **C.** Representative images of lung- and liver-associated cytokeatin-stained micro-metastases with high nuclear p-STAT3 levels and surrounding p-STAT3-positive CD4<sup>+</sup> T cells in lung and liver tissues of ovarian cancer patients that passed from the disease. CD4: magenta; Hoechst 33342: blue; pan-Cytokeratin: red; p-STAT3: green.

Our findings reveal that CD4<sup>+</sup> T cells accumulate in distant tumor-free sites, forming pre-metastatic niches and subsequently promoting tumor metastasis in mice. Moreover, STAT3 activation is necessary for CD4<sup>+</sup> T cell-mediated pre-metastatic niche formation. Depleting CD4<sup>+</sup> T cells and STAT3 activation prior to primary tumor establishment significantly reduced tumor growth and almost completely blocked spontaneous lung metastasis, as evidenced in CD4-Stat3<sup>-/-</sup> mice. Importantly, analysis of presumed disease-free lung and liver tissue sites of ovarian cancer patients showed CD4<sup>+</sup> T cell accumulation with activated STAT3 in non-tumor regions and surrounding micro-metastases.

**Conclusion/Implications:** Blocking the pre-metastatic niche has the potential to prevent tumor cell seeding at distant sites, and our studies now show that targeting STAT3 in CD4<sup>+</sup> T cells may be an effective strategy to prevent tumor metastasis.

EP019 / #184

Topic: *AS01. Basic/Translational Science*

## **VAGINAL MICROBIOME PORPHYROMONAS SOMERAE AFFECTS COMPLEMENT SYSTEM C3 TRANSLATION IN MENSTRUAL STEM CELLS**

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**Introduction:** Endometrial cancer is a growing health concern for women worldwide. Endometrial cancer is associated with several risk but less considering microbiota in cancer mechanism. Our published work indicates Porphyromonas somerae is associated with endometrial cancer and invade endometrial cancer cells. Our transcriptomic data indicates elevated C3 expression in benign host after exposing to P.somerae. Our hypothesis is that exposure of benign menstrual stem cells to P. somerae promotes a rise in complement system (C3) translation.

**Methods:** Menstrual stem cells and endometrial cancer cell line (KLE) were inoculated and incubated with P.somerae under hypoxic conditions (5% O<sub>2</sub>) for 4 h. Cell culture supernatant and host cells were collected at 0,4, 24,48,72 and 168 hours. Three replicates per experimental arm were used. Cell lysate and culture supernatant C3 concentrations were measured in duplicate through Enzyme-linked Immunosorbent Assays via manufacture protocols. T-test was used for statistics and P<0.05 was recognized as statistical significance.

**Results:** Cell culture supernatant and host cell's C3 protein level was higher in supernatant than host cells for both cell lines.(Figure 1,2) C3 level was higher in MSC exposed to P.somerae than unexposed MSC. KLE C3 protein levels were higher than MSC, but exposure to P.somerae did not significantly alter C3 levels in the KLE cell line.

Figure 1

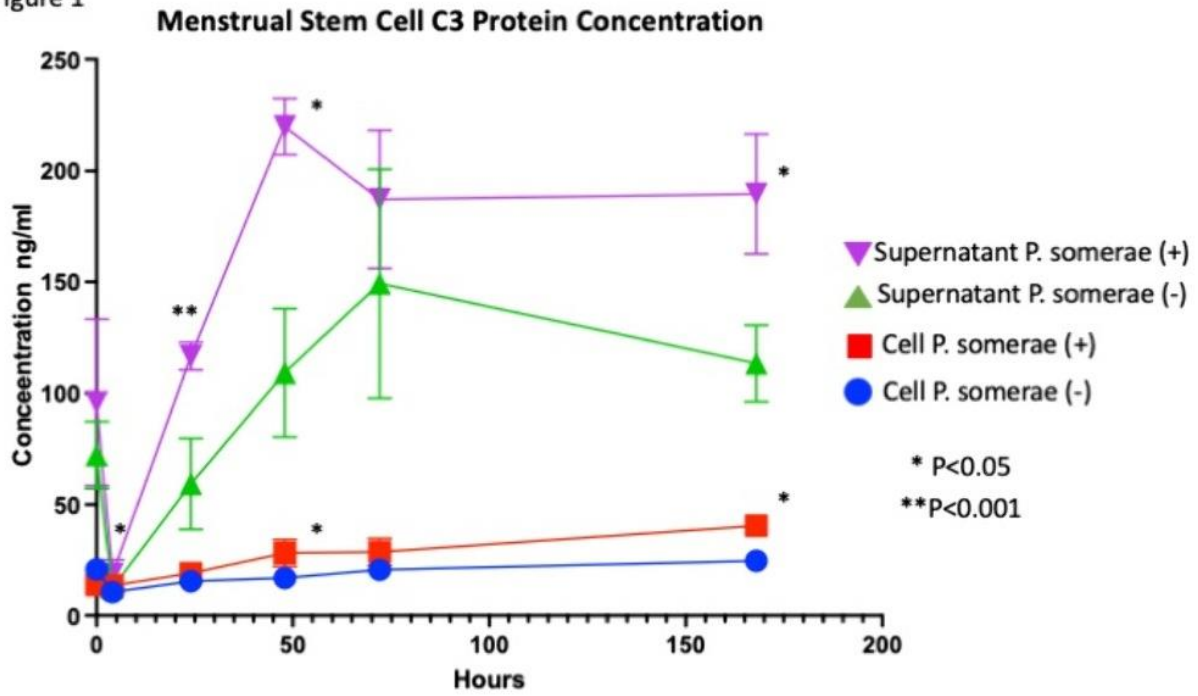
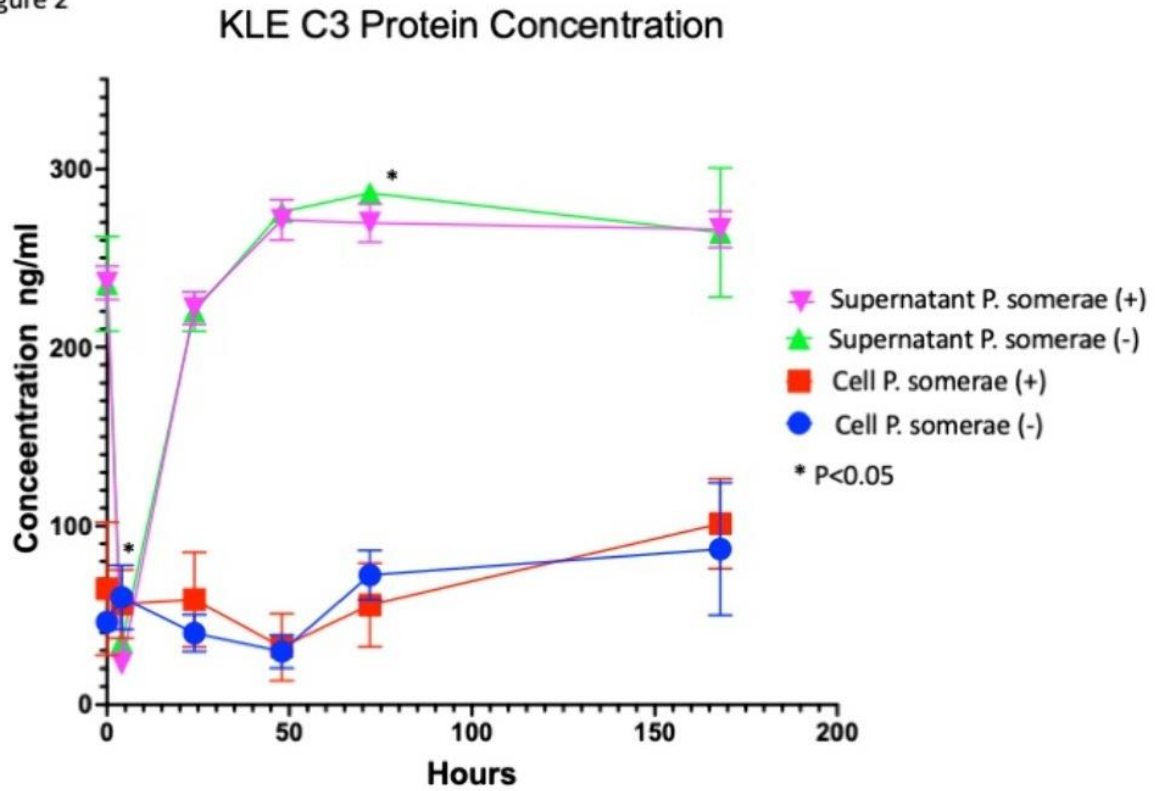


Figure 2



**Conclusion/Implications:** Our results indicate MSC exposing to *P. somerae* has higher C3 concentrations. We verified KLE cells have higher C3 concentration than MSC, as literature C3 elevated in endometrial cancer. Future work will explore the impact of other microbiome on C3 levels and downstream effects of endometrial cancer pathogenesis.

EP024 / #214

Topic: *AS02. Breast Cancer*

## **A RETROSPECTIVE ANALYSIS OF OUTCOMES OF MODIFIED HYPOFRACTIONATED BREAST RADIOTHERAPY FOR PATIENTS IN TYGERBERG HOSPITAL DURING THE 2020 CORONAVIRUS-19 PANDEMIC**

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**Introduction:** UK Standardization of Breast Radiotherapy (START) trials suggested that lower total doses of radiotherapy delivered in fewer fractions (40.05 Gy in 15 fractions) were as safe and effective as the historical 50 Gy in 25 fractions. The recent 26 Gy in 5 fractions regimen also compared favourably. The purpose was to retrospectively establish outcomes of a shorter hypofractionated schedule of adjuvant radiotherapy during COVID-19 pandemic for breast cancer patients at Tygerberg Hospital over one year (2020-2021), in terms of locoregional recurrence, distant metastasis, survival and side effects.

**Methods:** This study was conducted as a retrospective chart review of breast cancer patients treated with radiotherapy at Tygerberg Hospital over the period of April to September 2020. Patients with stages I-IIIc invasive breast carcinoma scheduled for adjuvant radiotherapy were eligible.

**Results:** Between 1st April and 30th September 2020, 161 patients were screened from Tygerberg Hospital breast multidisciplinary team meeting. 100 were eligible; 44 were assigned to 40.05 Gy in 15-day schedule and 56 to 26 Gy in 5-day fraction schedule. Over a median follow-up period of 15 months, it was reported that only four patients ( $p = 0.206$ , 95% CI;  $-0.316 - 0.71$ ) got locoregional recurrence and ten developed metastases ( $p = 0.691$  (95% CI,  $-0.235 - 0.157$ )). 16 patients passed away. No statistically significant difference was seen between schedules regarding side effect profile and survival analysis.

**Conclusion/Implications:** 26 Gy in five fractions over one week was relatively equivalent to 40.05 Gy in fifteen fractions over three weeks for local tumour control and was as safe in terms of normal tissue effects up to 1 year for patients prescribed adjuvant breast radiotherapy after primary surgery.

EP025 / #623

Topic: *AS02. Breast Cancer*

## **PROGNOSTIC VALUE OF TUMOR-INFILTRATING LYMPHOCYTE SCORE IN EARLY-STAGE TRIPLE-NEGATIVE BREAST CANCER: EXPERIENCE FROM A SINGLE CENTER IN VIETNAM**

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**Introduction:** To evaluate the prognostic value of tumor-infiltrating lymphocyte scores (TILs) and their correlation with clinicopathological features in patients with early-stage triple-negative breast cancer (TNBC) in Vietnam.

**Methods:** A retrospective study on 105 patients with early-stage TNBC who did not undergo neoadjuvant systemic therapy in Vietnam National Cancer hospital from January 2018 to May 2019. TILs assessment and the density of CD8+ TILs on IHC in intratumoural (iTILs) and stromal compartments (sTILs) were evaluated on surgical specimens. The relationship between clinicopathological features and immunoreactivity was evaluated with Pearson's Chi squared test or Fisher's exact test using median TIL value as the cut-off. Overall survival (OS) was analyzed using the Kaplan–Meier method, log-rank statistics and multivariable Cox regression.

**Results:**

**Table 1. Correlation between TILs, CD8+ iTILs, CD8+ sTILs and clinicopathological features (n = 105)**

Characteristic No. (%)	TILs (n=105)			CD8+ iTILs (n=105)			CD8+ sTILs (n=105)		
	Low	High	p value	Low	High	p value	Low	High	p value
Age, years, No. (%)									
≤ mean	9 (18.8)	5 (8.8)	0.13	9 (12.5)	5 (15.2)	0.46	10 (15.4)	4 (10)	0.32
> mean	39 (81.2)	52 (91.2)		63 (87.5)	28 (84.8)		55 (84.6)	36 (90)	
T stage, No. (%)									
1	19 (39.6)	31 (54.4)		35 (48.6)	15 (45.5)	0.77	25 (38.5)	25 (62.5)	
2	28 (58.3)	25 (43.9)	0.24	35 (48.6)	18 (54.5)		38 (58.5)	15 (37.5)	0.04*
3	1 (2.1)	1 (1.7)		2 (2.8)	0 (0)		2 (3.0)	0	
N status, No. (%)									
Negative	33 (68.8)	42 (73.7)	0.67	55 (76.4)	20 (60.6)	0.07	45 (69.2)	30 (75)	0.34
Positive	15 (31.2)	15 (26.3)		17 (23.6)	13 (39.4)		20 (30.8)	10 (25)	
Tumor grade, No. (%)									
1,2	24 (50)	20 (35.1)	0.12	33 (45.8)	11 (33.3)	0.16	31 (47.7)	13 (32.5)	0.09
3	24 (50)	37 (64.9)		39 (54.2)	22 (66.7)		34 (45.3)	27 (67.5)	
Local treatment, No. (%)									
BCS	1 (2.1)	2 (3.5)	0.56	3 (4.2)	0 (0)	0.32	1 (1.5)	2 (5.0)	0.32
Mastectomy	47 (97.9)	55 (96.5)		69 (95.8)	33 (100)		64 (98.5)	38 (95.0)	
Ki67, No. (%)									
<20	7 (14.9)	3 (5.6)	0.09	8 (11.2)	2 (6.1)		8 (12.5)	2 (5.0)	0.18
≥ 20	40 (85.1)	54 (94.7)		63 (88.7)	31 (93.9)		56 (88.5)	38 (95.0)	
Lymphovascular invasion									
No. (%)									
Absent	45 (93.8)	56 (98.2)	0.24	69 (95.8)	32 (97.0)	0.62	61 (93.8)	40 (100)	0.14
Present	3 (6.2)	1 (1.8)		3 (4.2)	1 (3.0)		4 (6.2)	0 (0)	
Her2 status, No. (%)									
Negative	40 (83.3)	55 (96.5)	0.02*	64 (88.9)	31 (93.9)	0.34	57 (87.7)	38 (95.0)	0.18
Her2-low	8 (16.7)	2 (3.5)		8 (11.1)	2 (6.1)		8 (12.3)	2 (5.0)	

(Pearson's Chi squared test or Fisher's exact test using median TIL value as the cut-off)



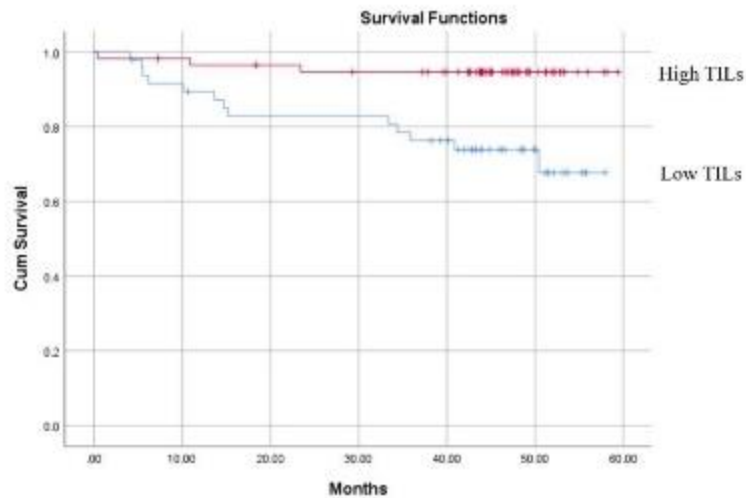


Figure 1. Kaplan-Meier curves for OS according to TILs categories defined by median TIL value as the cut-off

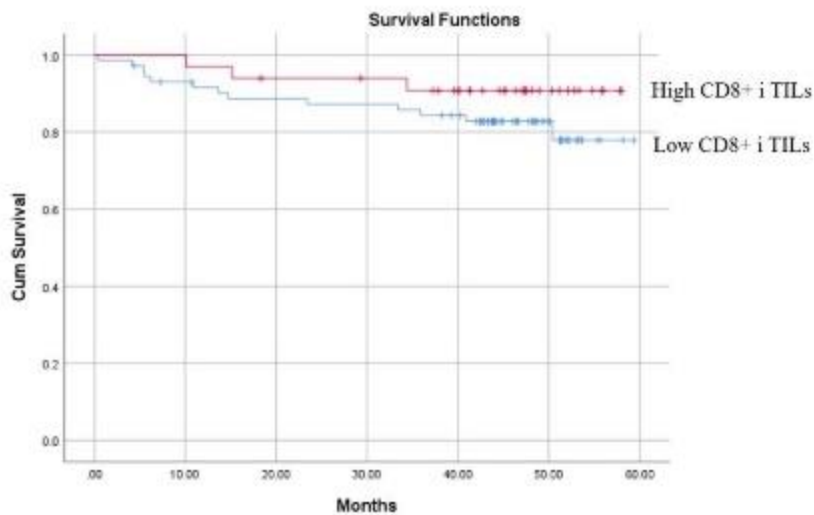


Figure 2. Kaplan-Meier curves for OS according to CD8+ iTILs categories defined by median iTILs value as the cut-off

The univariate analysis demonstrated that significant prognostic factors were T stage ( $p=0.000$ ), N status ( $p=0.000$ ), Her2 status (negative or Her2-low) ( $p=0.006$ ) and TILs ( $p=0.002$ ). The 5 year OS of patients with high TILs was significantly higher than those with low TILs (94.6% vs. 67.7%,  $P=0.002$ ). Cox regression multivariate analysis showed that independent predictors of OS were TILs ( $p=0.03$ ; HR=0.25; 95%CI 0.07-0.89) and CD8+ iTILs ( $p=0.04$ ; HR=0.20 95%CI 0.04-0.93). There was also a correlation

between TILs and Her2 status ( $P=0.02$ ) where low TILs were associated with Her2-low status, infiltration of CD8+ sTILs and T stage ( $p=0.04$ ).

**Conclusion/Implications:** High TILs and CD8+ iTILs were associated with better prognosis in early-stage TNBC patients. We recommend their inclusion in routine pathological reports. Further research is needed to explore the potential of TILs as predictive markers for immunotherapy in TNBC.

EP026 / #876

Topic: *AS02. Breast Cancer*

## **ADAPTATION OF SELF AND BODY IMAGE AFTER BREAST CANCER SURGERY IN YOUNG WOMEN : A QUALITATIVE STUDY**

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**Introduction:** From the diagnosis of breast cancer (BC), changes and adaptations are required in all the aspects of daily life in patients. The quality of life (QOL) during and after treatment of BC is an objective as important as the overall survival. Self image and body image are important characteristics of the QOL in BC patients, especially when breasts are symbols of femininity and maternity. They are often overlooked by healthcare professionals. We aim to study the adaptative changes in self and body image among young women after BC surgery.

**Methods:** A qualitative study was carried out until saturation occurrences among young BC patients. We included all sexually active women under 40 who had breast cancer surgery at our department during the last 2 years, from january to july 2022. In-depth semi-structured interviews with three axes: the diagnosis of BC, the fight against cancer and Self and body image after breast surgery were scheduled at participants concienience.

**Results:** Four themes were identified : the emotional crisis following breast surgery ; some participants had described the importance of spirituality and beliefs; others emphasized the need to have the support of their family and spouses in addition to caregivers and their informative and educational roles of source of information and education. Finally, bodily changes experienced by participants and their impact on their self-image with three sub-themes: sexual satisfaction, attribution and self-esteem.

**Conclusion/Implications:** Knowledge of the changes in women's self and body image after BC surgery is important to help improve their QOL.

EP027 / #915

Topic: *AS02. Breast Cancer*

## **IPSILATERAL SYNCHRONOUS MULTIPLE BREAST CANCER**

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**Introduction:** Breast cancer (BC) is the first cancer in women. The diagnosis, management and prognostic impact of ipsilateral synchronous multiple breast cancers (ISMBC) remain a dilemma in the scientific literature. We aim to study the specific clinical and pathological features of this entity.

**Methods:** A retrospective study was conducted at our institution over 11 years (2010-2020). We recruited all cases of ISMBC. We defined ISMBC as all cases of multifocal BC (multiple foci present in the same quadrant of the breast) and/or all cases of multicentric BC (multiple foci located in different quadrants) excluding bilateral synchronous BC.

**Results:** We recruited 159 cases of ISMBC representing 6.1% of all BC. The mean age was 51.6 years [26-85]. The sensitivity of breast MRI was superior to that of ultrasound-mammography in the detection of BC multiple locations. Invasive ductal carcinoma was the predominant histological type. The mean histological tumor size was 31mm ± 16.6mm. The most common SBR grade was grade II. There was a predominance of luminal subtype B. Mastectomy was performed in 81.8% of patients and 83% had axillary lymph node dissection. Locoregional recurrence was 5.96%. Distant metastases were found in 7.54%. The 5-year OS and DFS were 87.4% and 88.6%, respectively. In multivariate analysis, SBR grade was a significant prognostic factor for OS and DFS.

**Conclusion/Implications:** The current ISMBC clinical and pathological staging system is perfectible in order to customize the treatment options to the reality of the disease especially regarding breast surgery.

EP030 / #680

Topic: *AS02. Breast Cancer*

## **BREAST CANCER INCIDENCE FOLLOWING OVARIAN CANCER WITH BRCA MUTATION: SYSTEMATIC REVIEW AND META-ANALYSIS**

Migang Kim<sup>1</sup>, Seo Yeon Kim<sup>2</sup>, Young Tak Kim<sup>1</sup>, Chan Lee<sup>1</sup>, Sang Geun Jung<sup>1</sup>, Min Chul Choi<sup>1</sup>, Hyun Park<sup>1</sup>, Seung Hun Song<sup>1</sup>, Jung Hoon Lee<sup>1</sup>, Won Duk Joo<sup>1</sup>

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**Introduction:** Mutations in Breast Cancer Susceptibility Genes (BRCA) are associated with an increased risk of both breast and ovarian cancer. In previous studies, about 20% of ovarian cancer patients reported a BRCA gene mutation. However, there is currently no consensus on the incidence and risk management of breast cancer following ovarian cancer diagnosis in BRCA carriers. Therefore, we aimed to systematically review and perform a meta-analysis of the risk and management of breast cancer in ovarian cancer patients with BRCA mutation.

**Methods:** For published studies, we searched PubMed, EMBASE, and Cochrane Library databases for published studies to October 2022. The number of BRCA carriers with ovarian cancer, rate of BRCA-1 or BRCA-2 mutation, incidence of breast cancer, time interval between ovarian cancer diagnosis to breast cancer, and the breast cancer detection method were extracted.

**Results:** Eight studies met all inclusions and were included in the meta-analysis. Breast cancer incidence in BRCA-mutated ovarian cancer patients was 7.87% (160/2034). Breast cancer incidence with BRCA-1 or BRCA-2 mutation was 9.1% (90/991) and 8.65% (36/416), respectively. The primary breast cancer incidence following ovarian cancer was 7.52% (124/1648), and the recurrence rate was 10.31% (20/194) in patients with previous breast cancer history. The median time interval between ovarian and breast cancer diagnosis was 3.5-9 years. The most frequent screening method was mammography.

**Conclusion/Implications:** The risk of breast cancer after ovarian cancer was lower than the risk of breast cancer alone in BRCA carriers. Routine mammography could be helpful for the diagnosis of breast cancer in BRCA-mutated ovarian cancer patients.

EP031 / #1486

**Topic:** AS02. *Breast Cancer*

## **GENOMIC PROFILING AND SURVIVAL OUTCOMES IN YOUNG MOROCCAN WOMEN WITH BREAST CANCER**

Safaa Kriouile, Hind M'Rabti, Ibrahim Elghissassi, Saber Boutayeb, Hassan Errihani  
National Institute of Oncology Sidi Mohamed Ben Abdellah, Medical Oncology, Rabat, Morocco

**Introduction:** This study addresses the critical impact of genomic profiling on breast cancer severity and survival in young Moroccan women.

**Methods:** A 2021 study at Rabat's National Institute of Oncology characterized invasive breast carcinoma in Moroccan women under 40, assessing two-year survival rates.

**Results:** The study contained subgroups of "luminal" (53%), "triple-negative" (TN) (23%) and "HER2-positive" (HER2+) (24%) patients. In the "HER2+" group, 81% scored "+++" through immunohistochemistry, while 19% showed "++" plus positive in situ hybridization. Also, 29% were "non-luminal", the remaining 71% of this group being hormonereceptor positive. Patients' mean age was 35, with "Luminal", "TN", and "HER2+" subtypes ages averaging 35, 33, & 34 respectively. Family history of cancer was prevalent in 18% of cases. The "Ki67" biomarker was elevated in 24% of the total cases (cut-off = 20%). At diagnosis, 19% were already metastatic, including 26% "Luminal", 15% "TN", and 9% "HER2+". In nonmetastatic cases, 26% had "T3 or T4" tumors and 56% were N-positive. Two-year overall survival (OS) was 59%, with 81% ("HER2+"), 56% ("Luminal"), and 40% ("TN"). This was statistically significant according to the log-rank test ( $p=0,0433$ ). Non-metastatic and metastatic cases showed 60% and 53% OS respectively. Progression-free survival at two years was 56%, with 76% ("HER2+"), 56% ("Luminal"), and 35% ("TN"). This was also statistically significant ( $p=0,0321$ ). OS was 44% for initial "T3 or T4", and 59% for N-positive patients.

**Conclusion/Implications:** This research emphasizes genomic profiling's role in enhancing personalized therapies and survival rates for young Moroccan breast cancer patients, particularly "HER2+".

EP032 / #1390

Topic: *AS02. Breast Cancer*

## **TUMOR-INFILTRATING LYMPHOCYTES: A PROGNOSTIC BIOMARKER IN NEOADJUVANT-TREATED HR POSITIVE/HER2 NEGATIVE BREAST CANCER**

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**Introduction:** Anticancer immune responses contribute to the success of chemotherapy. We aimed to elucidate the value of tumor-infiltrating lymphocytes (TILs) as a prognostic marker for distant relapse-free survival (DRFS) in patients with HR positive/HER2 negative breast cancer in the taxane/anthracycline-based neoadjuvant chemotherapy (NACT).

**Methods:** The cell type enrichment analysis for 64 immune and stromal cell types was performed with the web-based tool xCell based on RNA expression profiles of breast cancer from National Center for Biotechnology Information (NCBI) Gene Expression Omnibus (GEO). Kaplan-Meier analysis and LASSO-Cox PH regression model were used to assess the correlation of TILs and stromal cells infiltration with breast cancer distant relapse-free survival.

**Results:** In this study, 123 HR positive/HER2 negative breast cancer patients derived from the dataset GSE25055 were eventually enrolled in the present study. LASSO-Cox PH regression analysis demonstrated that pre-NACT plasma cells and Th2 cells infiltration exhibited an independent prognostic value for DRFS (HR=11.26, P=0.036; HR= 15.13, P<0.001; respectively). A risk scoring model based on the TILs was conducted to divide patients into different risk groups with significantly different DRFS rates (P=0.0028). Compared with low risk group, high-risk group was comparatively associated with worse DRFS rates (3-year DRFS rate, 72.3% vs. 93.2%, P=0.0028).

**Conclusion/Implications:** These results suggested that pre-NACT immunological plasma cells and Th2 cells infiltration is an independent predictive factor of DRFS for the patients with HR positive/HER2 negative breast cancer, which provides valuable and profound perspective of immune microenvironment and NACT prognosis.

EP033 / #639

Topic: *AS02. Breast Cancer*

## **BREAST DESMOID FIBROMATOSIS: ABOUT FIVE CASES AND REVIEW OF THE LITERATURE**

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**Introduction:** Desmoid fibromatosis is a rare, locally aggressive fibroblastic tumor. It can occur in various parts of the body, including the breast. In this study, we describe five cases of breast desmoid fibromatosis and review the relevant literature.

**Methods:** We conducted a retrospective analysis of five cases of breast desmoid fibromatosis at our institution between 2010 and 2022. We collected data on patient demographics, clinical presentation, imaging findings, surgical management, and outcomes.

**Results:** The study cohort included five women with a mean age of 34 years. All patients presented with a breast mass, which was initially misdiagnosed as a benign lesion in three cases. Magnetic resonance imaging (MRI) was the most useful imaging modality for diagnosis. All patients underwent surgical excision, with clear margins achieved in four cases. The mean follow-up period was 36 months, during which there were no local recurrences or distant metastases.

**Conclusion/Implications:** Breast desmoid fibromatosis is a rare entity that can mimic benign breast lesions on imaging. MRI is the most reliable imaging modality for diagnosis. Surgical excision with clear margins is the treatment of choice, and long-term follow-up is necessary to monitor for local recurrences or distant metastases. Our study adds to the limited body of literature on breast desmoid fibromatosis and highlights the importance of considering this diagnosis in the differential diagnosis of breast masses.



EP034 / #855

Topic: *AS02. Breast Cancer*

## **ASSOCIATION BETWEEN CANCER STIGMA AND DEPRESSION AMONG TUNISIAN PATIENTS FOLLOWING BREAST AND GYNECOLOGIC CANCERS**

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**Introduction:** Cancer stigma can have a significant impact on cancer patient's mental health with risk of depression. Our study aimed to explore cancer stigma aspects among patients following breast and gynecologic cancers and to evaluate the association between cancer stigma and depression.

**Methods:** Patients (n=61) treated for breast or gynecologic cancers were asked to answer a questionnaire adapted from the "Cancer stigma scale". The "Hospital Anxiety and Depression Scale" was used to measure depression.

**Results:** Median age was 47.1 years. About 75% of patients had at least a high school educational level (EL). Around 78% of patients were urban and 32% reported low socioeconomic status. Breast cancer was the most common primary cancer (80%), followed by endometrial (10%) and ovarian (7%) cancers. About 29% of patients reported significant depressive symptoms. Fifty six percent of patients experienced at least one form of cancer stigma. Thirty nine percent of patients believed in the impossible total recovery after cancer experience and 46 % held stereotypical views of themselves. About 33% reported social discrimination due to their cancers. Patients who experienced cancer stigma were 4.4 times more likely to have depression than patients with positive attitudes (p=0.001). Depression were more registred in young (under 55 years) (OR=2.24, p=0.029) and rural patients (OR=4.94, p=0.001) with lower EL (OR=5.6, p=0.001) and socioeconomic status (OR=3.5, p=0.001).

**Conclusion/Implications:** Cancer patients who experienced cancer stigma are at increased risk of developing depression. Thus, it's important for healthcare providers to be aware of this relationship and provide an appropriate support.

EP035 / #866

Topic: *AS02. Breast Cancer*

## ADJUVANT TREATMENT FOR LUMINAL BREAST CANCER OF INTERMEDIATE PROGNOSIS

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**Introduction:** Our retrospective study analyzed the adjuvant treatment decision for localized intermediate risk breast cancer as well as the parameters leading to protocol de-escalation and its impact on outcome.

**Methods:** A retrospective study gathering 127 patients with localized (pT1-3pN1 or pT2-3pN0) luminal breast cancers; We analyzed the protocol decision and the parameters leading to de-escalation as well as the therapeutic results.

**Results:** Median age was 52 years and 47% were pre-menopausal. One third of the tumors were pN0, mean tumor size (pT) was 28 mm, and grade III in 27.4% of cases. Most of the tumors (66%) were of Luminal B and the mean ki67 was 26%. Adjuvant protocol was chemotherapy for 119 patients, sequential in 80.3% of cases and Docetaxel-Cyclophosphamide (TC) in 13.4% of cases. Twenty-four cases were reviewed by the medical committee, and a therapeutic de-escalation was decided for 12 patients among them, based on TC (6 patients) and hormone therapy for 6 patients. The patients characteristics are resumed in table 1. Concerning toxicity, we observed a higher rate of neutropenia (47.5% vs 11.8% p=0.04) and febrile neutropenia G3-4 (20.6% vs. 0% p=0.02) with sequential chemotherapy. With a median follow-up of 51 months, overall survival was 94% at 5 years. The choice of adjuvant treatment didn't significantly influence overall survival.

	Sequentiel chemotherapy	TC chemotherapy
Age	50 years	60 years
Premenopausal Status	51%	30%
3 positive axillary nodes	17.6%	11.8%
Grade III	32%	5.9%
mean ki67	25%	10%

**Conclusion/Implications:** De-escalation of adjuvant therapy in patients with intermediate risk localized breast cancer didn't impair overall survival.

EP036 / #930

Topic: *AS02. Breast Cancer*

## **BELIEFS ABOUT BREAST AND GYNECOLOGIC CANCER CAUSATION : A TRIP INTO THE TUNISIAN CONTEXT**

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**Introduction:** Patients try to find an explanation to their disease in order to accept it. We aimed in our study to evaluate patients' beliefs about breast and gynecologic cancer causation and to assess its impacts on their mental healths .

**Methods:** Patients (n=61) treated for breast or gynecologic cancers were asked to answer a questionnaire evaluating beliefs about cancer causation. The "Hospital Anxiety and Depression Scale" was used to measure depression.

**Results:** Median age was 47.1 years [30-76]. Breast cancer was the most common primary cancer (80%), followed by endometrial (10%) and ovarian (7%) cancers. Two patients thought that the cancer was a contagious disease. Eighty seven percent of patients believed that god was testing their faith. However, two patients thought that the cancer was a divine punishment. Twenty nine percent of patients believed that they were the cause of their disease : stressful lifestyle in 16%, diet in 6%, lack of breastfeeding in 6% and tobacco in 1%. Beliefs of being the cause of the disease were associated with more depression symptoms (OR :3.7 [1.16-12.3]). Being practising muslim or not did not impact depression symptoms.

**Conclusion/Implications:** Some beliefs could affect patients' mental health. Care providers should discuss with their patients, detect wrong belief and try to correct it.

EP040 / #789

Topic: *AS03. Cervical Cancer*

## **PREDICTIVE FACTORS OF COMPLETE HISTOLOGICAL RESPONSE IN PATIENTS MANAGED BY CHEMORADIOTHERAPY FOLLOWED BY RADICAL SURGERY FOR LOCALLY ADVANCED CERVICAL CANCER**

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**Introduction:** Exclusive chemoradiation represents the standard of treatment for locally advanced cervical cancer (LACC). Chemoradiation (CT/RT) followed by radical surgery (RS) may play a role for patients with a suboptimal response to CT/RT. This study aimed to identify predictive factors for complete histological response after CT/RT followed by RS.

**Methods:** We conducted a retrospective study at the Salah Azaiez Institute of Oncology from January 1, 2010, to December 31, 2020, including 118 patients with locally advanced cervical cancer treated with curative intentions. They underwent CT/RT followed by RS. Histologic assessment was made on the surgical specimen.

**Results:** Among 118 operated after CT/RT; 52 had Radical hysterectomy with pelvic lymph node dissection(RHPND), 1 patient underwent RHPND with paraaortic lymph node dissection, 4 patients underwent Radical hysterectomy, and 2 patients had hysterectomy with pelvic lymph node dissection. 59 patients (50.4.%) presented complete responses on histological examination of the specimen. In our study, lymphovascular space involvement p (0.016)) was identified as a predictive factor for complete histologic response after CT/RT. In contrast, tumor size p (0.794), parametrial involvement p (0.382), histologic grade p (0.959), FIGO stage p (0.520), type of CT p (0.150) and dose of RT p (0.990) were not factors affecting complete histologic response to CT/RT.

**Conclusion/Implications:** Lymphovascular space involvement was identified as a prognostic factor for complete response on the surgical specimen in locally advanced cervical cancer managed by CT/RT followed by surgery.

EP041 / #685

Topic: *AS03. Cervical Cancer*

## **PREDICTIVE FACTORS OF PELVIC LYMPH NODES METASTASES IN LOCALLY ADVANCED CERVICAL CANCER**

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**Introduction:** Pelvic lymph-nodal involvement is a major prognostic factor in cervical cancer. Lymph-node status is classically assessed by lymph-node dissection. This surgical approach is mainly of prognostic interest. In this study, we aimed to identify the risk factors associated with pelvic lymph node metastases (PLNM) in locally advanced cervical cancer.

**Methods:** We conducted a retrospective study at the Salah Azaiez Institute of Oncology from January 1, 2010, to December 31, 2020, including 118 patients with locally advanced cervical cancer who underwent radical hysterectomy, pelvic exenteration, and systematic pelvic lymphadenectomy. All removed pelvic nodes were pathologically examined. Risk factors for PLNM were evaluated.

**Results:** Among 118 operated patients, 115 underwent surgery after radiochemotherapy (97.5%) while 3 patients (2.5%) underwent exclusive surgery. Pelvic lymph node metastases were found in 12 cases (10.4%). In our study, lymphovascular space involvement p (0.00) and suspicious pelvic lymph nodes on MRI p (0.045) were identified as risk factors of PLNM. In contrast, tumor size p (0.897), parametrial involvement p (0.073), and histologic grade p (0.835) were not related to the risk of lymph node invasion.

**Conclusion/Implications:** Lymphovascular space involvement and suspicious pelvic lymph nodes on MRI were independent prognostic factors for pelvic lymph node involvement in locally advanced cervical cancer patients.

EP042 / #209

Topic: *AS03. Cervical Cancer*

## **CLPTM1L EXPRESSION PREDICTS RECURRENCE OF INTERMEDIATE- AND HIGH-RISK STAGE IB-IIB CERVICAL CANCER UNDERGOING RADICAL HYSTERECTOMY FOLLOWED BY TP AS ADJUVANT CHEMOTHERAPY.**

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**Introduction:** We examined the correlation between CLPTM1L (Cleft lip and palate transmembrane protein 1-like) expression and recurrence of intermediate- and high-risk stage IB-IIB (FIGO2008) cervical cancer undergoing radical hysterectomy followed by TP (paclitaxel plus cisplatin).

**Methods:** We reviewed 91 cases of intermediate- and high-risk stage IB-IIB cervical cancer patients who underwent TP after radical hysterectomy from 2014 to 2019. Cases were divided into two groups, one group in which the patients didn't recur within 2 years after initialization of treatment (group A; n=76), and the other group in which the patients recurred within 2 years (group B; n=15). CLPTM1L expression was examined immunohistochemically. Multiple logistic regression analysis was performed to identify predictor of recurrence. The effect of the siRNA-mediated knockdown of CLPTM1L on the sensitivity of cervical cancer cells to cisplatin was investigated. This study was approved by the institutional review board.

**Results:** The expression of CLPTM1L was significantly higher in group B than in group A ( $p < 0.001$ ). Cases were divided into two groups; low CLPTM1L expression group (weighted score  $\leq 4$ , n=59), and high CLPTM1L expression group (weighted score  $\geq 6$ , n=32). High CLPTM1L expression group was more likely to recur after adjuvant TP than low expression group ( $p < 0.01$ ). And multivariate analysis revealed that CLPTM1L expression was an independent predictor of recurrence ( $P = 0.003$ ). Furthermore, knockdown of CLPTM1L expression significantly increased cancer cell sensitivity to cisplatin in vitro.

**Conclusion/Implications:** High CLPTM1L expression might be associated with recurrence of intermediate- and high-risk stage IB-IIB cervical cancer undergoing radical hysterectomy followed by TP.

EP045 / #1275

Topic: *AS03. Cervical Cancer*

## IMPORTANCE OF EARLY INITIATION OF TREATMENT TO AVOID UPSTAGING IN LOCALLY ADVANCED CERVICAL CANCER

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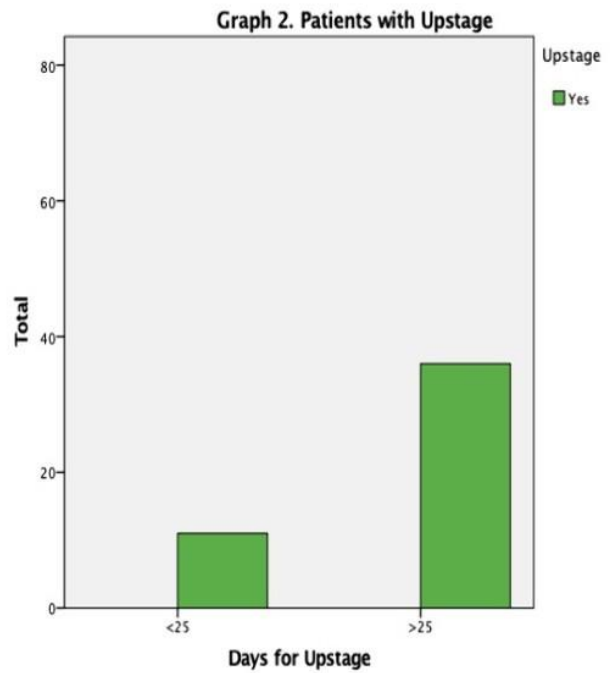
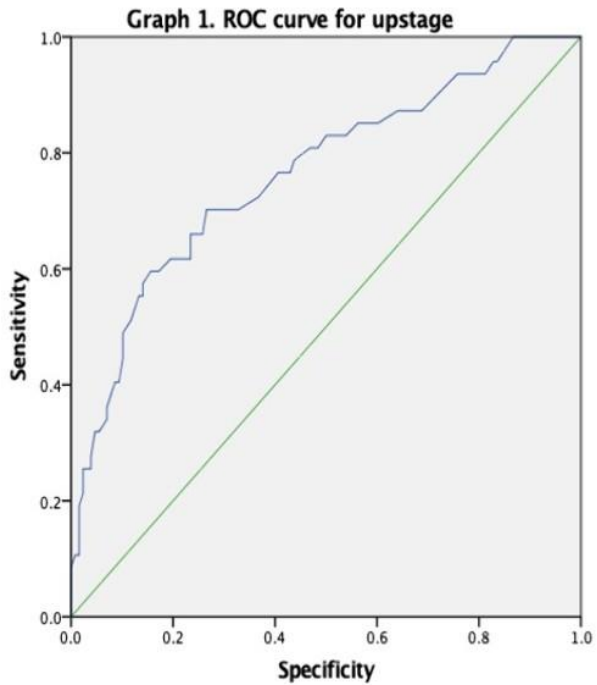
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**Introduction:** Locally advanced cervical cancer (LACC) is a public health problem. Objectives: Determine importance of initiation of treatment of LACC in limited-resource settings. Evaluate the concordance between CT and PET/CT for FIGO 2018 staging.

**Methods:** Retrospective analysis of 175 patients with LACC was performed in a national reference center. FIGO 2018 staging was established by clinical evaluation and CT scan. PET/CT was requested when CT was highly suspicious of more advanced disease or when initiation of treatment was delayed. Descriptive and inferential statistics, Cohen kappa index and ROC curve were performed.

**Results:** Population analyzed was Mexican with median age at diagnosis 47 years. Most common FIGO stage by clinic evaluation was IIB (43%), by CT was IIIC1 (46%), and IIIC1 (43%) by PET/CT. Concordance of CT with PET/CT within 25 days of initial study was substantial ( $k=0.719$ ,  $p = 0.0001$ ) and after 25 days with moderate agreement ( $k = 0.468$ ,  $p = 0.0001$ ). Time to upstage was 25 days by ROC (AUC 0.763,  $p = 0.0001$ ). FIGO IV was 9.2% with CT against 20.6% with PET/CT. Table 1:FIGO 2018 staging.

		CT STAGE		PET STAGE			
		Frequency	Percentage	Frequency	Percentage		
FIGO 2018	IA2	1	.6	FIGO 2018	IB3	6	3.4
	IB3	5	2.9		IIA1	1	.6
	IIA1	1	.6		IIA2	4	2.3
	IIA2	7	4.0		IIB	17	9.7
	IIB	24	13.7		IIIA	4	2.3
	IIIA	1	.6		IIIB	6	3.4
	IIIB	13	7.4		IIIC1	76	43.4
	IIIC1	80	45.7		IIIC2	25	14.3
	IIIC2	27	15.4		IVA	15	8.6
	IVA	8	4.6		IVB	21	12.0
	IVB	8	4.6		Total	175	100.0
	Total	175	100.0				



**Conclusion/Implications:** Image studies make FIGO 2018 in cervical cancer more accurate. PET/CT is not accessible and is expensive for the general population in limited resource settings. According to our results, we can rely on the initial staging with CT within 25 days from diagnosis to initiation of treatment, after this period, upstage must be considered and a more accurate image study such as PET/CT might be recommended to reconsider the therapeutic plan and prognosis.



EP046 / #1276

Topic: *AS03. Cervical Cancer*

## **PATHOLOGIC RESPONSE TO HYPOFRACTIONATED CHEMORADIATION IN LOCALLY ADVANCED CERVICAL CANCER**

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**Introduction:** Standard treatment for locally advanced cervical cancer (LACC) is chemoradiotherapy, in limited resource settings hypofractionated treatment might be an option. Objectives: Determine pathologic response to hypofractionated external concurrent chemoradiation followed by surgery in comparison to standard treatment in LACC.

**Methods:** Fifty-nine patients with LACC, as part of a clinical trial, were evaluated after being allocated to standard treatment (45gy in 25 fractions) (29 patients) or Hypofraction treatment (37.5Gy in 15 fractions) (30 patients) followed by a type C1 radical hysterectomy and pelvic node dissection. Pathologic response to treatment was evaluated. Descriptive and inferential statistics, chi-square and multivariable analysis with logistic regression were performed.

**Results:** In the standard external chemoradiotherapy group, complete pathology response was 22% (13 patients), partial response 5.1 % (3 patients), microscopic disease 22 % (13 patients). The hypofraction group, complete pathology response was 20.3% (12 patients), partial response 3.4 % (2 patients), microscopic disease 27.1 % (16 patients) ( $p=0.834$ ). Compared by histology, squamous cell carcinoma had complete response in 38% (19 patients), partial response 2% (1 patient), while adenocarcinoma with complete pathology response in 4% (2 patients), partial response 2% (1 patient) ( $p=0.296$ ), independently to treatment arm. In the multivariable analysis, treatment was not an independent factor for pathologic response OR 0.954 ( $p=0.938$ ).

**Conclusion/Implications:** Hypofractionation seems to be as effective, in relation to pathologic response, as standard treatment and could be implemented where economic limitations are important or patients have to travel long distances. More prospective studies are needed.

EP047 / #376

Topic: *AS03. Cervical Cancer*

## **MULTI-OMICS CHARACTERIZATION OF CELLULAR STATE DIVERSITY AND BIDIRECTIONAL TUMOR-STROMA/IMMUNE INTERACTIONS IN CERVICAL SQUAMOUS CELL CARCINOMA**

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**Introduction:** Cervical cancer ranks as the fourth leading cause of cancer-related deaths among women, with low response rates to immune-checkpoint blockade (ICB).

**Methods:** Here we conducted a multidimensional analysis encompassing single-cell RNA-seq (scRNA-seq), spatial transcriptomics, and spatial proteomics, combined with genetic and pharmacological perturbations to systematically develop a high-resolution and spatially-resolved map of intra-tumoral expression heterogeneity in cervical squamous cell carcinoma (CSCC).

**Results:** Three context-specific tumor states (Epithelial-cytokeratin (Epi-Krt), epithelial-immune (Epi-imm) and epithelial senescence (Epi-Sen)) that recapitulate squamous differentiation substantially alter the tumor immune microenvironment (TIME). Bidirectional interactions between Epi-Krt malignant epithelial cells and MMP11<sup>+</sup> CAF form an immune exclusionary microenvironment through TGF $\beta$  pathway signaling mediated by FABP5. Epi-Imm malignant epithelial cells and NK/T cells interact bidirectionally through interferon signaling. Notably, preliminary analysis of the NACI clinical trial (NCT04516616) demonstrated neoadjuvant chemotherapy (NACT) induce a state transition to Epi-Imm with the extent of this transition being associated with pathological complete remission (pCR) to subsequent ICB treatment.

**Conclusion/Implications:** These findings provide a comprehensive and nuanced understanding of cellular state diversity and have significant implications for developing novel therapeutic strategies in CSCC and potentially other squamous cancers.

EP048 / #911

Topic: *AS03. Cervical Cancer*

## **CD112 PROMOTES THE PROGRESSION OF CERVICAL CANCER THROUGH SLC7A11/GPX-4 PATHWAYS**

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**Introduction:** Expression of the immunoglobulin superfamily member CD112 was increased in multiple malignancies. Importantly, its expression was observed in both PD-L1 negative and positive tumors. However, the role of CD112 in tumorigenesis and tumor development in cervical cancer has not been elucidated.

**Methods:** The expression of CD112 in cervical cancer tissues was detected using immunohistochemistry (IHC) and gene expression profiling. CCK-8, Edu tests, wound healing and migration assays were used to assess the biological effects of CD112 overexpression and knockdown. Furthermore, proteomic analysis revealed the potential mechanism of CD112 in cervical cancer.

**Results:** CD112 is expressed at high levels in cervical cancer tissues and is negatively correlated with the level of infiltrating CD8+ T cells. In addition, *In vitro* and *in vivo*, reducing the expression of CD112 inhibited cell proliferation and migration. Antibody array-based profiling of protein analysis revealed that CD112 knockdown can inhibit the SLC7A11/GPX-4 pathway and activate ferroptosis; the opposite effects were observed upon CD155 overexpression. We further confirmed the mechanism between CD112 and SLC7A11/GPX-4 pathway through rescue experiments. CD112 over-expression reversed the ferroptosis effects and inhibition of the SLC7A11/GPX-4 pathway induced by GPX-4 inhibitor (rs13).

**Conclusion/Implications:** Our research demonstrated that CD112 can activate the SLC7A11/GPX-4 pathway and inhibit ferroptosis. Thus, CD112 is a potential screening and therapeutic biomarker for cervical cancer.

EP050 / #898

Topic: *AS03. Cervical Cancer*

## **DOES HIGHER NODAL DOSE IMPACT NODAL CONTROL IN CERVICAL CANCER: AN ANALYSIS OF PATIENTS TREATED WITH NODAL SIMULTANEOUS INTEGRATED BOOST FOR CERVICAL CANCER.**

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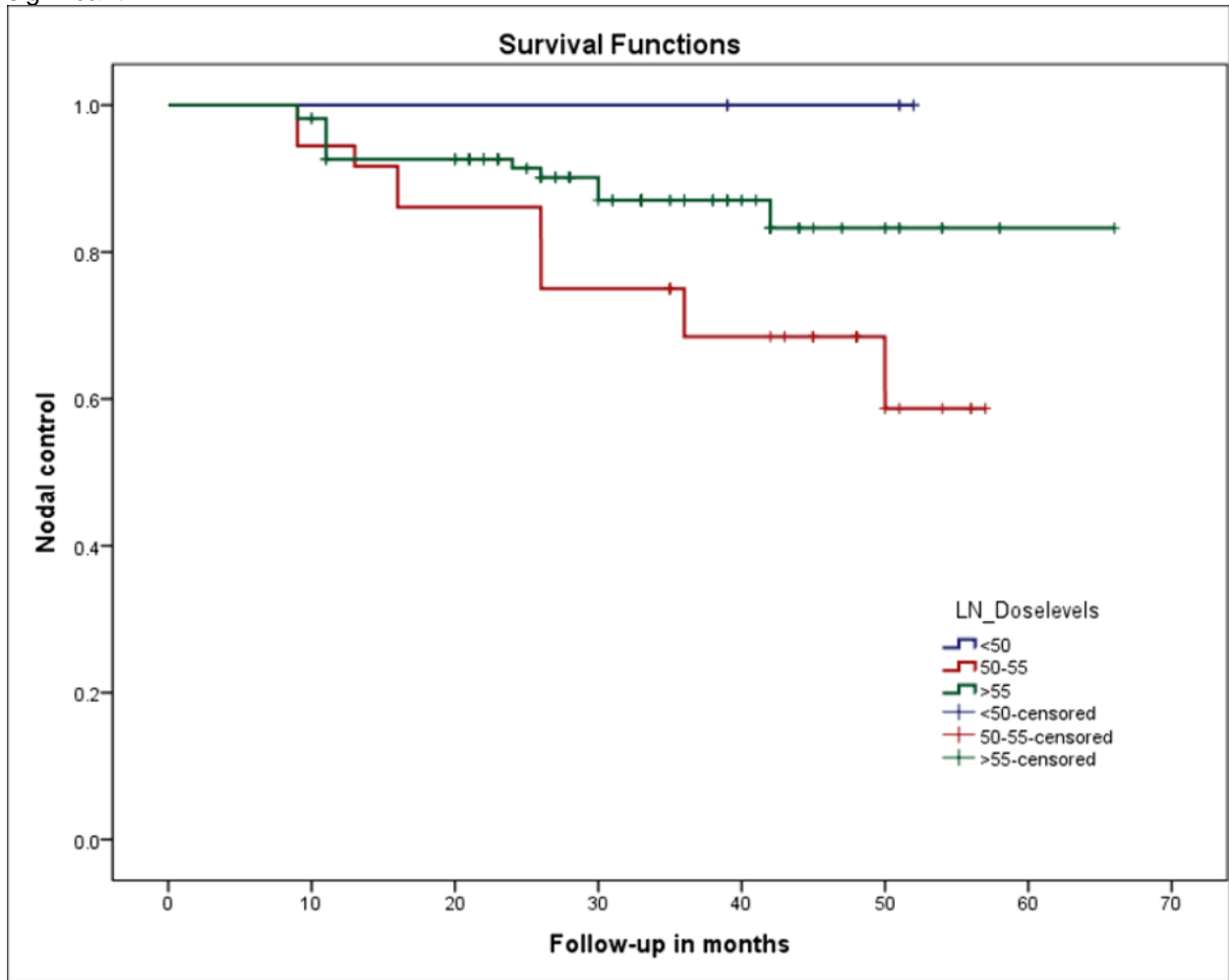
<sup>1</sup>Advanced Centre for Treatment Research and Education in Cancer, Tata Memorial Centre, Radiation Oncology, Navi Mumbai, India, <sup>2</sup>Tata Memorial Hospital, Radiation Oncology, Mumbai, India

**Introduction:** The dose prescription for nodes is heterogenous and choice of optimal dose is unclear. This study was designed to report nodal response in patients receiving simultaneous integrated boost (SIB) for stage IIIC cervical cancer.

**Methods:** Patients who received chemoradiation and nodal dose escalation through SIB followed by brachytherapy were included. As per RECIST 1.1, baseline lymph node was categorized as pathological if short axis diameter (SAD) was  $\geq 10$  mm and measurable if SAD  $\geq 15$  mm or as a non-target if SAD  $\geq 10$  mm, but  $< 15$  mm. On follow-up, if SAD was  $< 10$  mm, the node was considered non-pathologic. Nodal Control and Disease-Free Survival (DFS) was determined. Log-rank test was used for evaluation of impact of nodal RECIST baseline nodal category, nodal volume and dose on nodal control and disease-free survival (DFS).

**Results:** Sixty-six patients with 153 nodes were included. Patient characteristics and treatment details are depicted in table 1. Median SIB dose was 55Gy (45- 56.5Gy). Number of nodes receiving dose  $< 50$ Gy were 7 (4.6%), 51-55Gy: 36 (23.5%) and  $> 55$ Gy:110 (71.9%). At response assessment 92.2% nodes (n=141) had complete response, 6.5% (n=10) had partial response and 1.3% (n=2) had progressive disease. The median follow up was 33 months (9-66 months). Patients receiving  $> 55$ Gy had better 5-year nodal control (84.6% vs 58.7% p=0.02, figure 1). Reduced 5-yr DFS (76% vs 44%, p=0.15) was also observed based on RECIST definition though it was not statistically

significant.



**Conclusion/Implications:** Dose escalation to nodes leads to significantly better nodal control. Further dose escalation may need investigation.

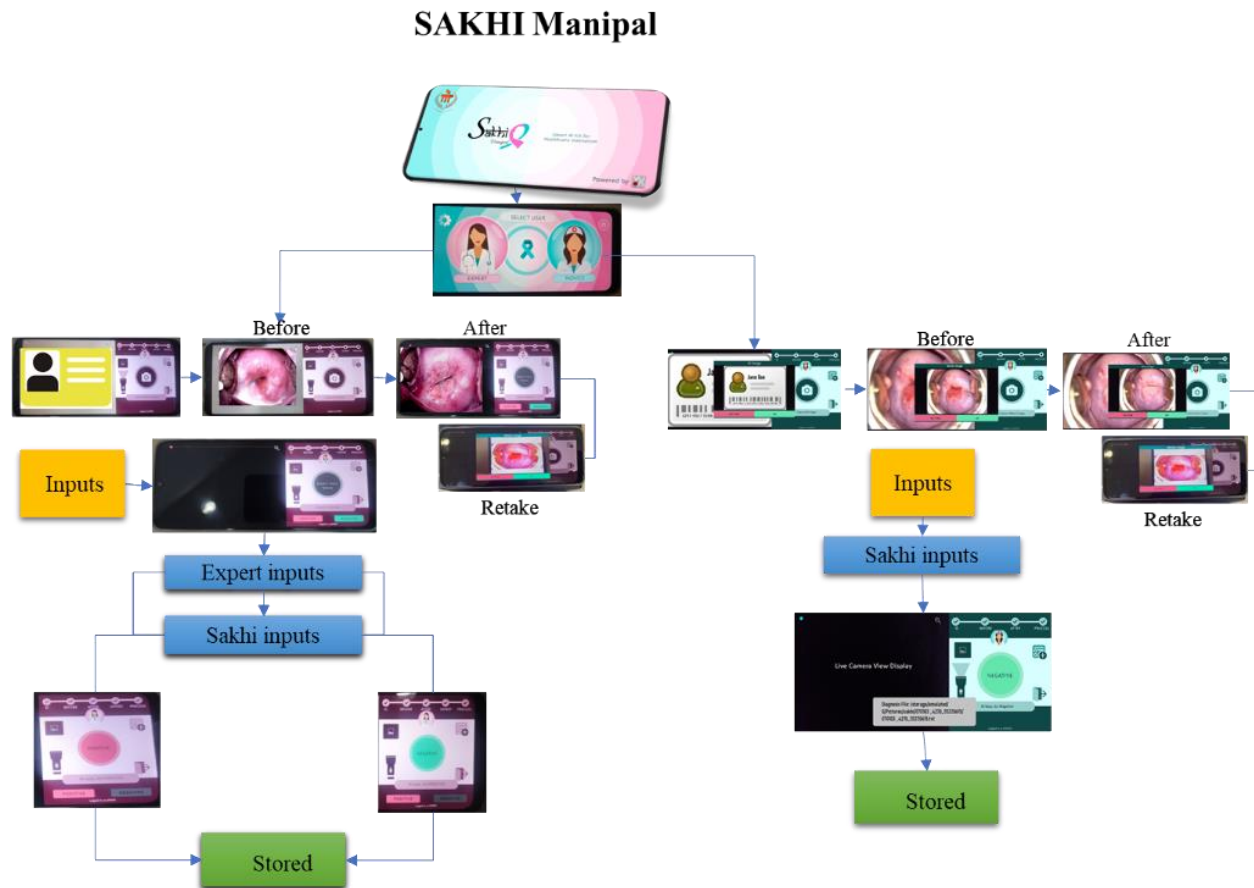
## SMART ARTIFICIAL INTELLIGENCE KIT FOR HEALTHCARE INNOVATION (SAKHI MANIPAL): ACCEPTABILITY AND USABILITY ANALYSIS

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**Introduction:** In resource-limited settings, a lack of trained professionals and testing facilities has halted the implementation of pre-existing screening programmes. SAKHI Manipal is a resource-effective device requiring minimally trained healthcare professionals. The further implementation of SAKHI requires the perspective of its users. Therefore, the study aims to evaluate the acceptability and usability of SAKHI among healthcare providers.

### Methods:





SAKHI Manipal is a secure, portable, standalone mobile-based device equipped with an algorithm based on deep learning to instantaneously analyse and interpret uterine cervix images for the presence of Cervical Intraepithelial Lesions after the application of acetic acid. The research group at Manipal Academy of Higher Education, Manipal, India, developed an Innovative device for resource-constrained settings. The field testing of the device is in progress in the PRESCRIP-TEC (Prevention and Screening Innovation Project Towards Elimination of Cervical Cancer) project as a triage test for HPV Positive women. The 40 healthcare professionals of tertiary hospitals were trained to use the device during the Visual Inspection with acetic acid (VIA) test, and their perspective as users of the SAKHI Manipal device was assessed using System Usability Scale (SUS).

**Results:** Of all device usability survey responses, 32.5% responded device was “Excellent” (SUS score >80.3), 42.5% felt it was “Good” (SUS 68-80.3) and would recommend it further, and 25% stated that the device was “Ok” (SUS 68). Overall, 91.9% of the user surveyed agreed that the device is helpful during the VIA procedure.

**Conclusion/Implications:** The study shows that the device was acceptable and usable by healthcare providers.

EP052 / #1533

Topic: *AS03. Cervical Cancer*

## **CERVICAL CANCER AND HPV VACCINATION: LESSONS LEARNT FROM A FOCUS GROUP DISCUSSION**

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**Introduction:** Cervical cancer is the most common gynecological malignancy in Nigeria. HPV vaccines are about to be rolled out for young girls aged 9-14 years in Nigeria. The key issue remains, how to deal with vaccine hesitancy and ensure adequate uptake. This study aims to assess the awareness level of Cervical cancer and HPV vaccination, as well as attitude towards Vaccine uptake.

**Methods:** A Focus Group Discussion was held with a representative sample of 100 Nigerian women aged 35-55 years, using a guide to assess their knowledge of Cervical cancer, HPV Vaccination, and willingness to consent to the uptake of vaccine by their young girls aged 9-14 years. Transcribed data was analyzed by Coding the text.

**Results:** Only 10 women had prior knowledge of Cervical Cancer, none of the women had ever undergone a screening test and none of them had prior knowledge of the HPV Vaccine. After the Focus group discussion, more than half of the women displayed proper understanding of the disease and the need for Vaccination, 5 women from the Sample population displayed willingness to Champion the cause.

**Conclusion/Implications:** From this study we can deduce that proper knowledge is key, an aware population can make health-conscious choices when given the right tools. It is however important to consider proper messaging and the education level of the Communities. Furthermore, pre-bunking myths help to reduce the incidence of Vaccine hesitancy.



EP053 / #200

Topic: *AS03. Cervical Cancer*

## **EARLY OUTCOMES AND TOXICITIES OF CHEMORADIATION THERAPY WITH VOLUMETRIC-MODULATED ARC THERAPY FOLLOWED BY 3D IMAGE-GUIDED BRACHYTHERAPY IN CERVICAL CANCER: VIETNAM NATIONAL CANCER HOSPITAL EXPERIENCE**

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**Introduction:** To evaluate early outcomes and toxicities among locally advanced cervical cancer patients treated with concurrent chemoradiation using volumetric-modulated arc therapy (VMAT) followed by 3D image-guided brachytherapy (3D-IGBT) To evaluate early outcomes and toxicities among locally advanced cervical cancer patients treated with concurrent chemoradiation using volumetric-modulated arc therapy (VMAT) followed by 3D image-guided brachytherapy (3D-IGBT).

**Methods:** A prospective, interventional study on 72 patients with 2018 International Federation of Gynecology and Obstetrics stage IB3-IIIC2 disease treated with concurrent chemoradiation using VMAT followed by 3D-IGBT according to EMBRACE-II protocol. Treatment response, locoregional control, systemic control, and toxicities were primary endpoints in all patients.

**Results:** Median of body volume received 43 Gy was 1589.1 cm<sup>3</sup> (range 1214.8-2574.8). Median of high-risk clinical target (CTV-HR) volume was 18.8 cm<sup>3</sup> (range 8.6 – 61.2), median dose to 90% of CTV-HR was 90.6 Gy (range 86.8-99.6). The mean of D2cc to bladder, rectum, and sigmoid were 75.8, 55.2, and 62.1 Gy, respectively. The complete response rate was 95.8%, and locoregional control and systemic control were 95.8% and 83.3%, respectively, at a median follow-up of 15 months (range 9-19). Grade ≥ 3 acute toxicities were observed in less than 10% of cases, except for neutropenia (accounted for 31.9%). Extended-field radiation increased the rate of nausea, fatigue, and thrombocytopenia. No grade ≥ 3 proctitis or cystitis was observed, but vaginal stenosis grade 3 was noted in 8.3% of patients.

**Conclusion/Implications:** Concurrent chemoradiation therapy using VMAT and 3D-IGBT resulted in a high response rate and locoregional control with manageable toxicities in patients with locally advanced cervical cancer.

EP059 / #412

Topic: *AS03. Cervical Cancer*

## **NRG ONCOLOGY CONSENSUS GUIDELINES FOR DELINEATION OF CLINICAL TARGET VOLUMES FOR INTENSITY-MODULATED RADIOTHERAPY FOR INTACT CERVICAL CANCER**

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**Introduction:** Accurate target delineation is essential when using IMRT for intact cervical cancer. In 2011, RTOG published a consensus guideline using MR images. The goal of the current project is to expand on the previous atlas by including CT-based contours without and with PET±MRI registrations, to add common and complex scenarios, and to ask about simulation and treatment planning techniques.

**Methods:** 28 experts contoured 3 cases, first on a non-contrast CT simulation scan, then with registered diagnostic images. The cases included (1) FIGO IIIC1 with a bulky tumor and a vaginal metastasis, (2) FIGO IIB with calcified uterine fibromas, and (3) FIGO IIIC2 with large lymph nodes. The contours were analyzed for consistency using an expectation-maximization algorithm for simultaneous truth and performance level estimation (STAPLE) with kappa statistics as a measure of agreement.

**Results:** Analysis of the contours showed considerable agreement between experts in each of the cases with kappa statistics of 0.67-0.72. For each case, use of diagnostic PET±MRI was associated with an increase in volume. The largest increase was in the CTV primary for Case 2 (20% increase in average volume, 64% increase in STAPLE estimate volume), which may be due to variance in registration priorities. For the third case, 92.9% of participants increased their CTVs based on the addition of the PET scan.

**Conclusion/Implications:** Here we show the value as well as the challenges of using co-registered diagnostic imaging. The main areas of variance remain determining the superior extent of CTV coverage, coverage of the mesorectum, simulation and planning protocols.

EP060 / #474

Topic: *AS03. Cervical Cancer*

## **POTENTIAL ANTI-HUMAN PAPILLOMAVIRUS THERAPEUTICS: MECHANISM AND ACTION OF COMBINATION THERAPY IN CERVICAL CANCER CELLS**

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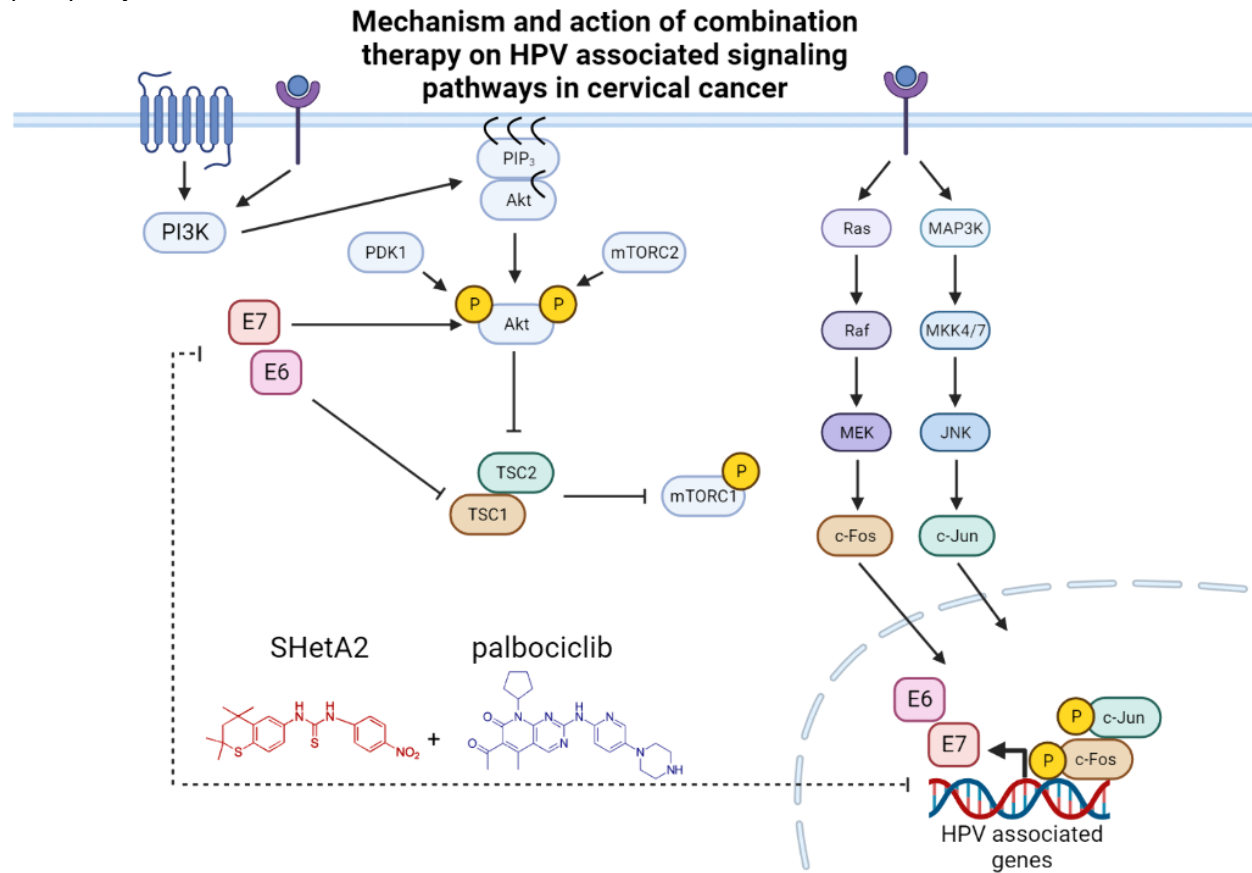
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**Introduction:** Cervical cancer is the most common malignancy among women caused due to persistent high-risk human papillomavirus (HR-HPV) infection. The carcinogenesis of HPV is attributed to its early viral onco-proteins E6/E7, which increase cellular proliferation and survival mechanisms by interacting with cellular survival pathways including AKT/mTOR kinases, and activator protein-1 (AP-1; Jun/Fos) and E2F transcription factors. Cervical cancer cells become addicted to E6/E7 expression and undergo apoptosis when E6/E7 are disrupted. Previously, we demonstrated functional synergism between the HSP70-inhibitor SHetA2 and the CDK4/6-inhibitor palbociclib in cervical cancer. However, this synergism's mechanism was not explored with respect to targeting HPV E6/E7 onco-proteins. Hence, the objective of this study was to evaluate the impact of SHetA2 and palbociclib alone, and in combination, on HPV E6/E7 and associated survival pathways.

**Methods:** Individual or combination treatments of SHetA2 and palbociclib in HR-HPV positive cervical cancer cell lines were evaluated for specific mRNA and protein modulation by western blotting, quantitative polymerase chain reaction (qPCR) and immunofluorescence.

**Results:** We demonstrated for the first time that combination treatment of SHetA2 and palbociclib causes significant down-regulation of E6/E7 viral proteins and up-regulation of c-Jun and c-Fos host proteins (Figure 1). The effects of the combination treatment were greater than either single treatment. Consistent with the down-regulation of E6/E7, SHetA2 impacted AKT/mTOR

phosphorylation.



**Conclusion/Implications:** This study identifies potential anti-HPV preventative and therapeutic strategies using combination therapy of SHetA2 and palbociclib. Future research will study SHetA2 and/or palbociclib mechanisms in pre-clinical models and conduct clinical trials of HR-HPV-driven pre-cancerous lesions.

EP064 / #761

Topic: *AS03. Cervical Cancer*

## **A POTENTIAL THERAPEUTIC METHOD FOR UTERINE CERVICAL CANCER BY ARSENIC TRIOXIDE VIA INDUCING CARBONYL REDUCTASE 1 EXPRESSION**

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**Introduction:** Carbonyl Reductase1 (CBR1) has been reported to be involved in cancer progression. Recently, we reported that CBR1 overexpression repressed malignant behavior of uterine cervical cancer (CC) via epithelial mesenchymal transition. Arsenic trioxide (ATO) is known as an effective chemotherapeutic agent for acute promyelocytic leukemia with a low toxicity. ATO is reported to upregulate CBR1 expression by activating the transcription factor activator protein-1. In this study, we investigated the effect of ATO on the malignant behavior of CC via CBR1 expression.

**Methods:** We investigated the effect of ATO on malignant behavior in CC cell lines (SiHa and SKGII) in vitro by Cell proliferation Assay, Wound healing Assay, and Invasion Assay, and using the mouse models transplanted with CC cells subcutaneously.

**Results:** ATO increased CBR1 expression dose-dependently in the cultured cells. ATO significantly inhibited the activities of cell proliferation, invasion, and migration.  $1.0 \times 10^6$  cells of SiHa or SKGII were subcutaneously injected into the back of immunodeficient mice (Bulb-C), and 5.0 mg/kg ATO were given intravenously every two days after the tumor development on the host mice. Seven weeks after injection of ATO, the tumor growth was significantly inhibited in SiHa and SKGII ( $P < 0.05$ ). The CBR1 expression level in the tumor treated with ATO was significantly higher than that of control.

**Conclusion/Implications:** ATO inhibited the cancer growth and malignant behavior with increased CBR1 expression in CC cells. This result suggests that ATO can be the novel agent targeting CBR1 in CC treatment.

EP066 / #602

Topic: *AS03. Cervical Cancer*

## **LESS THAN WHOLE UTERUS IRRADIATION FOR LOCALLY ADVANCED CERVICAL CANCER MAINTAINS LOCOREGIONAL CONTROL AND DECREASES RADIATION DOSE TO BOWEL**

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**Introduction:** Current consensus guidelines for definitive cervical cancer intensity modulated radiation therapy (IMRT) recommend inclusion of the entire uterus within the clinical target volume, however this is controversial. We aimed to evaluate outcomes of patients with cervical cancer who were treated with less than whole uterus irradiation.

**Methods:** We identified 112 patients with FIGO Stage IB-IVA cervical cancer treated definitively with concurrent chemoradiation, including IMRT and brachytherapy, from 2010 to 2022 at a single institution where the practice was to include the gross cervix tumor plus additional margin. Local, regional, and distant recurrences were analyzed using competing risk methods, and a Wilcoxon rank sum test was performed to assess differences in bowel dose based on the proportion of the uterus included in the planning target volume (PTV).

**Results:** With a median follow up time of 30.1 months, the 2-year cumulative incidence of local recurrence was 5%. Compared with patients who had  $\geq 90\%$  of the uterus included in the PTV (n=35), patients who had  $< 90\%$  (n=77) of the uterus included in the PTV had significantly lower bowel D200cc ( $p < 0.01$ ). The cumulative incidence of locoregional failure was not significantly different between the two groups. Only one patient experienced an isolated local failure and their PTV included  $\geq 90\%$  of the uterus.

**Conclusion/Implications:** Including less than the whole uterus for definitive cervix cancer IMRT does not compromise locoregional control. Less than whole uterus irradiation should be considered for cervix cancer patients to decrease bowel dose and treatment-related toxicity.

EP067 / #487

Topic: *AS03. Cervical Cancer*

## **EFFICACY OF INTERSTITIAL BRACHYTHERAPY FOR THE PATIENT WITH LOCALLY ADVANCED CERVICAL CANCER**

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**Introduction:** Locally advanced cervical cancers with bulky and asymmetrical tumors treated with intracavitary brachytherapy are more likely to relapse in a few years due to insufficient dose prescription to the entire tumor, resulting in poor prognosis. The purpose of this study is to evaluate the efficacy and safety of 3-dimensional (3D) image-guided multi-catheter interstitial brachytherapy, which could increase flexibility in dose distribution for patients with bulky ( $\geq 4$  cm) and high-risk, stage IIB–IVA advanced cervical cancer.

**Methods:** Twenty one patients who underwent concurrent chemoradiotherapy with multi-catheter interstitial brachytherapy between September 2014 and February 2023 were enrolled. The prescribed dose of external beam radiotherapy was 45–50.4 Gy, and the total dose of interstitial brachytherapy was 25–30 Gy per 5 fractions. The endpoints were 5-year local and pelvic control rates, 5-year disease-free and overall survival rates, and the adverse events rate.

**Results:** The median follow-up period was 53.5 months (4.1–102.0 months). Eighteen patients received concurrent cisplatin therapy (40 mg/m<sup>2</sup>, q1week). Five (23.9%), ten (47.6%), and six (28.6%) patients had T2b, T3b, and T4 cervical cancer, respectively. Pelvic and para-aortic lymph node metastases were detected in 13 (61.9%) and 3 (14.3%) patients, respectively. The median volume before interstitial brachytherapy was 42.6 cm<sup>3</sup>. The 5-year local control, pelvic control, progression free survival, and overall survival rates were 95.0%, 87.7%, 78.3%, and 83.2%, respectively. Four (19.0%) patients experienced grade 3 adverse events, and none experienced grade 4–5 adverse events.

**Conclusion/Implications:** 3D image-guided multi-catheter interstitial brachytherapy could be a promising therapeutic strategy for locally advanced cervical cancer.

EP068 / #553

Topic: *AS03. Cervical Cancer*

## **HPV-INDEPENDENT ADENOCARCINOMA HAS POORER PROGNOSIS THAN SQUAMOUS CELL CARCINOMA AND HPV-ASSOCIATED ADENOCARCINOMA, AND HPV-ASSOCIATED ADENOCARCINOMA HAS SIMILAR PROGNOSIS WITH SQUAMOUS CELL CARCINOMA**

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**Introduction:** In general, adenocarcinoma of the cervix is known to have a worse prognosis than squamous cell carcinoma (SCC). The World Health Organization classification divides endocervical adenocarcinoma (ADC) into human papillomavirus (HPV)-associated (HPVA) and HPV-independent (HPVI) types in 2020. This study aimed to compare the prognosis of HPVA ADC, HPVI ADC, and SCC.

**Methods:** We retrospectively reviewed the medical records of 185 patients with SCC, 61 patients with HPVA ADC, and 13 patients with HPVI ADC, who underwent radical hysterectomy and pelvic lymphadenectomy for cervical cancer 2018 FIGO stage IA2 – III from January 2005 to December 2016. Prognostic factors, recurrence rate, disease-free survival (DFS) and 5-year survival outcomes were compared between HPVA ADC, HPVI ADC and SCC.

**Results:** The incidence of deep stromal invasion ( $\geq$ middle or deep 1/3) was higher in HPVI ADC patients than in HPVA ADC and SCC patients (92.3%, 65.6%, 82.2%,  $P=0.0108$ ). HPVI ADC was associated with a higher recurrence rate compared to HPVA ADC and SCC (46.2%, 19.7%, 15.1%,  $P=0.0166$ ). HPVI ADC was associated with worse DFS compared with HPVA ADC, SCC (44.9 months, 127.9 months, 91.3 months,  $P=0.0123$ ). HPVI ADC was associated with worse 5-year survival rate compared with HPVA ADC, SCC (69.2%, 85.2%, 91.9%,  $P=0.0207$ ). There was no difference in 5-year survival rate between patients with HPVA ADC and patients with SCC.

**Conclusion/Implications:** HPVI ADC had a poorer prognosis compared to HPVA ADC and SCC. However, there was no difference in prognosis between HPVA ADC and SCC in 2018 FIGO stage IA2 – III cervical cancer.



EP069 / #511

Topic: *AS03. Cervical Cancer*

## **EVALUATION THE MULTILAYER SCANNER FOR LBC CYTOLOGY WITH SOFTWARE CONTAINING NEURAL NETWORKS AND MACHINE LEARNING ENABLING REMOTE SUPPORT FOR THE DIAGNOSIS ENHANCED WITH DIFFERENTIATING ALGORITHM**

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**Introduction:** Cervical cancer mortality in Poland is high. Access to diagnosticians is still insufficient. To deal with this problem a multilayer LBC sample scanner and software was built and implemented, which improved accuracy of diagnostics and limited time of obtaining results. Due to shortage of diagnosticians, a support system based on artificial intelligence algorithms was launched, offering the possibility of remote viewing of scans samples and medical history of the patient. The final diagnosis is always made by cyto-screeners on the basis of system results and cyto-screeners analysis.

**Methods:** The software is based on the artificial neural network (U-NET architecture) designed to recognize suspicious regions and a neural network (VGG) allowing to determine the type of disorder. A machine learning element (fuzzy K-Means) was added - responsible for the fusion of the patient's medical history with the neural network system results. A differentiating algorithm included is the crucial part of the system to increase sensitivity of the method especially in recognizing HSIL, ASC-US, ASC-H, Ca Plano.

**Results:** 3161 (LBC) samples were evaluated by cyto-screeners. Cytological abnormalities were found in 458 (14.3%) cases. Selected samples with diagnosed abnormality were a model to teach the artificial intelligence algorithms. Preliminary results obtained so far indicate 94-97% compliance with results obtained using standard methods. Implementing additional differentiating algorithm has improved results to the level of 96-98% compliance.

**Conclusion/Implications:** Further refinement of neural networks is necessary to improve sensitivity and specificity. A study with a larger sample size will be conducted to evaluate the software.

EP070 / #788

Topic: *AS03. Cervical Cancer*

## TARGETING TISSUE FACTOR WITH A BISPECIFIC T CELL ENGAGER FOR CERVICAL CANCER

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**Introduction:** To develop an effective and targeted therapeutic approach for solid tumors, including cervical cancer, with improved survival rates compared to standard treatments. Overcoming barriers to immunotherapies in solid tumors, such as limited therapy half-life, tumor penetrance, and precise targeting, is crucial. We aim to explore a durable and controllable local delivery method for therapeutic proteins, which can enhance antitumor efficacy while minimizing non-tumor tissue toxicities.

**Methods:** The Anti-Tissue factor x CD3 TCE is composed of two Tissue factor binding Fabs, which allow for preferential recognition of Tissue factor-high-expressing cancer cells, and one CD3 binding domain that facilitates Tissue factor-mediated CD3 crosslinking and subsequent T cell activation. Flow cytometry was used to study activation and degranulation assays. The immunomodulatory function of this sentence was able to confirm in vitro cell killing analysis through luciferase reporter cell analysis.

**Results:** Our study demonstrated that the functional tissue factor-targeted BiTE protein induced T cell activation, degranulation, and antigen-specific killing of cervical cancer cells. Importantly, this response was specific to tissue factor expression and was not observed in the absence of tissue factor expression.

**Conclusion/Implications:** The findings support the potential of the BiTE protein as a targeted therapeutic approach for cervical cancer, offering a promising strategy to address the challenges associated with solid tumors and improve treatment outcomes.

EP073 / #565

Topic: *AS03. Cervical Cancer*

## **SURVIVAL AND PATTERNS OF FAILURE IN SMALL CELL NEUROENDOCRINE CARCINOMA OF CERVIX TREATED WITH DEFINITIVE CHEMORADIOTHERAPY**

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**Introduction:** Small cell neuroendocrine carcinoma of cervix (SMNEC) is associated with poor prognosis on account of high incidence of nodal and systemic spread at diagnosis. Trimodality treatment often required if primary treatment was surgery even for early-stage disease. This study aims to investigate the survival and patterns of failure in immuno-histologically confirmed SMNEC treated with chemoradiotherapy-based primary treatment.

**Methods:** Thirty patients with FIGO 2009 1b-3b SMNEC treated consecutively with curative intent between 1997-2017 were identified from a prospectively collected institutional ethics-approved Gynaecology Unit database. Five patients had surgery as primary treatment whilst the remainder 25 who underwent primary radiotherapy were eligible for analysis. All patients had staging Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET). Treatment consisted of external beam radiotherapy and brachytherapy in combination with sequential and/or concurrent platinum-etoposide (EP)-based chemotherapy. Kaplan-Meier method and descriptive statistics were used to estimate survival and patterns of relapse.

**Results:** Twenty-five SMNEC patients followed-up for a median (IQR) of 69.5(20.8-120.0) months. Five-year overall survival was 55.5% (34.1%-72.4%). For node-negative patients (n=14) it was 76.9% (44.2%-91.9%) and for node-positive patients(n=11), it was 31.2% (8.5%-57.8%). Eleven patients (44%) relapsed, all of whom had distant failure. In addition, relapses in the primary(n=3), pelvic(n=6) and para-aortic(n=6) sites concomitantly. Primary and pelvic sites were controlled in 22(88%) and 19(76%) patients respectively. There were no primary site failures in the node-negative patients up to stage 2a.

**Conclusion/Implications:** Loco-regional control was obtained in 76% patients. However, distant failure rate was 39% and 58% in node-negative and node-positive patients respectively.

EP074 / #1447

Topic: AS03. Cervical Cancer

## CLINICALLY EARLY-STAGE CERVICAL CANCER WITH LYMPH NODE METASTASIS: A STUDY AND PROPOSAL FOR REVISING THE 2018 FIGO STAGING SYSTEM

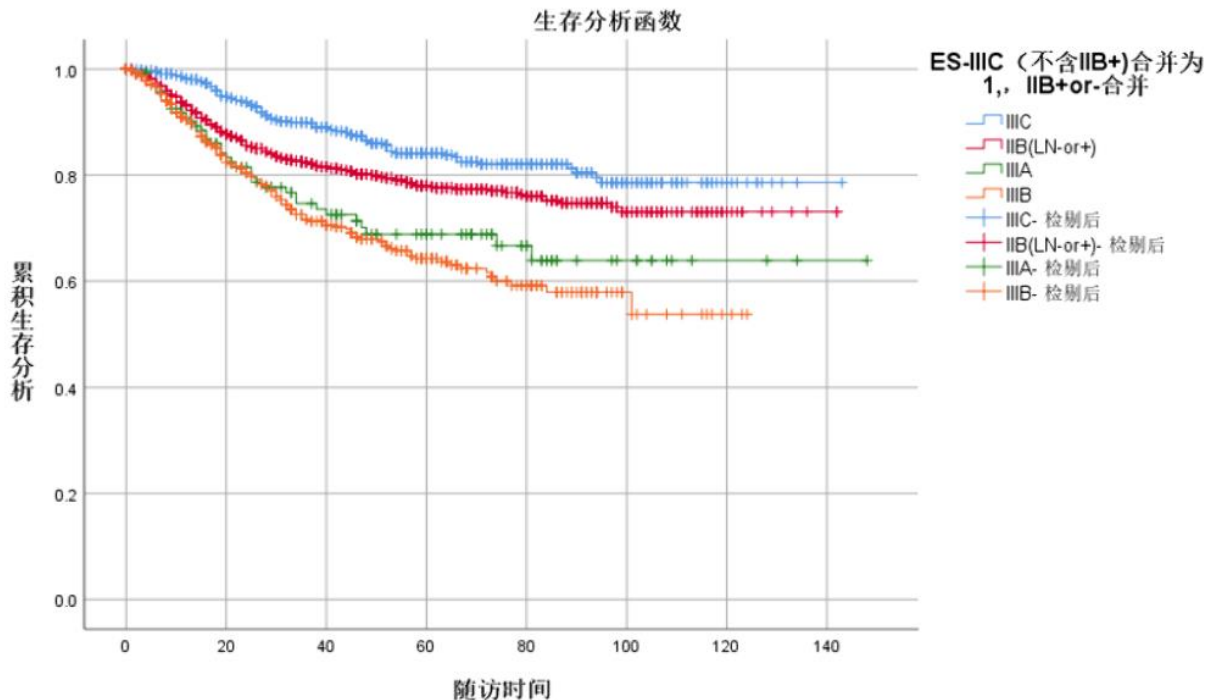
Jihong Liu<sup>1</sup>, Hua Tu<sup>1</sup>, Lewei Yang<sup>2</sup>, Ting Deng<sup>1</sup>, Guochen Liu<sup>1</sup>, Haifeng Gu<sup>1</sup>, Zhimin Liu<sup>1</sup>

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**Introduction:** To investigate optimal substage of lymph node metastasis in the FIGO staging system for cervical cancer.

**Methods:** Patients with early-stage cervical cancer who were surgically confirmed lymph-node metastases between 2008 and 2015 were analyzed for cancer-specific survival and compared with contemporaneous stage IIB, IIIA and IIIB patients.

**Results:**



A total of 2098 patients were included, comprising of 584 cases who were surgically confirmed node-positive with FIGO 2009 stage IA2 to IIA2 (cohort A) and 1514 cases with stage IIB to IIIB (cohort B). The median follow-up time was 62 and 48 months for cohort A and B, respectively. Patients in cohort A had significantly more favored overall survival than stage IIB ( $P = 0.003$ ), IIIA ( $P < 0.001$ ) and IIIB ( $P < 0.001$ ) patients. In cohort A, initial FIGO 2009 stage, the number of metastatic nodes and tumor size were independent prognostic factors for overall survival. In cohort B, lymph node metastases significantly decreased survival in patients with stage IIB ( $P=0.007$ ), but not in patients with stage IIIA ( $P=0.347$ ) or IIIB ( $P=0.486$ ) disease. When merged node-positive IIB patients into cohort A, the 5-year overall survival

were 81.3%, 78.1%, 68.8% and 64.3% for stage IIB (node-negative), regrouped cohort A (all node positive cases with FIGO stage IA2 to IIB), IIIA and IIIB patients, respectively ( $P < 0.001$ ).

**Conclusion/Implications:** The prognosis of early-stage cervical cancer with nodal metastases is significantly better than that of stage IIIA and worse than IIB. The findings support to stratify these patients into a new substage IIC in FIGO staging system.

EP075 / #462

Topic: *AS03. Cervical Cancer*

## **RADIATION QUALITY AND WORKFLOW IN NRG GY017: ANTI PD-L1 (ATEZOLIZUMAB) AS AN IMMUNE PRIMER OR CONCURRENTLY WITH RT FOR NODE POSITIVE LOCALLY ADVANCED CERVICAL CANCER.**

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**Introduction:** Advances in RT planning enhance the need for uniform quality oversight on clinical trials. NRG GY-17 was a randomized trial of the anti PD-L1 antibody, atezolizumab, before and concurrent (Arm A) or concurrent with CRT (Arm B). We describe the prospectively collected pre-treatment RT quality and workflow.

**Methods:** 40 patients were consented; 36 patients with locally advanced, LN+ cervical cancer were randomized. IMRT contouring guidelines and dose specifics were outlined in the protocol with deviations specified as per protocol and major. Each site had to pass a rigorous IMRT credentialing process. Sites were required to submit a pre-treatment IMRT plan for physician expert contour target and organ at risk review in a rapid pre-treatment manner. The expert physician then scored the contours and plan as per protocol or as a major deviation. For major deviations the sites were required to revise and resubmit the plans which were then re-reviewed prior to protocol start.

**Results:** The median follow-up time was 20 months. 37 participants had central review of the pre-treatment EBRT plan. 13 plans (35%) were scored as a major deviation requiring revision: 11 due to contours (5 bowel and 6 LN) and 2 due to incorrect expansion/dose. The major deviation plans were resubmitted and passed; 2 required revisions for a total of 3 plans.

**Conclusion/Implications:** Our data indicate that 35% of the submitted advanced technology IMRT plans required revision and resubmission in order to meet per protocol standards. Pre- treatment plan review is an important quality measure for cervical cancer clinical trials.

EP077 / #1445

Topic: *AS03. Cervical Cancer*

## THE HPV E4 IS A CANDIDATE BIOMARKER IN CERVICAL INTRAEPITHELIAL NEOPLASIA GRADE 2

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**Introduction:** HPV E4 protein is synthesized as a E1<sup>Δ</sup>E4 fusion protein as a result of mRNA splicing. The knowledge regarding the functions of E1<sup>Δ</sup>E4 during the viral life cycle remains incomplete. It is safe to suggest that the protein is involved in virus release and transmission and that it is a marker of the onset of productive infection. However, the potential role of E4 as a tool to stratify cervical intraepithelial neoplasia (CIN), and to detect HPV-associated lesions that may progress towards CIN2+, has been reported in multiple publications recently. The management of CIN2 is still controversial, prompting us to investigate the correlation between E4 expression and prognosis of lesions classified as CIN2.

**Methods:** We carried out a retrospective cohort study using the medical and histopathological records of 115 patients with CIN2 treated. E4 was detected as described previously (Griffin et al., 2015). Regression was defined as negative cytological and histological result for more than one year. Progression was defined as the appearance of histologically confirmed CIN3 during follow-up. We built Kaplan-Meier curves for progression/regression groups and compared unadjusted survival statistics using Log-rank test.

**Results:** The cases were 28, 67, and 20 for regression, persistence, and progression, respectively. Kaplan-Meier curves showed that E4 expression was significantly difference between progression and regression (Log-rank test= $p < 0.001$ ). CIN2 progressed in the E4 negative cases and regressed in the E4 positive cases.

**Conclusion/Implications:** The E4 expression was correlated with progression/regression of CIN2. These data suggest that the HPV E4 expression is a candidate biomarker for prognosis of CIN2.

EP078 / #759

Topic: *AS03. Cervical Cancer*

## **THE INFLUENCE OF DEMOGRAPHIC AND CLINICAL FEATURES ON THE RECEIPT OF RADIOTHERAPY FOR WOMEN WITH CARCINOMA OF THE CERVIX IN GHANA.**

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**Introduction:** Cervical cancer is a significant public health issue in Ghana. Most cases of the disease are diagnosed at an advanced stage where radiotherapy treatment will be required. We evaluated how demographic and clinical features of women with invasive cervical cancer influenced the receipt of radiotherapy in two large referral hospitals in Ghana.

**Methods:** We conducted a retrospective study of 1,725 women diagnosed with invasive cervical cancer between 1<sup>st</sup> January 2010 and 31<sup>st</sup> December 2013. Multivariable logistic regression was used to evaluate the odds of receiving radiotherapy by patient demographic and clinical features associated with financial barriers to care.

**Results:** Women who lived in other African countries but receiving treatment at one of the two centers in Ghana were more likely to receive radiotherapy compared with women who lived in a metropolis in Ghana (unadjusted OR: 4.1; 95% CI: 2.5-6.9). Additionally, women living in a semi-urban region of residence were more likely to receive radiotherapy compared with those living in a metropolis (unadjusted OR: 2.4; 95% CI: 1.6-3.5). Women less likely to receive radiotherapy tended to have three or more comorbidities (unadjusted OR: 0.2; 95% CI: 0.1-0.5), be recruited at the gynecology unit (unadjusted OR: 0.01; 95% CI: 0.002-0.01) and not have cancer histologically confirmed (unadjusted OR: 0.004; 95% CI: 0.002-0.01).

**Conclusion/Implications:** Conclusion: Women from other African countries may be fee-paying for radiotherapy treatment as opposed to being refugees. There are opportunities to improve the outcome for women with cervical cancer in Ghana by reducing financial barriers to access for radiation therapy.



EP079 / #533

Topic: *AS03. Cervical Cancer*

## **THE PREVALENCE AND DISTRIBUTION PATTERN OF CERVICAL HIGH-RISK HPV GENOTYPE INFECTIONS AMONG WOMEN WITH HIGH-GRADE PRE-INVASIVE AND INVASIVE CERVICAL CANCER IN LAGOS, NIGERIA**

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**Introduction:** High-risk HPV (hr-HPV) has been identified as the key etiology in the development of high-grade pre-invasive and invasive cervical cancer (CIN2+/ICC). However, little is known about the distribution of cervical hr-HPV genotypes associated with CIN2+/ICC in Lagos, Nigeria. We sought to investigate the hr-HPV genotypes responsible for CIN2+/ICC in Lagos, Nigeria.

**Methods:** The study was conducted as part of the Nigeria U54 study. DNA extract was obtained from cervical tissues obtained from women with confirmed CIN2+/ICC. Anyplex II HPV HR detection kit was used to detect the presence of 14 hr-HPV genotypes. Genotype-specific prevalence rates were computed and pattern of infection described.

**Results:** The overall prevalence of hr-HPV infection was 91.1%. Hr-HPV 16, 18, 35, and 51 were the most common genotypes isolated with genotype-specific prevalence rates of 50.0%, 33.3%, 12.2%, and 7.8% respectively. Hr-HPV 39 (0.0%), 31 (1.1%), 68 (1.1%), 56 (2.2%) & 66 (2.2%) were the least prevalent genotypes. The prevalence of single and multiple hr-HPV infections were 55.6% and 35.6% respectively. 27.8% had dual hr-HPV infections, while 7.8% had  $\geq 3$  hr-HPV infections. Hr-HPV 16, 18, and 35 were the most prevalent genotypes seen in single (23.3%, 14.4% & 5.6% respectively) and multiple infections (26.7%, 18.9% & 6.7% respectively). Though the presence of hr-HPV 16 & 18 was associated with having multiple hr-HPV infections, it was not predictive of having it on multivariable analysis ( $P > 0.05$ ).

**Conclusion/Implications:** Hr-HPV 16/18 remained a major cause of CIN2+/ICC, however, more attention needs to be given to hr-HPV 35 as an important cause of CIN2+/ICC.

EP080 / #648

Topic: *AS03. Cervical Cancer*

## **KNOWLEDGE AND PRACTICE OF CERVICAL CANCER SCREENING AMONG WUSE MARKET WOMEN IN ABUJA NIGERIA.**

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**Introduction:** Cervical cancer is the fourth most common cancer among women with estimated 604000 new cases and 342000 deaths in 2020. 90% of new cases and deaths worldwide in 2020 occurred in low middle income countries. The most important risk factor for cervical cancer is infection by human Papillomavirus (HPV). HPV can be spread during sex. Cervical cancer is highly preventable with screening but women rarely know the importance of cervix screening. Reports have shown that cervical cancer kills one woman every hour in Nigeria and ignorance remains the underlying risk factor for most Nigerian women.

**Methods:** It was a crosssectional semi descriptive study conducted among 200 market women randomly selected using systematic sampling technique. A questionnaire was used to collect data and the mean age of the study was 18- 65 years.

**Results:** Significant numbers of market women exhibited a low knowledge of cervical cancer screening 86%. Some of these women reported not having been screened for cervical cancer and reasons were Religious beliefs. Low income. Cultural and language barrier 14%. In line with a study done in Abuja hospital. 94.5% of cervical cancer patients presented their cases late due to ignorance.

**Conclusion/Implications:** There is a general need to educate market women. Governmental agencies should introduce cervical cancer educators with interpreters in market places. Most market women are not literates. It is important to use illustrative diagrams and 3D photographs to educate women on the importance of early cervical cancer screening and to enable them make an informed choice to prevent it.

EP081 / #404

Topic: *AS03. Cervical Cancer*

## **PROGNOSTIC VALUE OF RADIOLOGICAL AND PATHOLOGICAL EVALUATION OF PELVIC LYMPH NODES IN CERVICAL CANCER PATIENTS**

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**Introduction:** The presence of lymph node metastasis in cervical cancer is considered to be an independent prognostic factor for risk of recurrence and survival. Cases with lymph node metastasis are classified as stage IIIC in FIGO 2018 classification. In this study, we investigated the consistency of preoperative imaging of lymph node enlargement with pathologic diagnosis, and its impact on prognosis in cervical cancer.

**Methods:** We evaluated imaging and histological evaluation of pelvic lymph node, clinical stage, histological type, and oncologic outcome in 71 patients with cervical cancer who underwent radical hysterectomy in our hospital from 2014 to 2020.

**Results:** Of the 14 patients with enlarged lymph nodes on imaging (r+), 11 had pathologic lymph node metastasis (group:r+p+) and 3 had no pathological metastasis (r+p-). In contrast, of the 57 patients without lymph node enlargement by imaging, 20 had pathologic lymph node metastasis (r-p+) and 37 did not (r-p-). In histologic types of r-p+ group were squamous cell carcinoma in 11 of 36 patients (30.6%) and adenocarcinoma in 9 of 35 patients (25.7%). Among adenocarcinoma, mucinous carcinoma of gastric type was the most common at 4 of 5(80.0%). The mean survival of r+p+, r-p+, and r+p- group was 65.9, 54.3, and 69.8 months, respectively, while 96.6 months for r-p- group.

**Conclusion/Implications:** Patients with cervical cancer without lymph node enlargement on preoperative imaging but with pathologic lymph node metastasis had a similarly poor prognosis as those with enlarged lymph nodes on preoperative imaging.

EP084 / #264

Topic: *AS03. Cervical Cancer*

## **THE LANDSCAPE OF IMMUNE MICROENVIRONMENT AND THE POOR PROGNOSTIC VALUE OF TERTIARY LYMPHOID STRUCTURE IN GASTRIC-TYPE MUCINOUS CARCINOMA**

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**Introduction:** Gastric-type mucinous carcinoma (GAS) is the most common subtype in HPV-unrelated endocervical adenocarcinoma. GAS has aggressive behavior and worse clinical outcome compared with usual-type endocervical adenocarcinoma (UEA). In this research, we delineated the tumor immune microenvironment of GAS by comparing with UEA and found the adverse effect of TLS in them.

**Methods:** Multiplex immunofluorescence (mIF) and RNA sequencing were applied in this study. We optimized 4 mIF panels about tumor-infiltrating immune cell, the subtypes of macrophages, tertiary lymphoid structure (TLS) and regular T cell (Treg) and regular B cell (Breg)

**Results:** By analyzing mIF data, GAS tumors had less infiltration of CD4<sup>+</sup> T cells and CD8<sup>+</sup> T cells but more macrophages than UEA. In GAS patients, macrophage infiltration was significantly increased in patients with positive lymph node metastases and advanced stage, especially the M2 type macrophages. Functional pathway enrichment analysis also shew the immune-activated related pathways were more enriched in UEA tumors. By statistics, approximately 15% of patients had mature TLS. Surprisingly, mature TLS formation was associated with shorter overall survival time in both GAS and UEA. Patients with mature TLS had more Tregs and Bregs infiltrating in both the tumor region and the lymphocyte aggregation region. Gene expression analysis shew the tumor cell proliferation was increased, while the immune-activating was reduced in tumors with mature TLS.

**Conclusion/Implications:** We found GAS had less lymphocytes infiltration than UEA, but more macrophage infiltration, especially M2-type macrophages. And the formation of mature TLS was a crucial adverse prognostic factor in GAS and UEA.

EP085 / #241

Topic: **AS03. Cervical Cancer**

## **EVALUATION OF HPV TYPES AMONG WOMEN ENROLLED IN THE MULHER CERVICAL CANCER SCREENING STUDY IN MOZAMBIQUE**

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**Introduction:** The objective of our study is to describe the high-risk human papillomavirus (HR-HPV) types noted among women enrolled in the MULHER Study, a prospective trial of Mozambican women undergoing cervical cancer screening with HPV testing in conjunction with family planning services.

**Methods:** From January 2020 to January 2023, 9,014 women aged 30-49 years in Maputo City and Gaza Province, Mozambique underwent cervical cancer screening. Cervicovaginal samples were self-collected (97.5%) or provider-collected (2.5%) and primary HPV testing was performed using the GeneXpert HPV testing platform (Cepheid Inc, Sunnyvale, CA, USA) which provided genotyping for HPV16, HPV18/45 and non-16/18/45. Women with positive HPV testing underwent visual assessment for treatment (VAT) using visual inspection with acetic acid (VIA) and treated with ablation or excision as appropriate.

**Results:** Of the 9,014 women enrolled, 2,805 (31.1%) tested positive for at least one HR-HPV type: HPV16 (n=477, 17%), HPV18/45 (n=688, 24.5%) and non-16/18/45 (2,157, 76.9%). 23.2% of participants with HR-HPV had multiple types present. HR-HPV infection was more frequently observed among women living with HIV (WLWH) compared with HIV-negative women (39.5% vs, 24.2% respectively; p<0.001), with non-16/18/45 also being the most frequent type in this population (69.6%). Among women with cancer, HPV16 was the most frequent type noted (58%).

**Conclusion/Implications:** Our findings suggest that non-16/18/45 was the most frequent HR-HPV type among women in our study cohort in Mozambique overall; and HPV16 is the most common among women with cervical cancer. Further study is needed to determine the role of HR-HPV genotyping in follow-up and treatment, particularly among WLWH in Mozambique.

EP086 / #497

Topic: *AS03. Cervical Cancer*

## **SCALING CERVICAL CANCER SCREENING IN MOZAMBIQUE: ANALYSIS OF LOOP ELECTROSURGICAL EXCISION PROCEDURE (LEEP) SPECIMENS**

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**Introduction:** As cervical cancer screening programs are implemented, an increasing number of women require loop electrosurgical excision procedure (LEEP). Our objective was to describe the pathologic results of LEEP specimens performed as part of the MULHER Study, a prospective trial of primary HPV testing for cervical cancer screening in Mozambique.

**Methods:** 9,014 women underwent HPV testing followed by thermal ablation for those with positive results. 169 women had cervical lesions ineligible for ablation and underwent LEEP. Pathology reports were reviewed for specimen size/volume, number of pieces, pathologic diagnosis and margin status. A multivariable regression analysis was performed to identify variables associated with positive margins.

**Results:** The median age was 38 years (range 30-49). 65.1% were women living with human immunodeficiency virus (HIV). Pathologic diagnosis was available for 154 patients and included carcinoma (n=6,3.9%); cervical intraepithelial neoplasia (CIN)2-3 (n=75,48.7%); CIN1 (n=67, 43.5%) and normal/benign findings (n=6,3.9%). 31.8% of LEEP specimens were removed in >1 piece. The mean specimen volume was 2.9 mm<sup>3</sup> (range 0.2-15.0). LEEP margin status was available for 130 patients. Positive margins (ectocervical/endocervical only, or both) were noted in 76 (58.5%) patients and associated with HIV+ status (p=0.0499) and a diagnosis of CIN2 or worse (p=0.0197). There were no associations between margin status and age, number of pieces or specimen volume.

**Conclusion/Implications:** There were a high number of LEEP specimens with positive margins. As cervical cancer screening programs are scaled in Mozambique and other lower-resource countries, there is a need to train providers to perform high-quality LEEP as well as accurate pathologic interpretation.

EP087 / #716

Topic: *AS03. Cervical Cancer*

## **FREQUENCY OF PRIOR CERVICAL CYTOLOGY AND DETAILED HISTOLOGY IN PATIENTS DIAGNOSED WITH CERVICAL CANCER AT A NORTHERN REGIONAL HOSPITAL IN CHILE.**

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**Introduction:** The objective of this review is to know the frequency with which patients with cervical cancer have cervical cytology that is current, not current, or have never had one done before; in addition to knowing the results of the cytology and specifying the histology of the most frequent cervical cancer in patients with current cytology.

**Methods:** Retrospective descriptive study, with review of records of patients admitted to the Gynecology Oncology Unit of the Regional Hospital of Copiapó between 2020-2022, with diagnosis of cervical cancer. Current cytology was considered performed within 3 years of diagnosis. Cervical cytology was reported according to the classification of Bethesda.

**Results:** A sample of 68 patients who met the inclusion criteria was selected. 21% had a current Pap smear, 54% did not have a current pap smear, 25% had never had a Pap smear. Of the 14 patients with current cytology, the IG8 result predominates (64.3%), other results included IG7 (14.3%), H1 (14.3%) and G4 (7.1%). Histology results observed in the sample with current cytology included squamous (78.6%), adenocarcinoma (14.3%) and adenocarcinoma and clear cells (7.1%).

**Conclusion/Implications:** A large percentage of patients diagnosed with cervical cancer in our study population did not have a Pap smear in the last 3 years. Less than 5% of the population studied had a complete screening in the last 10 years, which highly decreases the possibility of preventing cervical cancer, therefore we recommend increasing awareness in the general population to obtain an effective and timely screening.

EP088 / #733

Topic: *AS03. Cervical Cancer*

## **INCIDENCE OF CERVICAL CANCER DIAGNOSED TOO LATE FOR SURGICAL TREATMENT; THIRD REGION, CHILE**

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**Introduction:** There are different types of treatment for cervical cancer, surgical treatment is carried out only in the early stages, this being the definitive treatment in many cases. In 2018 the European Society for Gynecologic Oncology (ESGO) together with the European Society for Radiotherapy and Oncology (ESTRO) and the European Society for Pathology (ESP) published evidence-based guidelines to improve the management of patients with cervical cancer within a multidisciplinary environment.

**Methods:** Retrospective review of statistical database analysis using clinical records, protocols, biopsies, and gynecology-oncology committee records of patients diagnosed with cervical cancer between November 2020 and April 2023.

**Results:** We found 95 patients with diagnosis of cervical cancer who were presented to the gynecology oncology committee between the aforementioned dates. 82 patients with ages between 22 to 82 years were newly diagnosed: 23 patients (28%) in initial stages who received curative surgical treatment and 59 patients (72%) who did not meet the conditions for surgical treatment. The FIGO stages were classified as: 6 IB3, 1 IIB, 1 IIA1, 2 IIA2, 7 IIB, 4 IIIB, 15 IIIC1, 4 IIIC2, 5 IVA, 14 IVB.

**Conclusion/Implications:** At present, after the pandemic and the decrease in screening, most patients with cervical cancer that arrive at our unit are in advanced stages and we cannot perform surgeries with curative intent. Therefore these results encourage us to improve public awareness to reach a greater population and to change the regional public health regulations to improve these data and decrease morbidity/mortality.



EP089 / #865

Topic: *AS03. Cervical Cancer*

## **COMPARATIVE ANALYSIS OF CERVICAL CANCER TREATMENT OUTCOMES IN CENTRAL ASIA**

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**Introduction:** Improving the results of treatment of patients with stage IIB cervical cancer by introducing the complex or combined treatment.

**Methods:** This study based on a prospective analysis of 215 women diagnosed with stage IIB cervical cancer. The median age was 47 years (28-64). The patients were divided into two groups: the NACT+S group, 105 patients who receive 2-3 cycles of neoadjuvant chemotherapy followed by surgical treatment. Chemo-Radiotherapy (1,8 Gy, 45 Gy ± SIB on the metastatically involved lymph nodes 2,2 Gy, 55 Gy). The second group (CRT group) included 110 patients who underwent radiotherapy.

**Results:** The median follow-up was 23 months (8-38). In the NACT+S group, thrombocytopenia and neutropenia of the 3 - 4 degree were more common than in the CRT group (6.6% and 7.6% vs. 0.9% and 0.9%, respectively;  $p = 0.026$ ;  $p = 0.015$ ). However, there was no significant difference between the two groups studied in relation to the 3 - 4 degree of radiation toxicity of the GI and genitourinary system. 26 cases of disease progression (24.8%) occurred in the NACT+S group, and 15 events (13.6%) occurred in the CRT group; the corresponding 3-year DFS rates were 75.2% and 86.4%, respectively (HR 1.83; 95% CI 1.99-3.40;  $p = 0.05$ ).

**Conclusion/Implications:** Cisplatin-based chemoradiation resulted in superior DFS compared with neoadjuvant chemotherapy followed by radical surgery in locally advanced cervical cancer. There was no significant difference between the two study groups with 3-year indicators of OS and respect to grade 3 or 4 GI and bladder toxicities.

EP090 / #413

Topic: *AS03. Cervical Cancer*

## **ROLE OF PET-CT AND MRI TO EVALUATE LYMPH NODE METASTASIS IN CERVICAL CANCER**

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**Introduction:** Cervical cancer is the fourth most common cancer in women in the world. Management usually includes surgery for early stage of the disease in cases with no contraindication for surgery. Lymph node metastasis is an indicator for primary chemoradiotherapy. Lymph node involvement is incorporated in FIGO's 2018 staging system. The involvement should be noted according to the method of detection as either radiological(r) or pathological(p). So, we evaluate MRI and PET CT values to detect nodal metastasis for single center.

**Methods:** This retrospective analysis was performed in patients treated with surgery, who had MRI and PET CT imaging in The Department of Obstetrics and Gynecology, Gynecologic Oncology Surgery division at Akdeniz University School of Medicine between 2004 to 2020. A Total of 139 cases were included in the study where mean age was 49.68.

**Results:** The most frequent symptom was postcoital bleeding. 29.5% cases had histologic node metastasis. Preoperative MRI showed that 56.1% of cases were node metastatic, and this rate was 38.1% for PET CT. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy for MRI were 60.9%, 63.2%, 40.9%, 79.4%, 72.5% respectively and 70.7%, 75.5%, 54.7%, 86%, 74.1% for PET CT respectively. Negative predictive values are acceptable for both imaging methods. Accuracy of PET CT is higher than MRI to detect nodal metastasis.

**Conclusion/Implications:** MRI and PET CT offer moderate value to detect lymph node metastasis for cervical cancer. Negative predictive value of PET CT is a better indicator for nodal involvement compared to MRI.

EP091 / #144

Topic: *AS03. Cervical Cancer*

## **COMPARISON OF SURVIVAL OUTCOMES BETWEEN DEFINITIVE CHEMORADIATION AND POST-RADIATION HYSTERECTOMY IN BULKY IB CERVICAL CARCINOMA**

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**Introduction:** Optimal treatment of bulky stage IB cervical cancer has long been a source of controversy. Definitive chemoradiation therapy (chemoRT) has been the preferred approach for large IB disease, however the role of post-radiation surgery has not been fully defined. The objective of the study was to compare the recurrence, complication, and survival data between patients with large primary cervical lesions undergoing definitive chemoRT with post-radiation surgery.

**Methods:** Retrospective cohort analysis of patients at a single institution with IB cervical cancer and primary lesions greater than 4 centimeters treated between January 1st, 2008 and December 31<sup>st</sup>, 2016. Data was extracted from patient's electronic or paper medical records. Data variables included patient demographics, comorbidities, oncologic treatments, complications, and survival. The Kaplan-Meier method was used to estimate recurrence-free survival and overall survival censored at 5 years and the log-rank test provided a statistical comparison between chemoradiation and post-radiation hysterectomy.

**Results:** 42 patients were identified: 16 receiving chemoRT (Arm A) and 26 receiving post-radiation hysterectomy (Arm B). Demographics, comorbidities, and tumor characteristics were comparable between groups, with a majority of patients identified as stage IB2. Rates of treatment-related complications requiring hospitalization were low in both groups: Arm A (25%) vs Arm B (15.4%) ( $p=0.45$ ). 5-year recurrence-free survival was comparable between both groups (62.5% vs 73%,  $p= 0.52$ ) and overall survival censored at 5 years in the post-radiation hysterectomy was more favorable although not statistically significant (68.75% vs 88.5%,  $p= 0.17$ ).

**Conclusion/Implications:** Post-radiation hysterectomy, while safe in terms of long-term morbidity, did not confer a significant survival advantage.

EP092 / #437

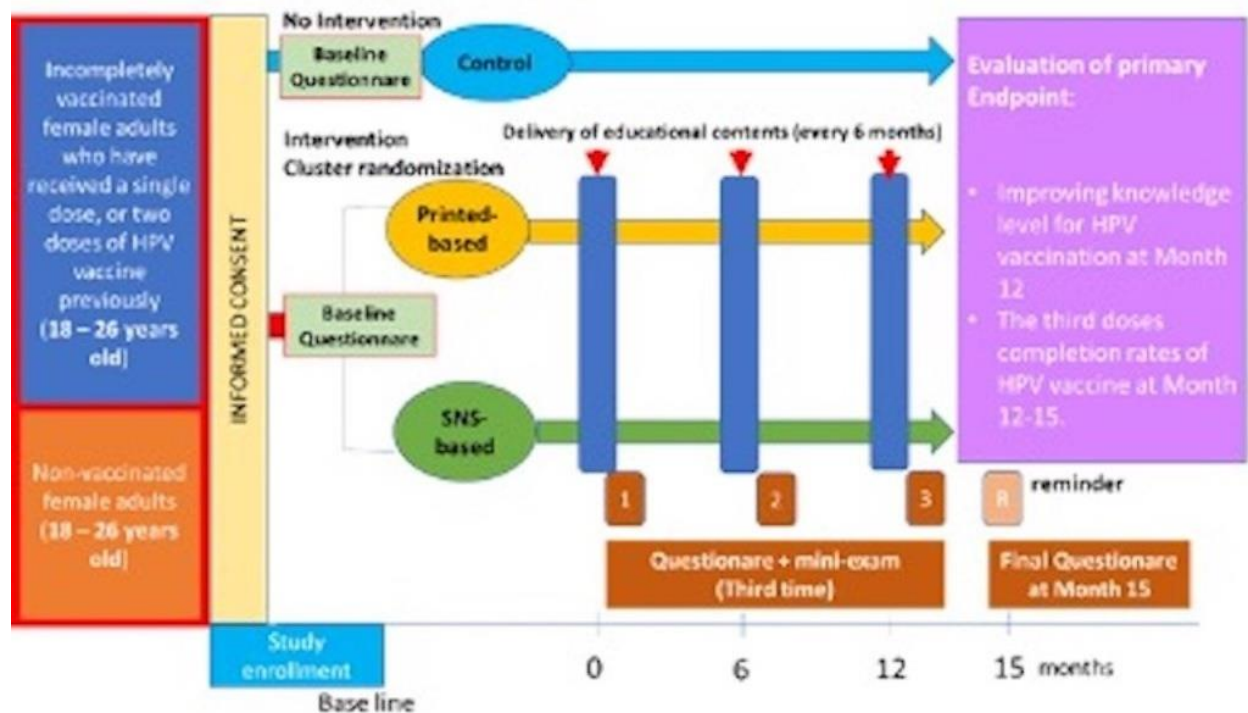
Topic: AS03. Cervical Cancer

## EFFECT OF DIFFERENT EDUCATIONAL INTERVENTIONS ON KNOWLEDGE OF HPV VACCINATION AND CERVICAL CANCER AMONG YOUNG WOMEN: AN INTERIM REPORT

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**Introduction:** The incidence and mortality rates of cervical cancer are rising among young women in Japan. In November 2021, the Japanese Ministry of Health, Labour, and Welfare reinstated the active recommendation for the human papillomavirus (HPV) vaccine, which was discontinued in June 2013 due to reports of adverse reactions, including chronic pain and motor dysfunction, following vaccination. However, vaccine hesitancy still remains. We aimed to conduct a randomized study using different methods of providing educational content to improve health literacy among female students in Japan.

**Methods:** Data was collected three times from students in our university who were divided into three groups: no intervention, print-based intervention, and social networking service-based intervention, using the health literacy scale and communicative and critical health literacy scale.



**Results:** As of April 2023, of the 267 participants in the study, 179 participants have completed the first questionnaires. One hundred forty-eight students (79.3%) were in medical-related faculties, 72 (40.2%) had relatives of medical professionals, 99 (55.3%) had never received the HPV vaccine, and 50 (28.0%)

had completed three doses. There were significant differences in the total scores of the health literacy questionnaire depending on the above backgrounds.

**Conclusion/Implications:** Our present analysis indicates that participants' knowledges due to lifestyles are related to health literacy. Therefore, medical professionals must provide accurate scientific knowledge about HPV vaccination and the risk of cervical cancer to improve students' health literacy and subsequently increase the HPV vaccination rates. The collected responses will be statistically reviewed and reported.

EP093 / #971

Topic: *AS03. Cervical Cancer*

## **ASSESSMENT OF QUALITY OF LIFE IN NEWLY DIAGNOSED CERVICAL CANCER PATIENTS IN NIGERIA – A MULTI-CENTER STUDY**

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**Introduction:** Most cervical cancer patients in LMICs tend to present at an advanced stage with associated health and psychological difficulties. This can affect their quality of life (QOL). There is limited published data about the QOL of women with cervical cancer in LMICs. AIM: To evaluate the QOL among women newly diagnosed with cervical cancer.

**Methods:** This was a cross-sectional study of the QOL in women recently diagnosed Cervical Cancer (treatment naïve) using a validated tool, the Quality of Life Questionnaire domains (EORTC QLQ30) administered by trained assistants. The study was conducted from May 2022 to April 2023 in 6 tertiary health facilities, selected by multistage stratified sampling technique in 120 eligible consenting participants. The QOL score was graded into 5 categories: ( $\leq 15$  - very good, 16-30– Good, 31-60– poor, 61-75– very poor, and  $\geq 76$ – worst). All data were exported into SPSS version 26 for analysis. Ethical approval was obtained.

**Results:** The commonest age range (23.33%) was 44-49 years, 64.17% were married and 59.17% had monthly income less than \$33.2. Stage 4 (39.83%) and 3 (33.90%) disease were commonest. Most (71.67%) had poor quality of life while 20% had good quality of life. Half of the participants rated their perception of quality of life as poor and very poor (36.67% & 13.33% respectively). Depression(53.3%), difficulty controlling bowel (30%), and painful sex (20.8%) were common complaints.

**Conclusion/Implications:** Majority of women newly diagnosed with cervical cancer in Nigeria had poor QOL. This needs to be a consideration when planning their treatment

EP094 / #1572

Topic: *AS03. Cervical Cancer*

## **UNRAVELING THE COMPLEXITIES OF CERVICAL CANCER: EXPLORATION OF MOLECULAR MECHANISMS AND IMMUNOLOGICAL DICHOTOMIES BETWEEN SQUAMOUS CELL CARCINOMA AND ADENOCARCINOMA**

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**Introduction:** This study aims to refine our understanding of the inherent heterogeneity in cervical cancer by exploring the differential gene expression profiles, immune cell infiltration dynamics, and implicated signaling pathways among the two predominant histological types: Squamous Cell Carcinoma (SCC) and Adenocarcinoma (ADC).

**Methods:** This study builds upon our previous research that included samples of primary cervical cancer patients [1]. The samples were grouped based on their histopathology; comparing SCC to ADC. Existed targeted gene expression data were reanalyzed using the advanced analysis module of nSolver software (nanoString Technology).

**Results:** The study included 22 cervical cancer patients, with 12 patients diagnosed with SCC and 10 with ADC. A total of 33 genes were found to be significantly differentially expressed between the two groups, 23 genes of them were overexpressed in SCC compared to ADC (Benjamini-Yekutieli (BY) adjusted p-value < 0.05). Importantly, the immune checkpoint CD274 and CTLA4 were identified as highly express in the SCC compared to ADC. In addition, the immune cell comparison revealed that B cells, T cells, and the cytotoxic cells infiltrated in higher abundance in SCC compared to ADC. In the same lines, the pathway analysis showed higher scores of cytotoxicity, interferon signaling, metabolic stress, and Notch signaling pathways (adjusted p-value = 0.01, 0.03, 0.03, and 0.01 respectively) in SCC samples.

**Conclusion/Implications:** Our findings elucidate distinctive gene expression patterns, signaling pathway activations, and immune cell infiltration trends in SCC compared to ADC. The findings of this study highlight that all primary cervical cancer is not the same and might be beneficial to subdivide it based on the histological and molecular differences.

1. de Geus V, Ewing-Graham PC, de Koning W, de Koning MN, van den Bosch TP, Nigg AL, van Eijck CH, Jozwiak M, van Beekhuizen HJ, Mustafa DA. Identifying molecular changes in early cervical cancer samples of patients that developed metastasis. *Frontiers in oncology*. 2022 Jan 11;11:715077.

EP095 / #141

Topic: *AS03. Cervical Cancer*

## **IGCS-MD ANDERSON PROJECT ECHO GYNECOLOGIC CANCERS IN LATIN AMERICA: TRANSFERRING KNOWLEDGE, BUILDING CONFIDENCE AND INCREASING COLLABORATION IN LATIN AMERICA THROUGH A TELEMENTORING MODEL**

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**Introduction:** Cancer rates in Latin America continue to increase significantly. There is a need for additional oncology specialists, however training and mentoring is not widely available in the region. The goal of the LAGO (Latin America Gynecologic Oncology) ECHO (Extension for Community Healthcare Outcomes) is to support Gynecologic Oncologists in Latin America through knowledge sharing and mentorship.

**Methods:** LAGO ECHO began in 2015 and is a collaboration among Latin American clinicians with support from the IGCS and MD Anderson. It consists of monthly one-hour virtual tumor boards (in Spanish) and includes case presentations as well as didactic lectures. In 2022, a formal learning curriculum was added consisting of a series of lectures focusing on evidence-based medicine. In Jan-Feb 2023, a survey was distributed to ECHO participants to assess satisfaction and knowledge changes from participation in LAGO ECHO.

**Results:** In 2022, 12 ECHO sessions were held with an average of 63 participants per session from 14 countries. Eleven patient cases were presented and discussed. 49 participants from 15 countries responded to the survey. 90% stated that they join to increase their knowledge on best clinical practices; 90% indicated that their knowledge improved or improved significantly; 96% agreed or totally agreed that they learned from the case presentations; and 98% thought the quality of the course was good or excellent.

**Conclusion/Implications:** The LAGO ECHO program facilitates collaboration among Latin American Gynecologic Oncologists. This allows sharing of best practices, increases knowledge, and provides mentoring to early career specialists.



EP096 / #1356

Topic: *AS03. Cervical Cancer*

## **COMBINATION OF CAFs AND CD8+ T CELLS TUMOR-TO-STROMA RATIO IN PREDICTING VALUE OF THE LYMPH NODE METASTASES OF CERVICAL CANCER**

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**Introduction:** Objective: To explore the cancer-associated fibroblasts (CAFs) and CD8+ T cells tumor-to-stroma ratio (T:S ratio) in cervical cancer tissue and its association with the clinicopathological indexes, and to study the predictive significance of CAFs combined with CD8+ T cells T:S ratio in lymph node metastasis of cervical cancer.

**Methods:** One hundred and ten cervical cancer tissues and thirty-nine biopsy tissues from patients were investigated immunocytochemically for the CAFs and the account of CD8+ T cells using the streptavidin-biotin-peroxidase method with respective monoclonal antibodies. The statistical correlation analysis was carried out using Spearman's correlation test and  $\chi^2$  test analysis by the SPSS system.

**Results:** Statistical analysis also revealed a correlation ( $r=-0.690$ ;  $P<0.001$ ) between CAFs and CD8+ T cells T:S ratio in cervical cancer. It was found that a higher CAFs and CD8+ T cells T:S ratio had a significant correlation with lymph node metastases ( $P < 0.001$ ). To further analysis, the combination of CAFs and CD8+ T cells T:S ratio correlated with lymph node metastases ( $P < 0.001$ ). ROC curves analysis showed that the ROC curves areas for CAFs, CD8+ T cells T:S ratio, and combination of both are 0.879 (95%CI 0.809-0.946), 0.747 (95%CI 0.654-0.841) and 0.951 (95%CI 0.912-0.991). The prediction model was verified by biopsy specimens and consistent results were obtained.

**Conclusion/Implications:** Conclusions: The combination of CAFs and CD8+ T cells T:S ratio has a high predictive value for lymph node metastasis in patients with cervical cancer. Their sensitivity and specificity are high, indicating they may hold considerable clinical value.

EP097 / #28

Topic: *AS03. Cervical Cancer*

## **IMMUNOGENICITY OF AS04-ADJUVANTED VACCINE IN FEMALES WITH EXISTING HIGH-RISK HPV INFECTION AT FIRST VACCINATION: POOLED ANALYSIS OF INDIVIDUAL DATA FROM FOUR LARGE CLINICAL TRIALS WORLDWIDE**

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**Introduction:** HPV vaccine protection has been proved in HPV naïve females, whereas there is a deficiency in the evidence of benefit in females with ongoing HR-HPV infection.

**Methods:** We pooled data from four large-scale RCTs (HPV-008 NCT00122681, HPV-039 NCT00779766, VIVIANE NCT00294047, and HPV-032/063 NCT00316693) to evaluate the immune response in females with HPV-16/18 infection at first vaccination (determined by DNA status). Seropositivity was defined as an antibody titer greater than or equal to assay cut-off: 7 ELISA units (EU)/mL for HPV-18 and 8 EU/mL for HPV-16.

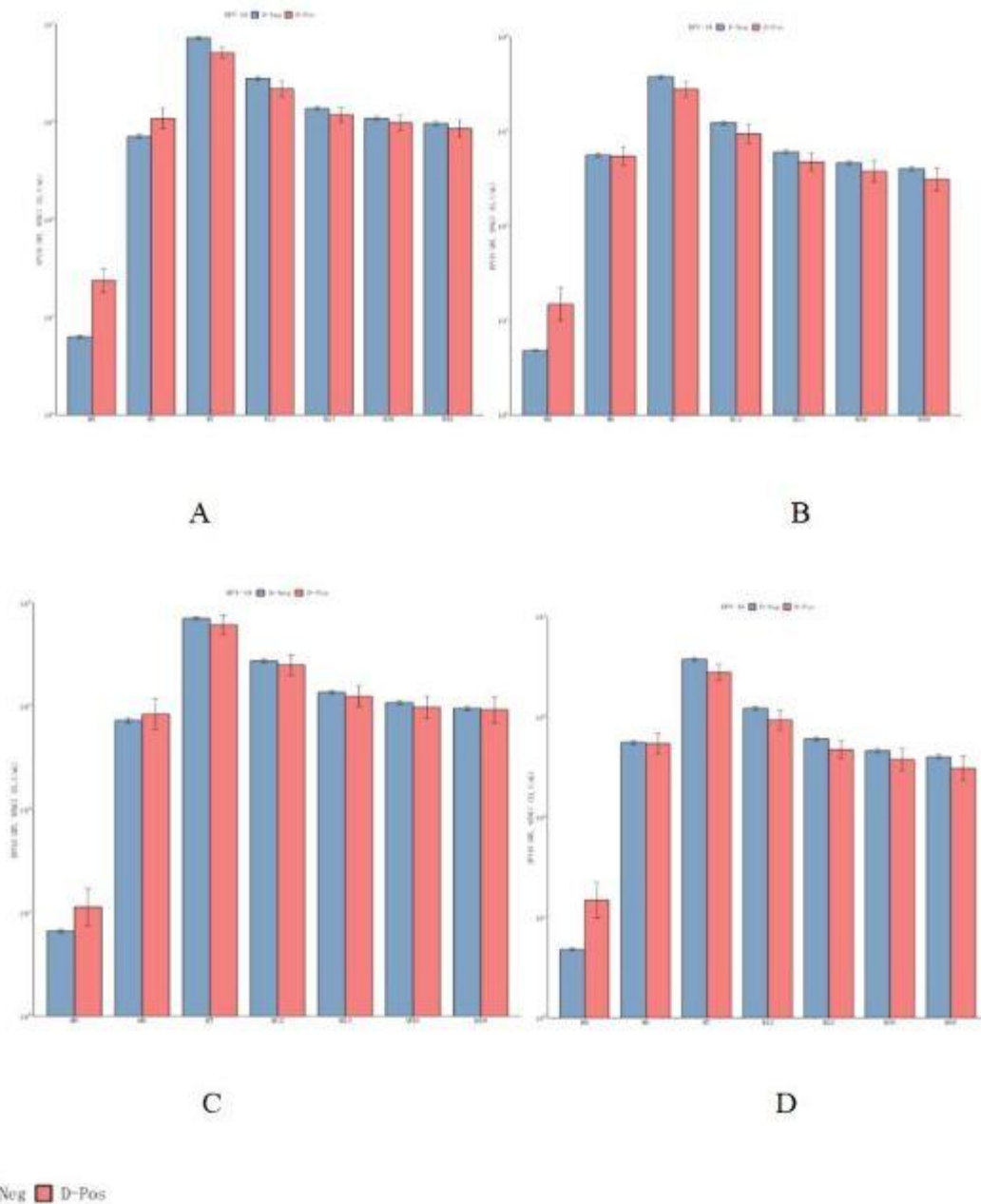
**Results:** At Month 7 after the first dose, the HPV-16/18 IgG GMTs reached peaks in both HPV-16/18 positive and negative females, and then slowly declined in a similar dynamic pattern. For antibodies in females DNA-positive for the considered HPV type at baseline, lower HPV16 GMTs were observed at Month 7 (GMT ratio 0.71 [95% CI: 0.60,0.83]) and Month 12 (0.78 [0.66,0.93]) in females HPV-16 positive, compared with those negative. Lower HPV-18 GMTs were also observed in HPV-18 positive females compared with those negative at Month 7 (0.74 [0.58,0.94]) and Month 12 (0.76 [0.59,0.99]). For antibodies in those HPV DNA-positive for one vaccine type but negative for the considered HPV type, no statistically significant differences in HPV-16/18 GMTs were observed between DNA-positive and negative females. However, until Month 48, the GMTs remained at much higher levels than those before vaccination, and the seropositive rates maintained at approximately 100%.

**Table 1. HPV-16/18 IgG GMT ratio grouped by baseline HPV-DNA status**

HPV antibody	Visit	HPV-16 DNA positive vs. negative		HPV-18 DNA positive vs. negative	
		GMT ratio	P value	GMT ratio	P value
HPV 16	Baseline	3.8 (3.20,4.51)	0.000	1.71 (1.30,2.24)	0.000
	M7	0.71 (0.60,0.83)	0.000	0.86 (0.67,1.11)	0.240
	M12	0.78 (0.66,0.93)	0.007	0.91 (0.70,1.19)	0.486
	M24	0.86 (0.72,1.03)	0.094	0.91 (0.70,1.18)	0.486
	M36	0.9 (0.73,1.1)	0.300	0.9 (0.67,1.22)	0.501
	M48	0.89 (0.72,1.11)	0.293	0.97 (0.71,1.33)	0.843

HPV antibody	Visit	HPV-18 DNA positive vs. negative		HPV-16 DNA positive vs. negative	
		GMT ratio	P value	GMT ratio	P value
HPV 18	Baseline	3.08 (2.5,3.81)	0.000	1.39 (1.21,1.60)	0.000
	M7	0.74 (0.58,0.94)	0.015	0.94 (0.81,1.11)	0.486
	M12	0.76 (0.59,0.99)	0.042	0.86 (0.72,1.03)	0.095
	M24	0.79 (0.6,1.04)	0.087	0.94 (0.78,1.14)	0.529
	M36	0.82 (0.6,1.12)	0.204	0.97 (0.79,1.21)	0.813
	M48	0.77 (0.55,1.08)	0.133	0.96 (0.77,1.21)	0.761

**Figure 1. HPV-16/18 IgG GMTs grouped by baseline HPV-DNA status**



A: HPV-16 IgG GMT grouped by baseline HPV-16 DNA status; B: HPV-18 IgG GMT grouped by baseline HPV-18 DNA status; C: HPV-16 IgG GMT grouped by baseline HPV-18 DNA status; D: HPV-18 IgG GMT grouped by baseline HPV-16 DNA status

**Conclusion/Implications:** HPV vaccine induced high and sustained immunity in women with existing HR-HPV infection. The results of our study would support vaccination recommendations and policy-making.

EP099 / #921

Topic: *AS03. Cervical Cancer*

## **RISK FACTORS OF RESIDUAL DISEASE IN PATIENTS WITH A DIAGNOSIS OF CERVICAL ADENOCARCINOMA IN SITU WHO WERE TREATED BY HYSTERECTOMY**

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**Introduction:** The incidence of cervical adenocarcinoma in situ (AIS) has recently risen in reproductive-age women. This study aimed to investigate the effects of various factors such as Pap smear, HPV, margin status, ECC, and crypt involvement on the residue of disease and outcomes of patients with AIS.

**Methods:** This study was conducted on 22 women with cervical AIS who were treated in a tertiary hospital, between 2004 and 2022.

**Results:** In this study, 22 women with AIS which was diagnosed in cone biopsy (84% in loop electrosurgical excision procedure and 16% in cold knife cone method), underwent hysterectomy. Positive internal and external margins were noted in 45.0% and positive internal margins in 9% of patients. Residual disease was detected in 7 (31%) patients; three of them had invasive carcinoma. In patients with invasive carcinoma, one had positive internal and external margins and ECC, and two others had positive internal and external margins. Although, CIN3 and SCC were noted in 3 and 1 patients of negative margins, respectively.

**Conclusion/Implications:** The results of this study indicated that hysterectomy should be recommended even in patients with negative margins; and in women with positive margins (internal or external), the re-cone biopsy should be performed before hysterectomy to detect invasive carcinoma.

EP100 / #579

Topic: *AS03. Cervical Cancer*

## **COMPARISON OF ONCOLOGICAL OUTCOMES AND COMPLICATION RATE BETWEEN RADICAL HYSTERECTOMY AND CONCURRENT CHEMORADIATION IN STAGE IIIC CERVICAL CANCER WITHOUT PARAMETRIAL INVASION**

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**Introduction:** In 2009 International Federation of Gynecology and Obstetrics (FIGO) staging, patients with stage IB or IIA with lymph node metastasis (LNM) underwent operation or concurrent chemoradiation (CCRT). However, in revised 2018 FIGO staging, patients with LNM were stage IIIC and have been underwent CCRT. The purpose of study was to compare outcome of CCRT and operation in patients with stage IIIC.

**Methods:** Total 106 patients treated either surgical treatment or CCRT for cervical cancer with pelvic and/or paraaortic lymph node metastasis were enrolled retrospectively in study. LNM was confirmed by either radiologically (IIICr) or pathologically (IIICp). We observed 55 patients underwent radical hysterectomy (type 3) between Jan 2011 and Dec 2019 and 51 patients with CCRT between Jan 2001 and Sep 2016.

**Results:** Pathological type was statistically different ( $p=0.006$ ). Operation group had more prevalence of adenocarcinoma than CCRT group (34.5% vs 7.8%). Kaplan-Meier survival curve showed both overall survival (OS,  $p=0.424$ ) and disease-free survival (DFS,  $p=0.183$ ) were not different in two group. However, operation group with LNM confirmed by both radiologically and pathologically (IIICr+p) had worse DFS than CCRT group. Complication rate (54.5% vs 19.6%,  $p<0.001$ ) and major complication (43.3% vs 20%,  $p=0.001$ ) were significantly greater in operation group. There was significant difference in recurrence pattern ( $p=0.026$ ). Operation group had less pelvic/paraaortic LN metastasis, however had more distant and pelvic side wall metastasis.

**Conclusion/Implications:** OS and DFS were not different in two groups. However, operation group with staging IIICr+p had worse DFS than CCRT group. Complication rate and grade were greater in operation group.

EP102 / #351

Topic: *AS03. Cervical Cancer*

## **SURVEY OF THE TRANSLATIONAL DYSREGULATION IN CERVICAL CANCER INITIATION AND PROGRESSION WITH RIBOSOME PROFILING**

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**Introduction:** As a critical position of the multilevel gene expression regulation program, translational regulation has been found to be widely involved in cancer initiation and progression. Cervical cancer is the second largest female malignant tumor in China. The high-resolution and genome-wide view of the landscape of RNA translation in cervical cancer is still limited.

**Methods:** We performed the ribosome profiling for 25 samples of human cervical cancer at various stages and 10 samples of normal cervical tissues, respectively. A series of bioinformatics tools was then utilized to these data for the mining of novel insights into the translational dysregulation in cervical cancer.

**Results:** This is the first translome data resource for dissecting dysregulated translation in cervical cancer at the sub-codon resolution. Our data suggested that there are significant differences in the transcriptome and translationome in cervical cancer initiation and progression. For example, multiple proteins involved in cell cycle or cell-cell adhesion exhibited significant translational upregulation and downregulation in cervical cancer when comparing with normal tissue (Fig 1). In addition, we analyzed the translome data with clinical features, which shown translational dysregulation leading to immune dysregulation may be an important reason for the progression of cervical cancer (Fig

Fig 1

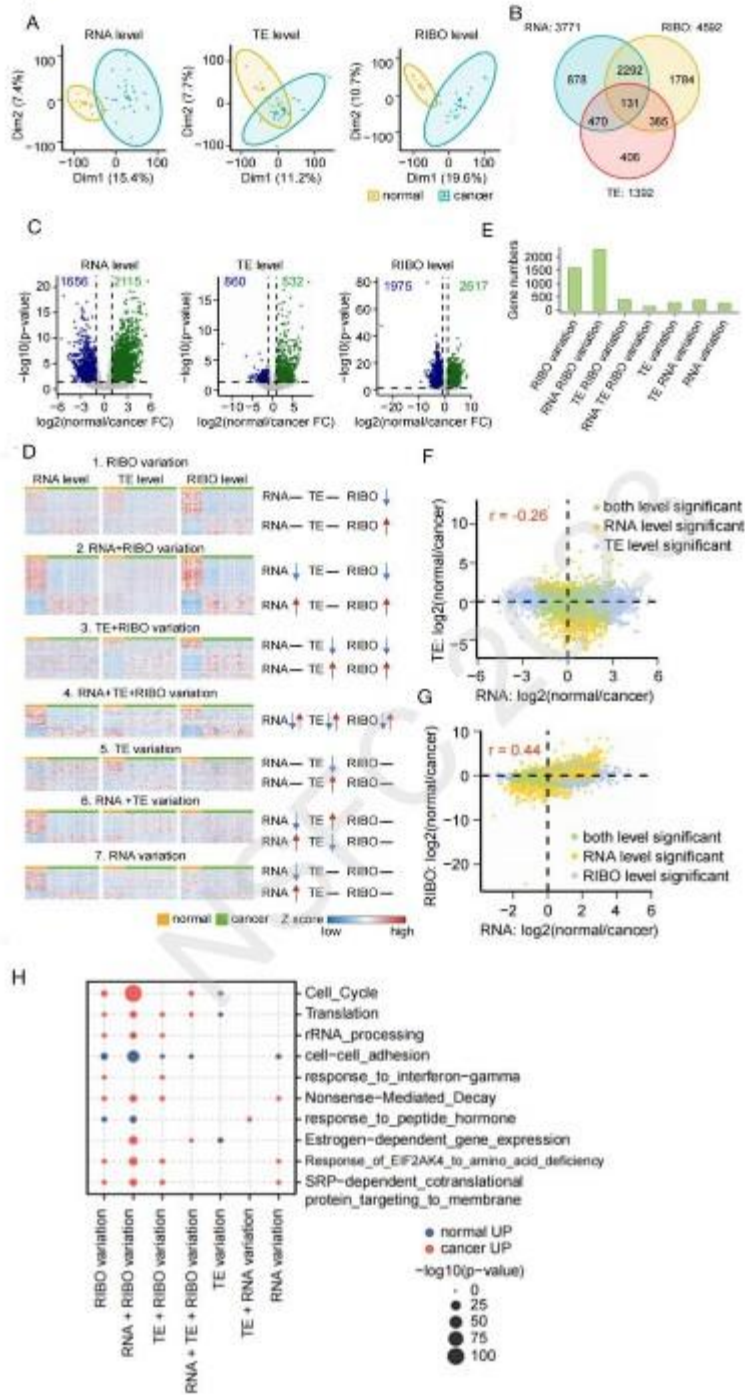


Fig 1 Translation landscape

2).



Fig 2

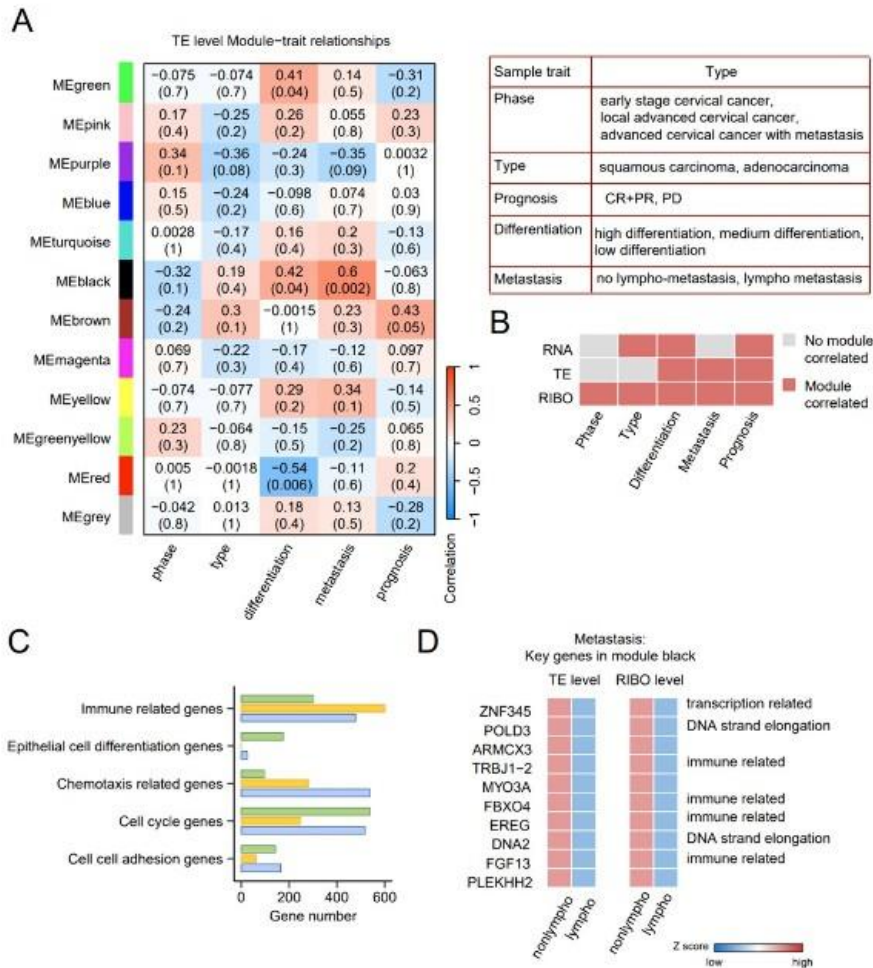


Fig 2 Analyzed the translome data with clinical features

**Conclusion/Implications:** This study has constructed the first translome of cervical cancer, which provides a valuable data resource and novel insights in cervical cancer initiation and progression.

EP103 / #441

Topic: *AS03. Cervical Cancer*

## **GENETIC ANALYSIS OF CERVICAL CANCER WITH LYMPH NODE METASTASIS**

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**Introduction:** To find out the differences in gene characteristics between patients with positive and negative cervical cancer lymph nodes, and to provide a reference for predicting lymph node metastasis of cervical cancer.

**Methods:** From January 2018 to June 2022, 112 cases of cervical cancer underwent genetic testing of 1021 cancer-related genes by next – generation sequencing were analyzed. Patients were grouped according to positive and negative lymph nodes, maftools software was used to analyze the somatic single nucleotide variation/insertion-deletion variation mutation frequency, mutation coexistence and mutual exclusion, cosmic mutation characteristics, and oncogenic signaling pathways in the two groups.

**Results:** The five genes with the highest frequency of somatic SNV/Indel mutations are: PIK3CA (39%), MLL3 (26%), MLL2 (21%), EP300 (15%), and FBXW7 (13%). Further differential analysis find EP300 and FBXW7 are significantly enriched in lymph node-positive patients. Mutation coexistence-mutual exclusion analysis find both lymph node-positive and negative patients have large number of coexisting mutations, while mutually exclusive mutations are rare, and the patterns of coexisting mutations are different between the two groups. Cosmic mutational signature analysis reveal the homologous recombination-mediated DNA repair defect signature is enriched in lymph node-positive, but not in negative patients.

**Conclusion/Implications:** The gene mutation characteristics of both are different, the somatic SNV/Indels of EP300 and FBXW7 are significantly enriched in lymph node positive patients. The co-occurrence and cosmic features of gene mutations are also different, homologous recombination-mediated DNA repair defects only exist in lymph node-positive patients. These different features may be potential molecular markers to predict lymph node metastasis in cervical cancer.

EP104 / #212

Topic: *AS03. Cervical Cancer*

## **A RETROSPECTIVE STUDY COMPARING WEEKLY VERSUS TRI-WEEKLY CISPLATIN PLUS PACLITAXEL CHEMOTHERAPY CONCOMITANT WITH RADIOTHERAPY IN THE TREATMENT OF LOCALLY ADVANCED CERVICAL CANCER**

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**Introduction:** To assess the tumor response following definitive concurrent chemoradiotherapy (CCRT) for locally advanced cervical cancer (LACC) using magnetic resonance imaging before and after treatment. The prognosis and side effects of CCRT with weekly cisplatin plus paclitaxel versus tri-weekly cisplatin plus paclitaxel should also be compared.

**Methods:** We collected clinical data from the medical records of patients diagnosed with International Federation of Gynecology and Obstetrics (FIGO 2018) stage IIB to IIIC1r LACC at Chongqing University Cancer Hospital from 1 March 2016 to 31 November 2020. A total of 191 patients who underwent MRI before CCRT and 1,3,6 months after CCRT were included in this analysis.

**Results:** With a median follow-up of 39 months, the complete response rates were 57.8% vs. 41.2% ( $P=0.026$ ) in the weekly and triweekly groups at 1 month, 72.2% vs. 60.7% ( $P=0.086$ ) and 76.6% vs. 71.3% ( $P=0.400$ ) at 3 and 6 months. Separately, the 5-year OS was 83.1% vs. 82.7% ( $P=0.690$ ) and the PFS was 80.4% vs. 83.5% ( $P=0.650$ ). Patients with residual disease  $>1\text{cm}$  and  $\leq 1\text{cm}$  had a median PFS rate of 88.3% and 57.4%, respectively ( $P=0.000$ ). An increase in toxicities were observed in the tri-weekly group in terms of grade 3/4 thrombocytopenia ( $P=0.000$ ) and grade 1/2 nausea/vomiting ( $p=0.049$ ).

**Conclusion/Implications:** Tri-weekly cisplatin & paclitaxel chemotherapy concurrent with radiotherapy showed worse short-term efficacy compared with the weekly group, and increased side effects but didn't improve PFS and OS. Patients with residual disease measuring more than 1 cm associated with worse PFS.

PR015 / #791

Topic: *AS03. Cervical Cancer*

## **MEASURING THE RISK-BENEFIT OF OBSTETRIC AND ONCOLOGIC ASPECTS OF FERTILITY-SPARING SURGERY AMONG EARLY CERVICAL CANCER $\geq 2$ CM: IMPLICATIONS CAPTURED IN SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Introduction:** Composing approaches to early cervical cancer (CC  $\geq 2$  cm in tumor size) in fertile years implicates around the preservation of the reproductive function; on whether the following intervention (i.e., operative procedures with/without neoadjuvant chemotherapy (NACT)) offer acceptable child-bearing potential within an estimable risk of cancer recurrence? This study aims to measure the obstetric and oncologic outcomes among woman with early CC  $\geq 2$  cm treated by fertility-sparing management.

**Methods:** This study is in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) to review cohorts from the last decade, focused on fertility-sparing intervention among woman with CC  $\geq 2$  cm. The obstetric outcome is consisted by pregnancy rate (PR), living-birth rate (LBR), and pre-term rate (PtR); supported by the recurrence rate (RR) and moderated by NACT status. The statistical analyses were performed with random-effect model (REM) in Comprehensive Meta Analysis (CMA) version 3.0.

**Results:** We included 16 studies encompassed by 499 individuals to the final analysis. The estimated overall obstetrical outcomes were 32.4%, 58.5%, and 37.1%, respectively. Prior NACT administration proved to increase the outcomes e.g., PR (47.6% vs. 22.5%) and LBR (73.1% vs. 35.7%); though the findings were not observed on PtR (37.1% vs. 33.3%). Interestingly, we also found that the RR was higher among NACT+ populations (12.1%) compared to its control (5.1%).

**Conclusion/Implications:** Fertility-sparing treatment may substantially affect the obstetric outcomes among women with CC  $\geq 2$  cm which can be improved by NACT administration, though our study revealed a possibility of worse oncologic outcomes among NACT-receiving individuals.

EP105 / #527

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **ABERRANT BETA-CATENIN DISTRIBUTION AS POTENTIAL PROGNOSTICATOR FOR ENDOMETRIOID ENDOMETRIAL CANCER**

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**Introduction:** Aberrant beta-catenin distribution has been theorized as a predictive biomarker for recurrence in early stage, low grade endometrioid endometrial cancer.

**Methods:** Retrospective single institution cohort study of 298 endometrioid endometrial cancer patients 5/2018-2/2022. Demographic and tumor molecular characteristics collected. Beta-catenin status defined as aberrant nuclear distribution, wild-type plasma membrane distribution. X<sup>2</sup> test, Fisher test, adjusted multivariable logistic regressions, sensitivity analyses were performed.

**Results:** Most tumors were stage IA (55.4%) grade 1 (65.8%). 45.3% of tumors aberrant beta-catenin, 70% MMR proficient, 94% p53 wild type, 95% POLE wild type, 98% ER positive, 97.3% PR positive. Aberrant beta-catenin distribution in 74.1% of FIGO grade 1 tumors, 22.5% of LVSI tumors and in 69% of patients younger than 70 years. Aberrant status in 39.6% of recurrences vs. 46.4% without recurrence (p=0.38). Recurrences in the vagina (29.2%), lung (25%). In early stage, low grade cohort, recurrence did not vary by beta-catenin status (42.9% of aberrant with recurrence versus 47.2% of aberrant without recurrence (p=0.71). In the NSMP cohort, recurrence did not vary by beta-catenin status (61.9% recurred vs. 53.2% did not recurred) (p=0.45). In adjusted logistic regression, aberrant beta-catenin distribution did not affect disease recurrence in the overall cohort with aOR 1.12 [95% CI 0.50-2.48], early stage/low grade cohort with aOR 1.03 [0.35-3.10], and the NSMP cohort with aOR 0.58 [0.14-2.56]. Among tumors that received adjuvant RT (n=84), 2.86% aberrant beta-catenin tumors recurred vs. 8.16% wild-type beta-catenin recurred.

**Conclusion/Implications:** Aberrant beta-catenin distribution did not significantly correlate with recurrence in early stage, low grade endometrioid uterine cancer

EP106 / #616

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **OUR SINGAPOREAN EXPERIENCE IN ADOPTION OF FERTILITY SPARING STRATEGIES FOR ENDOMETRIAL HYPERPLASIA AND CANCER**

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**Introduction:** Endometrial Cancer (EC) is the commonest gynaecological cancer in Singapore and affects an increasing number of women desiring fertility. With increasing recognition that fertility-sparing options of treatment are feasible in carefully selected cases, our institution developed a protocol to manage such patients. We report the characteristics of this pilot cohort of patients and describe their oncological and fertility outcomes.

**Methods:** Patients undergoing conservative treatment for EC and endometrial hyperplasia (EH) were identified from the gynaecologic oncology tumour group database. A total of 27 patients were identified between January 2015 to May 2022. Information was obtained from their electronic medical records.

**Results:** The average age of the women was 37 years, of which almost all of them were overweight. Of the 27 women desiring fertility, 16 women had EC, and 11 women had EH. Regression to benign histology was noted in 100% in EH group, and 81% in EC, median time to regression to benign histology was 11.4 and 10 months respectively. 26% in EH group and 31% in EC group recurred within 33 and 8 months respectively. 2 women in EC group underwent IVF and 1 patient became pregnant spontaneously and subsequently had a live birth. One patient failed fertility-sparing treatment, was diagnosed with stage IIIC serous cancer, and underwent definitive surgical debulking and adjuvant systemic therapy.

**Conclusion/Implications:** Fertility-sparing treatment appears to be a safe management option in women with EC or EH desiring fertility. Multi-disciplinary patient support improves patient compliance and treatment outcomes.

EP107 / #402

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **A PROSPECTIVE STUDY ON THE ROLE OF HISTOLOGICAL AND MOLECULAR FEATURES IN PREDICTING NODAL DISEASE IN ENDOMETRIAL CANCER**

Giorgio Bogani<sup>1</sup>, Jvan Casarin<sup>2</sup>, Fabio Ghezzi<sup>2</sup>, Mariangela Longo<sup>2</sup>, Elisa Ervas<sup>3</sup>, Antonino Ditto<sup>4</sup>, Francesco Raspagliesi<sup>1</sup>

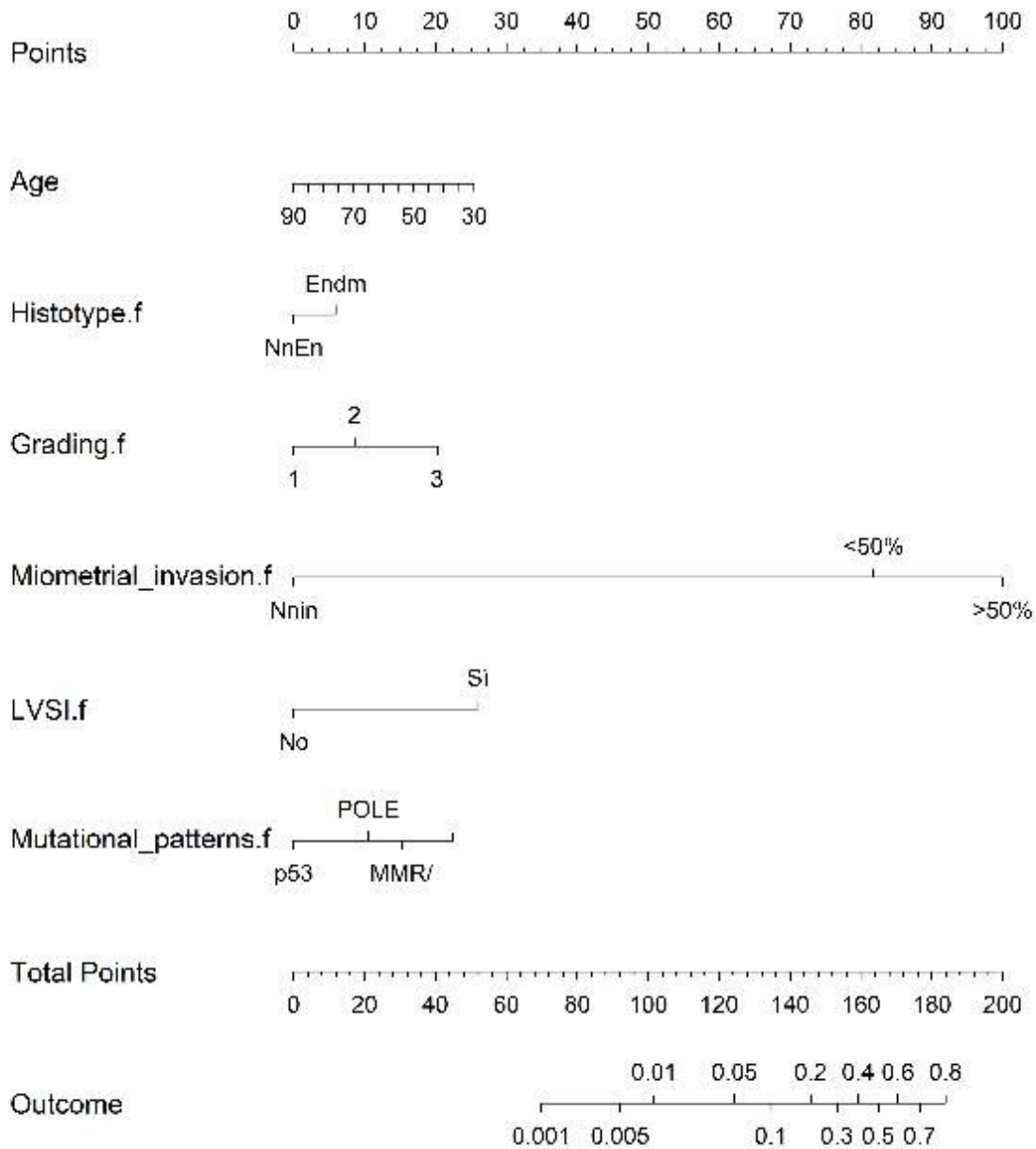
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**Introduction:** To assess the role of histopathological and molecular features in predicting the risk of nodal metastases in apparent early-stage endometrial cancer (EC) patients undergoing sentinel node mapping.

**Methods:** This is a prospective multicenter trial. Consecutive patients with apparent early-stage EC undergoing laparoscopic hysterectomy, bilateral salpingo-oophorectomy, and sentinel node mapping were enrolled. Histological and molecular features were recorded at the final pathological evaluation and were used to predict node positivity.

**Results:** Charts of 210 EC patients were evaluated. The study population included 178 (85%) and 32 (15%) patients with endometrioid and non-endometrioid EC, respectively. According to conventional pathological uterine characteristics, 94, 46, 41, and 32 were classified as low, intermediate, intermediate-high, and high-risk, respectively. According to molecular classification 10 (5%), 42 (20%), 57 (27%), and 101 (48%) were included in the POLE mutated, p53 abnormal, MMRd/MSI-H, and NSMP, respectively. Overall, 41 (19.5%) patients were detected with positive nodes. Molecular features were not associated with the risk of having nodal metastases (OR: 1.03 (95%CI: 0.21, 5.95; p=0.969) for POLE mutated; OR: 0.788 (95%CI: 0.32, 1.98; p=0.602) for p53 abnormal; OR: 1.14 (95%CI: 0.53, 2.42); p=0.733 for MMRd/MSI-H). At multivariate analysis, only myometrial invasion (OR: 3.33 (95%CI: 1.40,7.80); p=0.006) and LVSI (OR: 6.03 (95%CI: 2.56, 15.4); p<0.001) correlated with nodal status. A nomogram evaluating the impact of pathological and molecular features on nodal status was built (C-index 0.78,

Figure)



**Conclusion/Implications:** Our prospective study suggested that molecular features seem not helpful in tailoring the need for nodal dissection in EC. Further external validation is warranted.



Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **MULTIPLE CLASSIFIER ENDOMETRIAL CANCER: A MULTICENTER STUDY**

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<sup>1</sup>Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Gynecologic Oncology, Milano, Italy, <sup>2</sup>University of Insubria, Gynecologic Oncology Unit, Varese, Italy, <sup>3</sup>European Institute of Oncology, Gynecologic Oncology, Milan, Italy, <sup>4</sup>Mayo Clinic, Department Of Obstetrics And Gynecology, Rochester, United States of America, <sup>5</sup>Mayo Clinic, Obstetrics And Gynecology, Rochester, United States of America, <sup>6</sup>University of Parma, Gynecologic Oncology, Parma, Italy, <sup>7</sup>University of Udine, Gynecologic Oncology, Udine, Italy, <sup>8</sup>University of Sassari, Gynecologic Oncology, Sassari, Italy, <sup>9</sup>University of Florence, Gynecologic Oncology, Florence, Italy, <sup>10</sup>University of Milan-Bicocca and Gynecologic Oncology Program, European Institute of Oncology IRCCS, Department Of Medicine And Surgery, Milan, Italy, <sup>11</sup>Filippo Del Ponte Hospital, University of Insubria, Department Of Obstetrics And Gynecology, Varese, Italy, <sup>12</sup>University La Sapienza, Gynecologic Oncology Unit, Rome, Italy

**Introduction:** The growing adoption of molecular and genomic characterization is changing the current landscape of treatment of endometrial cancer (EC) patients. Using the surrogate molecular classification EC patients are classified in four subgroups: POLE mutated, MMRd/MSI-H, p53 abnormal, and no specific mutational profile (NSMP). However, there are few patients (called multiple classifier) harboring two or more mutational patterns. Since the rarity of this occurrence, evidence regarding multiple classifier is still limited. Here, we described characteristics and outcomes of multiple classifier.

**Methods:** This is a multi-institutional retrospective study. Apparent early-stage EC patients undergoing were evaluated via conventional pathological analysis and via immunohistochemistry and next generation sequencing.

**Results:** Charts of 72 multiple classifier were reviewed. Median (range) follow-up was 9.8 (1.2, 37.5) months. Overall, 31 (43%) patients had a POLE mutation. Patients with POLE plus MMRd/MSI-H, POLE plus p53, and POLE plus MMRd/MSI-H, and p53 were 6 (8.3%), 20 (27.8%), and 5 (6.9%), respectively. Among those 31 patients, six had postoperative adjuvant therapies, and no recurrence occurred (median follow-up: 10.5 months (seven patients had at least 2-year follow-up)). Forty-one (56.9%) patients were diagnosed with tumors harboring both p53 plus MMRd/MSI-H. Adjuvant therapy was administered in 25/41 patients (60.9%). Four (9.8%) recurrence occurred after a median follow-up of 8.9 months (eleven non-recurring patients had at least 2-year follow-up).

**Conclusion/Implications:** Multiple classifier EC are characterized by a good prognosis. POLE mutation seems confer protection in multiple classifier EC even in case of presence of MMRd/MSI-H and/or p53 abnormality. Prospective studies with long-term follow-up are needed.

EP109 / #1527

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **THE APPLICATION VALUE OF DUAL GENE METHYLATION DETECTION FOR ENDOMETRIAL CANCER IN WOMEN WITH ABNORMAL UTERINE BLEEDING**

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**Introduction:** To explore the clinical value of dual gene (CDO1 and CELF4) methylation test for endometrial cancer in women with abnormal uterine bleeding.

**Methods:** From July to June 2022, 216 female patients with abnormal uterine bleeding were enrolled in the gynecologic clinic of Gansu Provincial Woman & Child Medical Center. The exfoliated cervical cells were collected for dual gene methylation detection, and the basic information, tumor biological markers, and endometrial thickness of patients were collected. The clinical statistics of dual gene methylation detection for endometrial cancer in women with abnormal uterine bleeding were analyzed.

**Results:** The following factors were associated with endometrial cancer in univariate analysis: age, BMI, diabetes mellitus, number of births, menopause, CDO1 methylation, and CELF4 methylation (all  $p < 0.001$ ). Binary logistic regression analysis showed that BMI, diabetes mellitus, menopause, CDO1 methylation, and CELF4 methylation were independent risk factors for endometrial cancer (OR: 4.062, 3.504, 17.484, 20.555, and 66.599, respectively). The dual gene methylation assay had a sensitivity and specificity of >90% and >95%, respectively. The sensitivity and specificity of endometrial thickness by ultrasound and CA125 were <60% and <80%, respectively. Dual gene methylation detection is more sensitive and specific than the current gynecological examination for the detection of endometrial cancer.

**Conclusion/Implications:** Using non-invasive dual gene methylation assay to screen women with suspected endometrial cancer of abnormal uterine bleeding for hysteroscopy may reduce the risk of endometrial cancer and improve the ability of the clinic to perform noninvasive early detection, it also reduces the need for repeated invasive hysteroscopy in women.

EP111 / #1490

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **PROTEOGENOMICS DELINEATE PATHOGENESIS, MOLECULAR CHARACTERISTICS, AND PREDICTORS OF PROGESTIN RESPONSE IN EARLY-ONSET ENDOMETRIOID ENDOMETRIAL CANCER**

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**Introduction:** Endometrial carcinoma (EC) remains a public health concern with a growing incidence particularly in younger women. Women with early-onset endometrioid EC (EEEC) who wish to maintain fertility are a worldwide concern, and biomarkers for predicting which patients will respond to progestin-based fertility-sparing therapy are a major unmet clinical need.

**Methods:** To comprehensively characterize the proteogenomic characteristics of the early-onset endometrioid endometrial carcinoma (EEEC), we conducted a multi-omics study (genomics, and proteomics) with FFPE tissues from paired tumor and normal tissues of 222 endometrioid ECs (including 81 EEECs younger than 40 who mainly received fertility-sparing treatment ) and 14 atypical endometrial hyperplasia (AEH) patients from Tongji and Fudan Hospital (TJFD cohort) in China.

**Results:** EEEEC was featured by exclusive germline mutations, a higher BMI and downstream dysregulated lipid metabolism signaling. Our integrated multi-omics analysis unexpectedly revealed an exposome-related mutational signature to be associated with EEEEC leading to EEEEC specific CTNNB1 and SIGLEC10 hotspot mutations and downstream protein pathway disturbance. Interestingly, in EEECs SIGLEC10<sup>Q144K</sup> mutation resulted in aberrant Siglec-10 protein expression and promoted progestin resistance by interacting with ER $\alpha$ . We identified and validated four (EEF1E1, ILVBL, SRPK1 and NUDT5) biomarkers of progestin resistance.

**Conclusion/Implications:** Our study provides a unique high-quality proteogenomic resource of EEECs, and explicates the distinct clinical and molecular characteristics of EEECs, encompassing obesity, genetic susceptibility, and environmental exposure, that are concomitant with pathogenesis and progestin resistance. Furthermore, we identified biomarkers for progestin response in EEEEC fertility-sparing treatment. These attributes can be utilized to promote primary prevention and early detection of EEECs

EP112 / #1491

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **PROTEOGENOMICS DECIPHER DISTINCT METASTASIS PATTERNS AND BIOMARKERS OF ENDOMETRIAL CARCINOMA**

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**Introduction:** Endometrial carcinoma is a common gynecologic malignancy, and lymph node metastasis greatly affects patient outcomes. Proteogenomics analysis has emerged as a powerful tool for identifying molecular mechanisms involved in cancer progression and metastasis, offering potential for biomarkers discovery and personalized treatment strategies.

**Methods:** In this study, we utilized WES, proteomics, and multiplex immunohistochemistry to investigate the metastasis patterns of different molecular subtypes in a cohort of 96 EC patients with lymph-node metastasis and 126 without metastasis. Our aim was to elucidate the molecular characteristics that distinguish between these two groups and identify potential biomarkers for metastasis.

**Results:** Proteogenomics analysis identified two distinct metastasis patterns of EC associated with TME. One pattern is characterized by an immune-cold phenotype, which is predominantly observed in patients with the MSI subtype. These patients often exhibit JAK1 mutations, defects in immunoproteasome components and HLA complexes, leading to deficiencies in antigen presentation pathways, resulting in immune evasion. The other is characterized by an immune-hot phenotype, mainly distributed in the CNL and few MSI subtype, with significant infiltration of macrophages and upregulation of integrin pathways, promoting tumor cells to undergo mesenchymal transition. Additionally, we explored and validated three consensus biomarkers shared across different molecular subtypes for predicting lymph-node metastasis.

**Conclusion/Implications:** Our research provides an unprecedented large-scale multi-omics resource of lymphatic metastasis EC, offering novel insights and new biomarkers for effectively stratifying high-risk patients for lymphatic metastasis. We have deciphered two distinct metastasis patterns in EC, which can be exploited for the development of personalized screening and targeting strategies.

EP113 / #220

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **COMPOUND AC1Q3QWB UPREGULATES CDKN1A AND SOX17 VIA INTERRUPTING THE HOTAIR-EZH2 INTERACTION AND ENHANCES THE EFFICACY OF TAZEMETOSTAT IN ENDOMETRIAL CANCER**

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**Introduction:** Endometrial cancer (EC) is a common female reproductive system malignant tumor, with increasing incidence rates and poor prognosis in recurrent/metastatic cases. The interaction between long non-coding RNA HOTAIR and polycomb repressive complex 2 (PRC2) causes the abnormal suppression of tumor suppressors, which plays a crucial role in tumor development. This study aims to investigate the potential of AC1Q3QWB (AQB) to interrupt the HOTAIR-EZH2 interaction in EC and evaluate a novel combination therapy of AQB and tazemetostat (TAZ).

**Methods:** RNA immunoprecipitation (RIP) and chromatin isolation by RNA purification (ChIRP) assays were utilized to verify the interference of AQB with HOTAIR-EZH2 interaction in EC cells. The Agilent Human ceRNA Microarray was employed to identify tumor suppressors upregulated by AQB and TAZ, while the chromatin immunoprecipitation (ChIP) assay was performed to investigate the mechanism of genes activation. The combination therapy of AQB and TMZ was used for in vivo experiments.

**Results:** AQB inhibited HOTAIR and EZH2 binding in EC cells, restoring the expression of numerous tumor suppressors. In vitro, the combination of AQB and TAZ produced a synergistic effect, significantly upregulating CDKN1A and SOX17, which resulted in cell cycle arrest and inhibited the proliferation, migration and invasion of EC cells. Additionally, it showed that AQB can enhance the anti-tumor effect of TAZ in vivo.

**Conclusion/Implications:** AQB has demonstrated a promising inhibitory effect on EC cells. When combined with TAZ, the expression of CDKN1A and SOX17 was significantly upregulated, resulting in more potent anti-tumor effects. This combination therapy could provide a novel strategy for treating EC.

EP114 / #688

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **EVALUATING CDK 4/6 INHIBITORS IN COMBINATION WITH ENDOCRINE THERAPY IN ENDOMETRIAL CANCERS: A RETROSPECTIVE STUDY**

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**Introduction:** CDK 4/6 inhibitors (CDK4/6i) with endocrine therapy (ET) has promising phase II results in estrogen receptor (ER)+ recurrent/advanced endometrial cancer (EC). The purpose of our study is to evaluate characteristics and clinical outcomes of patients with ER+EC who have received a CDK4/6i+ET at our institution.

**Methods:** This is a multi-center institution retrospective chart review, which included patients diagnosed with endometrial cancer and treated with CDK4/6i+ET between 2016- March 2023 for  $\geq 1$  month in duration. Outcomes evaluated included time to treatment failure (TTF) and progression free survival (PFS).

**Results:** Thirteen patients were identified, with an average age of diagnosis at 61 years (IQR: 50-68). The most common histopathologic diagnosis was endometrioid (n=8, 61.5%), followed by endometrial stromal sarcoma (ESS) (n=4, 30.8%). The median follow-up after CDK4/6i was 8.6 months (IQR 4.7-17.5). The median number of treatments since recurrence was 2, including 9 with prior ET. The TTF in the endometrioid group was 5.1 months (95% CI 3.8-NR), where PFS was not reached (NR) (95% CI 5.4-NR). The TTF and PFS in the ESS group was the same at 9.8 months (95% CI 7.9-NR). Four patients were still on treatment upon study completion, five patients discontinued due to disease progression, and four discontinued because of toxicity.

**Conclusion/Implications:** Patients with ER+EC have reasonable responses to CDK4/6i+ET with the majority of patients with endometrioid histology discontinuing due to toxicity rather than progression. This data supports the findings from the previously published clinical trials that CDK4/6i+ET should be considered as a treatment option in recurrent ER+EC.

EP115 / #847

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **CORRELATION BETWEEN MISMATCH REPAIR STATUS AND LYMPH NODE METASTASIS IN ENDOMETRIAL CANCER**

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**Introduction:** Endometrial cancer is the most common gynecologic malignancy worldwide, and lymph node metastasis is a major prognostic factor for patients with this cancer. Mismatch repair (MMR) deficiency is known to play a critical role in the development of endometrial cancer, but its association with lymph node metastasis and recurrence remains unclear. In this study, we aimed to investigate the correlation between MMR status and lymph node metastasis/recurrence rate in endometrial cancer.

**Methods:** We retrospectively analyzed 59 patients with endometrial cancer who underwent surgery and received MMR testing at our institution between 2010 and 2022. Immunohistochemistry was performed to assess the expression of MMR, including MLH1, PMS2, MSH2, and MSH6.

**Results:** Of these patients, 14 (23.7%) had MMR deficiency. The MMR deficient group had a higher proportion of early stage (stage I and II) compared to the MMR proficient group (78.6% vs. 64.4%). However, lymph node metastasis was more common in the MMR deficient group (21.4%) compared to the MMR proficient group (13.3%) ( $p=0.038$ ). Furthermore, the recurrence rate was higher in the MMR deficient group (21.4% vs. 15.6%).

**Conclusion/Implications:** Therefore, MMR status may serve as a useful biomarker to predict the risk of lymph node metastasis and recurrence in patients with endometrial cancer. Based on our findings, knowing the MMR status before surgery may help in determining an appropriate surgical plan, which could potentially improve the prognosis and quality of life of the patients. Further studies with larger sample sizes are needed to validate our findings.

EP116 / #189

**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **RADIOGRAPHER LED INSERTION OF POST-OPERATIVE VAGINAL APPLICATOR FOR ENDOMETRIAL CANCER BRACHYTHERAPY: CLATTERBRIDGE CANCER CENTRE EXPERIENCE**

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**Introduction:** Vaginal vault brachytherapy (VBT) using post-operative vaginal applicator (POVA) has been a standard adjuvant treatment for endometrial cancer and reduces the risk of local recurrence. The Clatterbridge Cancer Centre (CCC) has offered VBT since the start of the service. Radiographer-led delivery of POVA was implemented to free up clinician time and improve service delivery. Historically all POVA insertions were carried out by the clinicians. More recently clinicians have performed the initial assessment and applicator placement for the first insertion and the subsequent insertions were then carried out by competent radiographers. The aim of this study was to evaluate the safety and effectiveness of radiographer-led delivery for subsequent treatments.

**Methods:** This is a retrospective audit of endometrial cancer patients treated with VBT between 31st March 2020 and 28<sup>th</sup> February 2023. The aim is to identify the frequency of clinician input for the subsequent treatments and identify any complications.

**Results:** During the specified time period, 278 patients were treated with VBT amounting to a total of 724 treatments. All of the 278 planned first fractions were carried out by the clinicians and only 15 of the subsequent 446 treatments required clinician input. 431 (96.6%) treatments were carried out solely by the radiographers. There were no procedure related complications noted. Some of the reasons requiring clinician input were radiographer unavailability, anxious and tense patients requiring change in the size of applicator and vaginal bleeding requiring examination.

**Conclusion/Implications:** Radiographer led VBT is safe, effective, frees up clinician time, improves service delivery and streamlines work force utilisation.



EP117 / #831

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **ARE WE UNDERUTILIZING STEREOTACTIC BODY RADIOTHERAPY IN THE TREATMENT OF OLIGOMETASTATIC UTERINE CANCER?**

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**Introduction:** Oligometastatic disease is an intermediate state between locoregional disease and widely metastatic disease. Previous work by our group showed a significant difference between the median survival of uterine cancer patients with a single metastatic site versus multiple sites, hence we defined our oligometastatic cohort as having one metastatic site at diagnosis. In our current analysis we explore the trends of stereotactic body radiotherapy (SBRT) use in this oligometastatic population.

**Methods:** The National Cancer Database was analyzed in patients diagnosed with uterine cancer between 2004-2019. We excluded patients with non-metastatic disease at diagnosis, lack of metastatic sites listed, multiple primaries and missing survival data. We included patients treated with radiotherapy and defined SBRT as  $\leq 5$  fractions and  $\geq 500$ cGy dose per fraction.

**Results:** Among 641,276 women with uterine cancer, 17,343 remained after exclusion and 12,214 had oligometastatic disease. 23.7% of metastatic patients received radiation (4.3% SBRT) and 22.0% of oligometastatic patients received radiation (3.2% SBRT). Among the oligometastatic SBRT cohort, patients received a median total dose of 21 Gy (range 800 cGy-67 Gy). SBRT sites include: brain (46.3%), uterus (11%), lung (9.8%), spine (8.5%), pelvis (7.3%), extremity bone (6.1%), other bone (4.8%), vagina (2.4%), liver (1.2%), lymph node (1.2%) and other (1.2%). SBRT patients had a median age of 63, low comorbidity index scores, and were high income earners.

**Conclusion/Implications:** SBRT is underutilized in the treatment of uterine cancers, particularly in oligometastatic disease. Increasing the use of SBRT may have implications for increasing overall survival in oligometastatic uterine cancer.

EP119 / #398

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **RECURRENT POSTMENOPAUSAL BLEEDING: PATHOLOGICAL OUTCOMES AND PROGNOSTIC FACTORS. A MULTICENTER OBSERVATIONAL STUDY.**

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**Introduction:** Recurrent postmenopausal bleeding (PMB) occurs in 6-25% of postmenopausal women. Controversy exists as to whether recurrent PMB leads to a higher risk of endometrial cancer (EC) in comparison to a first presentation of PMB. Additionally, little is known about predictive factors for recurrent PMB.

**Methods:** We conducted an observational multicenter prospective cohort study over a 7 year period in four hospitals in the Netherlands. Women aged  $\geq 40$  years with PMB undergoing endometrial sampling were included after written consent was obtained. Occurrence of recurrent PMB was retrospectively determined. Chi-square, univariate and multivariate analysis were performed using SPSS28 to compare pathological outcomes and identify predictive factors. Central study approval was obtained (MEC 2015-740).

**Results:** We included 468 women, of whom 28% experienced recurrent PMB. Median follow-up time was 61 months (IQR 54-69). Compared to women with recurrent PMB, women with one episode of PMB were more often diagnosed with a malignancy (RR 1.979, 95% CI 1.071-3.657,  $p=0.023$ ) and less frequently with benign polyps (RR 0.735, 95% CI 0.547-0.987,  $p=0.045$ ). Identified predictive factors for recurrent PMB include higher BMI (OR 1.041, 95% CI 1.004-1.079,  $p=0.03$ ) and use of hormone replacement therapy (HRT) (OR 2.754, 95% CI 1.476-5.138,  $p=0.001$ ). Presence of polyps was not independently associated with recurrence (OR 1.527, 95% CI 0.978-2.385,  $p=0.063$ ).

**Conclusion/Implications:** Recurrent PMB occurred in 28% of postmenopausal women. Women with recurrent PMB were less often diagnosed with malignancies and more frequently with benign polyps, compared to women with one episode of PMB. Predictive factors for recurrent PMB include high BMI and HRT.

EP123 / #1544

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **IDENTIFICATION OF A DNA DAMAGE RESPONSE RELATED PROGNOSTIC MODELS IN ENDOMETRIAL CANCER**

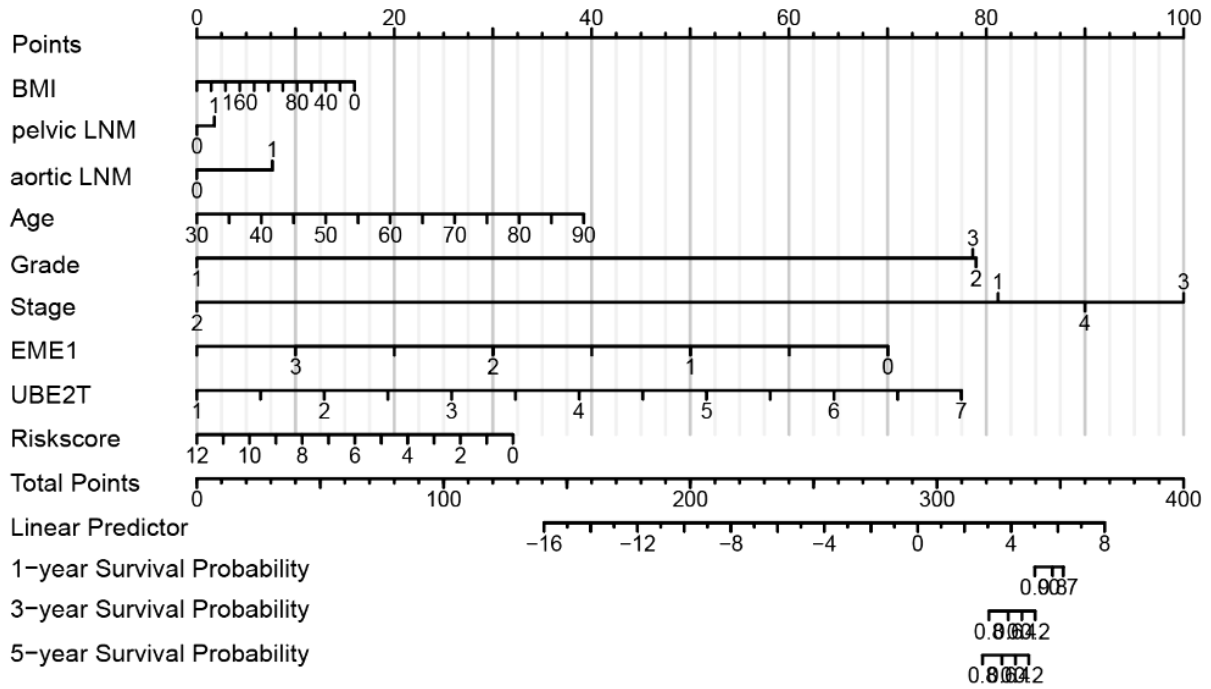
Xuan Feng, Jingyi Zhou, Jianliu Wang

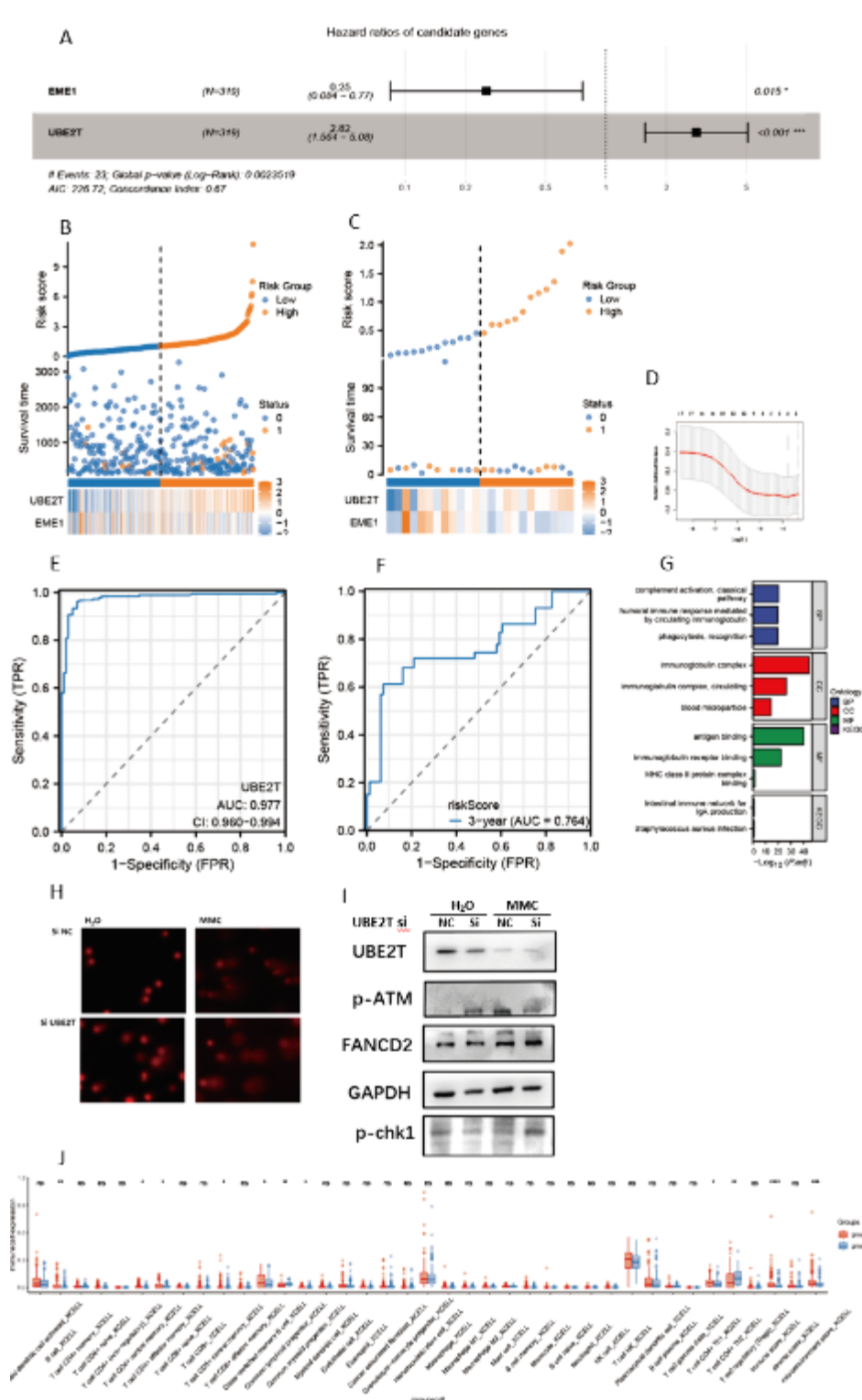
Peking university people's hospital, Obstetrics And Gynecology, Beijing, China

**Introduction:** Genomic instability is a hallmark of cancers, which leads to tumor heterogeneity and tolerance to chemoradiotherapy thus affecting the prognosis. Exploring the DDR gene in the prediction of prognosis, response of ICB and anti-tumor therapy is of great importance.

**Methods:** RNA-seq data was from 19 endometrial cancer patients. 585 patients' data were from TCGA. Cox, Kaplan Meier, and Lasso logistic regression were used to screen the univariate factor and build the DDR nomogram. R "limma" package was used to analyze the DEGs between the high and low-risk groups. Enrichment analysis was achieved. Immune infiltration status and ICB response prediction were performed. r-H2AX foci after UBE2T knockdown were analyzed. Comet assay was used to observe the DNA damage caused by UBE2T knockdown. Western blot was used to investigate DDR protein expression.

**Results:** A DDR-related nomogram containing UBE2T and EME1 was established. UBE2T expression increased in high-risk group. The high-risk group showed different infiltration patterns. DDR nomogram exhibits an AUC of 0.764 to predict 3-year prognosis. UBE2T showed an AUC of 0.977 to predict 3-year prognosis. UBE2T mono-ubiquitinating FANCD2 is a critical process in ICL repair. Comet assay showed UBE2T knockdown-induced DNA damage, which is enhanced after MMC treatment. FANCD2 ubiquitin decreased after UBE2T knockdown. p-Chk1 and p-ATM increased when exposed to MMC. UBE2T expression level is related to immune receptors such as TNFRSF14, etc.





**Conclusion/Implications:** A DDR genes nomogram with UBE2T as a key variable was identified. This study may help risk stratification and promote DDR agent and ICB use in endometrial cancer.

EP124 / #764

**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **NATURAL COMPOUND BAICALEIN SYNERGIZES WITH AMP-ACTIVATED PROTEIN KINASE ACTIVATOR SR04 IN ENDOMETRIAL CANCER BY INHIBITION OF PI3K/MTOR AND STAT3 WITHOUT ACTIVATING AKT OR MAPK**

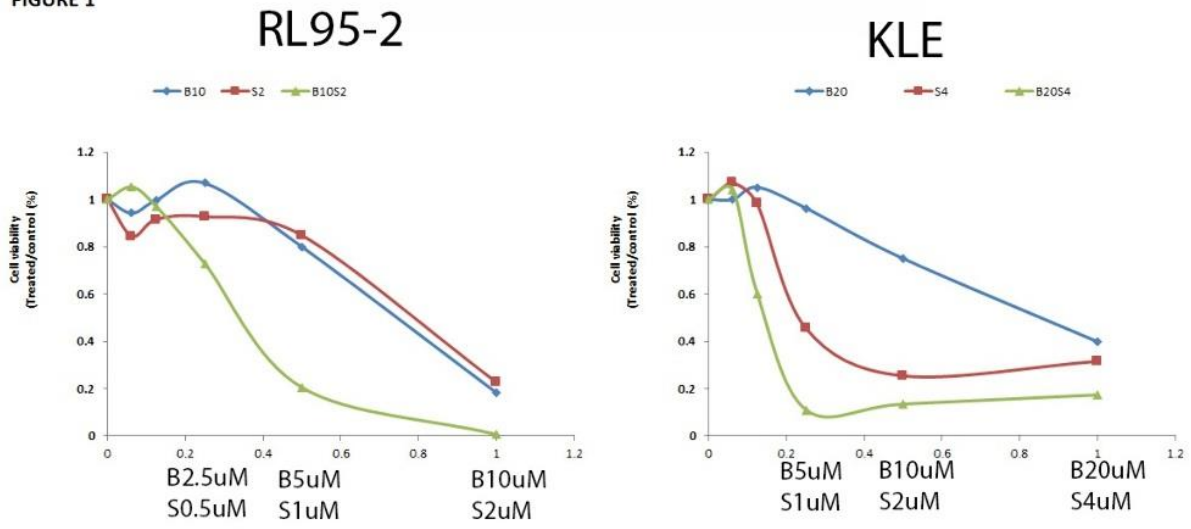
Ernest Han, Jin Yan, Quanhua Xing, Wei Wen, Alison Dumitriu, James Figarola, John Yim  
City of Hope, Department Of Surgery, Durate, United States of America

**Introduction:** Loss of PTEN expression is common in endometrial cancer. The PI3K/mTOR pathway has been a target, but counter-regulatory pathways via Akt and ERK may hinder efficacy. We previously showed that the natural flavonoid baicalein inhibits cell growth via mTOR pathway. We investigated the effects of a novel AMPK activator SR04 in combination with baicalein in endometrial cancer.

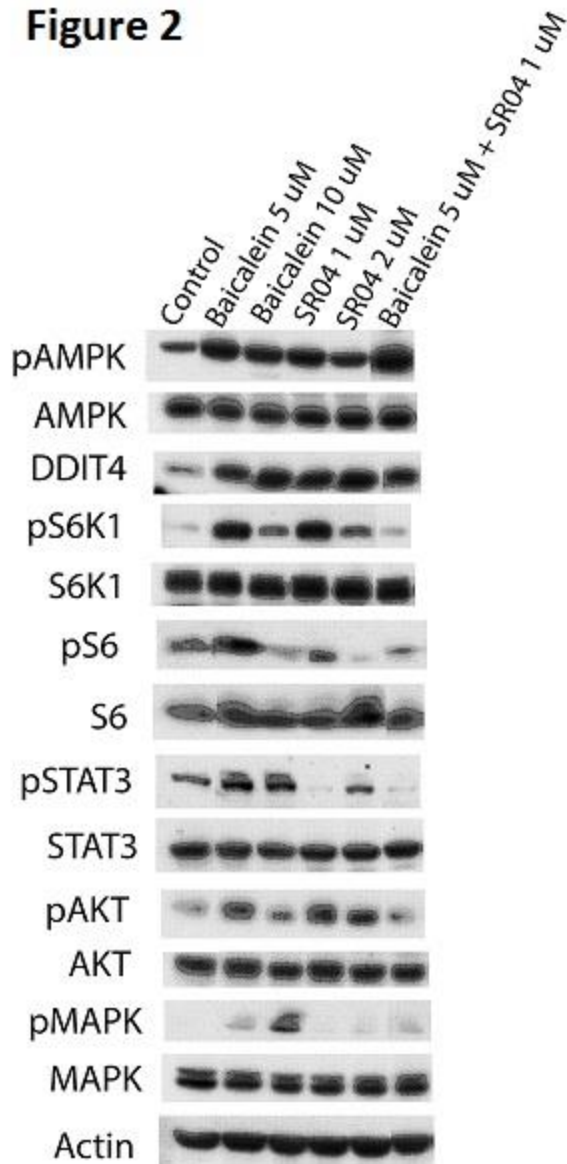
**Methods:** Endometrial cancer cell lines, RL95-2 and KLE were treated with varying concentrations of baicalein and SR04. Cell viability assessment at 72 hours was determined by MTT assay. Drug combination studies and synergy quantification was performed using Chou-Talalay method. Western blot analysis was utilized to evaluate PI3K/mTOR end targets.

**Results:** Baicalein or SR04 alone inhibited proliferation of endometrial cancer cell lines in a dose dependent manner. In combination, baicalein and SR04 acted synergistically to inhibit cell proliferation, especially at low concentrations (Figure 1). The synergistic effect was mediated by inhibition of STAT3 and PS6 as demonstrated on Western blot (Figure 2). Interestingly compensatory activation of AKT and MAPK pathways, which can oppose the anti-proliferative effects of PI3K/mTOR inhibition, was not observed with the combination of baicalein and SR04 on Western blots.

FIGURE 1



**Figure 2**



**Conclusion/Implications:** The combination of baicalein and AMPK activator SR04 inhibits endometrial cancer cell proliferation in a synergistic manner. The combination does not appear to activate AKT and MAPK pathways which can hinder efficacy. The combination of baicalein and SR04 may offer a novel treatment paradigm for endometrial cancer.



EP126 / #753

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **IGF2BP2 IS THE POOR PROGNOSTIC FACTOR OF ENDOMETRIAL CANCER AND REGULATES THE PLATINUM RESISTANCE**

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**Introduction:** Endometrial cancer (EC) is the most common gynecological cancer in Japan. The initial treatment of EC is surgery followed by platinum-based chemotherapy, therefore, platinum resistance is major factor of poor prognosis. In this study, we focused on IGF2BP2 which is highly expressed in platinum resistant EC cells and analyze its function.

**Methods:** We performed iTRAQ-based exhaustive and quantitative protein analysis using EC tissues of platinum sensitive and resistant cases, and detected high expression protein (IGF2BP2) among platinum resistant cases. Using 119 EC cases, we also performed survival analysis to reveal the correlation between IGF2BP2 expression levels and overall survival. Moreover, we generated IGF2BP2 knockdown EC cell lines using siRNA, and measured IC50 value of platinum reagent.

**Results:** iTRAQ-based protein analysis detected 2299 proteins, and IGF2BP2 was one of the highly expressed proteins in platinum resistant EC cases. High expression of IGF2BP2 was associated with poor prognosis of EC ( $p < 0.05$ ). Knockdown of IGF2BP2 decreased IC50 value of platinum reagent ( $p < 0.05$ ).

**Conclusion/Implications:** High expression of IGF2BP2 is poor prognostic factor and is related platinum resistance of EC.

EP127 / #784

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **ENDOMETRIAL CANCER FERTILITY SPARING TREATMENT - EFFECT OF BARIATRIC SURGERY ON CANCER REGRESSION**

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**Introduction:** Obesity is a major risk factor in the development of endometrial cancer in young patients in the reproductive age group. Fertility sparing treatment is a viable option for a select group of patients with early endometrial cancer, and involves systemic and intra-uterine hormonal therapy. Weight loss has been associated with improved outcomes in this group. Bariatric surgery has been shown to be the most effective and durable method of weight loss in obese patients. However, there is a paucity of data studying the benefit of bariatric surgery as part of fertility sparing management.

**Methods:** We present a retrospective case series of five patients who are undergoing fertility sparing treatment for early endometrial cancer, who also underwent bariatric surgery for treatment of obesity and related comorbidities. We aim to show early regression of endometrial cancer for all the patients and also report on the other health benefits of bariatric surgery.

**Results:** All five patients in this series achieved regression of endometrial cancer within six months of undergoing bariatric surgery. They also achieved significant weight loss and three patients with obesity-related comorbidities had remission of these conditions. One patient conceived via in-vitro fertilization and delivered a healthy baby.

**Conclusion/Implications:** Patients on fertility sparing treatment for endometrial cancer who underwent bariatric surgery achieved early cancer regression within six months, significant weight loss and resolution of obesity related comorbidities. Bariatric surgery could be a promising component of fertility sparing management for obese patients. Long term, prospective studies are required to confirm the benefits reported in this series.

EP128 / #505

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **IMPACT OF DIFFERENT ADJUVANT TREATMENT APPROACHES ON SURVIVAL IN HIGH-RISK ENDOMETRIAL CARCINOMA: A MULTICENTER STUDY**

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**Introduction:** This study aims to compare survival outcomes of various adjuvant treatments for high-risk endometrial cancer, including pelvic radiotherapy, chemotherapy, and combined chemotherapy and radiotherapy since there is limited research available that compares their outcomes.

**Methods:** This retrospective cohort study used data between January 1, 2000, and December 31, 2020 at two tertiary centers in Korea and Taiwan. Adjuvant therapy was divided into 3 categories: systemic chemotherapy, radiotherapy, and combination of chemotherapy and radiotherapy. Propensity score matching was done based on the stage and cell type.

**Results:** After removing patients with incomplete data from a total of 626 patients with high-risk endometrial cancer, 519 patients were included in the study. Among these, 176 received radiotherapy, 200 received chemotherapy, and 143 received a combination of radiotherapy and chemotherapy. After matching patients using propensity scores, 83 patients were included in each treatment group for analysis. There was no significant difference in survival between groups when all patients, early stage patients (stage I-II), and advanced stage patients (stage III-IV) were considered. Although statistical significance was not reached after matching, advanced stage patients had a higher survival rate when treated with combined chemotherapy and radiotherapy. Further analysis of the combined treatment by dividing it into different methods did not reveal any differences in survival.

**Conclusion/Implications:** There was no significant variation in the survival benefits among the different stages and treatment categories. However, for stage III and IV groups, the combination of radiotherapy and chemotherapy is believed to offer an advantage in terms of survival.

EP129 / #919

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **COMPARISONS OF CLINICAL OUTCOME OF UTERINE CONFINED ENDOMETRIAL CANCER BETWEEN LAPAROTOMIC, LAPAROSCOPIC AND ROBOTIC STAGING SURGERIES IN THE ERA OF SENTINEL LYMPH NODE MAPPING**

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**Introduction:** In the era of sentinel lymph node mapping, the clinical outcomes between laparotomic, laparoscopic and robotic surgeries were infrequently reported. Herein, we aimed to compare the clinical outcomes between the above surgical groups.

**Methods:** All consecutive women who received surgical treatment between January 2008 and May 2021 were reviewed from medical records. Only women with clinically determined uterine-confined disease based on preoperative physical examination and radiological survey were included. Chi-square test and Fisher's exact test were used as appropriate. Survival curves were generated using the Kaplan–Meier method, and the statistical differences in the survival curves were estimated with the log-rank test.

**Results:** A total of 334 cases were reviewed. Baseline characteristics were similar, despite a higher rate of sentinel lymph node mapping in the laparoscopy group (5% - laparotomy vs. 42% - laparoscopy vs. 21% - robot,  $p < 0.001$ , Table 1). The total number of dissected lymph nodes was higher in the laparotomic group, compared with the laparoscopic and robotic groups ( $p < 0.0001$ , Table 1); however, the positive lymph node rate did not differ between groups (8.6% - laparotomy vs. 3.8% - laparoscopy vs. 11.9% - robot,  $p = 0.15$ , Table 1). The recurrence-free survival and overall survival also did not differ between groups (log-rank test,  $p = 0.85$  and  $0.50$ , respectively, Figures 1 and

Table 1. Comparison of baseline data and clinical outcomes between the laparotomy, laparoscopy and robot groups in women with clinically uterine-confined endometrial cancer (n=334)

Variables	Laparotomy (n=187)	Laparoscopy (n=105)	Robot (n=42)	tP
Sentinel lymph node mapping	9 (5)	44 (42)	9 (21)	<0.001
Age (years)	56±10	56±11	56±10	0.93
Parity	2.1 ± 1.3	1.9 ± 1.3	2 ± 1.3	0.63
Body mass index (kg/m <sup>2</sup> )	26.7±6.1	28.3±5.7	26.8±4.2	0.07
ECOG score				
0	77 (41)	44 (42)	23 (55)	0.70
1	105 (56)	57 (54)	18 (43)	
2	3 (2)	2 (2)	1 (2)	
3	2 (1)	1 (1)	0 (0)	
CA-125 (U/mL)	64 ± 140	35 ± 52	89 ± 243	0.12
Endometrioid cell type	149 (80)	93 (89)	39 (93)	0.04
Cell grade				
1	76 (41)	58 (55)	22 (52)	0.06
2	63 (34)	28 (27)	14 (33)	
3	39 (21)	15 (14)	3 (7)	
Deep (>1/2) myometrial invasion	45 (24)	23 (22)	11 (26)	0.81
Lymphovascular space invasion	67 (36)	31 (30)	20 (48)	0.04
Tumor size (mm)	35 ± 27	24 ± 16	25 ± 20	0.002
Malignant cell in washing cytology	8 (4)	3 (3)	1 (2)	0.91
Total number of dissected lymph nodes	17 ± 8	13 ± 8	12 ± 6	<0.0001
Total cases of positive lymph nodes	16 (8.5)	4 (3.8)	5 (11.9)	0.15
Para-aortic lymph nodes dissection	123 (66)	9 (9)	24 (57)	<0.001
Stage				
IA	123 (66)	77 (73)	26 (62)	0.049
IB	30 (16)	20 (19)	9 (21)	
II	13 (7)	0 (0)	2 (5)	
IIIA	4 (2)	4 (4)	0 (0)	
IIIC1	13 (7)	2 (2)	4 (10)	
IIIC2	2 (1)	2 (2)	1 (2)	
IVB	2 (1)	0 (0)	0 (0)	
Operation time (min)	161±55	200±57	291±73	<0.0001
Blood loss (mL)	336±313	234±190	328±331	0.0008
Median follow-up (months)	71±43	37±25	48±28	<0.0001
Adjuvant radiotherapy	101 (54)	38 (36)	23 (55)	0.01
Adjuvant chemotherapy	36 (19)	12 (11)	6 (14)	0.21
Lymphocyst/lymphedema	29 (16)	3 (3)	4 (10)	0.11
Recurrence	14 (7)	8 (8)	4 (10)	0.85
Death	11 (6)	5 (5)	4 (10)	0.50

Data were presented with mean ± standard deviation or number (percentage).

†ANOVA test, chi2 test or log-rank test.

2).

Figure 1. Recurrence free survival

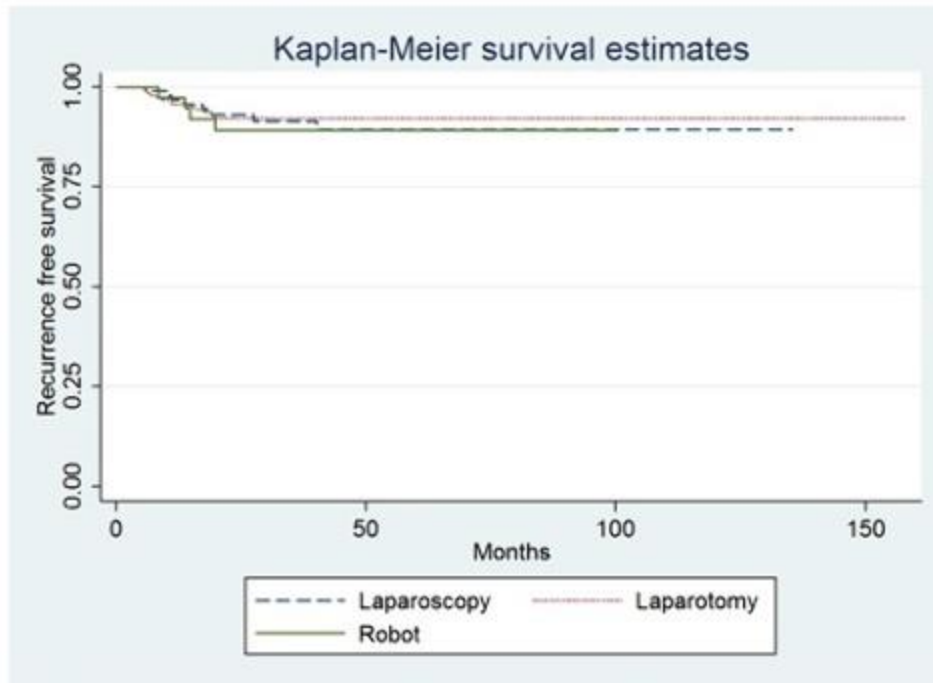
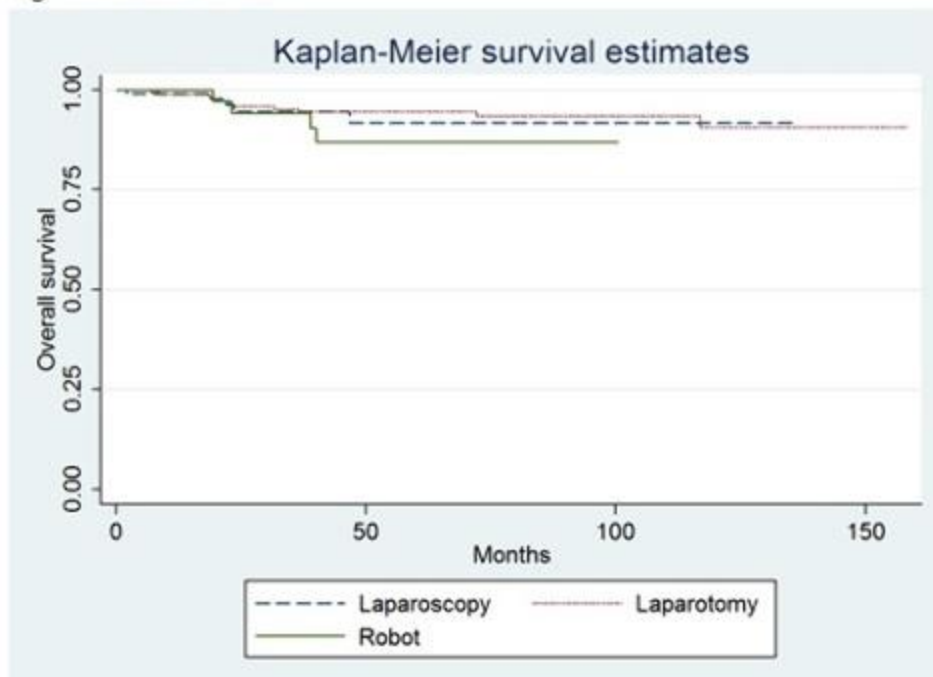


Figure 2. Overall survival



**Conclusion/Implications:** Less numbers of lymph nodes were dissected in the laparoscopy and robot groups, compared with laparotomy. However, recurrence-free survival and overall survival seem similar between the laparotomy, laparoscopy and robot surgical groups in women with uterine-confined endometrial cancer.

EP130 / #706

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **IGFBP2 REGULATES GLUCOSE METABOLISM REPROGRAMMING THROUGH PKM2 TO PROMOTE ENDOMETRIAL ADENOCARCINOMA PROGRESSION**

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**Introduction:** Endometrial cancer (EC) is one of the most common malignant tumors in the female reproductive system. The incidence and mortality of EC have been increasing in the past 40 years. As an important member of the insulin-like growth factor (IGF) family, IGF binding protein 2 (IGFBP2) is an important molecular target in many cancers, also plays a pivotal role in metabolic diseases, such as obesity and diabetes. However, whether IGFBP2 in EC can affect the metabolism of tumor cells and participate in the metabolic reprogramming of endometrial adenocarcinoma cells and consequently affect tumorigenesis and progression, these questions are still unclear and the specific mechanisms have not been elucidated.

**Methods:** Cancer and paracancer tissue specimens were collected from 80 patients with EC, and the expression of IGFBP2, PKM2 and glycolytic enzymes in the tissues were examined. The expression of IGFBP2 in EC cells was altered to detect the effect of IGFBP2 on cellular glycolysis, and the expression of key enzymes of intracellular glycolysis was examined.

**Results:** IGFBP2 and PKM2 were highly expressed in tumor tissues of EC patients and correlated with tumor stage and differentiation. After knockdown of IGFBP2 expression in EC cells, cell proliferation capacity was significantly reduced, tumorigenic capacity in vivo was decreased, cellular glycolytic function, glucose uptake, lactate production and ATP production were significantly reduced, the expression levels of various key enzymes of glucose metabolism were significantly reduced, and the nuclear plasma ratio of PKM2 was decreased.

**Conclusion/Implications:** We found IGFBP2 regulates glucose metabolism reprogramming through PKM2 to promote endometrial adenocarcinoma progression.

EP131 / #702

**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **CLINICAL CHARACTERISTICS AND PROGNOSIS ANALYSIS OF UTERINE SARCOMA: MULTI-CENTER RETROSPECTIVE STUDY**

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Eunpyeong St. Mary's Hospital. The Catholic university of Korea, Division Of Gynecologic Oncology  
Department Of Obstetrics & Gynecology, Seoul, Korea, Republic of

**Introduction:** To examine the histopathological features and treatment modalities in patients with uterine sarcoma according to subgroups (uterine leiomyosarcoma, low grade/high grade endometrial stromal sarcoma, adenosarcoma, undifferentiated uterine sarcoma) and to determine the factors affecting mortality rates.

**Methods:** We retrospectively evaluated patients diagnosed with uterine sarcoma in our eight multicenter institutions between March 2012 and December 2021. We compared the clinicopathological characteristics and treatment modalities of the subgroups and investigated the factors affecting mortality rates using logistic regression analysis.

**Results:** In the entire US group, the rate of 5-year OS was 51.2% and the rate of DFS was 39.9%. There was no difference between the subgroups in terms of age, body mass index, menopausal status, comorbidity, presenting complaint, primary diagnosis, surgical treatment protocol, adnexal and lymph node involvement and tumor size ( $p > 0.01$ ). High NLR was significantly associated with worse DFS ( $p = 0.007$ ) and OS ( $p = 0.039$ ). Advanced stage ( $p = 0.017$ ) and high mitotic index ( $p = 0.036$ ) retained their prognostic significance for DFS. Other clinical variables, including PLR, CA125, and lactate



dehydrogenase (LDH) failed to show significant impact.

N (%) <sup>±</sup>	ALL sarcomas <sup>±</sup>	LMS <sup>±</sup> (N=57) <sup>±</sup>	ESS <sup>±</sup> (N=29) <sup>±</sup>	UUS <sup>±</sup> (N=7) <sup>±</sup>	Adenosarcoma <sup>±</sup> (N=6) <sup>±</sup>	P <sup>±</sup>	<sup>±</sup>
Age (years) <sup>±</sup>							
≥60 <sup>±</sup>	21 (21.2%) <sup>±</sup>	13 (22.8%) <sup>±</sup>	4 (13.8%) <sup>±</sup>	1 (14.3%) <sup>±</sup>	3 (50.0%) <sup>±</sup>	0.224 <sup>±</sup>	
<60 <sup>±</sup>	78 (78.8%) <sup>±</sup>	44 (77.2%) <sup>±</sup>	25 (86.2%) <sup>±</sup>	6 (85.7%) <sup>±</sup>	3 (50.0%) <sup>±</sup>		
BMI (kg/m2) <sup>±</sup>							
Normal 18.5-22.9 <sup>±</sup>	41 (41.4%) <sup>±</sup>	22 (38.6%) <sup>±</sup>	14 (48.3%) <sup>±</sup>	2 (28.6%) <sup>±</sup>	3 (50.0%) <sup>±</sup>	0.718 <sup>±</sup>	
Overweight-obese ≥23 <sup>±</sup>	58 (58.6%) <sup>±</sup>	35 (61.4%) <sup>±</sup>	15 (51.7%) <sup>±</sup>	5 (71.4%) <sup>±</sup>	3 (50.0%) <sup>±</sup>		
History of hypertension <sup>±</sup>							
Yes <sup>±</sup>	25 (25.3%) <sup>±</sup>	16 (28.1%) <sup>±</sup>	4 (13.8%) <sup>±</sup>	3 (42.9%) <sup>±</sup>	2 (33.3%) <sup>±</sup>	0.238 <sup>±</sup>	
No <sup>±</sup>	74 (74.7%) <sup>±</sup>	41 (71.9%) <sup>±</sup>	25 (86.2%) <sup>±</sup>	4 (57.1%) <sup>±</sup>	4 (66.7%) <sup>±</sup>		
History of diabetes <sup>±</sup>							
Yes <sup>±</sup>	14 (14.1%) <sup>±</sup>	8 (14.0%) <sup>±</sup>	2 (6.9%) <sup>±</sup>	2 (28.6%) <sup>±</sup>	2 (33.3%) <sup>±</sup>	0.158 <sup>±</sup>	
No <sup>±</sup>	85 (85.9%) <sup>±</sup>	49 (86.0%) <sup>±</sup>	27 (93.1%) <sup>±</sup>	5 (71.4%) <sup>±</sup>	4 (66.7%) <sup>±</sup>		
Stage <sup>±</sup>							
I <sup>±</sup>	73 (73.7%) <sup>±</sup>	37 (64.9%) <sup>±</sup>	23 (79.3%) <sup>±</sup>	7 (100.0%) <sup>±</sup>	6 (100%) <sup>±</sup>	0.834 <sup>±</sup>	
II <sup>±</sup>	7 (7.1%) <sup>±</sup>	5 (8.8%) <sup>±</sup>	2 (6.9%) <sup>±</sup>	0 (0.0%) <sup>±</sup>	0 (0.0%) <sup>±</sup>		
III <sup>±</sup>	8 (8.1%) <sup>±</sup>	7 (12.3%) <sup>±</sup>	1 (3.4%) <sup>±</sup>	0 (0.0%) <sup>±</sup>	0 (0.0%) <sup>±</sup>		
IV <sup>±</sup>	11 (11.1%) <sup>±</sup>	8 (14.0%) <sup>±</sup>	3 (10.3%) <sup>±</sup>	0 (0.0%) <sup>±</sup>	0 (0.0%) <sup>±</sup>		
Tumor size (cm) <sup>±</sup>							
≥10 <sup>±</sup>	36 (36.4%) <sup>±</sup>	24 (42.1%) <sup>±</sup>	6 (20.7%) <sup>±</sup>	3 (42.9%) <sup>±</sup>	3 (50.0%) <sup>±</sup>	0.189 <sup>±</sup>	
<10 <sup>±</sup>	63 (63.6%) <sup>±</sup>	33 (57.9%) <sup>±</sup>	23 (79.3%) <sup>±</sup>	4 (57.1%) <sup>±</sup>	3 (50.0%) <sup>±</sup>		
Mitotic index (MF/10HPF) <sup>±</sup>							
≥15 <sup>±</sup>	44 (44.4%) <sup>±</sup>	33 (57.9%) <sup>±</sup>	7 (24.1%) <sup>±</sup>	2 (28.6%) <sup>±</sup>	2 (33.3%) <sup>±</sup>	0.015 <sup>±</sup>	
<15 <sup>±</sup>	55 (55.6%) <sup>±</sup>	24 (42.1%) <sup>±</sup>	22 (75.9%) <sup>±</sup>	5 (71.4%) <sup>±</sup>	4 (66.7%) <sup>±</sup>		
Nuclear atypia <sup>±</sup>							
≥severe <sup>±</sup>	20 (20.2%) <sup>±</sup>	16 (28.1%) <sup>±</sup>	2 (6.9%) <sup>±</sup>	2 (28.6%) <sup>±</sup>	0 (0.0%) <sup>±</sup>	0.050 <sup>±</sup>	
<severe <sup>±</sup>	79 (79.8%) <sup>±</sup>	41 (71.9%) <sup>±</sup>	27 (93.1%) <sup>±</sup>	5 (71.4%) <sup>±</sup>	6 (100.0%) <sup>±</sup>		
Vascular invasion <sup>±</sup>							
Yes <sup>±</sup>	24 (24.2%) <sup>±</sup>	12 (21.1%) <sup>±</sup>	7 (24.1%) <sup>±</sup>	4 (57.1%) <sup>±</sup>	1 (16.7%) <sup>±</sup>	0.220 <sup>±</sup>	
No <sup>±</sup>	75 (75.8%) <sup>±</sup>	45 (78.9%) <sup>±</sup>	22 (75.9%) <sup>±</sup>	3 (42.9%) <sup>±</sup>	5 (83.3%) <sup>±</sup>		
Tumor necrosis <sup>±</sup>							
Yes <sup>±</sup>	74 (74.7%) <sup>±</sup>	50 (87.7%) <sup>±</sup>	13 (44.8%) <sup>±</sup>	6 (85.7%) <sup>±</sup>	5 (83.3%) <sup>±</sup>	<0.001 <sup>±</sup>	
No <sup>±</sup>	25 (25.3%) <sup>±</sup>	7 (12.3%) <sup>±</sup>	16 (55.2%) <sup>±</sup>	1 (14.3%) <sup>±</sup>	1 (16.7%) <sup>±</sup>		
Lymphadenectomy <sup>±</sup>							
Yes <sup>±</sup>	29 (29.3%) <sup>±</sup>	21 (36.8%) <sup>±</sup>	5 (17.2%) <sup>±</sup>	1 (14.3%) <sup>±</sup>	2 (33.3%) <sup>±</sup>	0.219 <sup>±</sup>	
No <sup>±</sup>	70 (70.7%) <sup>±</sup>	36 (63.2%) <sup>±</sup>	24 (82.8%) <sup>±</sup>	6 (85.7%) <sup>±</sup>	4 (66.7%) <sup>±</sup>		
Recurrence <sup>±</sup>							
Yes <sup>±</sup>	30 (30.3%) <sup>±</sup>	21 (36.8%) <sup>±</sup>	6 (20.7%) <sup>±</sup>	1 (14.3%) <sup>±</sup>	2 (33.3%) <sup>±</sup>	0.373 <sup>±</sup>	
No <sup>±</sup>	69 (69.7%) <sup>±</sup>	36 (63.2%) <sup>±</sup>	23 (79.3%) <sup>±</sup>	6 (85.7%) <sup>±</sup>	4 (66.7%) <sup>±</sup>		

\* p value between different histologic type. Abbreviations: LMS: leiomyosarcoma, ESS: endometrial stromal sarcoma, UUS: undifferentiated uterine sarcoma<sup>±</sup>

**Conclusion/Implications:** Uterine sarcoma is an aggressive cancer with poorer survival in this specific cohort than has been described in other contemporary cohorts. Despite their different histopathological features, subgroups do not have distinctive features such as demographic features, presenting complaints, primary diagnosis and surgical treatment protocols. Therefore, prospective randomized

clinical studies should be performed to evaluate the prognostic influencing factor and the value of adjuvant treatments for patients with uterine sarcoma.

EP132 / #512

**Topic: AS04. Endometrial/Uterine Corpus Cancers**

## **LYNCH SCREENING AND GENETIC TESTING WITH ENDOMETRIAL CANCER IN A DIVERSE PATIENT POPULATION**

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**Introduction:** Lynch syndrome (LS) accounts for most of the inherited endometrial cancers. Screening for mismatch repair (MMR) defects is recommended using immunohistochemistry (IHC) to identify qualifying patients for genetic testing. We report LS screening and genetic testing rates at a tertiary care center with a large minority population.

**Methods:** Retrospective cohort study of patients with newly diagnosed endometrial cancer between January 2014 and June 2022 at the NewYork-Presbyterian Brooklyn Methodist Hospital.

**Results:** 373 patients included. 45% identified as white, 42% black; 8.3% were of Hispanic ethnicity and 18% were non-English speaking. 207(55%) patients were screened using MMR-IHC. 82(40%) of these patients had MMR deficiencies. Of these, 63(77%) received genetic counseling. 62(98%) subsequently underwent genetic testing, and 7(11%) were diagnosed with LS. The rate of LS detected was 1.9%. MMR-IHC testing rates reached 95% in 2021 and 100% in 2022. It was not influenced by race, language, BMI, family history of cancer, or stage. The proportion of patients that received genetic counseling and testing also increased over time ( $p<0.01$ ). Rates were different by ethnicity ( $p=0.03$ ), with only 3.0% of patients receiving services identifying as Hispanic. 98% of genetic counseling was performed by a gynecologic oncologist, as opposed to a genetic counselor.

**Conclusion/Implications:** There were no disparities in access to IHC screening in this diverse population, however more work must be done to reach all ethnicities for genetic counseling and testing. The rate of LS detected was less than the known prevalence in endometrial cancer, indicating demographic differences or gaps in screening.

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EP133 / #724

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **PROGNOSTIC VALUE OF THE PROGNOSTIC NUTRITIONAL INDEX IN ENDOMETRIAL CANCER**

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**Introduction:** The prognostic nutritional index (PNI) reflects the immuno-nutritional status of patients with cancer, estimated based on pre-operative lymphocyte counts and serum albumin levels. The PNI has been widely used to predict the prognosis of gynecologic cancer. However, endometrial cancer (EC) remains relatively understudied compared to ovarian and cervical cancers. Therefore, this study aimed to evaluate the prognostic value of PNI in patients with EC.

**Methods:** Laboratory and clinicopathological data from 370 patients who were diagnosed with EC between January 2010 and December 2021 were reviewed. PNI was analyzed for correlations with recurrence and survival. The receiver operating characteristic curves were generated for the PNI. Optimal cut-off values were determined. Based on the results of the ROC curve analysis, the patients were grouped into high and low PNI groups. Differences in the clinicopathological characteristics between patients with high and low PNI were compared between the two groups. The effects of the prognostic factors were analyzed using univariate and multivariate Cox proportional hazards model.

**Results:** The optimal cutoff value of the PNI was 52.74 for DFS (area under the curve: 0.817,  $p < 0.001$ ). Significantly more patients in the low PNI group experienced recurrence (30.6% vs. 5.2%,  $p < 0.001$ ) and cancer-related death (17.8% vs. 2.8%,  $p < 0.001$ ). In multivariate analysis, PNI were independent prognostic factors for both DFS and OS.

**Conclusion/Implications:** Low PNI was significantly associated with worse clinical outcomes in patients with EC. Our findings demonstrate that the PNI may be clinically reliable and useful as a prognostic marker for patients with EC.

EP134 / #1505

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **DOSTARLIMAB MONOTHERAPY IN MISMATCH REPAIR DEFICIENT/MICROSATELLITE INSTABILITY–HIGH ADVANCED OR RECURRENT ENDOMETRIAL CANCER IN THE KOREAN EXPANDED ACCESS PROGRAM**

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**Introduction:** Dostarlimab, a programmed death 1 inhibitor, is approved in Korea for patients with mismatch repair deficient/microsatellite instability–high (dMMR/MSI-H) recurrent or advanced endometrial cancer (EC) that has progressed on or after treatment with a platinum-based chemotherapy. Through the Korean expanded access program (EAP), patients at 16 major medical institutions were able to access dostarlimab treatment. For the first time, we present real-world data from these Korean patients.

**Methods:** Patients with recurrent/advanced dMMR/MSI-H EC with  $\leq 2$  lines of prior systemic chemotherapy and no prior anti-PD-(L)1 agent received 500 mg of dostarlimab intravenously once every 3 weeks for 4 cycles, then 1000 mg once every 6 weeks until disease progression or withdrawal from treatment. Tumor response and adverse events were recorded.

**Results:** At data cutoff of August 1, 2023, 17 patients were accepted into the EAP. Median age was 57 years (range, 42–71 years). With a median follow-up of 3.75 months, 10 patients were available for evaluation of tumor response. Of these, 6 had confirmed complete or partial responses; objective response rate was 60.0%. Treatment-related adverse events (TRAEs) were experienced by 5.9% (1/17) of patients, with no grade  $\geq 3$  TRAEs. No patients discontinued because of TRAEs.

**Conclusion/Implications:** Initial results from the Korean EAP of dostarlimab monotherapy treatment for patients with recurrent or advanced dMMR/MSI-H EC demonstrated encouraging antitumor activity with no new safety signals, further supporting dostarlimab use in Korean patients. Results were consistent with the GARNET clinical trial (NCT02715284) of dostarlimab monotherapy. Additional follow-up is

ongoing.

**Table**

	<b>Korean expanded access program dMMR/MSI-H EC N=17</b>
Median follow-up, months	3.75
<b>Tumor response</b>	
ORR, % (n/N)	60 (6/10)
Complete response, % (n/N)	20 (2/10)
Partial response, % (n/N)	40 (4/10)
Stable disease, % (n/N)	10 (1/10)
<b>Adverse events</b>	
TEAE, n (%)	6 (35.3)
Grade ≥3 TEAE, n (%)	2 (11.8)
TRAE, n (%)	1 (5.9)
Grade ≥3 TRAE, n (%)	0
SAE, n (%)	1 (5.9)
TRAE leading to discontinuation, n (%)	0

ORR, objective response rate; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## THE PROGNOSTIC SIGNIFICANCE OF THE NUMBER OF RESECTED PELVIC NODES IN ENDOMETRIAL CANCER: JAPANESE GYNECOLOGIC ONCOLOGY GROUP STUDY JGOG2043 POST HOC ANALYSIS

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**Introduction:** Objective: This study aimed to determine whether the number of resected pelvic lymph nodes (PLNs) affects the prognosis of endometrial cancer patients at post-operative risk of recurrence.

**Methods:** JGOG2043 was a trial to assess the efficacy of three different chemotherapeutic regimens as adjuvant therapy in endometrial cancer patients with post-operative recurrent risk. Two hundred fifty patients who underwent pelvic lymphadenectomy alone in JGOG2043 were analyzed retrospectively. The number of resected and positive nodes and other clinicopathologic risk factors for survival were retrieved.

**Results:** There were 167 patients in the group with 20 or more PLNs removed, while 83 patients had less than 20 PLNs removed. There was no significant difference in patients' backgrounds between the two groups, and the rate of lymph node metastasis was not significantly different (28.1% vs. 24.1%,  $P=0.49$ ). There was a trend toward fewer pelvic recurrences in the group with 20 or more PLNs removed (3.5% vs. 9.6%,  $P=0.0502$ ). Although Kaplan-Meier analysis showed no significant difference in survival rates between 20 or more and less than 20 groups (5-year OS: 90.3% vs. 84.3%,  $P=0.20$ ), multivariate analysis revealed that the number of resected nodes is one of the independent risk factors (HR, 0.49; 95%CI, 0.24-0.99;  $P=0.048$ ), as well as surgical stage, high-risk histology, and advanced age for overall survival.

**Conclusion/Implications:** Resection of 20 or more nodes in the pelvic region was associated with improved pelvic control and better survival outcomes in endometrial cancer patients who underwent pelvic lymphadenectomy alone at risk of recurrence treated with adjuvant chemotherapy.

EP136 / #225

Topic: **AS04. Endometrial/Uterine Corpus Cancers**

## EVALUATION OF UTERINE ENDOMETRIAL CARCINOMA HISTOLOGICAL GRADES USING MAGNETIC RESONANCE IMAGING TEXTURE ANALYSES

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**Introduction:** The histological tumor grade of uterine endometrial carcinoma (UEC) is one factor that can determine the prognosis. However, studies have shown that some histological grades assigned by preoperative biopsy results did not correspond to the final grades of the surgical specimens. This study evaluated the possibility of predicting the UEC histological grade using magnetic resonance imaging texture features (TFs).

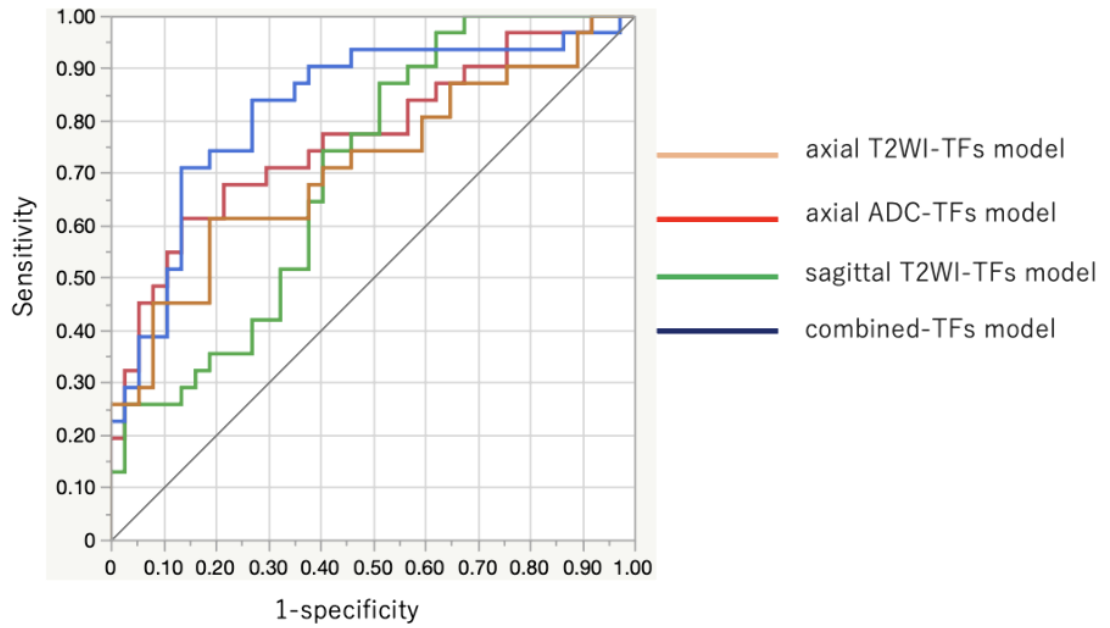
**Methods:** This retrospective study included 70 patients with UEC. We evaluated axial T2-weighted imaging (T2WI) TFs, axial apparent diffusion coefficient (ADC) TFs, sagittal T2WI TFs, and their combinations to determine histological class 1 (Grade 1: n=33) and class 2 (Grade 2 and Grade 3: n=37) using texture analyses. The least absolute shrinkage and selection operator was used to select four TFs for each model and construct a discriminative model. A binary logistic regression analysis and receiver-operating characteristic analysis of the axial T2WI TFs, axial ADC TFs, sagittal T2WI TFs, and combined TFs models were performed to compare the two histological class.

**Results:** Four models were constructed from each of the four selected features. The area under the curve (AUC) values of the discriminative model using these features were 0.71, 0.70, 0.77, and 0.82 for the sagittal T2WI TFs, axial T2WI TFs, axial ADC TFs, and combined TFs models, respectively. The AUC value of the combined TFs model was the highest.

Model	Feature	AUC	Sensitivity	Specificity
sagittal T2-TFs model	first order maximum glcm joint energy glszm large area low gray level emphasis ngtdm busyness	0.70	0.49	0.87
axial ADC-TFs model	first order skewness GlcM ldn3 ngtdm busyness glcm correlation	0.77	0.87	0.61
axial T2WI-TFs model	first order skewness first order total energy ngtdm contrast ngtdm busyness	0.71	0.81	0.62
combined TFs model	glcm correlation on axial ADC-TF ngtdm strength on sagittal T2WI-TF ngtdm contrast on axial T2WI-TF ngtdm busyness on sagittal T2WI-TF	0.82	0.86	0.71

**Table 1** Diagnostic performance of the model for differentiating histological class of uterus endometrial carcinoma





**Figure1** the receiver operating characteristic curves analysis of the diagnostic model

**Conclusion/Implications:** A combined TFs model may help distinguish UEC histological grades.

EP137 / #905

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **COMBINED PELVIC AND PARA-AORTIC LYMPHADENECTOMY IS NOT ASSOCIATED WITH SURVIVAL BENEFIT IN EARLY-STAGE HIGH-GRADE ENDOMETRIAL ADENOCARCINOMA**

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**Introduction:** The therapeutic effect of para-aortic lymphadenectomy in early-stage high-grade endometrial cancer remains controversial. In this study, we investigated whether combined pelvic and para-aortic lymphadenectomy has a survival benefit compared to pelvic lymphadenectomy alone in patients with pathologically diagnosed FIGO stage I-II grade 3 endometrioid and non-endometrioid endometrial cancers.

**Methods:** Weretrospectively reviewed themedical records of 281 patientswith histologically confirmed FIGO stage I-II grade 3 endometrioid and non-endometrioid endometrial cancers who underwent pelvic lymphadenectomy alone or combined pelvic and para-aortic lymphadenectomy in staging surgery at two tertiary centers in Korea and Taiwan. Prognostic factors to predict outcomes in these cases were also analyzed.

**Results:** Among 281 patients, 144 underwent pelvic lymphadenectomy alone and 137 underwent combined pelvic and para-aortic lymphadenectomy. Within amedian follow-up of 45 months, there was no significant difference in recurrence-free survival (RFS) and overall survival (OS) between the two groups. In multivariable analysis, age at diagnosis  $\geq 60$  years (HR = 2.20, 95% CI 1.25–3.87,  $p = 0.006$ ) and positive lymph-vascular space invasion (LVSI) (HR = 2.79, 95% CI 1.60–4.85,  $p < 0.001$ ) were associated with worse RFS, and only non-endometrioid histology was associated with worse OS (HR=3.18, 95% CI 1.42–7.12,  $p=0.005$ ). In further subgroup analysis, beneficial effects of combined pelvic and para-aortic lymphadenectomy on RFS and OS were not observed.

**Conclusion/Implications:** In this study, combined pelvic and para-aortic lymphadenectomy could not improve survival compared to pelvic lymphadenectomy alone in patients with FIGO stage I-II grade 3 endometrioid and nonendometrioid endometrial cancers. Therefore, para-aortic lymphadenectomy may be omitted for these cases.

## **PREDICTION OF FINAL PATHOLOGY DEPENDING ON PREOPERATIVE MYOMETRIAL INVASION AND GRADE ASSESSMENT IN LOW RISK ENDOMETRIAL CANCER PATIENTS: A KOREAN GYNECOLOGIC ONCOLOGY GROUP ANCILLARY STUDY**

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**Introduction:** Fertility-sparing treatment might be considered option for reproductive women with low risk endometrial cancer (EC). However, in low risk EC patients, concordance rates between preoperative assessment and postoperative pathology are not high enough. We aimed to predict postoperative pathology depending on preoperative myometrial invasion (MI) and grade in low risk EC patients to help extend current criteria for fertility-sparing treatment.

**Methods:** In Korean Gynecologic Oncology Group (KGOG) 2015, a prospective, multicenter study, 529 EC patients underwent preoperative assessment using MRI and endometrial biopsy followed by surgical staging. This ancillary study included patients who had no MI or MI <1/2 on preoperative MRI and endometrioid adenocarcinoma and grade 1 or 2 on endometrial biopsy. Among eligible patients, Groups 1 - 4 were defined with no MI and grade 1, no MI and grade 2, MI <1/2 and grade 1, and MI <1/2 and grade 2, respectively. New prediction model using machine learning was developed.

**Results:** Among 251 eligible patients, Groups 1 - 4 included 106 (42.2%) patients, 41 (16.3%), 74 (29.5%), and 30 (12.0%), respectively. Compared with conventional analysis, new prediction model showed somewhat better prediction values. In new prediction model, NPV, sensitivity, and AUC of preoperative each group to predict postoperative each group were 88.9%, 77.6%, and 0.714 for Group 1, 97.1%, 64.3%, and 0.676 for Group 2, 77.5%, 76.5%, and 0.641 for Group 3, and 92.4%, 64.9%, and 0.691% for Group 4.

**Conclusion/Implications:** In low risk EC patients, prediction of postoperative pathology was ineffective enough. New prediction model might provide better prediction.

EP139 / #824

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **WOULD PREOPERATIVE MOLECULAR PROFILING OF P53 MUTATION AND MISMATCH REPAIR DEFICIENCY BE USEFUL AS MARKERS TO PREDICT THE EXTENT OF SURGERY IN EARLY-STAGE ENDOMETRIAL CANCER?**

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**Introduction:** Staging operations for early stage endometrial cancer are performed uniformly, despite the fact that pathologic information can be obtained prior to surgery. According to molecular categories identified in the Cancer Genome Atlas, p53 mutation and MMRd are associated with poor prognosis. If there is a correlation between the molecular profile obtained from endometrial biopsy tissue and the extent of disease after surgery, it may be possible to personalize surgical planning.

**Methods:** This study compared the P53 and MMR status of 173 patients with newly diagnosed and clinically staged I-II endometrial cancer who underwent surgical staging, with their final pathological results. All were classified into three groups based on their molecular profiles: abnormal p53, MMRd, and NSMP (no specific molecular profile). The presence of involvement in the cervix, adnexa, and lymph nodes was analyzed using the Kruskal-Wallis test.

**Results:** Out of 173 patients, 17(9.8%) were assigned to p53 abnormal group, 33(19.1%) to MMRd group, and 123(71.1%) to NSMP group. Among them, 18(10.4%) had cervical involvement, 8(4.6%) had adnexal involvement, and 8(4.6%) had lymph node involvement. The p-values for the involvement of each group were 0.115 for cervix, 0.328 for adnexa, and 0.860 for lymph nodes, indicating no statistically significant relationship between molecular profile and disease extent.

**Conclusion/Implications:** Molecular profiles do not seem to determine the prognosis based on the difference in stage at first onset in early stage endometrial cancer. Staging operations should follow current guidelines, but It is necessary to make efforts to individualize treatment plans based on information obtained through preoperative histology.

EP140 / #1543

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## RESEARCH ON HOMOGENIZATION OF AI-ASSISTED MEDICAL IMAGING ANALYSIS SYSTEM FOR ENDOMETRIAL CELLS

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**Introduction:** With the endometrial cell test is widely used in the primary screening of high-risk population of endometrial cancer. It revealed the shortage of cytopathology experts and the imbalance of resources distribution. We introduced convolutional neural network into the screening and diagnosis of endometrial cancer and established a set of AI-assisted medical imaging analysis system that can automatically identify and differentiate benign and malignant endometrial cell mass. But the homogeneity in different hospitals has not been defined for clinical application.

**Methods:** A retrospective study was conducted to select endometrial fluid-based cytological pathological sections from the First Affiliated Hospital of Xi 'an Jiaotong University (Jiaotong University Group) and Xi 'an Daxing Hospital (Daxing Group) from September 2021 to May 2023 due to abnormal vaginal bleeding or uterine abnormalities indicated by ultrasound, with 100 cases each. The results were reported by the AI-assisted medical imaging analysis system of the same model in the two hospitals. The accuracy, sensitivity and specificity were analyzed based on the pathological results of the patient's endometrial tissue as the gold standard.

**Results:** The diagnostic accuracy of the AI-assisted endometrial cell medical imaging analysis system in the Jiaotong group and the Daxing group was 93.0% and 89.0%, respectively. The sensitivity was 87.8% and 82.1%, respectively, and the specificity was 96.6% and 91.7%, respectively. There was no significant difference in diagnostic accuracy, sensitivity, and specificity between the two systems ( $P > 0.05$ ).

**Conclusion/Implications:** The AI-assisted endometrial cell medical imaging analysis system shows homogenization in the diagnostic accuracy, sensitivity, and specificity when used in different medical institutions.

EP142 / #1526

**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **STUDY ON THE EFFECTIVENESS OF USING ARTIFICIAL INTELLIGENCE IMAGE RECOGNITION SYSTEM TO DIAGNOSE ENDOMETRIAL CYTOPATHOLOGY**

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**Introduction:** To explore the effectiveness of an image recognition system based on artificial intelligence (AI) in diagnosing benign and malignant endometrial cell clumps.

**Methods:** Endometrial cytological specimens from the First Affiliated Hospital of Xi'an Jiaotong University and Xi'an Daxing Hospital from August 2021 to February 2023 were selected, and histopathology was used as the gold standard. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of AI image recognition system (AI diagnosis) and professional pathologists' manual diagnosis (manual diagnosis) of benign and malignant endometrial cell clumps were compared and analyzed.

**Results:** Among the 126 patients included in the analysis, the overall coincidence rate of AI diagnosis and histological diagnosis was 92.1% (116/126), which was highly consistent with histopathological results (Kappa=0.841); the overall coincidence rate of manual diagnosis and histological diagnosis was 94.4% (119/126), which was highly consistent with histopathological results (Kappa=0.889). There was no statistically significant difference between AI diagnosis and manual diagnosis methods ( $\chi^2=0.568$ ,  $P=0.451$ ). The sensitivity, specificity, positive predictive value, and negative predictive value of AI diagnosis were 91.8%, 92.3%, 91.8%, and 92.3%, respectively. There were 126 cytology sections, each of which required 6.67 minutes for manual diagnosis and 5.00 minutes for AI diagnosis.

**Conclusion/Implications:** The AI image recognition system has high diagnostic accuracy, sensitivity and specificity, which is equivalent to the manual diagnosis level of professional pathologists, and this system has application value in the diagnosis of benign and malignant endometrial cell clumps.

EP143 / #483

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **A STUDY EVALUATING LIQUID-BASED ENDOMETRIAL CYTOLOGY TEST AND TRANSVAGINAL ULTRASONOGRAPHY AS A SCREENING TOOL FOR ENDOMETRIAL CANCER IN 570 POSTMENOPAUSAL WOMEN**

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**Introduction:** To evaluate the combination of transvaginal ultrasonography (TVS) and endometrial cytology test (ECT) as an potential diagnostic strategy for endometrial cancer and endometrial precancerous lesions in postmenopausal patients.

**Methods:** 570 postmenopausal patients admitted in our hospital due to abnormal bleeding or other symptoms and/or with endometrium thickness over 5 mm on ultrasound. The endometrial thickness was evaluated by TVS. Following obtainment with written consent, all patients underwent ECT, hysteroscopy and then dilatation and curettage (D&C). Cytological sampling was conducted by scratching the uterus cavity using SAP-1 and the samples were prepared as liquid-based smear using SurePath technology. The samples were stained using Papanicolaou method. The correlation between cytological diagnosis and TVS results with the D&C histological diagnosis was analyzed. The WHO classification was used for diagnosis.

**Results:** Sensitivity of ECT, TVS, ECT or TVS positive, ECT and TVS positive to diagnose atypical hyperplasia or worse were estimated at 80.7%, 86.8%, 97.4%, 70.2%, specificity at 94.7%, 20.4%, 17.5%, 88.4%, positive predictive value at 58.2%, 21.1%, 22.8%, 60.2%, negative predictive value at 94.4%, 86.1%, 96.4%, 92.2%, and accuracy at 84.6%, 33.7%, 33.5%, 84.7%, respectively.

**Conclusion/Implications:** transvaginal ultrasonography and Endometrial cytology test may be regarded as a effective first-line method in endometrial pathology detection in postmenopausal women.



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**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **PRELIMINARY STUDY OF CONFOCAL LASER ENDOMICROSCOPY FOR IN VITRO SPECIMENS OF THE ENDOMETRIUM**

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**Introduction:** This study observed and described the morphological characteristics of the endometrium of the resected uterus using confocal laser endomicroscopy. This included normal endometrium, non-atypical endometrial hyperplasia, endometrial hyperplasia without atypia, and endometrial carcinoma, thereby laying a foundation for finding the precise localization and resection of endometrial lesions, given the feasibility of confocal laser endomicroscopy-assisted hysteroscopy.

**Methods:** This prospective study included 74 patients who underwent hysterectomy. We used confocal laser endomicroscopy to observe the endometrium of resected uteruses and described the characteristics of endometrium in different states by comparing histopathological findings (primary objects). The secondary objects of observation were the myometrium, endocervical canal, and surface of the external os of the cervix.

**Results:** A total of 74 patients : 19 with EC , 3 with atypical endometrial hyperplasia,22 with benign diseases, 20 with CC, and 7 with OC and borderline tumor. The dynamic images of the endometrium were observed and recorded using pCLE. Considering histopathology as the gold standard, the diagnostic concordance rate of pCLE was 97.3% in patients with EC and precancerous lesions and 100% in EC.

**Conclusion/Implications:** Confocal laser endomicroscopy provides real-time high-resolution images of the normal endometrium and endometrial lesions. Compared with histopathology, confocal laser endomicroscopy has high diagnostic accuracy and may become an auxiliary examination tool for hysteroscopy, as it is useful for early identification of endometrial lesions, real-time diagnosis of tumor, and detection of tumor boundaries for complete tumor resection. These findings can lay a foundation for the feasible use of fertility-sparing local excision of tumor lesions by hysteroscopy.

EP145 / #573

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **NOMOGRAM PREDICTION MODEL OF SEVERE POSTOPERATIVE COMPLICATIONS AFTER CYTOREDUCTIVE SURGERY FOR ADVANCED OVARIAN CANCER**

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**Introduction:** It has been established that age, smoking, duration of operation, hypertension and other medical complications are independent risk factors for postoperative complications. Kumar et al. developed the first histogram prediction model for postoperative complications of ovarian cancer, which incorporated age, BMI, ASA score, preoperative albumin, stage, and surgical complexity to help clinicians and patients make patient-centered decisions about PDS. The purpose of this study was to analyze the influencing factors of postoperative complications, and then construct a nomogram prediction model for Clavien-Dindo grade 3-4 postoperative complications.

**Methods:** 200 patients undergoing cytoreductive surgery from January 2019 to January 2023 were collected. They were divided into SPC group (n=57) and no SPC group (n=143). Univariate analysis and logistic regression analysis were used to analyze the risk factors, and a nomogram model was established to predict the occurrence of SPC in cytoreductive surgery patients.

**Results:** Univariate analysis showed that there were significant differences in age, preoperative CA125, preoperative HE4, preoperative VEGF, preoperative tumor area score, tumor load score, albumin in the two groups ( $P < 0.05$ ). Multivariate logistic regression analysis showed that age (OR=4.82, 95%CI: 1.85~13.62), preoperative tumor area score (OR=6.24, 95%CI: 1.73~30.4), tumor load score (OR=6.25, 95%CI: 2.34~18.14), albumin (OR=0.19, 95%CI: 0.07~0.47) were independent influencing factors of SPC after cytoreductive surgery. The nomogram model was constructed by using the above indexes. The Area Under Curve of the model was 0.913 (95%CI: 0.866~0.959), the sensitivity was 82.50%, and the specificity was 88.80%.

**Conclusion/Implications:** Age, preoperative tumor area score, tumor load score, albumin are independent factors of SPC after cytoreductive surgery. Nomogram can provide an individualized postoperative SPC risk prediction for cytoreductive surgery patients.

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Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **NOMOGRAM BASED ON HUMAN EPIDIDYMIS PROTEIN 4 PREDICTED CONCURRENT ENDOMETRIAL CANCER FOR PATIENTS DIAGNOSED WITH ATYPICAL ENDOMETRIAL HYPERPLASIA BEFORE SURGERY**

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**Introduction:** This study aimed to investigate whether preoperative human epididymis protein 4 (HE4) could predict concurrent endometrial cancer (EC) for patients diagnosed with atypical endometrial hyperplasia before surgery and help to establish a nomogram for better clinical management.

**Methods:** Preoperative-AEH patients who underwent hysterectomy in a tertiary hospital from Jan 2020 to Dec 2022 were retrospectively analyzed. Independent predictive factors determined by multivariate logistic regression model were used to establish nomogram and internal validation was performed by a bootstrap resampling method.

**Results:** A total of 455 preoperative-AEH patients were included, 23.4% of whom had concurrent EC. HE4 level significantly increased in concurrent-EC patients compared with final-diagnosed AEH patients (median 50.5 vs 43.7 pmol/L,  $p < 0.001$ ). ROC curves also showed good predictive potential of HE4 for concurrent EC (AUC = 0.696, 95%CI=0.633-0.760,  $p < 0.001$ ) and concurrent intermediate-high-risk EC (AUC = 0.713, 95%CI=0.563-0.863,  $p = 0.005$ ). Multivariate analysis revealed the independent predictive factors for concurrent EC were HE4 level (OR = 3.84; 95% CI = 2.07-7.13), postmenopausal status (OR = 5.25; 95% CI = 2.26-12.22) and BMI (OR = 2.09, 95% CI = 1.12-3.91). The three factors were used to create the nomogram that showed a better goodness-of-fit for predicting concurrent EC. The bootstrap-corrected of concordance index of nomogram was 0.726 (95% CI=0.665-0.784), which was higher than that of each factor alone.

**Conclusion/Implications:** HE4 presented good predictive potential for concurrent EC in preoperative-AEH patients. The nomogram based on HE4, postmenopausal status and BMI might improve this predictive value to stratify high-risk patients for better clinical strategy.

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**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **MMR STATUS ACCORDING TO ETHNICITY IN NEW ENDOMETRIAL CANCER DIAGNOSES WITHIN THE AUCKLAND REGION**

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**Introduction:** Endometrial cancer (EC) is the most common gynaecological malignancy in New Zealand. Pacific women have the highest incidence, which is rising in those under 50 years of age. The introduction of immunohistochemistry for EC has important implications for identification of potential Lynch syndrome (LS). Universal testing of EC tumours for a mutation in one of the DNA mismatch repair genes (MMR) was introduced to New Zealand in 2017. The objective of this study was to investigate the rate of MMR deficient and proficient tumours within our population, and whether these rates vary according to ethnicity.

**Methods:** This is a retrospective population-based cohort study of all cases of EC diagnosed between 1st January 2017 until 31 December 2018 within the Auckland region. Incidence of MMR deficient and proficient tumours was assessed for each ethnicity and compared.

**Results:** 409 patients were diagnosed with EC, 81.6% (n=334/409) underwent MMR IHC testing. There were 266 pMMR (79.6%) and 68 dMMR (20.4%) EC tumours. 26.1% of EC in European patients were dMMR, compared with 10% in Māori (p=0.06, RR 0.4 (0.1 – 1.2)), and 11.4% in Pacific (p=0.004 RR 0.5 (0.3 – 0.9)), and 28.3% in Asian (ns). 8 patients (2.3%) were diagnosed with Lynch Syndrome: 4/8 (50%) European, 2/8 (25%) Asian, 1/8 (12.5%) Indian, 1/8 (12.5%) Middle Eastern.

**Conclusion/Implications:** Despite having an increased incidence of EC in New Zealand, Māori and Pacific people have significantly lower rates of MMR deficient tumours than the European population. None of the Pacific or Māori patients had Lynch syndrome.

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**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **THE ROLE OF DDIT4 AS A HYPOXIA-INDUCIBLE GENE AND PROGNOSTIC BIOMARKER IN TYPE II ENDOMETRIAL CANCER**

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**Introduction:** Although extensive research has been conducted on endometrial cancer and its hypoxic microenvironment, the role of DDIT4 in endometrial cancer remains unexplored. This study aimed to investigate the significance of DDIT4 as a prognostic biomarker for endometrial cancer using immunohistochemical staining and RNA-sequencing.

**Methods:** Four types of endometrial cancer cells were cultured under normoxia and hypoxia conditions, and RNA-seq was used to examine differentially expressed genes. Immunohistochemical staining for DDIT4 and HIF1A was performed in 86 patients with type II endometrial cancer treated at our hospital. Statistical methods were used to analyze the correlation between DDIT4 expression and other clinicopathological factors and to assess its prognostic role.

**Results:** The expression analysis of hypoxia-inducible genes using the four types of endometrial cancer cells revealed that DDIT4 was among the 28 genes upregulated in all cells. Our immunohistochemical analysis of DDIT4 expression in endometrial cancer tissues showed that high DDIT4 expression was significantly correlated with a favorable prognosis in both progression-free survival and overall survival according to univariate and multivariate COX regression analyses. In recurrent cases, metastasis only to lymph nodes was significantly related to high DDIT4 expression, whereas metastasis to other parenchymal organs was significantly dominant in patients with low DDIT4 expression.

**Conclusion/Implications:** DDIT4 expression can predict survival and recurrence in type II endometrial cancer, indicating its potential use as a prognostic biomarker.

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**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **CD47 EXPRESSION AND MACROPHAGE INFILTRATION IN TYPE 2 ENDOMETRIAL CANCER**

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**Introduction:** This study aimed to investigate the role of CD47 in type 2 endometrial cancer and its relationship with macrophage infiltration and patient prognosis.

**Methods:** A retrospective study was conducted on 75 patients with type 2 endometrial cancer who underwent hysterectomy between 2002 and 2017 at Nagoya University Hospital. Formalin-fixed paraffin-embedded tissue samples were collected and stained for CD47, CD68, and CD163 to assess macrophage infiltration. The correlation between CD47 expression, macrophage infiltration, and patient prognosis was analyzed.

**Results:** CD47 expression was not significantly associated with prognosis in type 2 endometrial cancer. However, higher CD47 expression in tumor cells was significantly associated with fewer CD68 macrophages at the tumor margins. A poorer prognosis was observed in patients with more CD68 macrophages and fewer CD163 macrophages at the tumor margins compared to the other patients. No significant differences were observed in age, stage, or histological type.

**Conclusion/Implications:** CD47 expression may not be a reliable prognostic factor for type 2 endometrial cancer. However, higher CD47 expression in tumor cells was found to be associated with fewer CD68 macrophages at the tumor margins, and a greater number of CD68 macrophages and a lower number of CD163 macrophages at the tumor margins were poor prognostic factors. Further investigation into the association between CD47 expression and macrophage subtypes in endometrial cancer is warranted.

**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **THE PROGNOSTIC SIGNIFICANCE OF PARA-AORTIC LYMPH NODE METASTASES IN ENDOMETRIAL CANCER: JAPANESE GYNECOLOGIC ONCOLOGY GROUP STUDY JGOG2043 POST HOC ANALYSIS**

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**Introduction:** Objective. This study aimed to examine the prognostic impact of para-aortic lymphadenectomy (PALX) in endometrial cancer patients at post-operative risk of recurrence.

**Methods:** JGOG2043 was a clinical trial conducted to assess the efficacy of three distinct chemotherapeutic regimens as adjuvant therapy in endometrial cancer patients with post-operative recurrent risk. A retrospective analysis was performed on patients who underwent pelvic lymphadenectomy (PLX) alone or both PLX and PALX in JGOG2043. Cases with residual disease or missing data were excluded. The number of resected and positive nodes and other clinicopathologic risk factors for survival were retrieved.

**Results:** Four hundred two patients underwent PLX and PALX, while 250 underwent PLX alone. It was difficult to evaluate the survival impact of PALX because the PALX was more frequently applied for higher-risk cases with high-risk histology, more than 1/2 myometrial invasion, and positive pelvic lymph nodes. In the PLX and PALX group, Kaplan-Meier analysis showed that patients with two or more para-aortic lymph node (PAN) metastases exhibited significantly inferior overall survival (OS) compared to those with 0-1 metastasis ( $P < 0.0001$ ). Multivariate analysis revealed that two or more metastases in PAN are one of the independent risk factors (HR, 2.52; 95%CI, 1.48-4.27;  $P < 0.001$ ), as well as high-risk histology and advanced age for OS.

**Conclusion/Implications:** The therapeutic significance of PAN removal was difficult to assess in the JGOG 2043 cohort, but two or more PAN metastases were identified as a significant poor prognostic factor.

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**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## UTERINE SARCOMA: A CASE SERIES OF 16 PATIENTS

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**Introduction:** Uterine sarcoma is a rare and aggressive malignancy arising from the smooth muscle or connective tissue of the uterus. Due to its rarity, there is limited information available on the clinical presentation, treatment, and prognosis of this disease. The aim of this study is to report the clinical and pathological features, as well as treatment outcomes of 16 cases of uterine sarcoma.

**Methods:** We conducted a retrospective analysis of 16 patients diagnosed with uterine sarcoma between 2015 and 2021 at our tertiary care hospital. Clinical data, including age, presenting symptoms, tumor characteristics, treatment modalities, and survival outcomes were collected from medical records.

**Results:** The mean age of the patients was 53 years (range: 35-72). The most common presenting symptom was abnormal uterine bleeding (n=11, 68.75%). The majority of the tumors were leiomyosarcoma (n=14, 87.5%). The mean tumor size was 7.4 cm (range: 4-15 cm). The most common treatment modality was surgery (n=14, 87.5%), with adjuvant therapy administered in some cases. 12 patients were treated with an initial hysterectomy with bilateral adnexectomy due to the strong preoperative suspicion of uterine sarcoma on radiological data. The overall 5-year survival rate was 43.8%. 4 patients had an initial myomectomy and then a complement by hysterectomy and bilateral adnexectomy was performed after the final anatomopathological examination.

**Conclusion/Implications:** Uterine sarcoma is a rare malignancy with a poor prognosis. The most common presenting symptom is abnormal uterine bleeding. Surgery is the mainstay of treatment, and adjuvant therapy may be considered in selected cases.



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Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **THE EFFICACY AND SAFETY OF LENVATINIB PLUS PEMBROLIZUMAB IN PATIENTS WITH RECURRENT ENDOMETRIAL CANCER; A JAPANESE SINGLE INSTITUTIONAL EXPERIENCE**

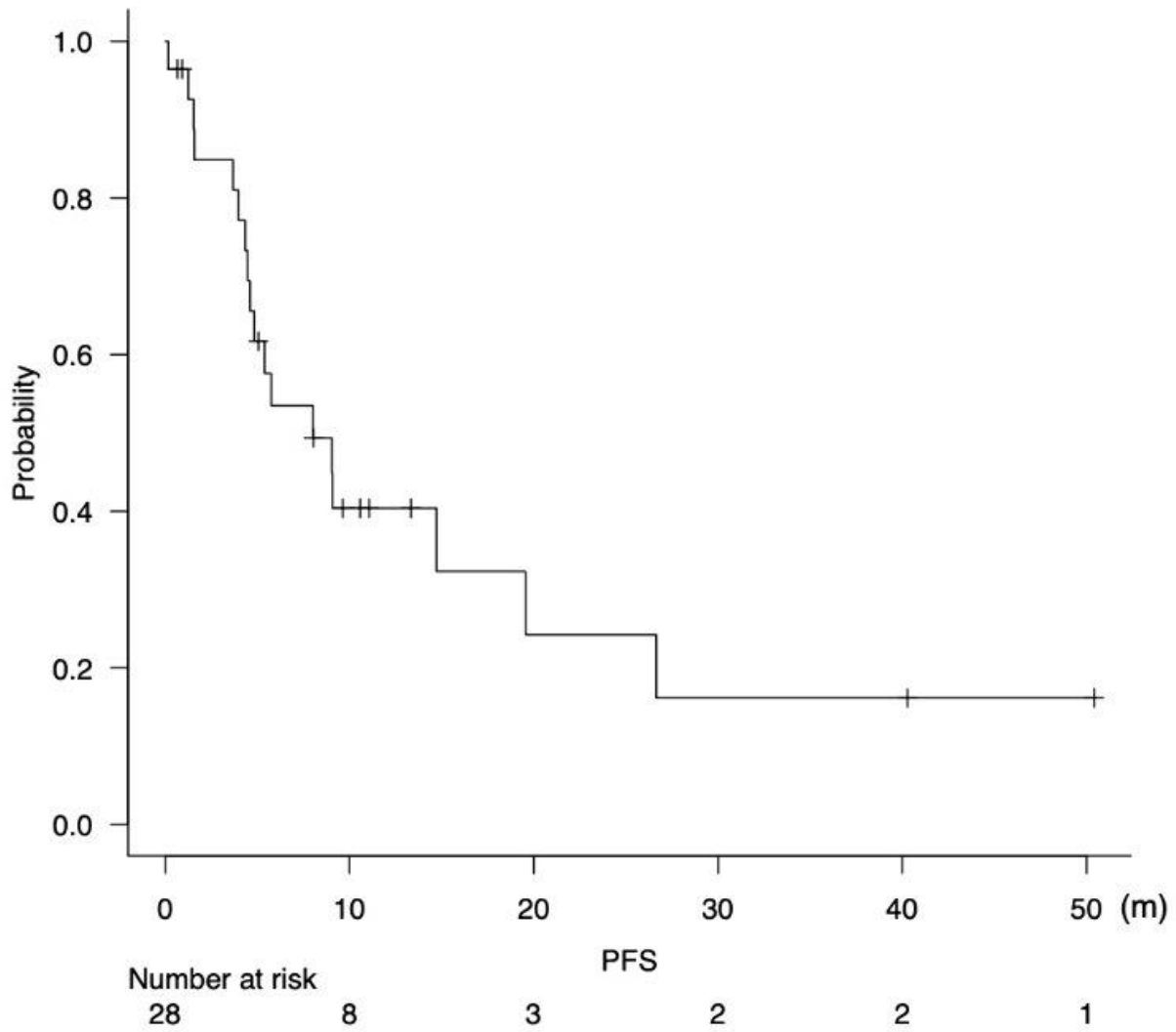
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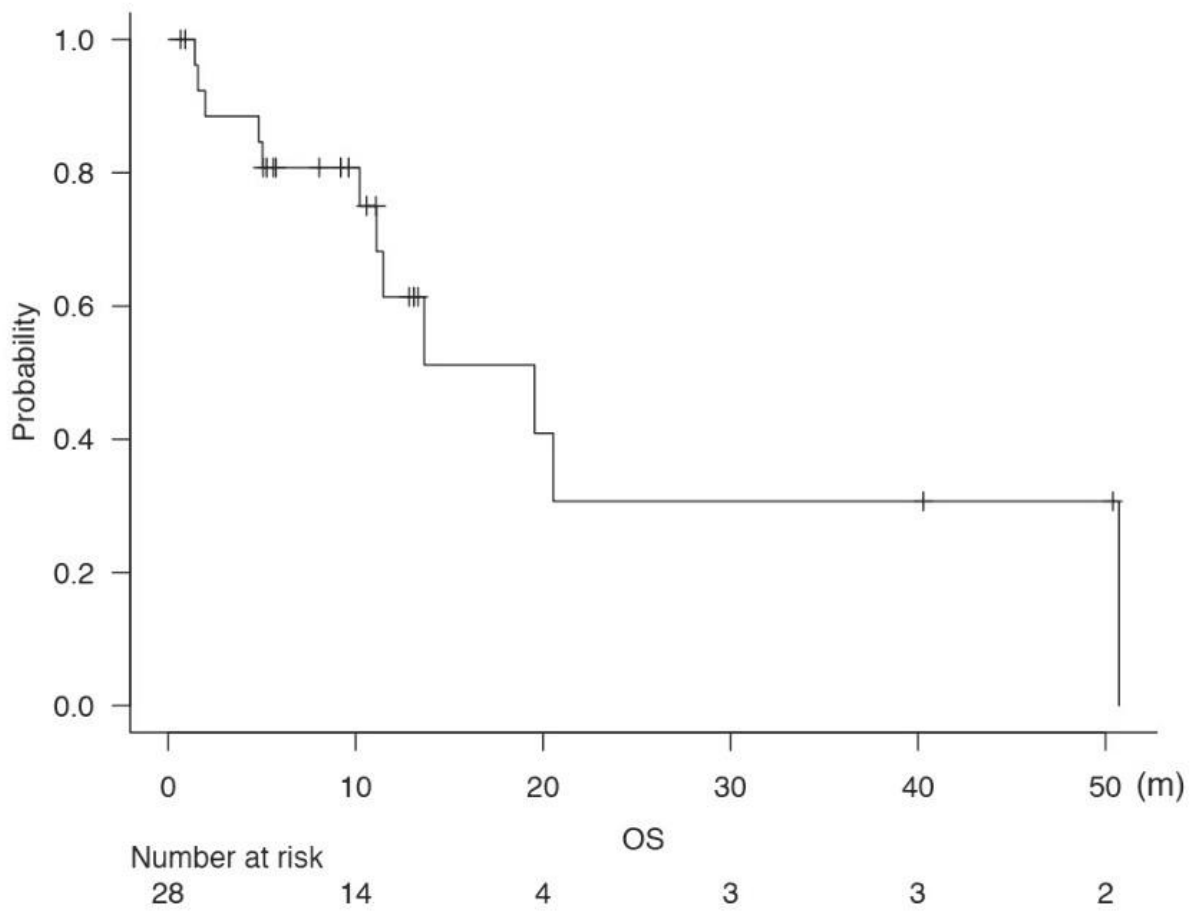
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**Introduction:** Lenvatinib plus pembrolizumab (LP) has been approved for the treatment of advanced or recurrent endometrial cancer, but there have been few reports in clinical practice. We aimed to investigate the efficacy and safety of LP in real clinical practice.

**Methods:** We retrospectively reviewed the medical records regarding patients who received LP for recurrent or advanced endometrial cancer at our hospital from 2018 to 2023. The overall response rate (ORR), progression-free survival (PFS), and overall survival (OS) were evaluated regarding efficacy, and adverse events were evaluated regarding safety.

**Results:** Twenty-eight patients were included. The median age was 59 (31-78) and the median observation period was 9 months (0.7-45). Regarding mismatch repair status, one patient was deficient and 27 patients were proficient. The histologic subtypes were endometrioid G1/2 in eight patients, endometrioid G3 in nine, carcinosarcoma in four, serous in three, mixed in three, and clear cell in one, respectively. The best response was complete response in one patient (4%), partial response in 11 (39%), stable disease in eight (29%), progressive disease in six (21%), not evaluated in two (7%), and the ORR was 43%. The median PFS and OS were 8.0 and 19.6 months, respectively. Adverse events with grade 3 or higher were observed in 17 patients (61%). Five patients (18%) had to discontinue treatment due to toxicities.





**Conclusion/Implications:** LP showed comparable efficacy to the phase III trial in clinical practice, however, it caused serious adverse events that were different from conventional cytotoxic chemotherapies. It was considered important to manage these toxicities.

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**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **SURVIVAL OUTCOMES IN ADVANCED STAGE OPERABLE CARCINOMA ENDOMETRIUM: EXPERIENCE OF SURGICAL TREATMENT AT A TERTIARY CARE CANCER CENTRE**

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**Introduction:** There is a lack of consensus regarding the surgical management of advanced-stage endometrial cancer. We aim to look at survival outcomes of advanced-stage carcinoma endometrium, managed through surgery and adjuvant treatment.

**Methods:** This was a retrospective study from a tertiary care cancer centre in India that included all women registered between 1st August 2011 and 31st January 2021 with operable advanced-stage carcinoma endometrium (stages 3 and 4). Their relevant data were collected from electronic medical records.

**Results:** Out of 1760 endometrial cancer cases screened 102 women with stage 3 and 4 disease were operable. The mean age was 59 years. Most women were parous (85%) with an ECOG status of 0 or 1 (90%). Histopathology was high grade in 73 women (71.6%). Surgeries performed were: Staging surgery 50(49%), debulking surgery 38(37.2%), surgery after chemotherapy 6(5.8%). Eight women (7.8%) were operable but given only chemotherapy for various reasons. 72 (76.6%) patients received planned adjuvant treatment. Overall, 50 patients (56.8%) were upstaged after surgery. At the time of analysis, 32 (31.4%) women were alive without disease. Median disease-free survival of stage 3, stage 4 and both combined were 32.8 months (95%CI: 0-87), 19 months (7.6-30.3), and 23.5 months (95% CI: 13.7-33.2) respectively. Median overall survival was not reached for stage 3. For stage 4 and both combined, it was 41 months (95% CI: 18.8-63.1) and 50.1 months (95% CI: 31.2-69.1) respectively.

**Conclusion/Implications:** Upfront surgery in advanced-stage endometrial carcinoma gives a respectable survival outcome after maximal surgical attempt.

EP157 / #814

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **THE DIFFERENCE BETWEEN ESTROGEN RECEPTOR AND PROGESTERONE RECEPTOR POSITIVITY IN TYPE I AND TYPE II ENDOMETRIAL CANCER**

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**Introduction:** Endometrial cancer is a major gynecological cancer in women and can be classified into two types: type I and type II. Type I endometrial cancer is often estrogen-dependent and typically express estrogen receptors (ER) and progesterone receptors (PR), while Type II endometrial cancer is known to do not typically express these receptors and has a poor prognosis. This study aims to investigate the differences in ER and PR positivity between Type I and Type II endometrial cancer.

**Methods:** A retrospective analysis was performed on medical records of 170 endometrial cancer patients who underwent molecular analysis between 2010 and 2022 at a single-center. Immunohistochemistry was used to assess ER and PR expression in tumor samples, and the results were compared between the two groups.

**Results:** Of 161 patients, 80(49.69%) were diagnosed with Type I endometrial cancer, and 81(50.31%) were diagnosed with Type II endometrial cancer. The study found that ER or PR positivity was significantly higher in Type I endometrial cancer compared to Type II endometrial cancer ( Type I – 84.21% vs. Type II – 65.45% ). Specifically, ER positivity was observed in 78.79% of Type I compared to 55.93 % of Type II. And PR positivity was 80.36% of Type I compared to 50.91% of Type II endometrial cancer.

**Conclusion/Implications:** In conclusion, the results of this study highlight the importance of distinguishing between Type I and Type II endometrial cancer and tailoring treatment strategies accordingly based on the expression of ER and PR.

EP158 / #445

**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **SURVIVAL AND QUALITY OF LIFE IN PATIENTS WITH UTERINE CARCINOSARCOMA: A TERTIARY CENTER OBSERVATIONAL STUDY**

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**Introduction:** Patients with uterine carcinosarcoma (UCS) have a dismal prognosis despite receiving extensive treatment which also may abate the quality of life (QoL). Our aim is to determine the survival in patients with UCS and to assess the QoL during and after treatment.

**Methods:** An observational study was performed in the Erasmus Medical center between 2016 – 2021, including all patients with UCS. Clinical data was collected from diagnosis until 5 years after treatment or death. EORTC QLQ-C30 and -EN24 were obtained at four time points: pre-operative, end of treatment (ET), one year, and two year after treatment. QLQ-C30 outcomes were also compared with normative data of a matching reference group.

**Results:** 52 patients were included in the study, with a mean age of 69 years (range 50-86 years) at the time of diagnosis. The majority of patients were diagnosed with early-stage disease (N=20, N=5, N=9, N=18 patients respectively with FIGO stage I-IV). Median overall survival (OS) was 18 months, with the poorest survival seen in patients with stage IV disease (median OS=9 months) (figure 1).

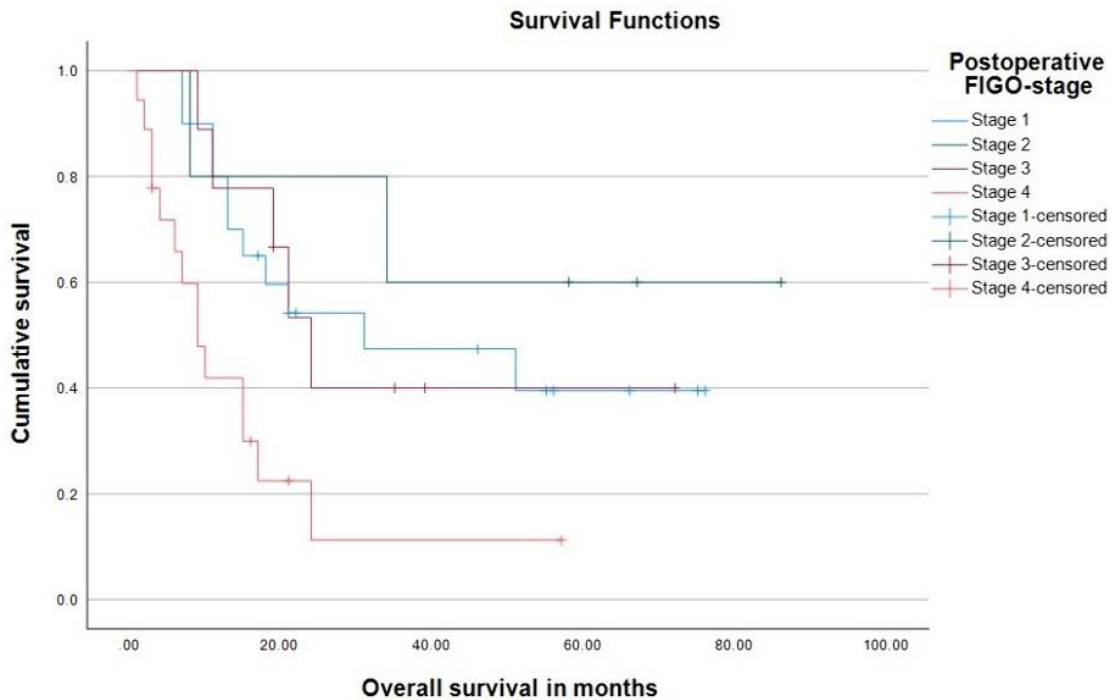


Figure 1. Kaplan-Meier curve for overall survival (OS) among patients with FIGO stage I, II, III and IV UCS. Patients who were lost to follow up or alive at end of follow up are censored.

QoL assessment indicated that patients with advanced stage disease reported significantly more deterioration on insomnia, financial problems, tingling/numbness and hair loss. Furthermore, comparing QLQ-C30 outcomes at ET showed a significant difference compared to normative data in overall quality of life, role, emotional, cognitive and social functioning (Figure 2).

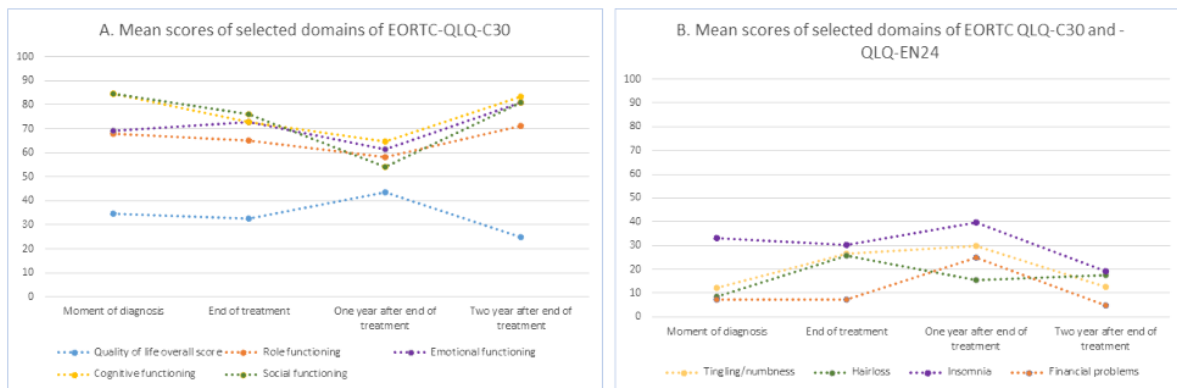


Figure 2. A) Mean scores of total study population at four time points of selected domains of EORTC-QLQ-C30: quality of life overall score and role, emotional, cognitive, and social functioning. These domains were statistically different compared to normative data of a matched reference group (women from 60-69 years) which was respectively 76.5, 83.8, 85.9, 91.3 and 91.3 (not depicted). For these domains, a higher score equals a higher quality of life. B) Mean scores of total study population at four time points of selected domains of EORTC-QLQ-C30 and QLQ-EN-24: Tingling/numbness, hair loss, insomnia and financial problems. These domains were statistically more affected at advanced stage disease (not separately depicted). For these domains, a lower score equals a higher quality of life. Data of patients who were deceased at later timepoints were not included in the analysis.

**Conclusion/Implications:** Patients with UCS face a poor prognosis, and the effect of treatment on QoL be considered in clinical decision-making, particularly in patients with advanced stage disease.

EP159 / #1534

**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **LEVERAGING PERSONALIZED CIRCULATING TUMOR DNA MONITORING TO PREDICT TREATMENT RESPONSE AND RECURRENCE IN HIGH-RISK ENDOMETRIAL CANCER**

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**Introduction:** Adjuvant therapy is often used in high risk endometrial cancer (HREC) due to increased risk of recurrence. Histology alone does not accurately predict recurrence. Circulating tumor DNA (ctDNA) is a validated prognostic biomarker for many solid tumors, yet its utility in HREC is unclear.

**Methods:** In an ongoing, prospective registry, serial plasma samples were collected pre- and post-hysterectomy, and post-adjuvant treatment (AT) from 25 patients with newly diagnosed HREC treated with primary surgery. CtDNA was detected using a tumor-informed assay (Signatera™ Natera, Inc.) and correlated with recurrence-free survival (RFS).

**Results:** Personalized ctDNA assays were successfully designed for 24/25 patients. Median age was 63 years (range: 30-74). Pre-operatively, ctDNA was detectable in 60.87% patients (median 1.3 mean tumor molecules/mL), with 55% and 80% in stage I and II-IV, respectively. ctDNA cleared with surgery in 83% (10/12) patients; only one (10%) of these patients recurred. Three patients were ctDNA-positive post-operatively; 2/3 remained ctDNA-positive post-AT and recurred; 1/3 cleared ctDNA post-AT and remained disease-free. Seven patients recurred; ctDNA-positivity was observed in 43% (3/7) pre-operatively, 33% (2/6) post-operatively, and 29% (2/7) post-AT. There was no association between pre-operative ctDNA and recurrence ( $p=0.27$ ). Post-AT, ctDNA-positivity was significantly associated with shorter RFS compared to ctDNA-negativity ( $p=0.02$ ; HR=7.92; 95%CI: 1.43-43.73).

**Conclusion/Implications:** Post-AT ctDNA negativity and/or clearance were associated with better response and RFS in HREC patients. ctDNA detection was feasible across multiple timepoints in early-stage HREC patients. Future studies will determine whether the addition of ctDNA to other molecular/histologic characteristics can identify patients who may benefit from escalation/de-escalation of AT.



EP160 / #126

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **SURVIVAL BENEFIT OF PARAAORTIC LYMPH NODE EVALUATION IN ENOMETRIOID ENOMETRIAL CARCINOMA; A 10-YEAR RETROSPECTIVE STUDY IN THAILAND**

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**Introduction:** To evaluate 5-year survival in patients with endometrioid endometrial carcinoma, who underwent evaluation of retroperitoneal pelvic lymph nodes alone, compared to evaluation of pelvic with paraaortic lymph nodes.

**Methods:** This retrospective cohort study enrolled 636 women who were diagnosed with endometrioid endometrial carcinoma and underwent surgical staging at Faculty of Medicine Siriraj Hospital, Thailand between January 2006 and December 2015. Patients who underwent pelvic lymph node evaluation (n = 257) and pelvic with paraaortic lymph node evaluation (n = 379) were included.

**Results:** The median follow-up time was 60 months. The 5-year overall survival rate (OS) in the pelvic lymph node (PLN) and pelvic with paraaortic lymph node (PPALN) groups was 81.6% and 87.7%, respectively (p = 0.073). However, the PPALN group had significantly longer survival than the PLN group after adjustment for other prognostic factors (adjusted HR 1.63 (1.06-2.52, p=0.028)). The five-year disease-specific survival rate (DSS) was 88.8% in the PLN group and 93.5% in the PPALN group (p =0.025). There was a trend to improve 5-year DSS for the ESGO/ESTRO/ESP high risk patients, who underwent PPALN evaluation (85.6%) compared with PLN evaluation (70.8%), p=0.061.

Figure 1. Kaplan-Meier analysis of (A) 5-year OS of PLN and PPALN evaluation, (B) 5-year OS of PLN evaluation, PPALN evaluation with negative and positive PALN, (C) 5-year DSS of PLN and PPALN evaluation, (D) 5-year DSS of PLN evaluation, PPALN evaluation with negative and positive PALN, (E) 5-year RFS of PLN and PPALN evaluation, (F) 5-year RFS of PLN evaluation, PPALN evaluation with negative and positive PALN

\* PPALN = pelvic and paraaortic lymph node, PLN = pelvic lymph node, PALN = paraaortic lymph node

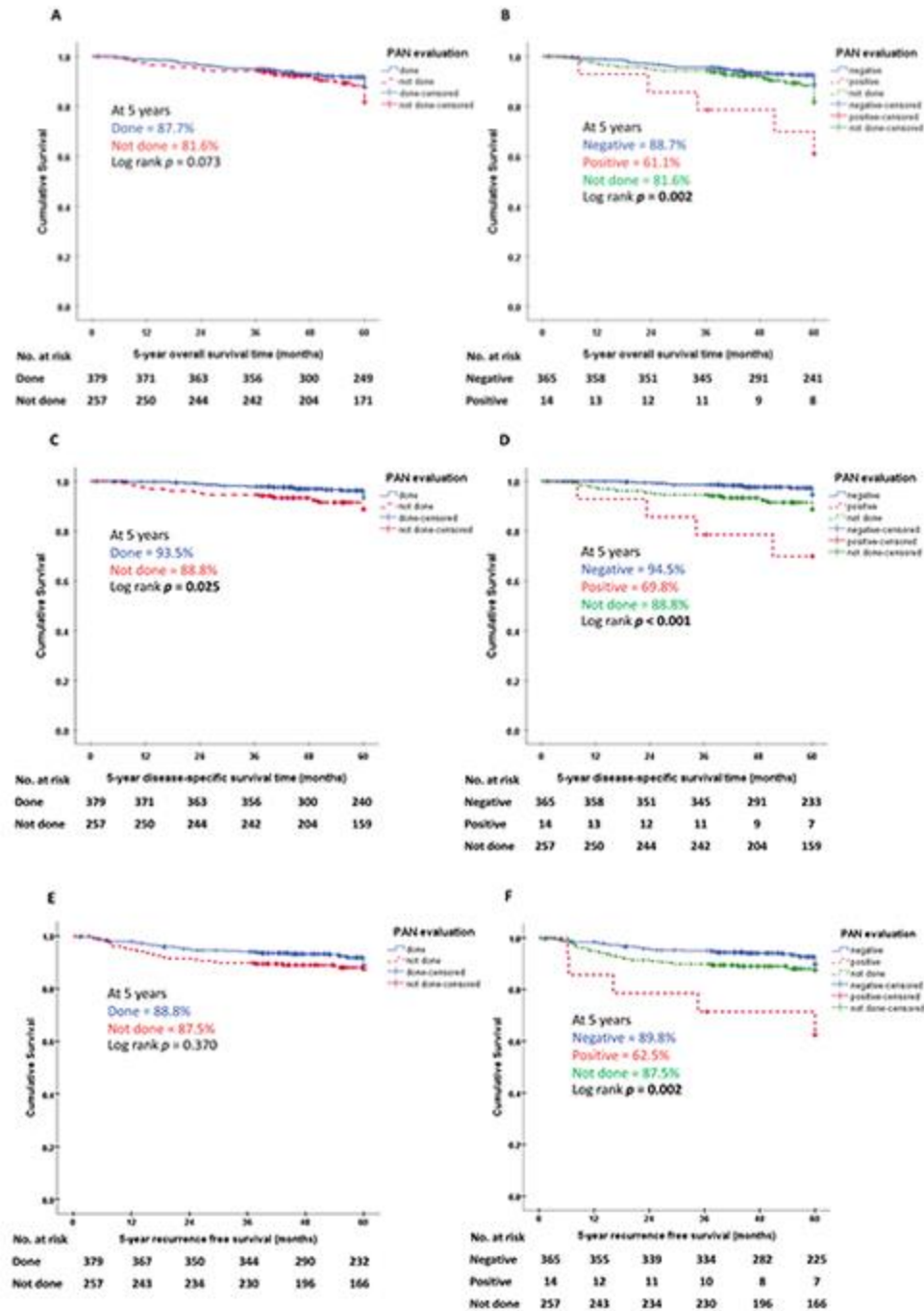
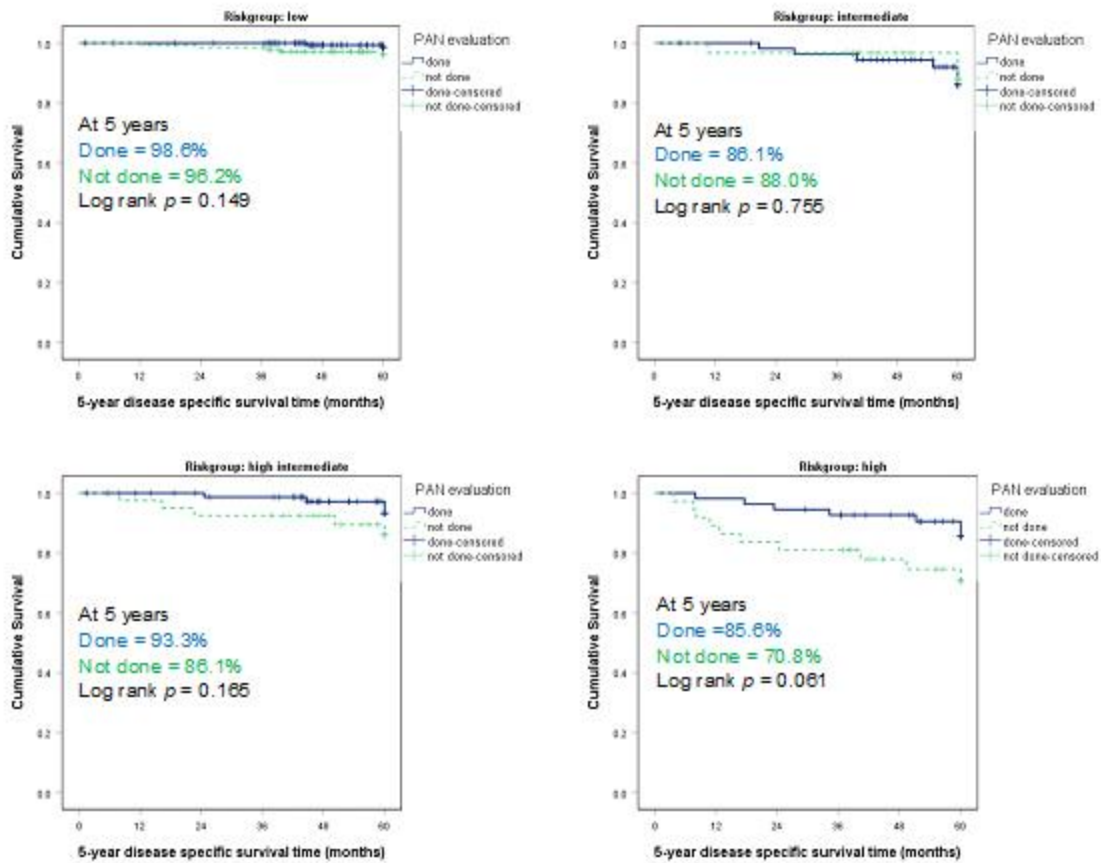


Figure 2: Kaplan-Meier analysis of 5-year DSS of PLN and PPALN evaluation stratified by ESGO/ESTRO/ESP risk groups (A) Low risk (B) Intermediate risk (C) High-intermediate risk (D) High risk



**Conclusion/Implications:** In endometrioid endometrial carcinoma, patients who underwent evaluation of the pelvic and paraaortic lymph nodes had a significantly 5-year lower risk of death compared to only pelvic lymph node evaluation. Currently, we suggest performing pelvic and paraaortic lymph node evaluations in each patient with endometrioid endometrial carcinoma, especially in the ESGO/ESTRO/ESP high-risk patients.

EP161 / #718

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **THE ASSOCIATION OF TUMOR MOLECULAR PROFILING AND CLINICAL TRIAL ENROLLMENT IN AN ADVANCED/RECURRENT ENDOMETRIAL CANCER COHORT**

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**Introduction:** To understand the utility of comprehensive genomic profiling (CGP) in endometrial cancer clinical trial enrollment

**Methods:** This was a retrospective chart review of three hospitals (large urban, smaller urban, and large suburban) within one health system. All patients undergoing surgical staging between Jan 2016- Jan 2022 with pathologically confirmed endometrial adenocarcinoma were included. The primary outcome of this study was proportion of patients who were enrolled in a clinical trial. Secondary outcomes were proportion of patients who underwent CGP, and the proportion of patients with an actionable mutation who enrolled in a clinical trial.

**Results:** Of 1099 patients included in this study, 45 (4.1%) patients were enrolled in a trial. 31 (68.9%) of those who were enrolled in a clinical trial had undergone CGP, compared to 14 (31.1%) who had not undergone CGP ( $p < 0.001$ ). Those who had CGP were more likely to be enrolled in a clinical trial compared to those who did not have CGP (OR 13.55, CI 5.82 - 31.56). Of the 31 patients enrolled in trials who had undergone CGP, 24 (77.4%) of patients had an actionable molecular finding on CGP (TP53, 14; HER2 positive, 4; MSI-H, 3; PIK3CA, 5; TMB-H, 2; CCNE amplification, 3; BRCA2, 1; BRCA1 0; POLE, 0). Of 114 patients (10.4%) who had CGP, 56 (49.1%) were White, while 36 (31.6%) were Black

(p<0.001).

N (%)	Not enrolled (n= 1054, 95.9%)	Enrolled in trial (n= 45, 4.1%)	p-value
Age at surgery (median, range in yrs)	64 (27-93)	64 (38-76)	0.86
BMI (mean +/- SD)	32.15 +/- 8.27	31.63 +/- 7.83	0.66
Race			<0.01
White	605 (55.1%)	16 (1.5%)	
Black	179 (16.3%)	20 (1.8%)	
Asian	80 (7.3%)	2 (0.2%)	
Other	190 (17.3%)	7 (0.6%)	
Ethnicity			0.99
Non-Hispanic	528 (48.0%)	22 (2.0%)	
Hispanic	47 (4.3%)	2 (0.2%)	
Unknown	479 (43.6%)	21 (1.9%)	
Insurance			0.90
Private	415 (37.8%)	20 (1.8%)	
Medicaid	141 (12.8%)	6 (0.5%)	
Medicare	485 (44.1%)	18 (1.6%)	
Uninsured	13 (1.2%)	1 (0.1%)	
Hospital			<0.01
Large urban	521 (47.4%)	25 (2.3%)	
Small urban	243 (22.1%)	17 (1.5%)	
Large suburban	290 (26.4%)	3 (0.3%)	
Year of surgery			<0.001
2016	53 (4.8%)	9 (0.8%)	
2017	129 (11.7%)	12 (1.0%)	
2018	135 (12.3%)	3 (0.3%)	
2019	157 (14.3%)	5 (0.5%)	
2020	236 (21.5%)	6 (0.5%)	
2021	269 (24.5%)	7 (0.6%)	
2022	75 (6.8%)	3 (0.3%)	
Stage			<0.001
Recurrent (I, II)	905 (82.3%)	15 (1.3%)	
Advanced (III, IV)	149 (13.6%)	30 (2.7%)	
Grade			<0.001
I	534 (48.6%)	3 (0.3%)	
II	175 (15.9%)	5 (0.5%)	
III	284 (25.8%)	29 (2.6%)	
N/A	61 (5.6%)	8 (0.7%)	
Histology			<0.001
Endometrioid	758 (69.0%)	15 (1.4%)	
Serous/clear	131 (11.9%)	14 (1.3%)	
Cardinosarcoma	70 (6.4%)	8 (0.7%)	
Other	95 (8.6%)	8 (0.7%)	

**Conclusion/Implications:** Patients who have undergone CGP were more 13 times more likely to enroll in a clinical trial. Race may be a barrier to undergoing CGP.

EP163 / #651

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **CLINICAL IMPACT OF THE NOVEL FIGO 2023 STAGING SYSTEM FOR ENDOMETRIAL CANCER**

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**Introduction:** FIGO staging for endometrial cancer will be revised in 2023. The novel staging will include major changes such as the addition of lymphovascular invasion and histological type. The aim of this study is to evaluate the revised FIGO2023 staging.

**Methods:** This study included 1,006 patients diagnosed with endometrial cancer between 2012 and 2021 at our institution. We analyzed them based on the pTNM classification and clinicopathological factors.

**Results:** Under the FIGO2023 classification, 59.7% of patients were classified as stage I (26.9% were classified as IA1, 27.4% as IA2, 0.5% as IA3, and 4.9% as IB), 23.2% as stage II (1.8% as IIA, 14.2% as IIB, and IIC as 7.2%), 12.0% as stage III (1.0% as IIIA1, 0.7% as IIIA2, 1.1% as IIIB1, 0.5% as IIIB2, 3.4% as IIIC1, and 5.4% as IIIC2), and 5.1% as stage IV (0.1% as IVA, 2.6% as IVB, and 2.4% as IVC). Among stage I, the 5-year overall survival rate (5y-OS) was 99.1% in IA1, 99.2% in IA2, 100% in IA3, and 100% in IB. Among stage II, the 5y-OS was 100% in stage IIA, 93.2% in IIB, and 85.2% in IIC. Among stage III, the 5y-OS was 100% in stage IIIA1, 66.7% in IIIA2, 66.7% in IIIB1, 100% in IIIB2, 84.2% in IIIC1, and 84% in IIIC2. Finally, the 5y-OS was 100% in stage IVA, 46.2% in IVB, and 33.3% in IVC among stage IV.

**Conclusion/Implications:** These findings indicate that the revised staging will result in upstaging of some cases with high-grade histologies and positive lymphovascular invasion.

EP164 / #666

**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **DOES PERINEPHRIC FAT PREDICT SURGICAL COMPLICATIONS AND SURVIVAL IN INDIVIDUALS WITH ENDOMETRIAL CANCER?**

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**Introduction:** The aim of this study was to evaluate the association between average perinephric fat (APF) and surgical complications and survival in individuals with endometrial cancer (EC).

**Methods:** This is a retrospective cohort study of individuals with EC who underwent surgical staging in a tertiary cancer centre in Canada (2015 – 2021). APF was measured on pre-operative CT scans. Baseline characteristics, surgical complications and survival data were compared between patients with APF < 2.2 cm and those with APF ≥ 2.2 cm. Cox proportional hazard model was used to evaluate the association between APF and overall survival (OS) and progression-free survival (PFS).

**Results:** Overall, 297 patients were included. Of whom, n=271 had APF <2.2 cm and n=26 had APF ≥ 2.2 cm. Baseline characteristics are presented in table. Patients with APF ≥ 2.2 cm had higher rates of failed sentinel lymph node mapping (31% vs 6%, p<0.001). There were no differences between groups in intraoperative (3% vs 4%, p=0.61) and postoperative complications (14% vs 19%, p=0.71). On univariable analysis, APF was not associated with OS (HR 1.58, 95% CI 0.90-2.78, p=0.11). However, increase in APF was significantly associated with worse PFS (HR 1.49, 95% CI 1.08 -2.06, p=0.02). In a multivariable analysis including age, stage, LVSI and deep myometrial invasion, the association between APF and PFS was not statistically significant (HR 1.35, 95% CI 0.96-1.91,

p=0.08).

Table 1 – Baseline characteristics

<b>Variable</b>	<b>AFP &lt; 2.2 cm (n=271)</b>	<b>AFP ≥ 2.2 cm (n=26)</b>	<b>P value</b>
Age at diagnosis, median, years	64.3 (28.7, 89.3)	70.2 (55.2, 83.5)	0.004
Diabetes, n (%)	57 (22)	13 (50)	0.003
Hypertension, n (%)	110 (42)	21 (81)	<0.001
Dyslipidemia, n (%)	43 (16)	9 (35)	0.003
BMI, median, kg/m <sup>2</sup>	29.6 (16.1, 65.0)	37.2 (28.6, 56.9)	<0.001
Average subcutaneous fat, median, cm	3.0 (0.7, 7.3)	3.2 (1.4, 7.9)	0.39
<b>Stage of disease: n (%)</b>			<b>0.92</b>
I	206 (76)	19 (73)	
II-IV	65 (24)	7 (27)	
<b>Histology: n (%)</b>			<b>0.13</b>
Endometrioid	157 (59)	19 (76)	
Other	107 (41)	6 (24)	

**Conclusion/Implications:** In this cohort of individuals with EC, there was a trend towards worse PFS with increased APF. However, increased APF did not impact perioperative complications or OS.



EP165 / #31

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **LAPAROSCOPIC SLN DETECTION IN PATIENTS WITH ENDOMETRIAL CANCER. EXPERIENCE IN KAZIOR.**

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**Introduction:** In Republic of Kazakhstan, endometrial cancer among malignant tumors occupies the 9th ranking position, and in the structure of gynecological cancer, the 3rd place, about 1000 cases of this disease are detected annually. The main method of treatment for EC is surgical treatment, with mandatory removal of regional lymph nodes (LN) for preventive purposes, regardless of their morphological state. However, prophylactic lymphadenectomy did not justify itself. Plenty of evidence suggests an improvement in survival only in groups of patients who have been diagnosed with metastatic changes in the lymph nodes.

**Methods:** In the period from January 1, 2021 to December 30, 2021, 37 patients with detection of sentinel lymph nodes were registered in KazIOR. We collected retrospective data from history of diseases.

**Results:** The mean age of the patients was 52 years. The average body mass index of patients was 30.2 kg/m<sup>2</sup>. Preoperative assessment of endometrial cancer risk groups showed: low risk in 19 (51.3%) patients, intermediate risk in 11 (29.7%) patients, high risk in 7 (18.9%) patients. Complete pelvic and para-aortic lymph node dissection was performed in 7 (18.9 %). In 30 (81%) patients, at least one sentinel lymph node was successfully mapped. 7 (18.9%) patients had positive nodes. In 37 patients, no postoperative complications were detected. The final histology revealed: 31 (83.7%) patients had endometrioid adenocarcinoma, 6 (16.2%) had clear cell carcinoma.

**Conclusion/Implications:** This study confirms the feasibility of the SLN procedure to assess recurrence risk in patients with early EC and the safety of sentinel lymph node detection.

EP166 / #912

**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **PREVALENCE OF PARAAORTIC LYMPH NODE METASTASIS IN PRESUMED CLINICAL STAGE I ENDOMETRIAL CANCER**

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**Introduction:** The aim of this study was to investigate the prevalence of paraaortic lymph node (LN) metastasis in patients with endometrial cancer, whose preoperative clinical stage was assumed to be FIGO stage I.

**Methods:** We retrospectively analyzed the medical records of 462 patients who underwent surgical staging for endometrial cancer at Yonsei Cancer Center from July 2014 to April 2021. The study population consisted of patients with clinical presumed stage I endometrial cancer and who underwent nodal assessment, including both pelvic and paraaortic LNs.

**Results:** A total of 311 patients met the eligibility criteria for the study. They were classified into low/intermediate and high-risk groups based on histology and myometrial invasion. Of the total patients, 66.9% were classified as low/intermediate risk group, while 33.1% were classified as high-risk group. After surgical staging, 28 patients (9.0%) were upstaged, and 12 patients (3.9%) were found to have LN metastasis. The incidence of LN metastasis was higher in the high-risk group (6.8%) than in the low/intermediate risk group (2.9%). However, the pattern of LN metastasis did not differ between the two groups (pelvic and paraaortic LN metastasis: 16.7% vs. 14.3%; pelvic only: 50% vs. 57.1%; paraaortic only: 33.3% vs. 28.6%, in the low/intermediate vs. high-risk group, respectively).

**Conclusion/Implications:** The incidence of paraaortic LN metastasis in endometrial cancer patients presumed to be FIGO stage I by preoperative radiologic evaluation is low. However, our findings emphasize the importance of nodal assessment, particularly in high-risk groups, as a significant number of patients were upstaged and found to have LN metastasis.

EP167 / #641

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **SENTINEL LYMPH NODE MAPPING USING INDOCYANINE GREEN DYE AND NEAR INFRARED FLUORESCENCE IMAGING METHOD FOR EARLY STAGE ENDOMETRIAL AND CERVICAL CANCER**

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**Introduction:** This study aimed to assess the feasibility and effectiveness of using ICG to detect SLNs & to investigate how patient and tumor-related factors may influence this process in patients with endometrial and cervical cancer in low-middle income country like India.

**Methods:** Patients with early stage cervical and endometrial cancer who underwent primary surgery with SLN identification using ICG Dye between July 2020 and March 2022 were analysed. Bilateral and overall SLN detection rates were calculated and univariate analysis was performed to estimate factors associated with SLN identification failure.

**Results:** 49 patients with endometrial and cervical cancer were included in the study. Successful SLN identification was done in 46 out of 49 patients (93.87%). Unilateral and bilateral detection rate was 89.79% & 83.67% respectively. Sensitivity, Specificity, False Negative Rate, Accuracy of SLN identification using ICG dye was 83.33%, 95.34%, 16.67%, 93.87% respectively. Negative predictive value of this test was 97.6%. In our study, myometrial invasion in endometrial cancer ( $p = 0.44$ ), LVI (with LVI  $p=0.12$ ), Grade of tumor (higher grade,  $p = 0.26$ ), menopausal status (postmenopausal,  $p = 0.09$ ), tumor size ( $>4\text{cm}$ ,  $p=0.62$ ), & Histopathology (adenocarcinoma,  $p = 0.157$ ) have association with decrease SLNs identification, but it did not found statistically significance. Only BMI ( $>30$ ) is found to be statistically significant to prove correlation between Obesity and SLN identification failure ( $p = 0.025$ ).

**Conclusion/Implications:** SLN identification using NIR fluorescence with ICG dye appears to be accurate method in our patients with early stage cervical or endometrial carcinoma. BMI is to be considered as an important factor for decrease SLN identification.

EP169 / #411

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **MACHINE LEARNING METHOD FOR DIFFERENTIAL DIAGNOSIS AND PROGNOSIS PREDICTION FOR EARLY-STAGE UTERINE SARCOMA USING PREOPERATIVE BLOOD BIOMARKER AND AGE**

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**Introduction:** Preoperative differential diagnosis of clinical stage I uterine sarcoma (US) is essential for surgical intervention. Many studies have been done using CT or MRI imaging for machine learning prediction models but not with blood biomarkers. We aimed to develop a new model for diagnosis and prognosis prediction in the US using preoperative blood biomarkers and patient age.

**Methods:** Overall, 143 US patients and 210 benign uterine myoma (UM) patients were randomly assigned to the "training and test" cohort. 78(55%) cases were on clinical stage I. 30 preoperative peripheral blood parameters and patient's age was surveyed. The Random Forest (RF) classifier was used to construct an algorithm. The accuracy, the area under the receiver operating characteristic curve (AUC), and the variable importance were calculated in the test cohort. The Ethics Committee approved this study.

**Results:** The accuracy and AUC values for segregating stage I US from UM were 87% and 0.89, respectively. Variable important parameters for this classifier included age, CRP, and Hematocrit. Additionally, they were 85% and 0.95 in leiomyosarcoma, and 92% and 0.81 in ESS, respectively. Furthermore, unsupervised clustering analysis based on RF showed significant differences in two clusters in clinical stage I US with a median progression-free survival of 47 (3-115) vs. 13 (1-93) months ( $P < 0.001$ ).

**Conclusion/Implications:** The RF approach using common blood biomarkers and patient age can differentiate its malignancy and prognosis of US patients before primary intervention. This predictive model may provide a clinically useful approach to preoperative diagnosis distinct from conventional imaging techniques.

EP170 / #355

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **MELK-MEDIATED PHOSPHORYLATION OF RB1 AND MAD2L1 PROMOTES CHROMOSOMAL INSTABILITY IN UTERINE LEIOMYOSARCOMA**

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**Introduction:** This study aimed to investigate the molecular pathogenesis of Uterine Leiomyosarcoma (ULMS), a highly lethal gynecologic malignancy with limited treatment options, and identify potential therapeutic strategies. ULMS is characterized by chromosomal instability (CIN), and its molecular mechanisms remain poorly understood.

**Methods:** We conducted Whole Genome and Target Region Sequencing to investigate genomic alterations in ULMS. mRNA profiling analysis identified differential expression of genes involved in mitosis and nuclear division pathways, including MELK. In vitro and in vivo experiments assessed the effects of MELK overexpression on cellular proliferation, migration, and invasion.

**Results:** Our study revealed that global chromosomal instability (CIN) was more prevalent than nucleotide alterations in ULMS. Additionally, mRNA profiling analysis showed differential expression of many genes involved in mitosis and nuclear division pathways, including MELK. We demonstrated that MELK promotes cellular proliferation, migration, and invasion in ULMS by phosphorylating MAD2L1 at the S170 site, causing its dissociation from CDC20 and subsequent conversion to its inactive form, O-MAD2, leading to uneven chromosomal distribution in daughter cells. MELK also promotes cell cycle progression by phosphorylating RB1 at the S252 site, leading to high cellularity and nuclear atypia formation in vitro and in vivo.

**Conclusion/Implications:** Our study provides a comprehensive analysis of genomic alterations underlying CIN in ULMS and identifies MELK as a potential therapeutic target. The MELK-mediated molecular mechanism of CIN in ULMS provides insight into developing new therapies targeting this pathway. Further research is needed to develop effective therapeutic strategies for treating ULMS.

EP171 / #796

**Topic: AS04. Endometrial/Uterine Corpus Cancers**

## **THE NEED FOR LYMPH NODE EVALUATION IN LATE-STAGE UTERINE CARCINOSARCOMA – A MULTICENTER RETROSPECTIVE STUDY**

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**Introduction:** Uterine carcinosarcoma (UCS) is a highly aggressive, rare, biphasic tumor. Lymph node evaluation by either lymphadenectomy (LND) or sentinel lymph node biopsy (SLNB) is recommended. However, its value in late-stage disease remains unclear.

**Methods:** Clinical data of patients with UCS from four different hospitals between February 2006 and December 2021 were reviewed. Patients with prior radiotherapy and/or chemotherapy were excluded. Progression-free survival (PFS) and overall survival (OS) were determined.

**Results:** Among 103 UCS patients, 91 UCS patients had enough follow-up data. 47 (51.6%) were diagnosed at stage III-IV, among which 24 (51.1%) had LND. 16 patients (34.0%) had lymph node metastases (LNM). Patients undergoing LND was associated with longer median PFS (20.2 months vs. 5.7 months,  $P = 0.009$ ) and OS (29.1 months vs. 14.1 months,  $P < 0.009$ ) compared to those without LND. Multivariate analyses demonstrated that LND (hazard ratio, HR 0.447, 95% confidence interval (CI) 0.23 – 0.86,  $P = 0.16$ ) and chemotherapy (HR 0.070, 95% CI 0.03 – 0.19,  $P < 0.001$ ) were significant prognostic factors for PFS in late-stage patients. Additionally, LND (HR 0.133, 95% CI 0.04 – 0.50,  $P = 0.003$ ) and chemotherapy (HR 0.102, 95% CI 0.03 – 0.33,  $P < 0.001$ ) were independent significant prognostic factors for OS.

**Conclusion/Implications:** Despite the use of adjuvant therapy, LND remains an integral part of the surgical treatment. Further prospective studies are needed to elucidate its value in late-stage disease.

EP172 / #839

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **SEROUS ENDOMETRIAL INTRAEPITHELIAL CARCINOMA: AN OBSERVATIONAL STUDY**

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**Introduction:** Serous endometrial intraepithelial carcinoma is described as a malignant, superficial spreading lesion with risk of extrauterine spread at time of diagnosis and poor outcome. The main objective of this study was to evaluate the surgical management of patients with serous endometrial intraepithelial carcinoma and its impact on oncologic outcomes and complications.

**Methods:** This Dutch observational retrospective cohort study evaluated all patients diagnosed with pure serous endometrial intraepithelial carcinoma in The Netherlands, from January 2012 to July 2020. The pathological examination was reviewed by two pathologists with expertise in gynecological oncology. Clinical data were obtained when the diagnosis was confirmed. Primary outcome is progression free survival, secondary outcomes are duration of follow-up, adverse events related to surgery and overall survival.

**Results:** A total of 23 patients from 13 medical centers were included, of whom 15 (65.2%) presented with postmenopausal blood loss. In 17 patients (73.9%) the intraepithelial lesion was present in an endometrial polyp. All patients underwent hysterectomy of whom 12 patients (52.2%) were surgically staged. None of the staged patients showed extrauterine disease. Two patients received adjuvant brachytherapy. There were no recurrences of disease (median follow-up duration of 35.6 months (range; 1.0-108.6) and there were no disease-related deaths in this cohort.

**Conclusion/Implications:** In patients with serous endometrial intraepithelial carcinoma median progression free survival reached nearly three years and no recurrences have been reported. Our results do not endorse the WHO 2014 advice to treat serous endometrial intraepithelial carcinoma as high grade, high risk endometrial carcinoma. Full surgical staging might possibly lead to overtreatment.

EP175 / #1348

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **ANALYSIS OF ENDOMETRIAL CARCINOGENESIS AND PROGNOSTIC-RELATED GENES IDENTIFIES ECT2 AS A POTENTIAL TARGET**

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**Introduction:** Based on bioinformatics analysis and clinical tissue sample verification, this study sought potential targets for prediction and diagnosis in uterine corpus endometrial carcinoma (UCEC).

**Methods:** The DEGs in endometrial carcinoma cohorts of GEO and TCGA were analyzed by R and the series test of cluster was performed by STEM software. GO and KEGG analysis and PPI analysis were performed to screen for Hub genes. The expression level and prognostic analysis of these genes were verified in the online database. The expression of ECT2 was validated by immunohistochemistry in local clinical endometrial samples.

**Results:** There are 763 common DEGs (368 up-regulated genes and 395 down-regulated genes) and 530 genes of endometrial carcinogenesis related cluster. 13 Hub genes were selected for further analysis, 9 significantly differential genes were selected as follow: ASPM, ATAD2, BUB1B, ECT2, KIF14, NUF2, HELLS, NCAPG and SPAG5. The ROC curves of candidate genes revealed that ECT2 had the best diagnostic efficacy for UCEC. The expression level of ECT2 was significantly higher in endometrial carcinoma than that in normal endometria and differently among different FIGO stages and pathological grades in UCEC. The level of ECT2 in local endometrial samples, including normal endometria (30 cases), simple hyperplasia (30 cases), atypical hyperplasia (52 cases), and endometrial carcinoma (83 cases) revealed an increase gradually trend from normal to cancer. ECT2 can significantly distinguish and help diagnose normal endometrium, simple hyperplasia, atypical hyperplasia and endometrial cancer.

**Conclusion/Implications:** ECT2 is expected to become a potential marker for the screening and diagnosis of endometrial carcinoma.



EP177 / #720

**Topic: AS04. Endometrial/Uterine Corpus Cancers**

## **THE EFFECT OF TCGA MOLECULAR TYPING AND IMMUNOHISTOCHEMICAL MARKERS ON THE PROGNOSIS OF ENDOMETRIOD CARCINOMA WITH FERTILITY-SPARING TREATMENT**

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**Introduction:** For early young and non-pregnant patients with endometrioid carcinoma. Drug treatment can reverse the carcinoma. But there are several problems: ① there is a significant individual difference in reaching complete regression(CR) after 3-month treatment. ② The recurrence rate after CR is high. The purpose of this study is to investigate the correlation between TCGA molecular typing and immunohistochemical markers with 3-month CR and recurrence in patients with conservative treatment.

**Methods:** The paraffin pathological specimens of 71 patients with stage IA and G1-G2 endometrioid carcinoma who underwent conservative treatment in Peking University Third Hospital from January 2010 to October 2022 were collected retrospectively for TCGA molecular typing and immunohistochemical staining (including PTEN, PIK3CA,  $\beta$ -catenin, ARID1A, ER, PR) to explore the influencing factors of 3-month CR and recurrence.

**Results:** There were 2 MSI-H subtypes, 1 high copy-number subtype, 68 low copy-number subtypes and no POLE mutations. Univariate and multivariate logistic analysis showed those PTEN-positive, ER and PR high-expression were more likely to achieve 3-month CR (OR=24.811, P=0.034; OR=9.428, P=0.025; OR=29.178, P=0.011). Univariate and multivariate COX regression analysis showed that patients with high-expression PIK3CA were more likely to recurrence (OR=12.750, P=0.017).

**Conclusion/Implications:** Patients with PTEN positive, ER and PR high-expression are more likely to achieve 3-month CR after treatment. Individuals with high expression of PIK3CA are more likely to relapse after CR. Further expansion of sample size is needed to confirm the impact of TCGA molecular typing on the prognosis of endometrioid carcinoma with fertility-sparing treatment.

EP178 / #1561

**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **EFFECT OF BLOOD LIPIDS ON THE CLINICAL EFFICACY OF FERTILITY-PRESERVING TREATMENT IN PATIENTS WITH ENDOMETRIAL CANCER**

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**Introduction:** The age of onset of endometrioid adenocarcinoma is progressively younger, and changes in dietary habits have led to an increase in dyslipidemia problems in young people. This study intends to analyze the effect of blood lipids on the clinical efficacy of fertility-preserving treatment in patients with atypical endometrial hyperplasia and endometrial cancer.

**Methods:** The clinical data of 109 patients with atypical endometrial hyperplasia and endometrial cancer who received fertility-preserving treatment in the Department of Obstetrics and Gynecology, Peking University People's Hospital (Dec. 2005 to Sep. 2022) were collected, and a retrospective analysis was performed on the clinical characteristics, histopathology results, outcomes, and blood lipids.

**Results:** Divide patients into three groups based on age:  $\leq 29$  years old( $n=36$ ),  $>29$  years old or  $\leq 35$  years old( $n=45$ ),  $>35$  years old( $n=28$ ). It was found that blood lipids gradually increase with age. Especially low density lipoprotein cholesterol ( $P=0.013$ ) and total cholesterol ( $P=0.045$ ). After 3 months of progesterone treatment, both low-density lipoprotein cholesterol and high-density lipoprotein cholesterol in the patient's blood significantly increased ( $P<0.05$ ). According to the clinical efficacy of progesterone, patients were divided into an insensitive group and a sensitive group. Low density lipoprotein cholesterol ( $P=0.004$ ) and free fatty acids ( $P=0.02$ ) were found to be influencing factors for progesterone insensitivity ( $P=0.004$ ).

**Conclusion/Implications:** Pay attention to the whole process of blood lipid management in patients of atypical endometrial hyperplasia and endometrial cancer, especially in patients with dyslipidemia treated with progesterone.

EP179 / #734

Topic: *AS04. Endometrial/Uterine Corpus Cancers*

## **POSTOPERATIVE COMBINED CHEMOTHERAPY AND RADIOTHERAPY FOR STAGE III ENDOMETRIAL CANCER: AN UPDATED SURVIVAL ANALYSIS OF A MULTICENTER RETROSPECTIVE STUDY**

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**Introduction:** Our previous report showed the efficacy and toxicity of adjuvant combination chemotherapy and radiation therapy (CRT) compared with chemotherapy alone (CT) in patients with stage III endometrial cancer. Here we present updated survival data with a median follow-up period of 60.0 months.

**Methods:** Medical records of patients who received standard surgical treatment for stage III endometrial cancer at six hospitals from January 2009 to December 2019 were retrospectively reviewed. Patients who received postoperative adjuvant CRT or CT were included. Disease-free survival (DFS) and overall survival (OS) was compared using Kaplan-Meier method and log-rank test. The data cutoff date was May 1, 2013.

**Results:** A total of 133 patients were included in the analysis, 80 (60.2%) in the CRT group and 53 (39.8%) in the CT group. In the overall population, 5-year DFS (CRT, 73% vs. CT, 65%, log-rank P = 0.290) and OS (81% vs. 75%, log-rank P = 0.400) rates were similar between treatment groups. In the subgroup of patients with stage IIIC endometrioid endometrial cancer, the CRT group had a significantly longer 5-year DFS rate compared with the CT group (76% vs. 55%, log-rank P = 0.037), but not for OS (81% vs. 71%, log-rank P = 0.450). Multivariable Cox regression analysis identified that CRT was the only independent favorable prognostic factor for DFS in this subgroup (adjusted HR, 0.43 (95% CI 0.19-0.97), P = 0.044).

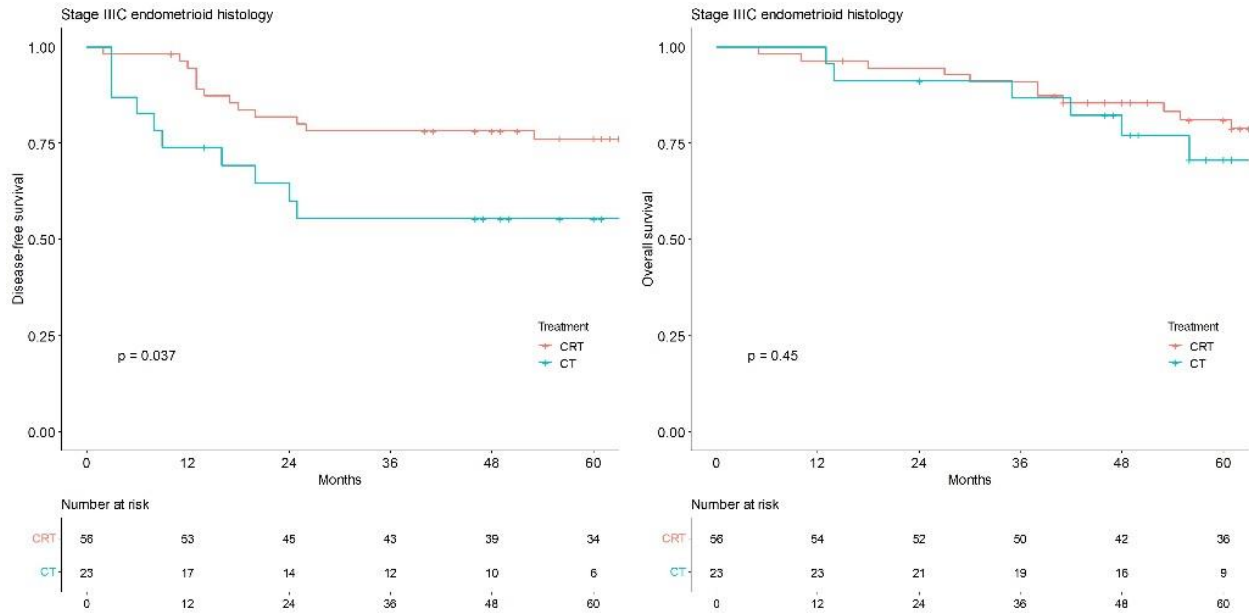


Table 1. Factors associated with disease-free survival in FIGO stage IIIC endometrioid endometrial cancer

Characteristics	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
Age ( $\geq 60$ vs. $<60$ )	1.99	(0.87-4.55)	0.102			
BMI ( $\geq 24$ vs. $<24$ )	0.98	(0.42-2.22)	0.960			
Medical comorbidities						
Hypertension (yes vs. no)	0.82	(0.37-2.19)	0.820			
Diabetes (yes vs. no)	1.01	(0.24-4.32)	0.986			
WHO performance status score (3-4 vs. 1-2)	3.49	(1.02-11.91)	0.046	Eliminated		
Tumor size ( $\geq 4$ cm vs. $<4$ cm)	2.26	(0.83-6.16)	0.112			
Invasion depth ( $\geq 50\%$ vs. $<50\%$ )	2.78	(0.82-9.40)	0.100			
Stage (IIIC2 vs. IIIC1)	0.91	(0.40-2.06)	0.815			
Grade						
2-3 vs. 1	1.16	(0.39-3.40)	0.792			
3 vs. 1-2	0.90	(0.36-2.29)	0.829			
Open surgery vs. MIS	1.77	(0.76-4.09)	0.183			
CRT vs. chemotherapy alone	0.43	(0.19-0.97)	0.044	0.43	(0.19-0.97)	0.044
Dose reduction or discontinuation (yes vs. no)	1.91	(0.83-4.43)	0.130			

Covariates with  $P < 0.1$  on univariate analysis were included in multivariate model.

FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; CI, confidence interval; WHO, World Health Organization; MIS, minimally invasive surgery; CRT, chemoradiotherapy.

**Conclusion/Implications:** For patients with stage IIIC endometrioid endometrial cancer, CRT was associated with an improved long-term DFS compared with CT.

EP180 / #587

Topic: **AS04. Endometrial/Uterine Corpus Cancers**

## **VALIDATION OF THE 2023 FIGO ENDOMETRIAL CANCER STAGING SYSTEM**

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**Introduction:** Objective: To validate the revised 2023 International Federation of Gynecology and Obstetrics (FIGO) endometrial cancer staging system, focusing on stage I and II diseases.

**Methods:** Endometrial cancer patients [A1] who received minimally invasive surgery between 2015 and 2017 were enrolled in a retrospective cohort research utilizing the Japan Society of Obstetrics and Gynecology Tumor Registry database. [A2] Stage I disease comprised IA1 (tumor limited to the endometrium), IA2 (< half of myometrial invasion [MI] without LVSI [A3] in non-aggressive tumor), IA3 (low-grade endometrioid tumor limited to the uterus and ovary), and IB (more than half of MI without LVSI in a non-aggressive tumor). Stage II comprised IIA (stromal invasion), IIB (substantial LVSI), and IIC (aggressive tumor with MI). Multivariable analysis was performed for survival assessment based on cancer stage.

**Results:** In stage I (n=2937), IA2 was not associated with an increased mortality risk rate compared to IA1 (adjusted hazard ratio [aHR], 1.04; 95% confidence interval [CI], 0.55–1.96; P=0.902). IA3 and IB were independently associated with an increased mortality risk (aHR, 3.8; 95% CI, 1.01–14.30; P=0.048; and aHR, 2.39; 95% CI, 1.04–5.48; P=0.039, respectively [A2]) compared to IA1. In stage II (n=696), IIB had a worse, though non-significant, survival rate tendency compared to IIA (aHR, 5.35; 95% CI, 0.74–39.34; P=0.099). IIC was independently associated with an increased mortality rate (aHR, 14.86; 95% CI, 2.02–106.8; P=0.008).

**Conclusion/Implications:** The 2023 FIGO staging system for endometrial cancer might be useful to distinguish survival groups among stages IA3, IB, IIA, IIB, and IIC.

EP181 / #16

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **IMPACT OF THE TYPE OF HYSTERECTOMY ON PROGNOSIS IN PATIENTS WITH STAGE II ENDOMETRIAL CANCER: A RETROSPECTIVE COHORT ANALYSIS**

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**Introduction:** In patients with stage II endometrial cancer, a radical hysterectomy is recommended. Nevertheless, it is associated with complications such as longer operative time, greater blood loss, and post-operative urinary retention. Thus, a simpler hysterectomy can be done with adjuvant treatment to reduce local recurrence and with lesser postoperative morbidity. The aim of this study is to determine the impact of hysterectomy type on prognosis and the pattern of relapse in patients with stage II endometrial cancer.

**Methods:** The study was approved by the Institutional Review Board; patient charts from the outpatient department of a tertiary hospital Section of Gynecologic Oncology of endometrial cancer patients with stage II disease from January 1, 2011 to December 31, 2020 were reviewed.

**Results:** The recurrence-free survival was higher among patients who underwent intrafascial and extrafascial hysterectomies at 12- and 24 months. However, at 36 months, those in the radical hysterectomy group have better recurrence-free survival (66%). For patients who underwent intrafascial hysterectomy, the overall survival at 12 and 24 months were 100%. For the extrafascial hysterectomy group, at 12 and 24 months, 100% overall survival; 88.89% (CI 43.3-98.36) at 36 months. For the radical hysterectomy group, at 12, 24, and 36 months, 100% overall survival, respectively. At 36 months, the radical hysterectomy group has better overall survival.

**Conclusion/Implications:** The result of the retrospective study proposes that patients with stage II endometrial cancer who underwent radical hysterectomy had fewer recurrences. The radical hysterectomy group has also better overall survival as compared to the extrafascial hysterectomy group.

EP182 / #276

**Topic:** AS04. Endometrial/Uterine Corpus Cancers

## **MOLECULAR CHARACTERIZATION OF STAGE I, GRADE 3 ENDOMETRIOID ENDOMETRIAL CANCER**

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**Introduction:** Endometrioid endometrial cancers (EECs) are clinically and molecularly heterogeneous. We sought to investigate the molecular landscape of stage I, grade 3 EECs.

**Methods:** Patients with stage I, grade 3 EECs who underwent surgical staging from 1/2014-1/2020 were identified. Clinicopathologic data were curated from electronic medical records. All EECs underwent tumor-normal targeted panel sequencing of up to 505 cancer-related genes and were classified by molecular subtype. POLE-mutated EECs were excluded from mutational analyses, as they are ultramutated tumors.

**Results:** Seventy-five patients were identified. Unlike stage I, grade 1 EECs, which are mostly of copy number (CN)-low molecular subtype, most of our stage I, grade 3 EECs were of POLE (25/75, 33%) or microsatellite instability (MSI)-high (24/75, 32%) molecular subtypes; 20% (15/75) were CN-high and 15% (11/75) CN-low. Patients with MSI-high EECs, compared to other subtypes, were more likely to have deep myometrial invasion ( $p=0.02$ ) and to have received chemotherapy ( $p=0.01$ ). After exclusion of POLE EECs, 50 patients met criteria for mutational analyses. The most common alterations affected PTEN (68%), ARID1A (46%), PIK3CA (42%), and PIK3R1 (38%). Stage I, grade 3 EECs with positive lymphovascular space invasion, compared to those without, more frequently harbored PTEN (86% vs 56%,  $p=0.03$ ), PIK3R1 (57% vs 28%,  $p=0.04$ ), and MAP2K4 (19% vs 0%,  $p=0.03$ ) mutations. Stage IB cases, compared to stage IA cases, were more likely to harbor FBXW7 (29% vs 6%,  $p=0.04$ ) and KMT2D (64% vs 25%,  $p=0.02$ ) mutations.

**Conclusion/Implications:** Stage I, grade 3 EECs are a heterogeneous group of tumors with varying mutational profiles and molecular subtypes.

EP183 / #1565

**Topic:** *AS04. Endometrial/Uterine Corpus Cancers*

## **META-ANALYSIS OF THE APPLICATION VALUE OF SENTINEL LYMPH NODE MAPPING IN EARLY STAGE HIGH-RISK ENDOMETRIAL CANCER**

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**Introduction:** Endometrial cancer is a common gynecological malignancy. Lymph node information is important for evaluating the prognosis. Current studies have shown that sentinel lymph node mapping (SLNM) in early stage low-risk endometrial cancer has satisfactory SLN detection rate, sensitivity without affecting PFS and OS. However, the feasibility of SLNM in early stage high-risk endometrial cancer is still under hot debate.

**Methods:** The PubMed, Embase, Cochrane Library, Web of science, and Scopus were retrieved. The search deadline is November 1, 2022. Inclusion criteria was, over 10 patients, only high-risk endometrial cancer, detection rate, sensitivity and PFS, OS, recurrence rate were reported.

**Results:** A total of 17 articles met the inclusion criteria, of which 12 were diagnostic studies, 7 were therapeutic studies. The total SLN detection rate is 85%. The bilateral detection rate of SLN is 62.5%. The detection rate of para-aortic SLN is 11.1%. The detection rate of isolated para-aortic SLN detection rate is 0.3%. The sensitivity is 91%. The SLNM group has a lower recurrence rate than that in the LAD group (OR: 0.504;  $p = 0.0001$ ); SLNM group reduces the risk of death compared to LAD group, 36-month OS is better (HR = 0.30;  $p = 0.02$ ),

**Conclusion/Implications:** The application of SLNM in early stage high-risk EC patients is feasible with good SLN detection rate and sensitivity. Compared with traditional LAD, SLNM has similar positive lymph node detection rate and adjuvant therapy rate, not affecting PFS and OS. It may even reduce the risk of recurrence by identifying the lymph nodes which are most relevant to metastasis.



EP184 / #803

Topic: *AS05. Fertility/Pregnancy*

## **ONCOFERTILITY IN OVARIAN TUMOURS AT A TERTIARY REFERRAL CENTRE IN SINGAPORE**

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**Introduction:** The gynaecological oncofertility service was set up with the aim to provide holistic counselling to young women with gynaecological cancers, to optimize their fertility potential in survivorship. We report our experience in fertility sparing management in ovarian tumours.

**Methods:** Over a period of 30 months, 69 young women with suspicious ovarian masses were reviewed at the oncofertility clinic. Patients were jointly counselled by gynaecological oncologists and fertility specialists, elaborating fertility-sparing staging surgery (FSS) and fertility preservation (FP) options. FP was offered prior to completion surgery or adjuvant chemotherapy, and when the ovarian reserve was deemed diminished and at risk. Dedicated counselling and psychosocial support was provided by a specialty nurse.

**Results:** The median age was 28 years. 88.4% of patients were nulliparous. Of 64 patients who underwent surgery, there were 23 borderline, 32 malignant, 1 Krukenberg and 9 benign ovarian tumours. FSS was performed in 90.6% of ovarian cancer (OC) cases. Among patients with borderline ovarian tumours (BOT), ovarian cystectomies and unilateral salpingoophorectomies were performed in 77.3% and 22.7% of cases respectively. The median stage was IC1 for OC and IB for BOT. 50% of patients had adjuvant chemotherapy. There were 6 suspected recurrences, 5 of whom underwent surgery with benign histology. Twenty-two patients were offered FP and 4 patients underwent oocyte or embryo cryopreservation. There were 4 spontaneous pregnancies with 2 livebirths, and 3 patients currently undergoing assisted reproductive therapy.

**Conclusion/Implications:** Through multidisciplinary oncofertility care, young females with ovarian tumours can achieve favourable oncologic and reproductive outcomes with FSS and early FP counselling.

EP185 / #904

Topic: *AS05. Fertility/Pregnancy*

## **KNOWLEDGE OF YOUNG WOMEN REGARDING THEIR REPRODUCTIVE HEALTH AT THE TIME OF BREAST CANCER SURGERY**

Ons Kaabia

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**Introduction:** We aim to identify patients' knowledge about their future fertility and reproductive health at the time of breast cancer surgery in order to adapt the preoperative patients' counselling.

**Methods:** This is a single-institution cross-sectional observational study based on in person interview with an Arabic questionnaire to collect quantitative and qualitative data from a cohort of young women diagnosed with breast cancer before the age of 40 between January 2022 and February 2023. All interviews took place within a month prior to the breast cancer surgery in patients that had no neoadjuvant treatment.

**Results:** A total of 48 women took part in the study. The mean age of the patients was 35 [24–40]. Of the 18 married participants, 10 were childless. Fertility was not a spontaneous concern reported by women when asked about their greatest fears before breast surgery. Among the single participants, 80% think that their cancer will be an obstacle to and/or delay their marital project. Among the participants, 31.2% fear a negative impact on their fertility due to a delay to conceive related to the prescription of contraception. 20.8% were aware of the possibility of fertility preservation but had no information about the availability of such options for them. The main concerns raised by the possibility of fertility preservation were the delay of cancer treatment (93.7%), the safety regarding the recurrence and/or flare up of their cancer (95.8%).

**Conclusion/Implications:** Before breast cancer surgery, reproductive health and potential fertility issues are not spontaneously expressed by patients but are present in their minds.

EP187 / #658

Topic: *AS05. Fertility/Pregnancy*

## **CHEMOTHERAPY-INDUCED AMENORRHEA IN PATIENTS WITH OVARIAN CANCER**

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**Introduction:** For young cancer patients, the possible impact on their fertility after treatment is important concern. If ovarian function is expected to decrease after chemotherapy, fertility preservation may be an option prior to treatment. We aimed to clarify the proportion of amenorrhea after platinum-and taxane-based chemotherapy.

**Methods:** Twenty-eight patients who underwent fertility-sparing surgery for ovarian malignancies from 2000-2022 were included. Clinical information were collected retrospectively from medical records.

**Results:** The median follow-up duration was 81 (6-252) months. Median age was 27 (range: 19-38) years. 15 patients had epithelial ovarian tumors, and 13 had germ cell tumors. Treatment details: no chemotherapy in 9 patients, BEP (bleomycin, etoposide, cisplatin) in 10, TC(Paclitaxel, carboplatin) in 7, DC(Docetaxel, carboplatin) in 1, PVB (Cisplatin, Vinblastine, Bleomycin) in 1. The median time to the resumption of regular menstrual cycle was 1 (1-4) M in the no-chemotherapy group, 4.1 (3-4) M in the BEP group, and 2.7 (1-5) M in the TC/DC group. While the proportion of amenorrhea at 3 months was 20% in the no-chemotherapy group, it was 68% in the chemotherapy group (80% in the BEP group and 50% in the TC/DC group). The amenorrhea at 6 months was found in only 1 patient in the PVB group.

**Conclusion/Implications:** After TC/DC therapy, amenorrhea at 3 months was found in about half of the patients, but regular menstruation had resumed by 6 months. The impact on ovarian function after platinum- and taxane-based chemotherapy is considered to remain short-term.

EP190 / #845

Topic: *AS06. Genetics and Epidemiology*

## **IMPACT OF OBESITY AND MENOPAUSAL STATUS ON DEVELOPMENT OF GYNECOLOGIC CANCERS IN KOREAN WOMEN**

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**Introduction:** To investigate the risk of gynecologic cancers according to obesity and menopausal status using a nationwide cohort in Korea.

**Methods:** We identified 2,708,938 women from the National Health Insurance Service cohort, and obtained baseline body mass index (BMI), waist circumference (WC), and other healthcare data, measured and collected during a health examinations and cancer-screening survey. By setting a normal weight/WC group (BMI, 18.5–22.9 kg/m<sup>2</sup> or WC, 80.0–84.9 cm) as the reference, we conducted multivariate analyses.

**Results:** The total follow-up duration was 22389854.63 person-years. In post-menopausal women, as the BMI classification level increased from normal to class II obesity, the risk of endometrial cancer (aHR, 2.11; 95% CI, 1.81–2.46) and ovarian cancer (aHR, 1.38; 95% CI, 1.20–1.58) significantly increased. The risk of endometrial cancer also increased as the WC classification increased from <75.0 to ≥95.0 cm. With a WC of 80.0–84.9 cm as the reference, the lowest risk of endometrial cancer was observed in WC <75.0 cm (aHR, 0.75; 95% CI, 0.67–0.84) while the highest risk was observed in WC ≥95.0 cm (aHR, 1.56; 95% CI, 1.33–1.82). In pre-menopausal women, the trends of endometrial and ovarian cancer incidence in pre-menopausal women were similar to those observed in post-menopausal women. For cervical cancer, only class II obesity was significantly associated with increased risks in both post-menopausal women (aHR, 1.18; 95% CI, 1.01–1.39) and pre-menopausal women (aHR, 1.27; 95% CI, 1.02–1.57).

**Conclusion/Implications:** In Korean women, the impact of obesity on the development of gynecologic cancers differs according to the malignancy type and menopausal status.

EP191 / #664

Topic: *AS06. Genetics and Epidemiology*

## **FACTORS ASSOCIATED WITH UPTAKE OF RISK-REDUCING SALPINGO-OOPHORECTOMY IN BRCA 1/2 MUTATION CARRIERS: SINGLE CENTER EXPERIENCE**

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**Introduction:** Risk-reducing salpingo-oophorectomy (RRSO) is one of key prevention strategies for female BRCA1/2 mutation carriers. The purpose of this study was to identify the factors associated with uptake RRSO among patients with BRCA1/2 mutation.

**Methods:** We reviewed the medical records of 786 patients who underwent BRCA1/2 gene testing at Ewha Womans University Mokdong Hospital from June 13, 2007 to July 28, 2020. Socio-demographic and clinical characteristics were compared between non-RRSO group and RRSO group, and the factors affecting the uptake of RRSO were analyzed.

**Results:** Among the final study population of 70 patients with BRCA1/2 mutation, 39 (55.7%) and 31 (44.3%) were in the non-RRSO group and RRSO group, respectively. There were significant differences in age ( $41.38 \pm 13.65$ yr vs.  $44.35 \pm 7.78$ yr,  $P=0.042$ ), marital status (30.8% vs. 3.2% in single; 66.7% vs. 87.1% in married,  $P=0.002$ ), parity (43.6% vs. 6.5% in nullipara; 53.4% vs. 93.6% in primi-/multipara,  $P<0.001$ ) and employment status (41.0% vs. 32.3%,  $P=0.019$ ) between non-RRSO group and RRSO group. However, no significant differences between the two groups were observed in personal and familial histories of breast or gynecologic cancer. Univariate analysis found significant associations between RRSO uptake and parity, marital and employment status. In RRSO group, the median time interval between BRCA1/2 testing and RRSO uptake was 8.8 (6.2-19.6) months. No subsequent cancer cases occurred in either group during the surveillance.

**Conclusion/Implications:** RRSO uptake in patients with BRCA1/2 mutation was affected by parity, marital and employment status. These findings may be of useful assistance to clinicians when counseling patients with BRCA1/2 mutations receiving RRSO.

EP192 / #809

Topic: *AS06. Genetics and Epidemiology*

## CLINICAL FEATURES OF CANCERS DIAGNOSED IN PATIENTS WITH LYNCH SYNDROME-ASSOCIATED GENE GERMLINE MUTATIONS

Ji Eun Lee<sup>1</sup>, Dongju Won<sup>2</sup>, Ji Soo Park<sup>3</sup>, Tae Il Kim<sup>4</sup>, Eunji Nam<sup>1</sup>

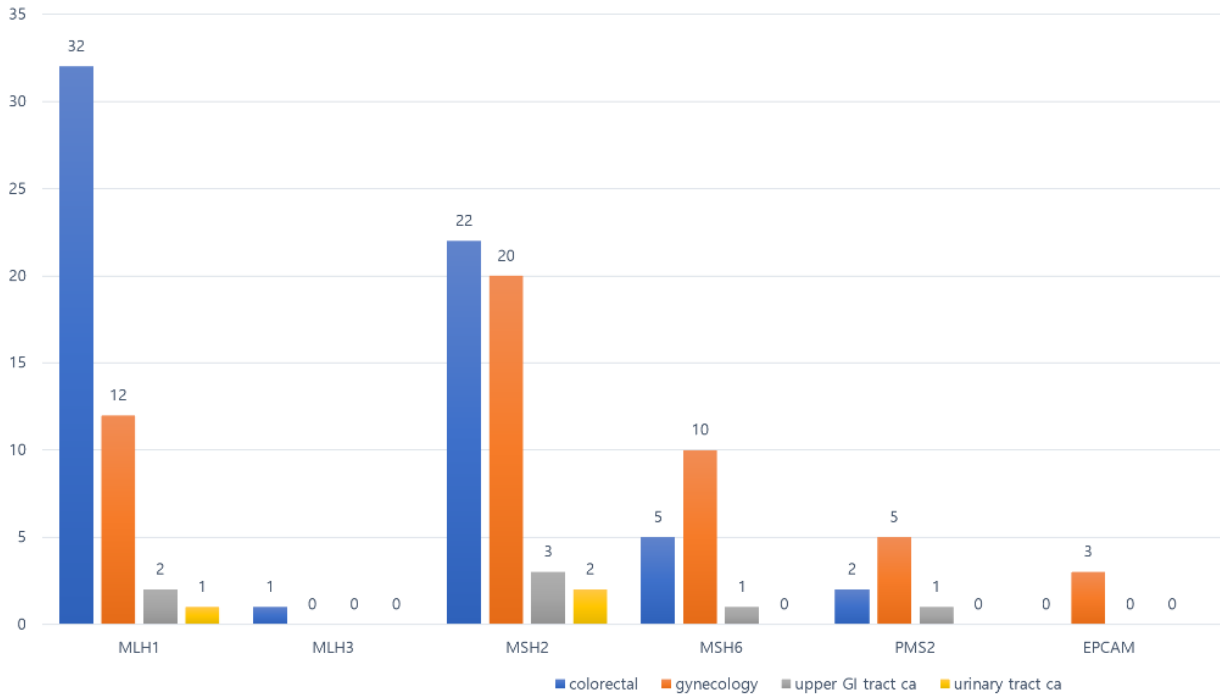
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**Introduction:** The purpose of this study is to determine the clinical features of comorbid cancers by gene (MLH1, MSH2, MSH6, PMS2, EPCAM) in patients diagnosed with Lynch syndrome (LS).

**Methods:** A multipanel NGS (oncorisk®) test for 56 cancer predisposition genes was performed in patients diagnosed with cancer at an early age or suspected of having an inherited cancer syndrome based on family history. Lynch syndrome associated genes were found in 112 patients. A medical record review was performed to examine the clinical features of the various cancers diagnosed in the patients.

**Results:** Among a total of 112 patients diagnosed with Lynch syndrome, 36 (32.14%) patients were MLH1 variants, 38 (33.92%) patients had mutation in the MSH2 gene. And 16 (14.28%) patients had mutation in the MSH6 gene, 15 (13.39%) patients were PMS2. Pathogenic MLH1 and MSH2 variants caused high penetrance dominant cancer syndromes sharing similar colorectal, endometrial cancer risks, but pathogenic MSH6, PMS2 variants caused high penetrance endometrial, ovary cancers. Older MSH2

variant carriers had higher risk of cancers of the urinary tract.



**Conclusion/Implications:** MLH1 and MSH2 are the genes with the highest number of mutations among the patients, with MLH1 being associated with a higher incidence of colorectal cancer, while MSH6, PMS2, and EPCAM are associated with a higher incidence of gynecologic cancer.

EP194 / #91

Topic: *AS06. Genetics and Epidemiology*

## **ATTITUDE OF BRCA1/2 MUTATION CARRIERS TOWARDS SURGICAL RISK REDUCTION FOR BREAST, OVARIAN AND UTERINE CANCER**

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**Introduction:** BRCA1/2 mutation carriers are subjected to high rates of ovarian and breast cancer, thus recommendations for minimizing malignancy risk include risk reduction bilateral salpingo-oophorectomy (RRBSO), with or without hysterectomy and risk reduction mastectomy (RRM).

**Methods:** This cross-sectional study was conducted by distribution of an anonymous questionnaire in social media platforms and BRCA1/2 mutation carriers medical clinic.

**Results:** 530 BRCA1/2 mutation carriers answered the survey. RRBSO was discussed with 91% of patients and performed in 53%. Hormonal replacement therapy was discussed in 53% of patients. Addition of hysterectomy to RRBSO was discussed in 27% of patients and performed by 10%. Age over 35 years at time of mutation detection was found significant in raising RRBSO and hysterectomy performance rates. RRM was discussed in 83% of patients and performed in 33%. In a multivariate analysis, BRCA1 mutation carriers (OR 1.66 (95% CI 1.07-2.57)  $p=0.024$ ) and a personal cancer history (OR 4.75 (95% CI 1.82-12.4)  $p=0.001$ ) leading to the mutation detection were found significant in increasing the likelihood of opting RRM. Additionally, highest RRM performance rates were observed in the group of patients with a first-degree family history of breast cancer under the age of 50 years (OR 1.58 (95% CI 1.07-2.32)  $p=0.01$ ).

**Conclusion/Implications:** The data presented provides insights for the clinician counseling patients about their BRCA1/2 mutation, with not only explaining the risks and the acceptable recommendations, but also understanding their concerns and fears towards treatment and management alternatives and finally to construct a personalized management medical plan.



EP196 / #369

Topic: *AS07. Global Health/Economic Challenges*

## **GYNAECOLOGIC ONCOLOGY SURGICAL CANCELLATIONS IN ZAMBIA SECONDARY TO THE LACK OF BLOOD**

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**Introduction:** Cancellations of elective surgery in low-and middle-income countries (LMIC) are common and a major hindrance for patients who are in need of this therapeutic modality. There is a knowledge gap in the literature related to cancellation of gynecologic oncology surgeries due specifically to lack of blood products. Herein we report our experience at the University Teaching Hospital (UTH) and Cancer Diseases Hospital (CDH) in Lusaka, Zambia.

**Methods:** From January 1 through December 31, 2021, we retrospectively evaluated the surgical registry for gynecologic oncology at UTH) and (CDH) to assess the number and causes of surgical cancellations with focus on lack of blood availability and/or low hemoglobin. A hemoglobin value of 10 mg/dL or more, coupled with availability of blood for possible peri-operatively transfusion were considered minimum requirements for performing major gynaecologic oncology surgeries.

**Results:** There were a total of 24 (16.4%) surgical cancellations out of 146 scheduled gynecologic oncology cases. Table 1 Lack of available blood and/or low hemoglobin was the most frequent cause of surgical cancellations 11 cases (45.8%). Table 2 Cancelled cases and their diagnosis are listed. Table

Table 1

Total number of cases and cancellations

Number of planned surgical Cases	Number of Cancelled Cases	Percentage
122	24	16.4%

Table 2

Causes and percentage of surgical cancellation

Cause of Surgical Cancellation	Number of Cancellations	Percentage
No blood Availability and/or Low Hemoglobin	11	45.83%
Reason Undetermined	3	12.50%
Failed Intubation	2	8.33%
Deep Venous Thrombosis	2	8.33%
Unavailable Anesthesiologist	2	8.33%
Unavaialbe Surgeon	1	4.17%
No Longer Operable	1	4.17%
Uncontrolled Hypertension	1	4.17%
Unavailable Anesthetic Agents	1	4.17%
<b>Total</b>	<b>24</b>	<b>100%</b>

Table 3

Specific cancers diagnosis and procedures that were canceled (excluding the 2 cases of failed intubation)

Cancer Diagnosis	Operative procedure Cancelled	Number
Cervix cancer	radical hysterectomy with pelvic lymphadenectomy	5
Ovarian Cancer	ovarian cancers for debulking/cytoreductive surgery	7
Endometrial Cancer	total abdominal hysterectomy with pelvic and paraaortic lymph node sampling	3
Vulva Cancer	radical vulvectomy with inguinal-femoral lymphadenectomy	2
Vulva Condyloma Extensiva	Simple Vulvectomy	3
Cervical Dysplasia	Simple Hysterectomy	4

**Conclusion/Implications:** As gynecologic oncology services scale up in LMIC, given the blood loss associated with these extensive cancer surgeries and the limited availability of radiation and chemotherapy; it is important to address and understand the need to have available blood on the scheduled date of surgery to prevent treatment delays.

EP197 / #453

Topic: *AS07. Global Health/Economic Challenges*

## **ECONOMIC BURDEN OF MANAGEMENT OF PLATINUM-RESISTANT OR -REFRACTORY OVARIAN CANCER: AN UPDATE OF A SYSTEMATIC LITERATURE REVIEW**

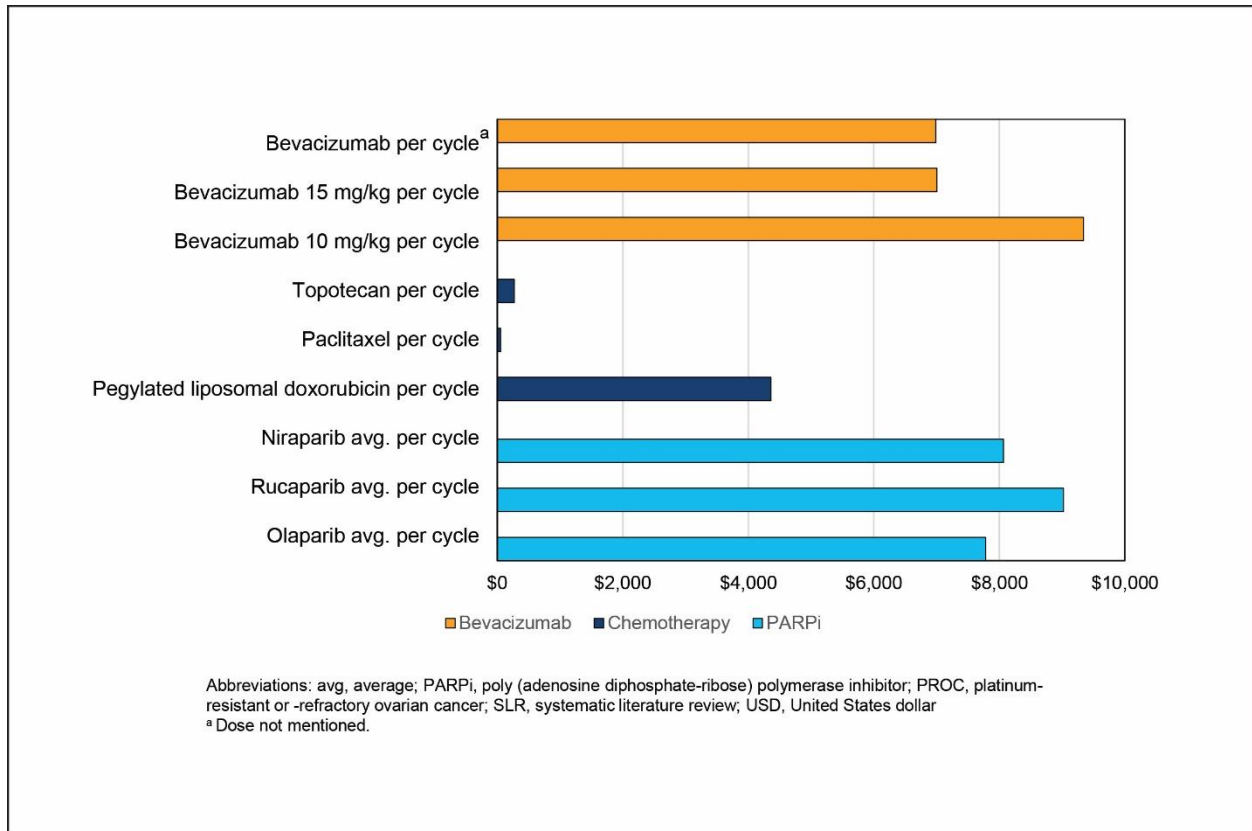
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**Introduction:** Platinum-resistant or -refractory ovarian cancer (PROC) is associated with a considerable economic burden, including high costs of treatment. Here we present the results from an update of a systematic literature review (SLR) conducted to characterize the costs associated with the management of PROC.

**Methods:** The initial SLR included studies published January 2010–July 6, 2021, and the current update included studies from July 2021 to March 2, 2023. MEDLINE®, Embase®, EconLit, Cochrane, and relevant conference proceedings were searched for economic evaluations and studies reporting costs associated with the treatment of advanced ovarian cancer recurring within six months of the last platinum-based chemotherapy. The SLR was conducted per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement.

**Results:** A total of 19 records from 18 studies were included, two of which were US cost-effectiveness analyses (CEAs) from the updated SLR. A 2022 US CEA reported that olaparib was cost-effective vs niraparib for BRCA1 and BRCA2-mutation-positive PROC at a willingness-to-pay threshold of \$100,000. In another CEA from 2022, total parenteral nutrition was not cost-effective for the management of inoperable malignant bowel obstruction in PROC. Overall, the cost-per-cycle for PROC treatment ranged from \$53 to \$4,360 for chemotherapy, \$6,989 to \$9,806 for bevacizumab, and \$7,780 to \$9,022 for poly-(adenosine diphosphate-ribose) polymerase inhibitors (Figure 1). Reported incremental cost-effectiveness ratios were high and most interventions were not considered cost effective (Table 1).



**Table 1: Cost-effectiveness of PROC therapies reported in the studies included in the SLR**

Year	Country (Currency)	Intervention(s)	ICER
2022 <sup>1</sup>	United States (\$)	Olaparib vs niraparib	159,232 per PFSY
2022 <sup>2</sup>	United States (\$)	Total parenteral nutrition + chemotherapy vs hospice	918,538 per QALY
		Total parenteral nutrition vs hospice	1.1 million per QALY
		Chemotherapy vs hospice	3.7 million per QALY
2022 <sup>3</sup>	United States (\$)	Total parenteral nutrition + chemotherapy vs chemotherapy	3.8 million per QALY
2020 <sup>4</sup>	United States (\$)	Niraparib vs non-platinum-based therapies	74,569 per QAL <sub>month</sub> *
		Niraparib vs bevacizumab + non-platinum-based therapies	189,924 per QAL <sub>month</sub> *
		Rucaparib vs non-platinum-based therapies	41,563 per QAL <sub>month</sub> *
		Rucaparib vs bevacizumab + non-platinum-based therapies	38,230 per QAL <sub>month</sub> *
		Olaparib vs non-platinum-based therapies	59,768 per QAL <sub>month</sub> *
		Olaparib vs bevacizumab + non-platinum-based therapies	115,920 per QAL <sub>month</sub> *
2018 <sup>5</sup>	Belgium (€)	Bevacizumab + chemotherapy vs chemotherapy	172,370 per QALY
2018 <sup>6</sup>	Canada (CAD)	Bevacizumab + chemotherapy vs chemotherapy	213,424 per QALY
2017 <sup>7</sup>	United States (\$)	Bevacizumab + chemotherapy vs chemotherapy	410,455 per QALY
2016 <sup>8</sup>	Thailand (Baht)	Doxorubicin + topotecan vs best supportive care	420,299 per QALY
		Gemcitabine + topotecan vs best supportive care	385,856 per QALY
		Doxorubicin + best supportive care vs best supportive care	385,322 per QALY
		Gemcitabine + best supportive care vs best supportive care	344,643 per QALY
2016 <sup>9</sup>	United States (\$)	Genomic-based tumor testing vs standard of care	479,303 per QALY
2013 <sup>10</sup>	United States (\$)	Early palliative care vs standard of care	37,440 per QALY

Note: \* ICER is reported in QAL<sub>month</sub> gained before progression

Abbreviations: CAD, Canadian dollar; ICER, incremental cost-effectiveness ratio; PFSY, progression-free survival year; PROC, platinum-resistant or -refractory ovarian cancer; QAL<sub>month</sub>, quality-adjusted life month; QALY, quality-adjusted life year; SLR, systematic literature review

Sources: <sup>1</sup>Alkhuzam, K et al. (2022) Value In Health: 25(7), S363; <sup>2</sup>Peters, PN et al. (2022) Gynecologic Oncology: 167(3), 523 – 531; <sup>3</sup>Peters, P et al. (2022) Gynecologic Oncology: 166, S54; <sup>4</sup>Wolford, JE et al. (2020) Gynecologic Oncology: 157(2), 500-507; <sup>5</sup>Neyt, M et al. (2018) PLoS ONE: 13(4), e0195134; <sup>6</sup>Ball, G et al. (2018) Pharmacoeconomics Open: 2, 19–29; <sup>7</sup>Wysham, WZ et al. (2017) Gynecologic Oncology: 145(2), 340-345; <sup>8</sup>Lucalon, P. et al. (2016) Asian Pacific Journal of Cancer Prevention. Asian Pacific Organization for Cancer Prevention: 17(2), 799–805; <sup>9</sup>Wallbillich, JJ et al. (2016) Gynecologic Oncology: 142(1), 144-149; <sup>10</sup>Lowery, WJ et al. (2013) Gynecologic Oncology: 130(3), 426-430

**Conclusion/Implications:** High healthcare and treatment costs associated with the management of PROC emphasize the need for cost-effective treatment options in PROC.

EP198 / #422

Topic: *AS07. Global Health/Economic Challenges*

## **KNOWLEDGE, ATTITUDE, AND ACCEPTANCE TOWARD COVID-19 VACCINE OF GYNECOLOGIC CANCER PATIENTS IN THAILAND: A MULTICENTER STUDY**

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**Introduction:** To evaluate the knowledge, attitudes, and acceptance toward covid-19 vaccine of gynecologic cancer patients in Thailand

**Methods:** Participants from Chiang Mai University Hospital, Khon Kaen university hospital, Khon Kaen Hospital, Prince of Songkla university hospital, and the National Cancer Institute (NCI) were surveyed on these issues using a WHO survey tool.

**Results:** Between February and September 2022, 1,263 patients participated in this project and 1,084 (85.8%) received the COVID-19 vaccine. The highest rate of vaccination was from NCI followed by Khon Kaen, Chiang Mai, and Songkhla. 356 participants (28.2%) were infected with COVID-19 and 46 infected participants (12.9%) were unvaccinated. Regarding knowledge and attitudes, most participants felt quite easy to get health literacy, moderate probability to get the severity of covid-19 infection, proper behavior for prevention, little stress of COVID infection, quite a lot to trust in healthcare workers, quite agreed with lifting regular rules for control covid-19 pandemic, and often general well-being. The significantly different level (level 0-6: the least to the most) vaccination decision factors in unvaccinated versus vaccinated participants were as follows: health ministry recommendation (3.92 vs.4.16), how easy to get the vaccine (3.6 vs. 3.9), no need to vaccine due to rare disease (2.6 vs.2.2), stress made me not want to vaccinate (2.6 vs 2.1), if everyone is vaccinated, no need for me to vaccinate (2.5 vs 1.9), and the importance of covid-19 vaccines (3.7 vs.4.2)

**Conclusion/Implications:** Most gynecologic cancer patients received covid-19 vaccine and revealed a good knowledge and attitude toward this pandemic



EP199 / #26

**Topic:** *AS08. Gynecologic Pathology/Cytology and Disease Pathogenesis*

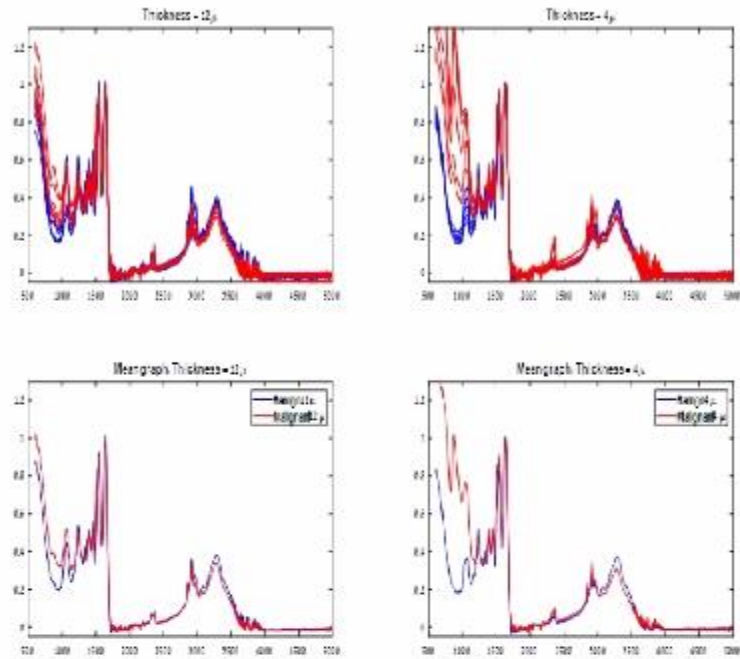
## **ATR-FTIR SPECTROSCOPY ANALYSIS OF GYNECOLOGICAL TUMOR PARAFFIN BLOCKS**

Ariel Polonsky, Hila Weinberger, Moran Gawie- Rotman, Fatme Kedan, [Ilan Bruchim](#)  
Hillel Yaffe medical center, Ob/gyn, Hadera, Israel

**Introduction:** Epithelial ovarian cancer (EOC) is the most lethal cancer among gynecological malignancies worldwide, accounting for 90% of all ovarian cancers. Our study's primary objective is to discriminate benign from malignant ovarian tumors using tissue samples that underwent formalin fixation using ATR-FTIR spectroscopy.

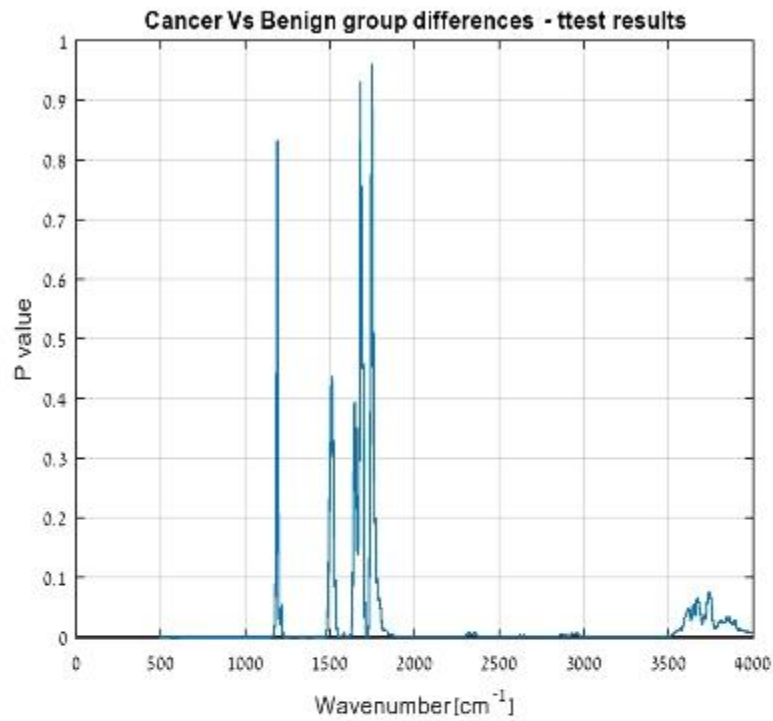
**Methods:** This is a retrospective, single center study. Inclusion criteria were of formalin fixed tissue taken from pathology archive samples, resected from females ages 18 and above. Two sets of slides from malignant tumors and 2 sets of slides from benign tumors were used to study the effect of tissue thicknesses on the measured absorption spectra: a set of 4 microns and a set of 12 microns from each tumor type were compared. Spectroscopic measurements were performed on the different slides. The 4 microns tissue thickness group was chosen. Each slide was measured in multiple locations. PCA-LDA Discrimination analysis was performed using the measured spectra. The cross-validation process was repeated five times. The results of these validations were then averaged to produce a single

estimation.



**Results:** A total of 74 tissue samples were examined. Absorption spectra of the malignant tumors were consistently different from that of benign tumors at many spectral ranges. Using K-fold cross validation technique, the study showed that the model correctly classified the samples into malignant and benign groups with an accuracy of

94.5%.



**Conclusion/Implications:** Our study exhibits a sensitive method to differentiate between a benign and malignant paraffin block preparation. With further research, this technique could become an alternative to conventional histopathology.

EP200 / #131

Topic: *AS08. Gynecologic Pathology/Cytology and Disease Pathogenesis*

## **INVASIVE STRATIFIED MUCIN-PRODUCING CARCINOMA OF THE UTERINE CERVIX: COMPARISON OF ITS CLINICOPATHOLOGICAL CHARACTERISTICS AND PROGRAMMED DEATH-LIGAND 1 EXPRESSION STATUS WITH OTHER ENDOCERVICAL ADENOCARCINOMAS**

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**Introduction:** Invasive stratified mucin-producing carcinoma (ISMC) is a rare histological type of human papillomavirus-associated (HPVA) mucinous-type endocervical adenocarcinoma (EAC). Compared to other HPVA EACs, ISMC shows more frequent post-treatment recurrences and metastases as well as worse survival. We investigated the differences in clinicopathological characteristics, patient outcomes, and programmed death-ligand 1 (PD-L1) expression status among ISMC, usual-type EAC (UEA), and gastric-type EAC (GEA).

**Methods:** PD-L1 22C3 immunostaining was performed using 20 ISMCs, 20 UEAs, and 20 GEAs. PD-L1 expression was assessed using combined positive score (CPS). We examined whether there are significant differences in clinicopathological characteristics and PD-L1 expression status among ISMC, UEA, and GEA.

**Results:** ISMC showed significantly younger age, more advanced stage, and shorter survival than UEA. Recurrence-free and overall survival rates of ISMC patients were comparable to those of GEA and significantly lower than those of UEA. All 20 ISMCs showed PD-L1 over-expression with a mean CPS of 43.5 (range=10-100), which was significantly higher than that of UEA (mean CPS=8.2;  $p=0.017$ ) and GEA (mean CPS=6.5;  $p=0.004$ ). In spite of PD-L1 over-expression, ISMC patients who treated with pembrolizumab showed no clinical responses. PD-L1 overexpression was found to be a significant predictor for RFS and OS in patients with ISMC. All examined ISMCs over-expressed PD-L1.

**Conclusion/Implications:** All examined ISMCs over-expressed PD-L1. ISMC showed significantly higher PD-L1 expression than other EACs and worse survival than UEA. Our data suggest that PD-L1 over-expression is associated with poor prognosis of ISMC.

EP201 / #746

**Topic:** *AS08. Gynecologic Pathology/Cytology and Disease Pathogenesis*

## **ASSOCIATION BETWEEN ESTROGEN RECEPTOR/PROGESTERONE RECEPTOR STATUS AND RISK FACTORS IN POSTMENOPAUSAL WOMEN WITH ENDOMETRIOID TYPE ENDOMETRIAL CANCER**

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<sup>1</sup>Haeundae Paik University, Obstetrics Gynecology, Busan, Korea, Republic of, <sup>2</sup>Inje University, Haeundae Paek Hospital, Obstetrics And Gynecology, Busan, Korea, Republic of, <sup>3</sup>Inje University Haeundae Paik Hospital, Department Of Obstetrics And Gynecology, Busan, Korea, Republic of

**Introduction:** Estrogen receptor(ER)/Progesterone receptor(PR) status has been known as a prognostic factor in endometrial cancer. Our study aimed to analyze the association between ER/PR status and risk factors including stage, histologic grade, myometrial invasion, lymphovascular space invasion(LVSI), lymph node(LN) metastasis, and cytology washing results in order to determine their relevance in postmenopausal women with endometrioid type endometrial cancer.

**Methods:** We retrospectively analyzed 114 postmenopausal patients who underwent staging surgery after being diagnosed with endometrioid type endometrial cancer at Haeundae Paik Hospital between 2010 and 2022. The associations between ER/PR status and risk factors were compared using the chi-square test.

**Results:** ER status showed statistically significant associations with histologic grade, myometrial invasion, LVSI, LN metastasis, and the results of washing cytology (p-values were 0.001, 0.016, 0.033, 0.018, and 0.013, respectively). On the other hand, PR status showed only significant association with histologic grade statistically (p-value 0.001).

**Conclusion/Implications:** ER status was observed to have a more significant role as a prognostic factor than PR in postmenopausal endometrioid type endometrial cancer.

EP202 / #750

**Topic: AS08. Gynecologic Pathology/Cytology and Disease Pathogenesis**

## **PROGNOSTIC FACTORS IN EARLY ENDOMETRIAL CANCER : A COHORT STUDY OF POSTMENOPAUSAL WOMEN**

Jisoo Lee<sup>1</sup>, Minjeong Park<sup>2</sup>, Minseong Choi<sup>2</sup>, Eunhyun Lee<sup>2</sup>, Yong-Il Ji<sup>2</sup>, Youngjin Lee<sup>3</sup>

<sup>1</sup>Haeundae Paik University, Obstetrics Gynecology, Busan, Korea, Republic of, <sup>2</sup>Inje University, Haeundae Paik Hospital, Obstetrics And Gynecology, Busan, Korea, Republic of, <sup>3</sup>Inje University Haeundae Paik Hospital, Department Of Obstetrics And Gynecology, Busan, Korea, Republic of

**Introduction:** Estrogen receptor(ER), progesterone receptor(PR) status and P53 has been known as a prognostic factor in endometrial cancer. The aim of this study is to analyze the significance of P53,ER,PR status as risk factors for recurrence in postmenopausal early endometrial cancer and to provide useful information for selecting patients who require adjuvant treatment.

**Methods:** A total of 122 postmenopausal patients who were diagnosed with endometrial cancer and underwent staging surgery, histological, immunohistochemical, and molecular genetic tests at Haeundae Paik Hospital from 2010 to 2022 were included in this study. Kaplan-Meier analysis was conducted to compare the recurrence rates between the subgroups.

**Results:** The recurrence rate was lowest in the endometrioid subgroup without P53 mutation(3.9%), and highest in the non-endometrioid subgroup with PR negative(32.7%). When comparing recurrence rates among the four subgroups based on P53 mutation and histologic type, the non-endometrioid subgroup with P53 mutation had the highest recurrence rate(28.8%). When comparing recurrence rates among the four subgroups based on ER expression and histologic type, the non-endometrioid subgroup with ER negative had the highest recurrence rate(21.3%). Similarly, in the PR subgroup, the non-endometrioid type with PR negative had the highest recurrence rate(32.8%).

**Conclusion/Implications:** In postmenopausal patients with early endometrial cancer, it was observed that the recurrence rate was lower in cases with endometrioid tumors without P53 mutation and ER(+) and PR(+). Therefore, adjuvant treatment should be considered in cases with P53 mutation or without ER and/or PR expression, especially non-endometrioid type.

EP203 / #368

**Topic:** *AS08. Gynecologic Pathology/Cytology and Disease Pathogenesis*

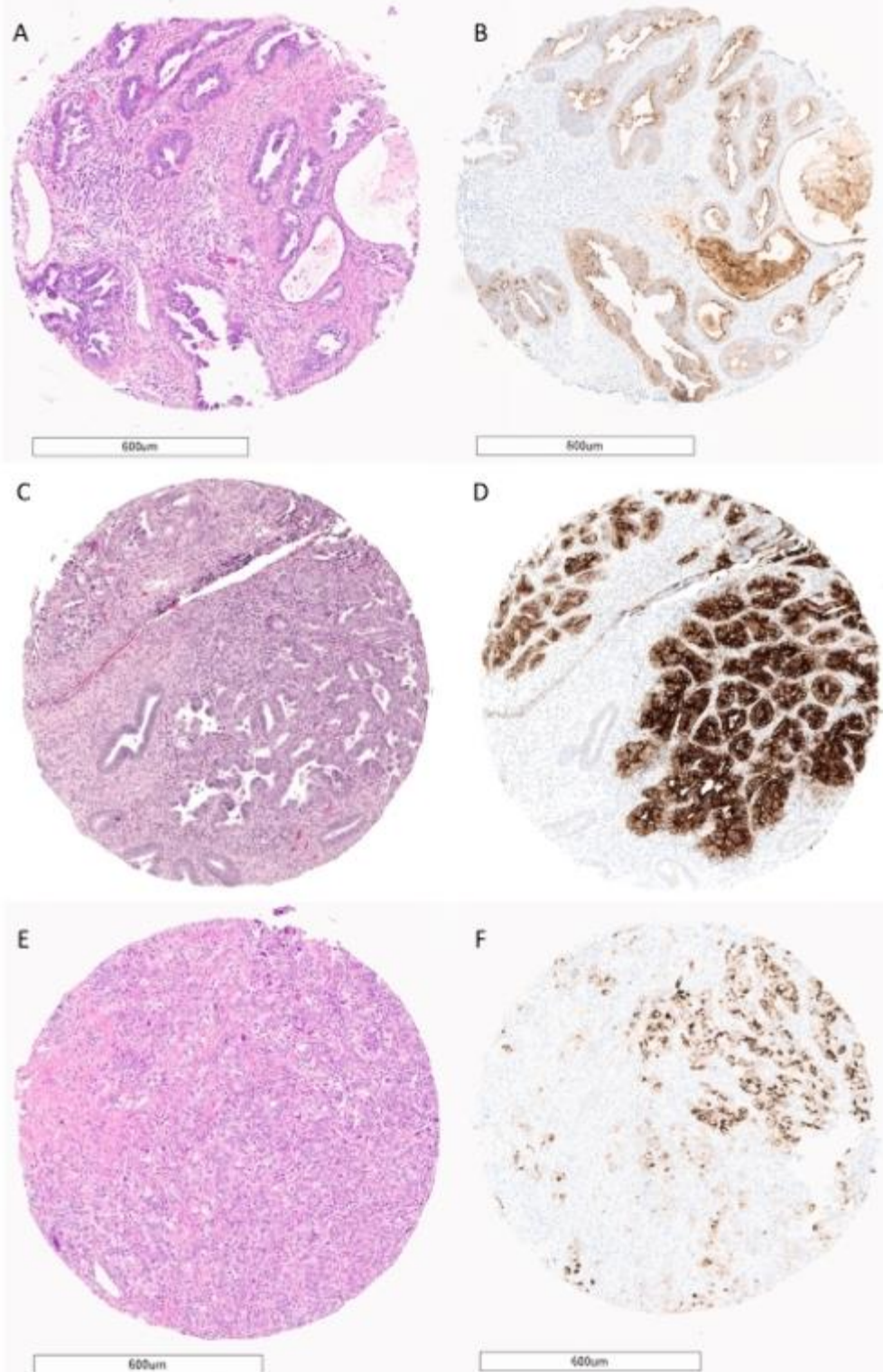
## **CHARACTERIZATION OF FOLATE RECEPTOR ALPHA EXPRESSION IN NON-HIGH-GRADE SEROUS GYNECOLOGIC TUMORS**

Brooke Liang, Troy Tenney, Minami Tokuyama, Phoebe Hammer, Sabrina Zdravkovic, Brooke Howitt  
Stanford Health Care, Department Of Pathology, Stanford, United States of America

**Introduction:** Mirvetuximab soravtansine (MIRV) is an anti-folate receptor alpha (FOLR1)-drug conjugate. Following the results of the SORAYA trial, MIRV was approved for the treatment of FOLR1-positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer. All 106 participants enrolled in SORAYA had high-grade serous carcinoma tumors on histology. Here, we report FOLR1 expression in gynecologic tumor histologies not represented by the SORAYA trail.

**Methods:** Archived gynecologic tumor samples from the Stanford University Department of Pathology were retrieved. Cores of formalin-fixed paraffin-embedded tissue were arranged into tumor microarrays (TMAs). TMA slides were stained using the VENTANA FOLR1 (FOLR1-2.1) RxDx Assay. PS2 scores (percentage of tumor cells with moderate (2+) or strong (3+) staining) were assigned according to the product insert.

**Results:** 41 cervical squamous cell carcinoma (SCC), 35 endocervical adenocarcinoma, 21 uterine serous carcinoma, 14 uterine carcinosarcoma, and 48 ovarian clear cell carcinoma (OCCC) cases were represented in the TMAs and stained with FOLR1 (see Figure 1). 0% of cervical SCC, 0% of endocervical adenocarcinoma, 14% of uterine serous carcinoma, 0% of uterine carcinosarcoma, and 0% of OCCC cases met current FOLR1 positivity criteria (PS2  $\geq$  75%) (see Table 1). Figure 1: Examples of H&E and FOLR1 staining in endocervical adenocarcinoma (A-B), uterine serous carcinoma (C-D), and ovarian clear cell carcinoma (E-



F)  
PS2 scores of different tumor

Table 1: FOLR1



types

Tumor type (N)	Median PS2 [range]	PS2 < 25 (n, %)	25 ≥ PS2 < 50 (n, %)	50 ≥ PS2 < 75 (n, %)	PS2 ≥ 75 (n, %)
Cervical squamous cell carcinoma (41)	0 [0-2]	41 (100)	0 (0)	0 (0)	0 (0)
Endocervical adenocarcinoma (35)	0 [0-21]	35 (100)	0 (0)	0 (0)	0 (0)
Uterine serous carcinoma (21)	8 [0-100]	14 (67)	4 (19)	0 (0)	3 (14)
Uterine carcinosarcoma (14)	4 [0-58]	11 (79)	2 (14)	1 (7)	0 (0)
Ovarian clear cell carcinoma (48)	0 [0-34]	45 (94)	3 (6)	0 (0)	0 (0)

**Conclusion/Implications:** Variable FOLR1 expression was seen in different gynecologic tumor types. Tumor types with higher FOLR1 staining (e.g., uterine serous carcinoma) may benefit more from FOLR1-targeting therapies than low FOLR1 staining tumor types would.

## CORRELATION BETWEEN HER2 TESTING BY IMMUNOHISTOCHEMISTRY-ISH AND ERBB2 DETERMINED BY NEXT GENERATION SEQUENCING

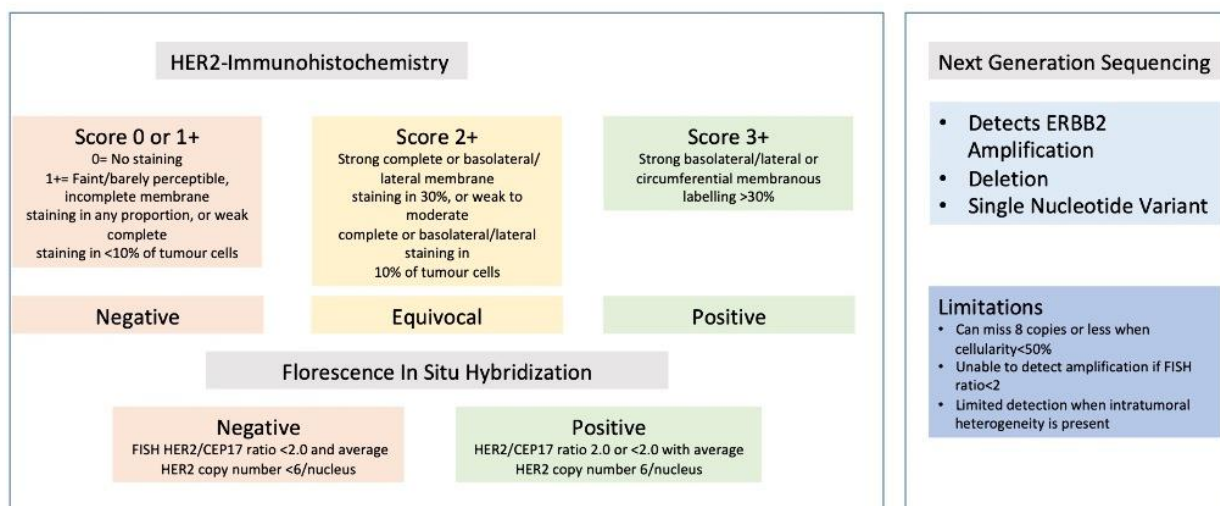
Anna Plotkin<sup>1,2</sup>, Ekaterina Olkhov-Mitsel<sup>1</sup>, Weei-Yuarn Huang<sup>1,2</sup>, Sharon Nofech-Mozes<sup>1,2</sup>

<sup>1</sup>Sunnybrook Health Sciences Centre, Department Of Laboratory Medicine And Molecular Diagnostics, Toronto, Canada, <sup>2</sup>University of Toronto, Department Of Laboratory Medicine And Pathobiology, Toronto, Canada

**Introduction:** Women with advanced or recurrent endometrial carcinoma (EC) exhibiting HER2 overexpression or gene amplification are candidates for HER2-targeted therapy. Determining HER2 status involves immunohistochemistry (IHC) and, in equivocal cases, fluorescence in situ hybridization (FISH), which is costly, requires proficiency training and is not widely available. Many well-resourced centers have adopted next generation sequencing (NGS) platforms to detect pathogenic POLE mutations using gene panels that include the ERBB2 gene. Herein, we examine the correlation between HER2 status determined by IHC-FISH and NGS.

**Methods:** Retrospective cases tested by IHC/FISH and NGS in a large academic center over 18 months. IHC (Ventana 4B5) and FISH (PathVysionHER2 DNA Probe kit) were evaluated on whole slide and scored according to ISGyP guideline recommendations. NGS used Oncomine Comprehensive Assay v3 on the S5 Prime NGS platform (Thermo Fisher) to detect ERBB2 deletions, single nucleotide variants (SNV) and amplification (Figure 1).

### HER2 testing in Endometrial Carcinoma



**Results:** HER2 status was determined by IHC/FISH and NGS in 45 cases: 19 serous, 18 high-grade (unspecified histologic type, HGU), 5 endometrioid 1 carcinosarcoma, 1 undifferentiated and 1 gastric-type. IHC-FISH HER2 was positive in 11/45 (24.4%) of cases, all serous or HGU. NGS identified 3 cases as amplified (concordant) and 1 non-pathogenic SNV. Although NGS had positive predictive value of

100% and negative predictive value of 81.0%, sensitivity was low (27.3%, 3/11). Table 1 describes the discordant cases.

Table 1: IHC/FISH and NGS details in discordant cases

Discordant case	Specimen	Tumor	Histology	IHC score	FISH: HER2/CH17; Ratio	Heterogeneity present	HER2 NGS	Tumor Cellularity
1	Biopsy	Primary	HGU	2+	9/3; 3	Yes	3.79	80
2	Biopsy	Recurrence	HGU	2+	6.5/2.2; 2.95	No	3.08	40
3	Resection	Primary	HGU	3+	6.5/5.5; 1.2	Yes	1.94	75
4	Biopsy	Primary	Serous	2+	6/2; 3	Yes	3.99	50
5	Resection	Primary	HGU	3+		Yes	4.23	75
6	Resection	Primary	Serous	3+	3.5/2; 1.75	Yes	3.49	75
7	Resection	Primary	Serous	3+		Yes	3.48	60
8	Resection	Primary	Serous	2+	8/2.3; 3.47	Yes	2.29	40

**Conclusion/Implications:** IHC/FISH are more sensitive than NGS for identification of HER2 positive cases. Intratumoral heterogeneity, tumour cellularity and HER2/CH17 ratio play significant role in reduced detection of HER2 amplification by NGS.

EP205 / #562

Topic: *AS08. Gynecologic Pathology/Cytology and Disease Pathogenesis*

## **PROGESTERON RECEPTOR STATUS IS A PROGNOSTIC MOLECULAR MARKER IN PATIENTS WITH P53 ABNORMAL ENDOMETRIOID ENDOMETRIAL CANCER.**

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<sup>1</sup>Chang Gung Memorial Hospital, Gynecologic Oncology, Taoyuan, Taiwan, <sup>2</sup>Chang Gung Memorial Hospital, College of Medicine, Chang Gung University, Department Of Pathology, Taoyuan, Taiwan, <sup>3</sup>Chang Gung Memorial Hospital, Biostatistics And Informatics Unit, Taoyuan, Taiwan, <sup>4</sup>Chang Gung Memorial Hospital, Gynecologic Cancer Research Center, Taoyuan, Taiwan, <sup>5</sup>Chang Gung Memorial Hospital, Cancer Registry, Taoyuan, Taiwan

**Introduction:** The Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) has developed as a molecular classification tool for endometrial cancer. Abnormal expression of p53 (p53abn) is identified as the worst prognostic group. We explored the association of p53abn and progesterone receptor (PR) in endometrioid endometrial cancer.

**Methods:** We included 397 consecutive endometrial cancer cases of endometrioid histology with adequate tumor tissue in the formalin-fixed, paraffin-embedded (FFPE) block and available follow-up information. This study was granted by Chang Gung Medical Foundation IRB 201702242B0D001. Immunohistochemical staining on FFPE tumor tissue sections for p53, and PR were performed. We arbitrarily defined intensity of the immunohistochemical p53 expression of cancer cell nucleus as abnormal or wild, and progesterone receptor score as positive or negative. Progression-free survival (PFS) and endometrial cancer-specific overall survival (OS) starting at the date of diagnosis were evaluated using Kaplan-Meier method and compared by log-rank test between groups.

**Results:** 48 and 339 cases were identified as p53abn and p53wt, respectively. Thirty-five (73%) p53abn cases were PR+. With a median follow-up of 74 months, the PFS and OS of patients with PR+ tumors (N = 310) were 93% and 96.8%, respectively, compared with 75% and 85.7% of those with PR- tumors (N = 70) (both  $p < 0.001$ , log-rank test). Among those with P53abn, PR+ expression was associated with a favorable PFS ( $p = 0.081$ ) and better OS ( $p = 0.044$ ).

**Conclusion/Implications:** Our study showed that incorporating PR into prognostic molecular markers for endometrioid endometrial cancer might provide further risk stratification.

EP206 / #943

Topic: *AS08. Gynecologic Pathology/Cytology and Disease Pathogenesis*

## THE SPECTRUM OF HER2 EXPRESSION IN ENDOMETRIAL CARCINOMA

Anna Plotkin<sup>1,2</sup>, Ekaterina Olkhov-Mitsel<sup>1</sup>, Weei-Yuarn Huang<sup>1,2</sup>, Sharon Nofech-Mozes<sup>1,2</sup>

<sup>1</sup>Sunnybrook Health Sciences Centre, Department Of Laboratory Medicine And Molecular Diagnostics, Toronto, Canada, <sup>2</sup>University of Toronto, Department Of Laboratory Medicine And Pathobiology, Toronto, Canada

**Introduction:** HER2-targeted therapy improves outcomes of HER2-positive endometrial cancer (EC). A novel class of HER2-directed antibody drug conjugate (ADC) that has demonstrated significant benefit in HER2-Low breast carcinoma, is being evaluated in clinical trials for other solid tumors, including uterine carcinoma with varying levels of HER2 expression. ADC efficacy in HER2-Low cancers may be partially attributed to bystander effect in tumors with heterogenous HER2 expression. We characterize the spectrum of HER2 expression in EC cases tested in a large tertiary care centre.

**Methods:** An audit of HER2 testing in EC was conducted, utilizing ISGyP criteria for immunohistochemistry (IHC) scoring. Akin to the DESTINY clinical trials, HER2-P (positive) was defined as IHC score 3+ or FISH-amplified; HER2-L (low) defined as IHC2+ (not-amplified) or IHC1+ and HER2-N (negative) defined as IHC score 0.

**Results:** There were 95 primary, 4 local recurrences and 10 metastatic EC HER2 tests, with 33 (30%) HER2-N, 46 (42%) HER2-L and 30 (28%) HER2-P. 60 were serous carcinoma, 29 high-grade EC, 9 carcinosarcomas, 8 Endometrioid and 3 others. Among 79 p53 abnormal cases, 22 (28%), 34 (43%), 23 (29%) were HER2-N, HER2-L and HER2-P, respectively. Table 1 summarizes p53, MMR and ER status by IHC and presence of pathogenic POLE mutations. None of the POLE-mutated or MMR-deficient molecular subgroup cases were HER2-P.

Table 1. Stratification of p53, MMR and ER status by immunohistochemistry, pathogenic *POLE* mutation analysis via Next Generation Sequencing, by HER2 Status

	HER2-N N=33	HER2-L N=46	HER2-P N=30
P53 (Ab/ W-T/ NA)	22/8/3	34/4/8	23/0/7
MMR (Intact/ Loss/ NA)	25/1*/11	34/2**/10	25/0/5
POLE mutation (Not detected/detected/NA)	21/1*/11	18/1/27	12/0/18
ER	9/12/12	34/4/8	8/11/11

NA=unavailable

\*Same case

**Conclusion/Implications:** The majority of ECs tested by IHC/FISH demonstrated some level of HER2 expression, with 42% meeting the criteria for HER2-L designation, potentially doubling the patients that may be considered for novel ADC therapies compared to the legacy HER2 targeted therapies.

EP207 / #760

**Topic: AS08. Gynecologic Pathology/Cytology and Disease Pathogenesis**

## **INVESTIGATING THE CLINICOPATHOLOGICAL CHARACTERISTICS OF 11 CASES OF GLIOMATOSIS PERITONEI AND EXPLORING THE POTENTIAL ROLE OF SOX 2 AND OCT 4 IN THEIR DEVELOPMENT**

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<sup>1</sup>All India Institute of Medical Sciences, New Delhi, Department Of Pathology, New Delhi, India, <sup>2</sup>All India Institute of Medical Sciences, New Delhi, Obstetrics And Gynaecology, New Delhi, India

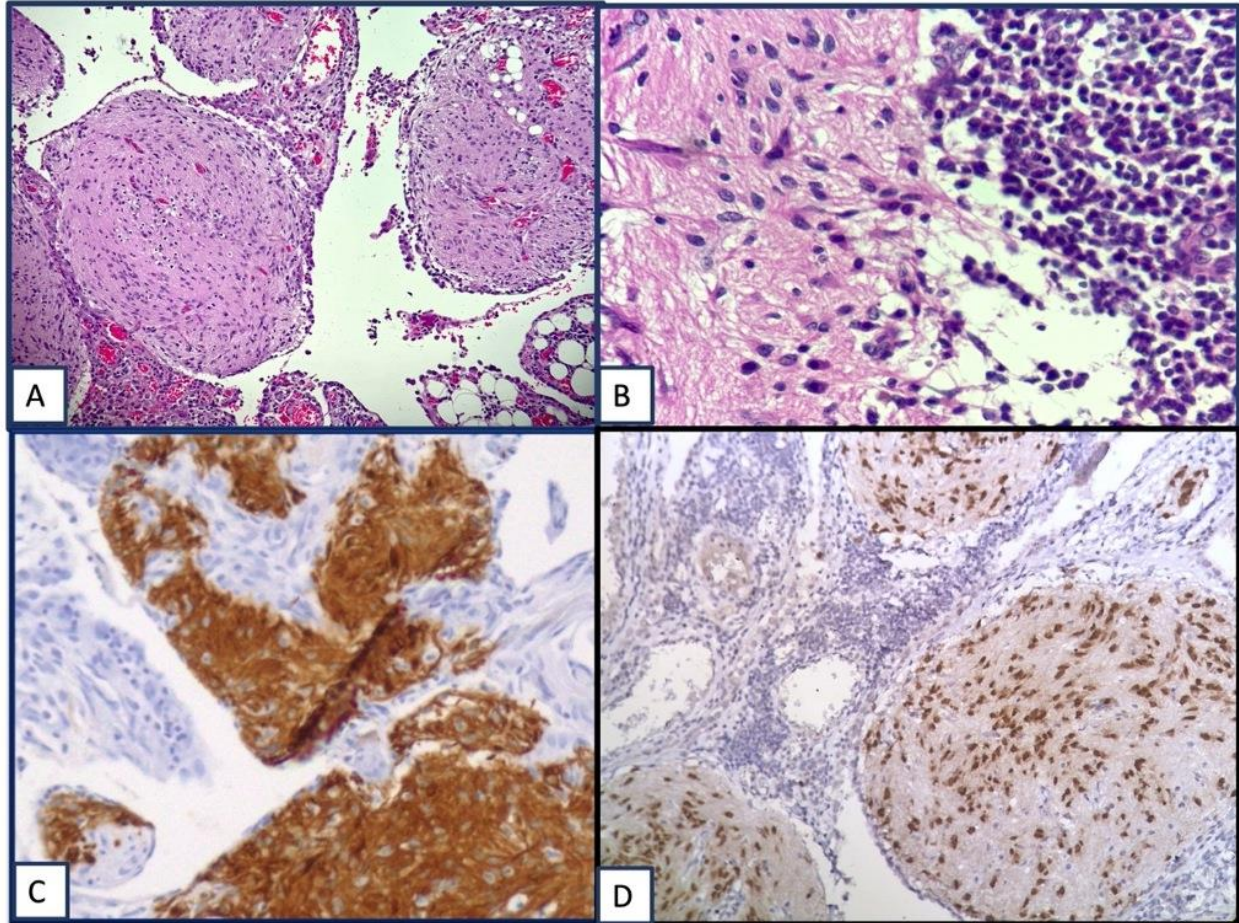
**Introduction:** Gliomatosis peritonei (GP) is a rare condition characterized by multiple mature glial tissue implants in the peritoneum and omentum. Mostly associated with immature teratomas (IMT), these are benign nodular implants that remain dormant for years. But due to their clinical presentation they are often misdiagnosed as metastasis or tuberculosis, clinically and radiologically. In recent years, OCT 4 and SOX2 (SRY-box containing gene 2) , two transcription factors that play crucial role in embryonic development and stem cell maintenance, have been implicated in various cancers. The aim of this study was to elucidate the role of SOX 2 and OCT 4 in the development and progression of GP and to analyze the clinicopathologic characteristics of 11 cases of GP.

**Methods:** It was an ambispective study of 6 years (2017-2022). Data from 11 cases of GP, was retrieved and analyzed. Immunohistochemistry (IHC) for OCT 4 and SOX 2 was put using Avidin Biotin method. Descriptive statistics was used and results were expressed as percentages.

Case	Age	Clp	CA, 125 U/ml	Site	Tumor size	Procedure	Diagnosis	Initial GP	% of positive slides in the tumor	Capex / Brachy	Rac / Met	HR / AP	HR / SOX2	HR / OCT4	Outcome	
1	22	AD* PA* x 1m	392	Rt	20	RSO, om PLND	IMT grade 3	GP	10-20%	No	No	NA	NA	+	-	Alive ; 60 month s
2	27	AD* PA* x 3m	NA	Lt	23	TAIH- BSO, Oms, P LND, Perito neal om	MCT	GP with Nodal GP	20-30%	+	No	+	NA	+	-	Alive at 48 month s
3	32	AD* x 3m	NA	Lt	23	LSO, Perito neal om	IMT grade 3	GP	10-20%	+	No	+	NA	+	-	Alive ; 46 month s
4	31	AD* x 1m	387	Rt	23	RSO, Oms, PLND	IMT grade 2	GP	30-35%	+	No	+	+	+	-	Alive ; 38 month s
5	23	AD* PA* x 1m	324	Rt	20	LSO, Rt cystect omy, O ms, Perito neal om	Rt MCT	GP	40-45% in Rt and 5- 10% in Lt	No	No	+	NA	+	-	Alive ; 34 month s
6	30	AD* x 2m	238	Lt	19	LSO, Oms	IMT grade 2	GP	20-25%	+	No	NA	+	+	-	LTFL
7	35	PA* AD* x 1y	NA	Rt	29	TAH, BSO, Oms	MCT	GP	5-10%	No	No	NA	+	+	-	Alive ; 15 month s
8	34	AD* x 3m	NA	Lt	14	TAH BSO, Oms	IMT grade 3	GP	20-25%	+	No	+	+	+	-	LTFL
9	27	AD* x 1m	906	Lt	17	LSO, Oms om	IMT grade 3	GP	20-25%	+	No	NA	+	+	-	Alive ; 18

10	14	AD* PA* x 1m	NA	Lt	24	LSO, p erito neal Biopsy	IMT grade 3	GP	15-20%	+	No	+	+	+	-	Alive ; 6 month s
11	30	AD* x 3m	NA	Rt	24	RSO, Lt cystec tomy, om	IMT grade 3 rt MCT Lt	GP	30-40%	No	No	+	+	+	-	Alive at 3 month s
AVG	29	AD 1.5m			21.4	USO+ Bx.7 TAH/ BSO -3	IMT G2-3; MCT3	1No dal GP	20%	7/10	0	6/6	6/6			8/10 Alive 2/10. TFU

**Results:**



1.6% (11/615) of all teratomas were associated with GP. The median age of patients was 29 years. 8/11 cases were IMT and 4/11 were mature cystic teratomas (MCT). All cases of GP were immunopositive for SOX 2 (nuclear) and immunonegative for OCT 4.

**Conclusion/Implications:** A possibility of GP should be considered in cases of omental nodularity with primary ovarian tumors. A conservative approach must be preferred along with long term follow up in these cases. SOX 2, in association with other transcription factors, may play a crucial role in development of GP.



EP208 / #617

**Topic:** AS08. *Gynecologic Pathology/Cytology and Disease Pathogenesis*

## **PREDICTING SURVIVAL FROM PRIMARY CERVICAL CANCER BASED ON DEEP LEARNING IN HISTOPATHOLOGICAL IMAGES**

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**Introduction:** The aim of the present study was to develop deep learning-based models to assist in predicting the overall survival (OS) of patients with cervical cancer (CC) by directly analysing scanned conventional haematoxylin and eosin (H&E)-stained whole-slide images (WSIs).

**Methods:** In total, 1161 HE-stained WSIs of primary cervical tumors from 405 patients who underwent radical CC surgery at the Fudan University Shanghai Cancer Center (FUSCC) between 2008 and 2014 were used in this retrospective study. The primary outcome was OS. Our deep learning model (CCOSNet) were developed using artificial intelligence (AI) for predicting outcome of CC. Performance was primarily evaluated using the sensitivity, specificity, and area under the receiver operating characteristic curve (AUROC).

**Results:** We constructed and trained a multi-instance deep convolutional neural network (CCOSNet) based on a multiscale attention mechanism, in which an internal independent test set (50 patients in total) were used to evaluate the predictive performance of the network. Our network achieved an AUROC=0.88 in the cross-validation set and an AUROC=0.79 in the internal independent test set of the FUSCC cohort. The biomarker provided a hazard ratio for poor versus good prognosis of 7.058 (P = 0.009) in the primary analysis of the validation cohort.

**Conclusion/Implications:** A clinically useful prognostic marker was developed using deep learning allied to digital scanning of conventional H&E-stained tumour tissue sections, which will offer assistance to choose appropriate treatment to improve the survival status of CC patients.

EP209 / #654

Topic: AS09. Nursing and Health Care

## **NUGENA (NURSE-LED GENETIC COUNSELLING AND AWARENESS): A PROVIDER SURVEY ON BARRIERS OF IMPLEMENTATION IN LMICS**

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**Introduction:** Availability and affordability of genetic testing and counselling for gynaecological malignancies remain an unmet clinical need in LMICs. Through KolGoTrg, we started an implementation research project NuGenA to overcome these barriers by training nurses to improve genetic testing uptake and identifying at-risk family members([www.kolgotrg.org/nugena/](http://www.kolgotrg.org/nugena/)). Training workshops were held for nurses in India and Nepal. We aimed to explore knowledge attitude practice (KAP) and perceived barriers from the provider end in implementing nurse-led hereditary cancer clinics using an EASE model(Table 1).

<b>EASE MODEL : KPI for success of (provider and patient level) implementating nurse led genetic counselling services</b>	
Ethical	No. of patients willing to participate versus no. who could participate No. of persons who opted out of the study Willingness to pay for genetic testing using a Co-Pay model
Acceptable	No. of patients who underwent counselling No. of patients who underwent testing No. of at-risk family members who underwent counselling No. of at-risk family members who underwent testing
Sustainable and scalable	No. of nurses trained in genetic counselling No. of set-ups/ centres for genetic counselling initiated No. of patients recruited from different sites No. of patient/family members who wanted to organise screening(PPI/snowballing) and awareness camps Local Policy making and guidelines
Effective	Effectiveness of the model calculated based on patient uptake and cost of a prevention strategy vis a vis treatment costs for cancer
Early diagnosis and treatment	No. of set-ups developed for preventive oncology No. of patients referred to preventive oncology follow-ups No. of patients undergoing preventive surgery 5 year follow-up of patients and response assessment

**Methods:** Gyn Oncology leads interested in setting up genetic clinics in India and Nepal were invited to send nurses for 3-day structured training workshops. The lead nurse, trained in genetic counselling (Co-PI) was the key educator. Pre-and post-training assessment of KAP was done and a survey (27 items) was sent out one month after the workshop to assess success/challenges faced in implementing nurse-led service/family history

clinics.

## Questionnaires that need to be implemented to develop the service and their rationale

- **Pre-screening form Inclusion/Exclusion criteria:** To identify whether a patient can be enrolled in the study
- **Baseline questionnaires:** Demographic questionnaires of each patient
- **Cancer Awareness Measures(CAM):** Interview based questionnaires to identify the knowledge level of each patient and their family members.
- **Family History form:** Pedigree diagrams briefing all necessary details of the family, including histories of cancer/developmental delays/abortions/TB etc.
- **Willingness to pay:** Patient willing to pay on basis of the benefits versus the actual cost the patient can bear.
- **Pre-test counselling satisfaction-regret scale:** Satisfaction/regret after counselling
- **Post-test counselling satisfaction-regret scale:** Satisfaction/regret after the test results
- **MICRA:** Anxiety/worry questionnaires encompassing genetic counselling

## Research/ services team required for study implementation



**Results:** 30 nurses participated: 11 from 5 centres in India and 19 from 10 centres in Nepal. Significant improvement occurred in post-workshop level of KAP. 11(39%) nurses commenced a service by setting up clinics (6 centres)/ starting counselling patients. > 90% expressed interest in further courses, workshops and setting up clinics. Barriers identified included: institutes not interested, lack of awareness amongst doctors (59% respondents), patient overburdening in clinics/lack of clinic time, requirement for administrative approval, staff crisis, cost of genetic tests, lack of local dedicated labs

**Conclusion/Implications:** Continued effort is required for provider training and awareness for scalability of nurse-led genetic counselling services including inclusion in Gyn Oncology nursing curriculums.

EP210 / #473

Topic: *AS09. Nursing and Health Care*

## **A PILOT STUDY OF NURSES' PERSPECTIVE ON AND EXPERIENCE IN HEALING ENVIRONMENT BETWEEN THE CANCER AND GENERAL WARDS IN A TERTIARY CENTER IN TAIWAN**

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**Introduction:** The growing incidences of various cancers greatly threaten people's health and even quality of life, which therefore calls for acknowledgement of creating a healing environment from the perspectives of patients and health professionals. This study aims to examine the difference (if any) in perceptions of healing environment and quality of life (QoL) between nurses in the cancer ward and general ward based on the ASPECT instrument and WHOQoL.

**Methods:** In the first stage, the English version ASPECT toolkit was translated forward and backward systemically using Jones' model. To test for the validity and reliability, Cronbach's coefficient and content validity index (CVI) were used and satisfactorily tested. In the second stage, 435 copies of questionnaires were distributed to nurses (195 in the cancer ward; 235 in the general ward). Descriptive analysis, inferential testing, and regression modeling were conducted.

**Results:** Of the 435 copies of questionnaires, 430 (98.9%) were satisfactorily collected. Overall, the instrument has a high content validity with an item-CVI of 1, and a Cronbach's  $\alpha$  of 0.944. No significant difference was found in terms of perspectives towards healing environment between the two groups of respondents. Nurses in the cancer ward, however, had significantly higher level of satisfaction with QoL. Moreover, the regression models show that 19.2% and 14.5% of variance in QoL could be explained by nurse' perceptions toward healing environment between the two wards, respectively.

**Conclusion/Implications:** The Chinese version ASPECT was demonstrated to be suitable as a predicative toolkit for nurses' QoL in the targeted tertiary center. Future studies might examine its applicability to patients in corresponding wards.

EP211 / #383

Topic: *AS09. Nursing and Health Care*

## **CURRENT PERCEPTIONS OF THE ROLE OF NURSES IN CANCER CLINICAL TRIALS**

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**Introduction:** Clinical (bedside) nurses play a crucial role in supporting cancer patients in making decisions regarding clinical trials, but this role is currently not being fulfilled sufficiently. The purpose of this study was to clarify the current perceptions of clinical nurses regarding their role in cancer clinical trials.

**Methods:** Nurses who participated in a study; "Development of Learning Program to Nurses Supporting Patients' Decision Making in Cancer Clinical Trials" were surveyed using an originally developed questionnaire (Kohara.2023). Descriptive statistics of these responses were conducted using SPSS Statistics ver. 25.

**Results:** The analysis included 101 nurses from two university hospitals in Japan, with a median clinical nursing experience was 12 years. 51% of the nurses worked for in-patient units. About half of the nurses reported experiencing the burden of communicating with patients in clinical trials, with the main reason being their inability to explain the trial properly due to insufficient understanding (36%). Furthermore, 90% of the nurses felt a lack of knowledge about clinical trials, and the fear of being able to provide proper answers to patient-nurse relationships (75%). Only 17% of nurses had the opportunity to be involved in caring for patients and making decisions regarding their participation in cancer clinical trials in the last three months.

**Conclusion/Implications:** Clinical nurses play an important role in supporting patients' decision-making process about participating in cancer clinical trials. However, their limited knowledge and burdens might hinder their nursing care, which calls for educational programs to improve their practice in clinical research nursing.

EP212 / #606

Topic: *AS09. Nursing and Health Care*

## **OCCUPATIONAL SAFETY AND THERAPEUTIC EFFECT OF PACLITAXEL ACCORDING TO TYPES OF FORMULATION AEROSOLIZED DURING ROTATIONAL INTRAPERITONEAL PRESSURIZED AEROSOL CHEMOTHERAPY FOR PERITONEAL METASTASIS**

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**Introduction:** To evaluate the occupation safety and effect of paclitaxel based on types of formulation aerosolized during rotational intraperitoneal aerosol chemotherapy (RIPAC) in pigs

**Methods:** In terms of occupational safety, we first conducted RIPAC using paclitaxel twice over two days (n=2), and then performed RIPAC using paclitaxel (n=3) and polymeric nanoparticle micellar paclitaxel (PM-Pac, n=3) three consecutive times a day in eight pigs for estimating airborne and surface contamination. Moreover, we tried to make ten piglets with peritoneal metastasis (PM) using SNU-008 cells. We evaluated the pattern of PM by using the modified peritoneal cancer index (PCI) score five weeks after the first inoculation. After RIPAC only on piglets with successful PM, we compared the rate of tumor reduction between paclitaxel and PM-Pac used in RIPAC.

**Results:** The airborne detection rate of paclitaxel was 75-100% despite no detection of PM-Pac during RIPAC. The number of airborne particles increased in the abdominal closure period during RIPAC using paclitaxel despite no increase in them during RIPAC using PM-PAC. Among surface wipe samples, the concentration above the limit of detection (LOD) was more common in paclitaxel than in PM-Pac (100% vs. 66.7% for laparoscopic instruments, P=0.03; 87% vs. 3.6% for healthcare personnel equipment). On the other hand, the modified PCI score increased after PM-Pac despite no change after paclitaxel for RIPAC in seven piglets with PM.

**Conclusion/Implications:** PM-Pac may be safe occupationally for RIPAC, whereas it may not be effective in suppressing PM of ovarian cancer when compared with paclitaxel.

EP216 / #619

**Topic:** *AS10. Oncologic Care During and Post-Pandemic*

## **SAFETY OF COVID-19 VACCINATION IN GYNECOLOGIC CANCER PATIENTS AT KING CHULALONGKORN MEMORIAL HOSPITAL, THAILAND**

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**Introduction:** There are scarce data on the safety of the COVID-19 vaccines in Gynecologic cancer patients. This study evaluated the safety of COVID-19 vaccines among gynecologic cancer patients.

**Methods:** A descriptive study was performed on gynecologic cancer patients who received at least one COVID-19 vaccine at King Chulalongkorn Memorial Hospital, Thailand, from January 2020 to August 2021. The evaluation was conducted via telephone interviews. Logistic regression was conducted to assess the association between demographics, clinical factors, cancer treatment status, and the occurrence of any grade adverse event. The number of COVID-19 infections of patients receiving at least two vaccine doses was studied.

**Results:** Of 294 patients interviewed, the most common adverse effects were the grade 1-2 injection site reaction. One patient developed grade 3 fever and seizure ten days after the first dose of the AstraZeneca vaccine. Between the 2nd to 4th dose of the vaccination, most of the adverse events were the grade 1-2 injection site reaction. No severe allergic reactions or grade 4 adverse events were reported. The study found that patients under 60 had more adverse events than older patients (Adjusted odds ratio 1.99 [95% CI 1.08-3.71];  $p=0.029$ ). The treatment status did not affect the adverse events. Of 283 who received two doses, 27.6% were infected with COVID-19.

**Conclusion/Implications:** COVID-19 vaccines are safe among gynecological cancer patients, both those receiving active anticancer therapy and those in surveillance. The younger patients frequently reported more adverse effects.



EP217 / #745

Topic: *AS10. Oncologic Care During and Post-Pandemic*

## **COVID-19 EFFECTS ON OVARIAN CANCER DIAGNOSIS, TREATMENT PATTERNS, AND SURVIVAL**

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**Introduction:** The impact COVID-19 had on cancer rates and outcomes will take years to fully assess. International studies have shown that non-emergency cancer surgeries were postponed in favor of neoadjuvant treatment. The impact the pandemic had on ovarian cancer patients has not yet been systematically examined in a US population-based cohort.

**Methods:** Stage III and IV ovarian cancer patients were ascertained using the National Cancer Database (NCDB). Patients were stratified by timeperiod (2017-2018 v 2020) to assess whether treatment patterns differed across time periods.

**Results:** 26,409 ovarian cancer patients were included, 18,585 diagnosed prior to 2019 and 7,824 in 2020. No differences were found in age at diagnosis, race, or ethnicity across timeperiods. On multivariable logistic regression, patients diagnosed during the COVID timeperiod were more likely to be on Medicare than private insurance (OR=1.19;CI=1.07-1.32) and were more likely to have stage IV disease than stage III disease (OR=1.11;CI=1.05-1.17). Multivariable results also showed that, compared to adjuvant treatment, neoadjuvant chemotherapy (OR=1.13;CI=1.03-1.25) or chemotherapy alone (OR=1.17;CI=1.08-1.27) were more often given during COVID than pre-COVID.

**Conclusion/Implications:** While the emergency threat posed by COVID-19 appears to have subsided, the experiences gained during the COVID-19 pandemic can inform future decisions in times of crises or resource shortages. Our findings show that patients on Medicare were diagnosed with ovarian cancer during the COVID era more often than patients on private insurance and that chemotherapy was used as the first treatment line more often than surgical resection. These results are consistent with international

studies.

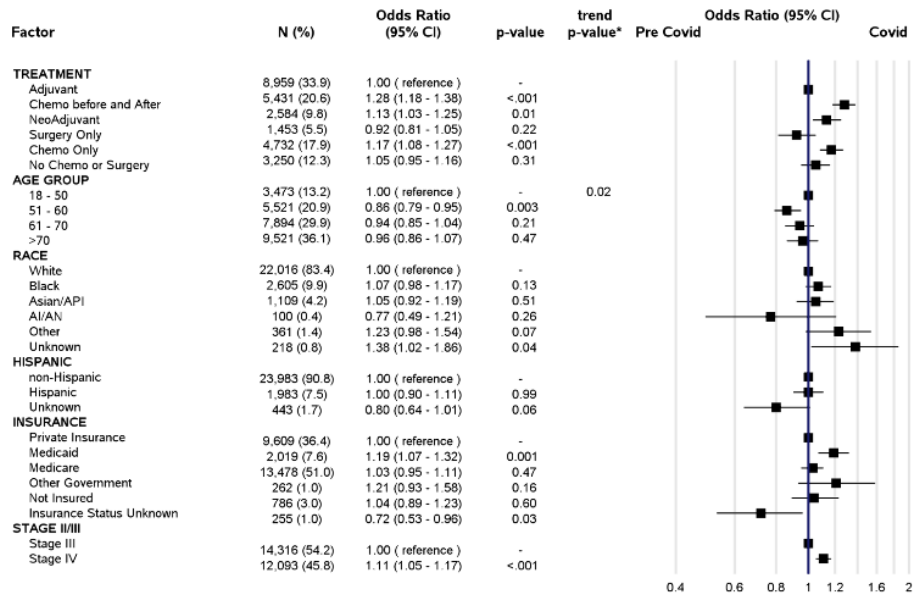


Figure 1: Multivariate Logistic Regression Examining Odds Ratio for COVID-Era Factors

EP219 / #902

Topic: *AS11. Ovarian Cancer*

## **PRIMARY DEBULKING SURGERY VERSUS NEOADJUVANT CHEMOTHERAPY IN ADVANCED STAGE OVARIAN CANCER; REALITY IN A SINGLE CENTER**

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**Introduction:** The aim of study was to compare the outcomes of stage III-IV ovarian cancer patients treated with NACT+IDS or PDS and to demonstrate the real life experience of a single center

**Methods:** This retrospective case control study was carried out in Baskent University, Ankara, Turkey. Patients with high grade serous histology who diagnosed between 2007 and 2022 were evaluated. Patient's characteristics and tumoral features like age, type of surgery, complications, OS, DFS were retrospectively documented.

**Results:** 473 patients included in PDS group and 143 patients included in NACT group. PDS group were slightly younger 57 y vs 59 y ( $p=0.006$ ). Median follow up time was 44 months. PDS group were more subjected to extended surgery 46 % vs 26 % ( $p=0.001$ ), however grade III-IV complications rates and RO resection rates were similar 6,8 % vs 11,8 % ( $p=0.18$ ) and 78 % vs 85 %  $p=0.06$  respectively. Median OS was 37 months (95 % CI ;28,9-45,0) and 53 months (95 % CI 48,2-57,2) for NACT and PDS group respectively ( $p<0.00$ ). Median DFS for NACT group was 12 months (95 % CI ;10.2-13.7) and 15 months (95 % CI 13.6-16.3) for PDS group ( $p=0.002$ ). In the cox proportional hazard model NACT was associated with diminished DFS and OS (HR:1.3 ,95 % CI:1.0-1.7;  $p=0.001$ ) and (HR:1.6 ,95 % CI:1.1-2.4;  $p=0.001$ )

**Conclusion/Implications:** In our retrospective cohort PDS seems to be more effective in the treatment of Stage III-IV ovarian cancer and patients who treated with PDS had better DFS and OS.

EP220 / #33

Topic: **AS11. Ovarian Cancer**

## **IMPACT OF FRAGMENTATION OF HEALTHCARE ON OVARIAN CANCER SURVIVAL**

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**Introduction:** Fragmentation of healthcare results when cancer care are provided at different institutions due to health insurance payer restrictions. The impact of this is studied on survival of ovarian cancer. The objective to examine the impact of fragmented healthcare on progression free survival(PFS).

**Methods:** Patients with stage IIIC high-grade ovarian cancer analysed between 2011-2018. Patients who had a delay in chemo-initiation (> 28 days following surgery) due to fragmentation of healthcare analyzed as cohort-1, compared to the patients who did not have any delay as cohort-2. We included patients' surgical, tumor, perioperative, surgical, chemotherapy data to control for factors affecting chemo-initiation and PFS. Descriptive statistics and multivariate analyses were performed. The primary outcome was a Progression free survival attributable to fragmented healthcare.

**Results:** Total of 491 ovarian cancer identified. There was 178/284 (67%) patients who had a delay in chemo-initiation. Cohort-1 (n=128) included patients who experienced a delay in chemo-initiation due to fragmentation of healthcare, cohort-2 (n=106) who did not have a delay. Both cohorts were ballanced. Multivariable-adjusted analysis showed that delay of chemo-initiation due to fragmented healthcare in cohort-1 was associated with shorter PFS compared to cohort-2 (18.1 months vs. 22.1 months; p<0.01); odds ratio [OR] 0.32 (0.23-0.68). Other factors contributing to shorter PFS included age OR 0.52 (0.32-0.78); stage OR 0.72 (0.52-0.87); grade OR 0.76 (0.53-0.99); and suboptimal cytoreduction OR 0.42 (0.25-0.67).

**Conclusion/Implications:** Patients with advanced ovarian cancer who had a delay in chemo-initiation due to fragmented healthcare, had a shorter progression-free interval after controlling for all other relevant factors.

EP221 / #1446

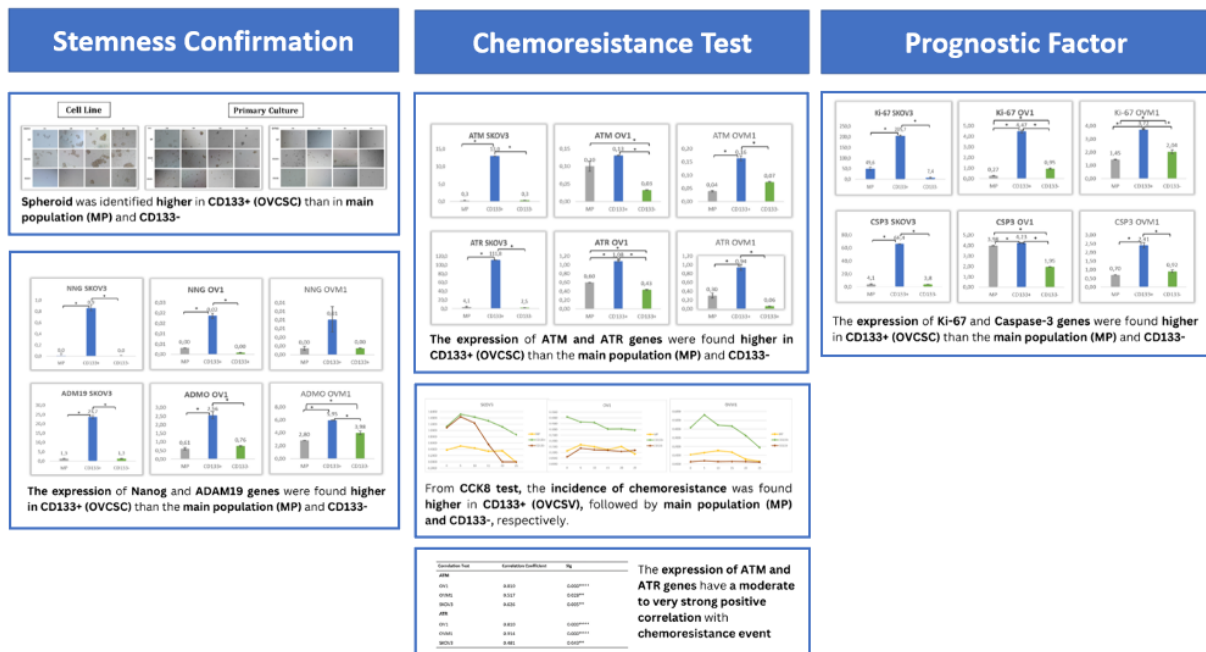
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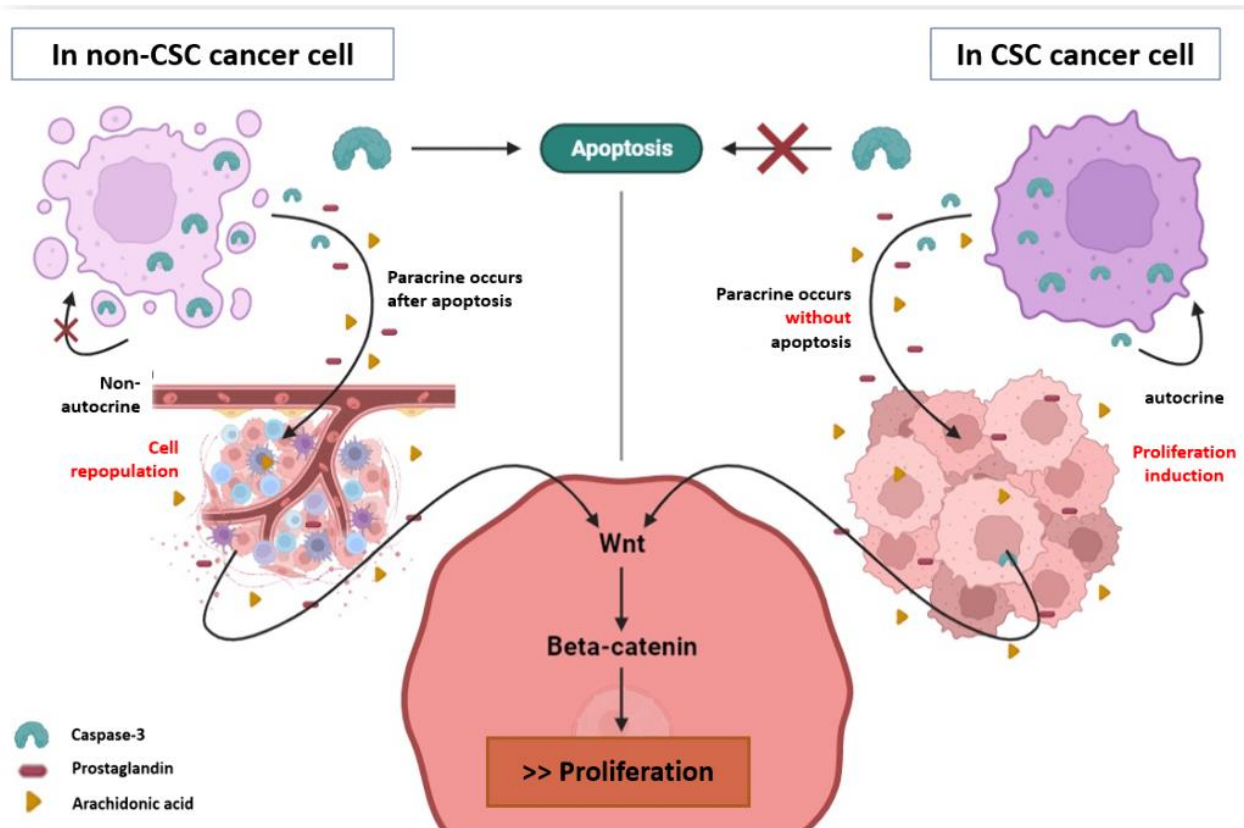
## THE ROLE OF ATM ATR GENE ON RESISTANCE OF CANCER STEM CELL SUBPOPULATIONS IN ADVANCED OVARIAN CANCER: THERAPY RESPONSE TO IN VITRO APOPTOSIS AND PROLIFERATION

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**Introduction:** Approximately 85% of ovarian cancer patients were diagnosed at an advanced stage which has a high mortality rate. More than 80% of them respond to first-line chemotherapy using platinum-based regimen. However, the median disease-free survival is only 18 months. Most patients relapse and do not respond to subsequent lines of chemotherapy. Intervening the presence of cancer stem cells (CSC) is preferred in managing chemoresistant ovarian cancer. One of chemoresistance mechanisms identified in CSC is the high activity of ATM and ATR proteins that bind competitively to DNA against platinum-based regimen. Therefore, this study aimed to explore correlation of ATM and ATR gene expression in ovarian cancer CSC chemoresistance.





**Methods:** The culture cells of 67 advanced ovarian cancer patients were sorted using MACS with the CD133 marker to obtain CSC. The obtained CSCs were prepared with the spheroid method (using SKOV3 cell line, OV1, and OVM1). They were then tested with RT-qPCR (ATM, ATR, NANOG, ADAM19, Ki-67, and Caspase-3) and chemoresistance test (to carboplatin chemotherapy).

**Results:** It was found that the number of spheroids obtained, all gene expression, and number of chemoresistance to carboplatin regimen in CD133+ CSC cultures were higher than the main population and CD133-. CSCs with CD133+ had a higher ability to proliferate with increased Ki-67 gene expression, stronger stemness with higher NANOG gene expression, and greater chemoresistance ability with increased ATM and ATR gene.

**Conclusion/Implications:** It can be concluded that ATM and ATR gene expression are positively correlated with the resistance of CSC in ovarian cancer patients.

EP222 / #246

Topic: *AS11. Ovarian Cancer*

## **QUANTIFYING PLATINUM SENSITIVITY AS A MARKER FOR RESPONSE TO PARP INHIBITION IN PATIENTS WITH ADVANCED OVARIAN CANCER**

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**Introduction:** All patients with high grade epithelial ovarian cancer(HGEOC) do not benefit equally from PARP inhibitors, but all are exposed to PARP-associated toxicities. This study aims to assess the correlation between the pathology-based Chemotherapy Response Score(CRS) at the time of interval debulking surgery(IDS) and progression free survival(PFS) in patients who received PARP maintenance, to determine this score's potential as a marker of expected benefit from PARP.

**Methods:** This is a retrospective cohort study of patients with HGEOC who underwent IDS between January 2016 and September 2022. Demographic and clinical parameters were collected.  $\chi^2$  test and Student t-test were used to compare descriptive variables and Kaplan-Meier survival analysis with log rank test comparison for PFS.

**Results:** On 169 patients, 47 received PARP maintenance and the majority needed dose reduction due to toxicity(53.2%). Patients with CRS 1(No/Minimal response) or CRS 2-3(Moderate/Complete response) were comparable in terms of baseline characteristics. Patients CRS 1 compared to CRS 2-3 had lower PFS regardless of maintenance( $p=0.017$ ). Patients with CRS 2-3 who received PARP showed significantly improved PFS(20 vs 15 months,  $p=0.029$ ) compared to those who did not, while in those with CRS 1 maintenance was not associated with improved PFS( $p=0.27$ ). Results were similar on multivariate analysis, adjusting for BRCA status and surgical outcomes.

**Conclusion/Implications:** In HGEOC patients demonstrating response(CRS 2-3) to NACT, PARP maintenance was associated with a significant improvement in PFS. CRS can be a helpful tool in counseling prior to PARP inhibitor initiation, in patients BRCA-intact, and in settings where homologous recombination deficiency testing is not easily available.

EP223 / #840

**Topic: AS11. Ovarian Cancer**

## **KAZAKHSTAN NATIONAL EXPERIENCE: GRANULOSA CELL TUMORS OF THE OVARY**

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**Introduction:** Objectives: Ovarian granulosa cell tumors (OGCT) are rare, and Eurasian data have not been published. This study objective was to describe OGCT among the 19 million residents of Kazakhstan.

**Methods:** The Kazakhstan Cancer Registry Database was queried for descriptive and outcomes data of all consecutive patients with histologically verified OGCT from 2014-2020. Descriptive statistics and log likelihood ratios were performed using JMP Version 14.0.

**Results:** 240 patients with OGCT were included, representing 3.9% of ovarian cancer in Kazakhstan. The median age was 52 years (range, 15-87 years). Nationality of origin was 55% Kazakh, 30.8% Russian, 3.8% Ukrainian, and 11% other. Stage distribution was 53.7% Stage I, 20.4% Stage II, 22% Stage III, 2.5% Stage IV, and 1% unknown. In total, 89 patients (37.6%) received chemotherapy; this did not correlate with stage. Common regimens included paclitaxel/carboplatin; bleomycin, etoposide, and cisplatin (BEP); and EP. Of the 240 patients, 67 patients (28%) recurred; recurrence correlated with stage ( $p < 0.001$ ). Treatment for recurrent disease included surgery, chemotherapy, and radiation therapy. After 16-month median follow up (range, 0-90 months), 186 patients (77.5%) were without evidence of disease, 12 patients (5%) were alive with disease, and 42 patients (17.5%) had died. Risk of death increased with advancing stage ( $p < 0.001$ ). Stage I OGCT patients who received adjuvant chemotherapy were significantly less likely to die than those who had not ( $p = 0.003$ ).

**Conclusion/Implications:** This is the first description of OGCT in Kazakhstan. There is a survival advantage to chemotherapy administration in early-stage patients, supporting the importance of access to chemotherapy.



EP224 / #880

Topic: **AS11. Ovarian Cancer**

## **BRCA MUTATIONS IN HIGH GRADE SEROUS OVARIAN CANCER IN KAZAKHSTAN**

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**Introduction:** Objectives: More than 1,000 new cases and 500 deaths from ovarian cancer are detected annually in Kazakhstan. The aim of this study was to examine the BRCA1/2 mutation rate in a cohort of Kazakhstani women with high-grade serous ovarian carcinoma (HGSOC).

**Methods:** We performed a retrospective review of the Kazakhstan Cancer Registry Database and identified all patients with HGSOC who had undergone genetic testing between 2018-2022. Gynecologic oncologists and genetic counselors initiated genetic testing within the KazIOR health care system. All testing was performed on site through DNA isolation from tumor tissue using the cobas® DNA sample preparation kit (Roche Diagnostics, Basel, Switzerland). Genomic DNA was amplified using the AmpliSeq BRCA1 and BRCA2 panel. The DNA Libraries were pooled, barcoded, and sequenced. Data was analyzed using SPSS 23.0. Study covered by MOH BR11065390

**Results:** 96 patients underwent genetic testing. The median age was 55.3 years (range, 26-83 years). Of the 96 patients, 34 tested positive for a pathogenic mutation in either BRCA1 or BRCA2, yielding a prevalence of 35.4%. Median age did not differ based on mutation status. Patients with BRCA mutations were more likely to recur. Of the 96 patients, 18 of 34 BRCA+ patients (52.9%) recurred, compared with 13 of 62 BRCA- patients (21%, p=0.001). Median overall survival was similar for BRCA+ patients (23.6 months) compared with BRCA- patients (22.1 months).

**Conclusion/Implications:** Pathogenic mutations in BRCA1/2 are more common than expected in women with HGSOC in Kazakhstan. All women diagnosed with HGSOC should undergo genetic testing to guide personalized treatment using PARP inhibitors.

EP225 / #828

Topic: *AS11. Ovarian Cancer*

## **DIFFERENCE IN HEMODYNAMIC PARAMETERS IN PATIENTS (PTS) WITH ADVANCED EPITHELIAL OVARIAN CANCER (EOC) UNDERGOING PRIMARY (PDS) OR INTERVAL DEBULKING SURGERY (IDS)**

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**Introduction:** To examine the impact of PDS versus IDS on hemodynamic and transfusion characteristics as well as the length of care in the intensive care unit (ICU).

**Methods:** All consecutive pts with EOC (FIGO stage  $\geq$ IIIC) undergoing PDS or IDS between 01/2018 and 12/2019 were included in the analysis. All data were collected in a prospectively maintained database and retrospectively analyzed regarding anaesthesiological characteristics.

**Results:** 270 pts could be included, 181 pts (67%) were treated with PDS, 89 pts (33%) underwent IDS. IDS pts showed a higher rate of thromboembolic events in history (10.1%) vs. PDS pts (1.1%,  $p < 0.001$ ), further differences in comorbidities or medications were not found. Table 1 shows patient and tumor characteristics. The initial median hemoglobin value in IDS pts was 10.5g/dl (9.3;11.5) vs. PDS pts 11.7g/dl (10.8;12.7,  $p < 0.001$ ) and IDS pts were more frequently transfused intraoperatively (PDS 21.5% vs. IDS 42.7%,  $p < 0.001$ ). PDS pts had higher fluid demands of crystalloid [4500ml (3500;5000) vs. 4000ml (3000;4500),  $p = 0.015$ ] and colloid infusions [2000ml (1500;2000) vs. 1500ml (1000;2000),  $p = 0.003$ ], whereas other hemodynamic characteristics like highest heart rate, lowest arterial pressure, norepinephrine requirements, highest lactate level, or the amount of urine output were comparable. Table 2 demonstrates further anesthesiological and surgical parameters.

**Table 1 Patient and tumor characteristics**

	<b>PDS (n=181)</b>	<b>IDS (n=89)</b>	<b>P-value</b>
<b>ECOG PS</b>			0.558
0	172 (95.0%)	86 (96.6%)	
1	8 (4.4%)	2 (2.2%)	
2	0 (0%)	1 (1.1%)	
3	1 (0.6%)	0 (0%)	
<b>ASA PS</b>			0.010
1	17 (9.4%)	1 (1.1%)	
2	111 (61.3%)	52 (58.4%)	
3	47 (26.0%)	35 (39.3%)	
4	1 (0.6%)	0 (0%)	
<b>Charlson Comorbidity index</b>			0.791
0	136 (75.1%)	68 (76.4%)	
1	23 (12.7%)	13 (14.6%)	
2	15 (8.3%)	2 (2.2%)	
3	3 (1.7%)	4 (4.5%)	
4	3 (1.7%)	2 (2.2%)	
5	0 (0%)	0 (0%)	
6	1 (0.6%)	0 (0%)	
<b>Arterial hypertension</b>	65 (35.9%)	33 (37.1%)	0.893
<b>Cardiac diseases</b>	21 (11.6%)	5 (5.6%)	0.130
<b>Diabetes mellitus</b>	10 (5.5%)	7 (7.9%)	0.439
<b>Renal insufficiency</b>	3 (1.7%)	2 (2.2%)	0.666
<b>Pulmonary diseases</b>	18 (9.9%)	12 (13.5%)	0.413
<b>Beta blocker</b>	38 (21.0%)	14 (15.7%)	0.329
<b>ACE inhibitor</b>	47 (26.0%)	15 (16.9%)	0.123
<b>FIGO stage</b>			0.020
IIIC	70 (38.7%)	42 (47.2%)	
IVA	5 (2.8%)	8 (9.0%)	
IVB	109 (60.2%)	41 (46.1%)	
<b>Ascites (ml)</b>	200 (30; 1200)	0 (0; 50)	<0.001

Data are shown as median (25%; 75%) quartiles or as n (%) patients.

P-values calculated using the exact Wilcoxon-Mann-Whitney test or the exact Fisher test in contingency tables as appropriate.

ECOG PS: Eastern Cooperative Oncology Group performance status, ASA PS: American Association of Anesthesiologists physical status, FIGO: Fédération Internationale de Gynécologie et d'Obstétrique| ACE: Angiotensin-converting-enzyme.

**Table 2 Anaesthesiological and surgical parameters**

	<b>PDS (n=181)</b>	<b>IDS (n=89)</b>	<b>P-value</b>
Duration of surgery (minutes)	280 (220; 330)	240 (180; 293)	<0.001
Peritoneal cancer index (points)	19 (13; 23)	12 (6; 16)	<0.001
Rectosigmoid resection	122 (67.4%)	35 (39.3%)	<0.001
Tumor residuals (mm)			0.294
0	129 (71.3%)	65 (73.0%)	
<5 mm	19 (10.5%)	9 (10.1%)	
5-10 mm	11 (6.1%)	9 (10.1%)	
11-19 mm	7 (3.9%)	0 (0%)	
>= 20 mm	15 (8.3)	6 (6.7%)	
Intraoperative estimated blood loss (ml)	500 (338; 700)	500 (300; 700)	0.745
Blood transfusion intraoperatively	39 (21.5%)	38 (42.7%)	<0.001
Patients admitted to ICU	165 (91.2%)	81 (91.0 %)	0.814
LOS in ICU (days)	1 (1; 2)	1 (1; 1)	0.175
LOS hospital (days)	15 (12; 20)	13 (10; 18)	0.016
Blood transfusion postoperatively	67 (37%)	45 (50.6%)	0.024
Clavien-Dindo classification			0.090
0	70 (38.7%)	42 (47.2%)	
I	7 (3.9%)	5 (5.6%)	
II	70 (38.7%)	31 (34.8%)	
IIIa	10 (5.5%)	2 (2.2%)	
IIIb	16 (8.8%)	9 (10.1%)	
IVa	5 (2.8%)	0 (0%)	
IVb	2 (1.1%)	0 (0%)	
V	1 (0.6%)	0 (0%)	

Data are shown as median (25%; 75%) quartiles or as n (%) patients.

P-values calculated using the exact Wilcoxon-Mann-Whitney test or the exact Fisher test in contingency tables as appropriate.

LOS: Length of stay, ICU: intensive care unit.]

**Conclusion/Implications:** In comparison to PDS the IDS showed intraoperatively lower fluid but higher transfusion demands and was not associated to a reduced stay in ICU. The hemodynamic characteristics did not show any benefits neither. These data indicate that IDS is similarly associated to a high impact on the anaesthesiological and ICU management.

EP226 / #560

**Topic: AS11. Ovarian Cancer**

## **VOC ANALYSES IN PLASMA SHOW HIGH SENSITIVITY TO DISTINGUISH OVARIAN CANCER PATIENTS FROM HEALTHY CONTROLS.**

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**Introduction:** Ovarian cancer (ovarian-/tubal-/peritoneal cancer) give dull symptoms why early diagnosis is challenging. Endogenous Volatile Organic Compounds (VOC) are products of metabolic activity in cancer and elevated glycolysis leads to increases in lactate, fumarate, and other metabolites. VOC analyses in plasma and urine have shown to indicate early cancer.

**Methods:** With highly sensitive gas sensors, preoperative plasma from 87 women with stage I–IV ovarian cancer was examined and compared to that from 26 healthy control women. Data analyses were performed using feature extraction from 32 gas sensors per sample. The dataset has been processed by principal component analysis (PCA) for dimensionality reduction and feature reduction (9 principal components were kept retaining 95 % of the original information in the features–observations dataset). A support vector machine model was then trained towards algorithmic binary classification: positive (cancer) or negative (no cancer). To avoid overfitting while not losing any observations, 5-fold cross validation was used during training of the classification algorithm.

**Results:** The analysis of VOCs revealed positive results in 85 out of 87 ovarian cancer patients, yielding a sensitivity of 97.7% (95% confidence interval [CI] 91.9 – 99.7%). Out of the healthy controls 22 were negative and 4 showed positive results (specificity 84.6 % 95 % CI 65.1 – 95.6 %). Positive predicted value 95.5 % (95 CI: 88.9 - 98.8%) and accuracy of 94.7 % (95 % CI: 88.8 - 98.0 %).

**Conclusion/Implications:** VOC analyses in plasma show very high sensitivity to distinguish ovarian cancer patients' stage I-IV from healthy controls.

EP227 / #389

Topic: *AS11. Ovarian Cancer*

## **COMBINATION OF IGF1R INHIBITION WITH PD-1 BLOCKADE RESULTS IN SIGNIFICANT ANTI-TUMORAL ACTIVITY IN EPITHELIAL OVARIAN CANCER**

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**Introduction:** The insulin-like growth factor 1 receptor (IGF1R) plays a key role in regulating growth and invasiveness in epithelial ovarian cancer (EOC), therefore is regarded as a promising therapeutic target. Recently, it has been shown that IGF1 can regulate dendritic cell (DC) maturation and T cell activation. Our study aims to investigate the combination effect of IGF1R inhibition and anti-PD-1 treatment on EOC.

**Methods:** EOC cell lines were co-cultured with IGF1R inhibitor (AEW-541)-treated-DCs. DC differentiation and EOC proliferation levels were evaluated by Flow Cytometry Assay (FACS). C57BL/6 mice with established peritoneal ovarian cancer were injected with single or combined anti-PD-1 and AEW-541 treatment, and their survival was evaluated. conventional DCs and T-cell population levels were analyzed by FACS. Finally, RNA was extracted from tumors and RNA sequencing was performed.

**Results:** IGF1R inhibitor treatment significantly induced DC differentiation in AEW-541 pre-treated-DCs compared to control after 24 h. In addition, Differentiated AEW-541-treated-DCs significantly decreased EOC cell proliferation. In vivo experiment showed that combined anti-PD-1/IGF1R treatment decreased tumor weight compared to single treatments. Moreover, the anti-PD-1/IGF1R treatment significantly increased the conventional DCs compared to AEW-541 and anti-PD-1 treatments. The Gene Ontology (GO) analysis indicate that the most significant differential biological process terms were immune response by increased lymphocytes cells activation.

**Conclusion/Implications:** IGF1R pathway inhibition in differentiated DCs suppressed EOC cell proliferation. IGF1R inhibitor combined with anti-PD-1 may result in enhanced anti-tumor activity. Thus, restoring the anti-tumor immune response by IGF1R targeting in combination with immunotherapy may be an effective therapy for EOC.

EP228 / #418

**Topic: AS11. Ovarian Cancer**

## **DISPARITIES IN TREATMENT MODALITIES AND SURVIVAL AMONG ELDERLY HIGH GRADE SEROUS OVARIAN CANCER PATIENTS**

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**Introduction:** Elderly women with ovarian cancer are often undertreated. We aimed to evaluate the treatment modalities of elderly patients and its impact on overall survival.

**Methods:** A total of 5,055 high grade serous ovarian cancer patients and 3584 advanced stage (IIIC+IV) patients aged 65 years or older were hereby identified, all from the Surveillance, Epidemiology, and EndResults (SEER) database from January 1, 2010 to December 31, 2017. Overall survival (OS) and ovarian cancer-specific survival (OCSS) was compared across age and Cox proportional-hazards model was created to adjust for case-mix.

**Results:** The very elderly patients ( $\geq 75$  years old) had significantly: less surgical complexity like undone lymphadenectomy (59.7% vs 48.6%;  $p < 0.001$ ), less chemotherapy (78.2% vs 89.4%;  $P < 0.001$ ), less standard treatment (70.6% vs. 85%;  $p < 0.001$ ) and less optimal debulking surgery (44.0% vs 52.7%;  $p < 0.001$ ). The very elderly and elderly patients all had a high use of NACT, but no significant difference was found (38.7% vs 36.2%;  $P=0.212$ ). Patients  $\geq 75$  had significantly worse OS and OCSS.

**Conclusion/Implications:** The survival of women with EOC strongly decreases with increasing age, EOC patients over 75 years old received less standard treatment and more elderly patients were treated with NACT.

EP229 / #1265

Topic: *AS11. Ovarian Cancer*

## **PROGNOSTIC NUTRITIONAL INDEX AS A PROGNOSTIC BIOMARKER IN ADVANCED OVARIAN CANCER**

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**Introduction:** The prognostic nutritional index (PNI) is a biomarker of nutritional and immunological status that has been validated as a prognostic factor in cancer. In ovarian cancer (OC) it has been studied in the Asian population. The aim of our study was to evaluate the association of PNI in Mexican patients with advanced ovarian cancer treated with neoadjuvant chemotherapy followed by debulking surgery.

**Methods:** Retrospective cohort study of 220 patients with OC. PNI was calculated with de formula: albumin (g/L) + 0.005 X lymphocyte count (mm<sup>3</sup>). The cut-off point was obtained using ROC curves. Categorical variables were analyzed with Chi square and multivariate analysis with logistic regression. DFS was obtained with Kaplan Meier. P value 0.05 was considered significant.

**Results:** The PNI cut-off values at diagnosis and post chemotherapy to predict complete and optimal surgery were 40.5 (AUC 0.62, OR: 1.07; p = 0.0023) and 44.5 (AUC 0.67, OR: 1.16; p = 0.00014), with significant association with high levels of PNI (p = 0.003 and p = 0.000), respectively. In logistic regression high levels of PNI were protective for residual disease (OR: 0.349, p = 0.005) and (OR: 0.168, p = 0.001). Median DFS was 15 (p = 0.054) and 13 (p = 0.640) months, respectively for cut-off points.

**Conclusion/Implications:** In our study PNI behaves as an independent prognostic factor in advanced OC. High levels are associated with complete and optimal surgery and may be a predictor of DFS.



EP230 / #827

Topic: *AS11. Ovarian Cancer*

## **ASSOCIATION BETWEEN OVARIAN CANCER AND ASBESTOS EXPOSURE: A META-ANALYSIS**

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**Introduction:** Despite the publication of numerous well-designed studies on the association between asbestos exposure and ovarian cancer since the 2012 IARC Monograph on asbestos, no comprehensive meta-analysis has been conducted to date. In the present study, a meta-analysis was performed by integrating studies published both before and after the 2014 Helsinki update on Asbestos.

**Methods:** A systematic review of the literature available on PubMed, EMBASE, and the Cochrane Library in July 2022 was conducted to identify relevant studies. Mesh terms and queries were selected based on the advice of a librarian, and included key concepts such as "asbestos," "crocidolite," "serpentine," "ovarian cancer," "ovarian neoplasms," and "ovary tumor."

**Results:** The present analysis includes 18 studies published between 1982 and 2022, reporting data from 1941 to 2015 and involving more than 74,574 participants from 9 countries. An analysis of 16 studies before and after the 2014 Helsinki update found that the overall summary Standardized Mortality Ratio (SMR) was 1.74 (95% CI, 1.46-2.08; P = 0.0440; 17 records). Among the integrated studies, five cohort studies reported a strong correlation between mortality from ovarian cancer and occupational high-intensity asbestos exposure.

**Conclusion/Implications:** The significance of the current study is that it is the first meta-analysis to incorporate both the Helsinki-included studies and subsequent publications. It revealed a significant increase in SMR for ovarian cancer, even in the studies published after the 2012 IARC Monograph. To enhance future research, it is recommended to investigate women diagnosed with ovarian cancer after 1999 using the SIR method, particularly regarding environmental exposure.

EP232 / #103

Topic: *AS11. Ovarian Cancer*

## **DOES THE DIAGNOSTIC TIMING OF CANCER-ASSOCIATED THROMBOEMBOLISM INFLUENCE THE SURVIVAL OUTCOME IN OVARIAN CANCER PATIENTS?**

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**Introduction:** Efforts were made to explore the influence of diagnostic timing for cancer-associated thromboembolic events on survival of ovarian cancer patients.

**Methods:** We reviewed the medical records of 75 ovarian cancer patients with thromboembolism and evaluated the prognostic factors affecting disease-free survival and overall survival.

**Results:** These 75 patients were classified into two categories by the diagnostic timing of the thromboembolism, during (33 cases) and after (42 cases) initial diagnosis of ovarian cancer groups. The diagnostic timing of thromboembolism was not related to disease-free survival or overall survival of the studied population. Advanced disease stage, clear cell histology, interval debulking surgery, no recurrence/persistence of ovarian cancer, and patients treated with anticoagulant(s) treatment >3 months were associated with the disease-free survival. Advanced disease stage, clear cell histology, body mass index (BMI)  $\geq 24$  kg/m<sup>2</sup> at the diagnosis of ovarian cancer, and no recurrence/persistence of ovarian cancer influenced the overall survival. In the subgroup analysis, compared to the after initial ovarian cancer diagnosis group, patients with stage I/II disease, BMI <24 kg/m<sup>2</sup> at the diagnosis of ovarian cancer, or primary debulking surgery in the during cancer diagnosis group had longer disease-free survival, and overall survival benefit was observed in cases with stage I/II disease, or primary debulking surgery.

**Conclusion/Implications:** The diagnostic timing of thromboembolism was not related to disease-free or overall survival of ovarian cancer patients, but associated with that of specific patient subgroups.

EP236 / #459

Topic: **AS11. Ovarian Cancer**

## **DEVELOPING A WHOLE EXOME SEQUENCING-BASED HOMOLOGOUS RECOMBINATION DEFICIENCY TEST OF EPITHELIAL OVARIAN CANCER**

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**Introduction:** Some studies revealed a very good correlation in HRD detection between Myriad testing and WGS/WES method for breast cancer. However, the clinical value of WES based HRD analysis was less validated in EOC.

**Methods:** We developed a HRD test by WES-based tissue samples (N=44) of EOC patients. Samples were concordantly examined by Myriad myChoice. The correlation of HRD and clinical outcomes among the three tests were analyzed

**Results:** High correlation of HRD score was observed between Myriad and our WES-based scarHRD test (coefficient 0.82,  $p < 0.001$ ) in the linear regression model. In compared to positive HRD status of Myriad test, the sensitivity, specificity, PPV and NPV was 93.5%, 76.9%, 90.6% and 83.3% respectively in our WES-based scarHRD test. The percentages of EOC patients with positive HRD status of our test/ Myriad test were higher in advanced FIGO stage (Early vs Advanced: 0% vs 76.2%;  $p = 0.018$ )/ (Early vs Advanced: 0% vs 73.8% ,  $p = 0.025$ ), and sensitive platinum-response (Sensitive vs Resistant: 84.6% vs 55.6%,  $p = 0.033$ )/(Sensitive vs Resistant: 84.6% vs 50%,  $p = 0.013$ ). In multivariate Cox regression model, optimal debulking surgery (H.R; 0.39,  $p = 0.017$ ) and positive HRD status of our test (H.R; 0.42,  $p = 0.026$ ) were independent factors for lower risk of disease recurrence. Only optimal debulking surgery (H.R; 0.41,  $p = 0.023$ ) but not positive HRD status of Myriad test (H.R; 0.99,  $p = 0.083$ ) was independent factor for lower risk of disease recurrence.

**Conclusion/Implications:** This test had favorable sensitivity, specificity and PPV/NPV and will provide a new feasible option to determine the HRD status of EOC patients

EP237 / #97

Topic: *AS11. Ovarian Cancer*

## **THE DOWNREGULATION OF MIR-509-3P EXPRESSION BY COL11A1-REGULATED HYPERMETHYLATION FACILITATES CANCER PROGRESSION AND CHEMORESISTANCE VIA THE DNMT1/SUMO-3 AXIS IN OVARIAN CANCER CELLS**

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**Introduction:** It has been revealed that miR-509-3p is a strong tumor suppressor that attenuates migration and disrupts multicellular spheroids in multiple ovarian cancer cell lines, sensitizes to cisplatin, and remarkably downregulates in recurrent and metastatic ovarian cancer. In this study, we hypothesize that miR-509-3p downregulated by promoter hypermethylation through COL11A1 leads to ovarian cancer progression.

**Methods:** The A2780CP70 and OVCAR-8 cells transfected with miR-509-3p mimic, while the A2780 and OVCAR-3 cells transfected with miR-509-3p inhibitor. The A2780CP70 cells transfected with a small interference RNA of COL11A1, and the A2780 cells transfected with a COL11A1 expression plasmid. The mRNA of COL11A1 and miR-509-3p and miR-509-3p hypermethylation of 137 ovarian tumors were determined by real-time reverse transcription-polymerase chain reaction and sequencing.

**Results:** We found that miR-509-3p is aberrantly downregulated in ovarian cancer tissues and correlated with disease progression, survival, and COL11A1 expressions. The invasive EOC cells phenotypes are regulated by miR-509-3p. The miR-509-3p promoter region (p278) hypermethylation is an extremely important mechanism by which miR-509-3p transcription is regulated. The frequency of hypermethylation was significantly higher in EOC tumors with miR-509-3p downregulation than that in those with high miR-509-3p expression. Additionally, Kaplan-Meier curve, stratified by the hypermethylation site of miR-509-3p, showed patients with hypermethylation had significantly shorter OS than those without hypermethylation. Mechanistic studies indicated that miR-509-3p transcription downregulated by COL11A1 through increased DNMT1 stability was achieved by combined DNMT1 and miR-509-3p promoter. Moreover, miR-509-3p targets SUMO-3 in ovarian cancer cells.

**Conclusion/Implications:** We propose that the miR-509-3p/SUMO-3 axis potentially uncovers new targets for drug resistant metastatic ovarian cancer treatment.

EP238 / #102

Topic: *AS11. Ovarian Cancer*

## **SUPPORT FOR STANDARDIZATION: ULTRASOUND RISK STRATIFICATION MODELS ACCURATELY DISCRIMINATE BENIGN FROM MALIGNANT ADNEXAL LESIONS IN THE HANDS OF NOVICE OPERATOR**

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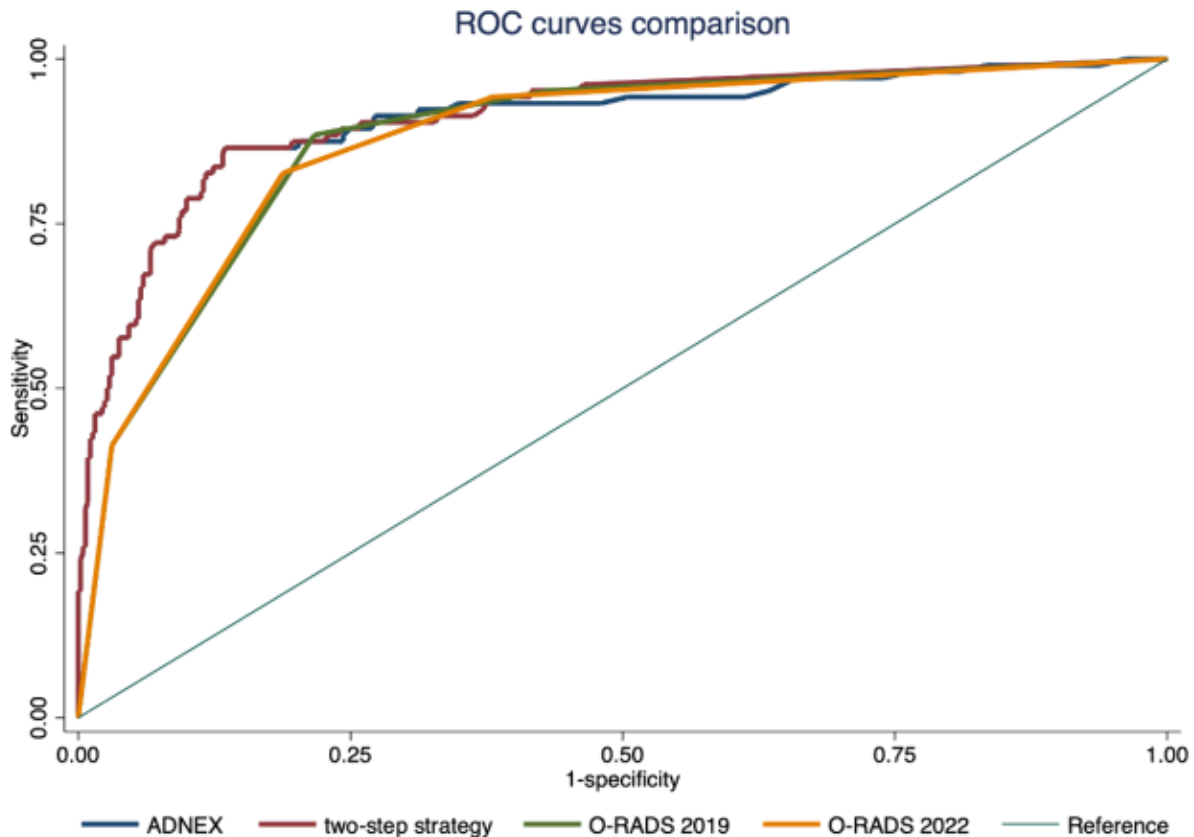
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**Introduction:** It is unclear whether ultrasound risk stratification models for adnexal lesions perform well when used by novice providers. We aim to compare the performance of four commonly used models to detect ovarian cancer, when the operator has only basic experience.

**Methods:** Women with adnexal masses treated in 2019 were identified retrospectively. Patients were included if they underwent surgery within 3 months of diagnosis or had at least 12±2 months of follow-up. A non-expert operator (European Federation of Societies for Ultrasound in Medicine and Biology level I) classified each lesion using ADNEX, two-step strategy (benign descriptors followed by ADNEX), O-RADS 2019, and O-RADS 2022. The primary outcome measure was AUC [95% confidence interval], compared across the four models.

**Results:** A total of 556 women were included in the analyses: 452 benign and 104 malignant. The AUCs of ADNEX, the two-step strategy, O-RADS 2019, and O-RADS 2022 were 0.90 [0.87-0.94], 0.91 [0.88-0.94], 0.88 [0.85-0.91], and 0.88 [0.84-0.91], respectively (Figure 1).

**Figure 1.** Diagnostic performance of ADNEX, two-step strategy, O-RADS 2019 and O-RADS 2022. Above, ROC curves for the four models. Below, AUC, sensitivity, specificity, accuracy, positive and negative predictive values with 95% confidence intervals. Abbreviations: AUC, area under the curve; ROC, receiver operating curve; PPV, positive predictive value; NPV, negative predictive value.



	ADNEX	Two-step strategy	O-RADS 2019	O-RADS 2022
AUC	0.9046 [0.8676-0.9415]	0.9106 [0.8773-0.9440]	0.8790 [0.8450-0.9131]	0.8757 [0.8405-0.9110]
Sensitivity	86.54% [83.70-89.38]	86.54% [83.70-89.38]	88.46% [85.81-91.12]	82.69% [79.55-85.84]
Specificity	84.73% [81.75-87.72]	84.96% [81.98-87.93]	78.32% [74.89-81.74]	81.19% [77.95-84.44]
Accuracy	85.07% [81.83-87.93]	85.25% [82.03-88.10]	80.22% [76.66-83.45]	81.47% [77.99-84.62]
PPV	56.60% [52.48-60.72]	56.96% [52.85-61.08]	48.42% [44.27-52.58]	50.29% [46.14-54.45]
NPV	96.47% [94.94-98.01]	96.48% [94.95-98.01]	96.72% [95.24-98.20]	95.32% [93.57-97.08]

The two-step strategy performed significantly better than the O-RADS algorithms (both  $p=0.01$ ). With all the algorithms, the observed malignancy rate was 1.91-2.17% among lesions categorized as “almost certainly benign”, two-fold higher than the expected <1% (Table 1).

**Table 1.** The calibration (i.e., the observed malignancy rate compared to the expected rate) is shown in Table 1A. Data are reported as number of malignant cases per cell/total number of patients in the cell (cell %). Table 1B describes the clinical and radiological characteristics of malignant cases misclassified as “almost certainly benign” by at least one of the models. Abbreviations: BD, benign descriptor; EC, endometrial cancer; GI, gastro-intestinal; na, not available; N, number; US, ultrasound.

Table 1A		Observed rate of malignancy			
		ADNEX	Two-step strategy	O-RADS 2019	O-RADS 2022
Expected rate of malignancy	<1%/score 2	1/46 (2.17)	5/261 (1.92)	5/262 (1.91)	6/286 (2.10)
	1-<10%/score 3	13/351 (3.70)	9/137 (6.57)	7/104 (6.73)	12/99 (12.12)
	10-<50%/score 4	36/92 (39.13)	36/91 (39.56)	49/133 (36.84)	43/114 (37.72)
	≥50%/score 5	54/67 (80.60)	54/67 (80.60)	43/57 (75.44)	43/57 (75.44)

Table 1B		1	2	3	4	5	6	7
Risk of malignancy								
ADNEX		0.4%	1.8%	3.8%	4.9%	6.0%	4.2%	1.5%
Two-step strategy		0.4%	BD	BD	BD	BD	4.2%	1.5%
O-RADS 2019		3	2	2	2	2	2	3
O-RADS 2022		3	2	2	2	2	2	2
US characteristics								
Max dimension (mm)		24.2	13.8	54.9	35.3	26.6	51.2	14.0
N Locules		1	1	1	1	1	1	2
Internal wall		irregular	smooth	smooth	smooth	smooth	irregular	smooth
N Papillations		0	0	0	0	0	0	0
Content		anechoic	anechoic	anechoic	anechoic	anechoic	anechoic	anechoic
Shadowing		yes	no	no	no	no	no	no
Color score		1	1	1	1	2	1	1
Age		62	75	52	55	51	62	62
Menopausal status		post	post	pre	post	pre	post	post
CA125 (KU/L)		36	13	na	109	276	na	na
Histology		Borderline clear cell adenofibroma	Serous borderline	Metastatic Lymphoma	Seromucinous borderline	Metastatic GI tumour	Metastatic EC	Serous borderline
Stage		IA	IB	na	IIB	na	na	IA

Out of the four methods, lesions wrongly classified as “almost certainly benign” were borderline tumors (n=4) and metastases (n=3).

**Conclusion/Implications:** In the hands of a novice provider, all algorithms performed well, and were able to distinguish benign from malignant lesions. ADNEX misclassified only one malignant patient as “almost certainly benign”, compared to 5-6 patients by the other models.

EP239 / #122

Topic: *AS11. Ovarian Cancer*

## THE NEOANTIGENS LANDSCAPE ASSOCIATED WITH HISTOLOGICAL SUBTYPES IN EPITHELIAL OVARIAN CANCER

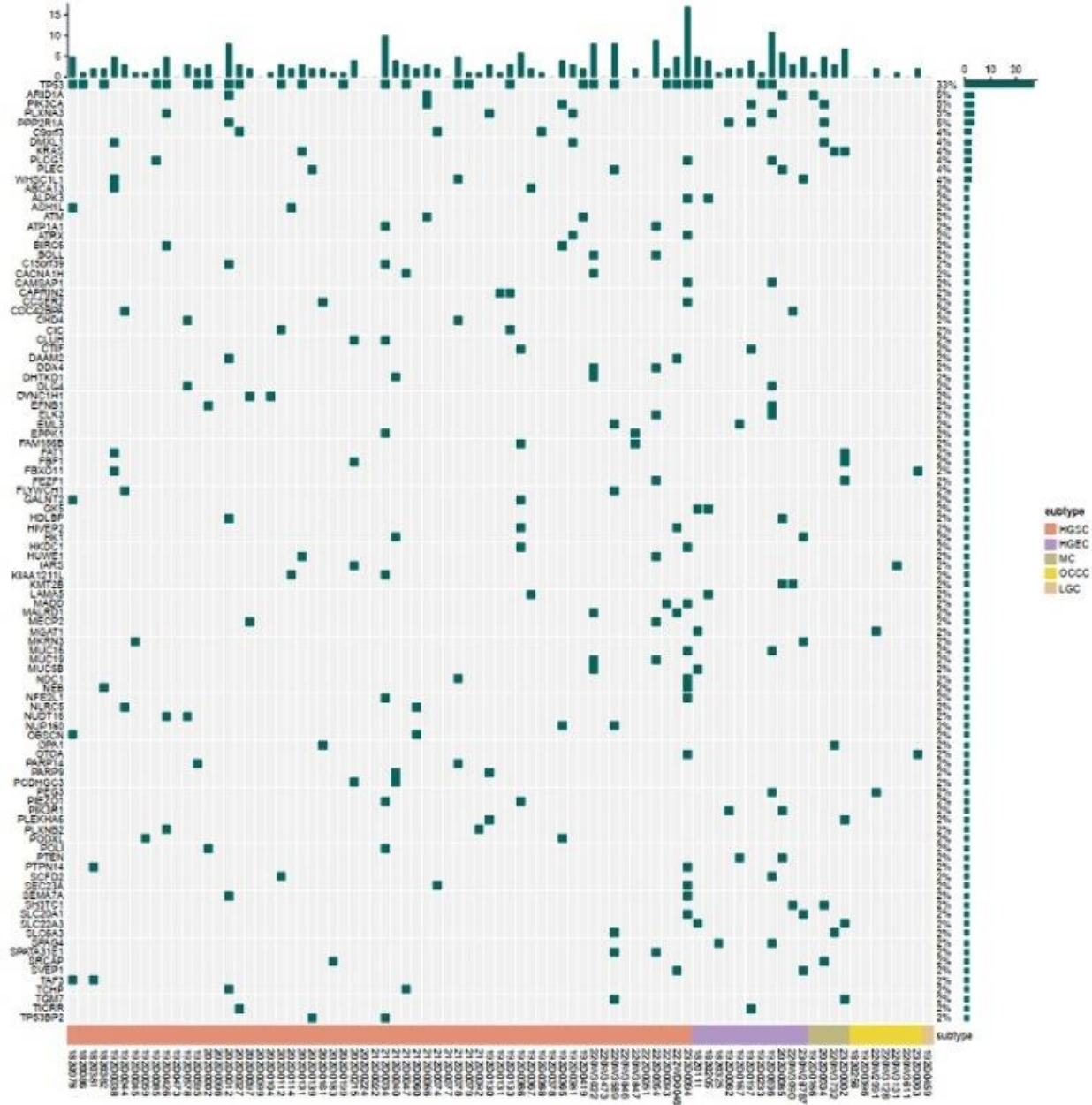
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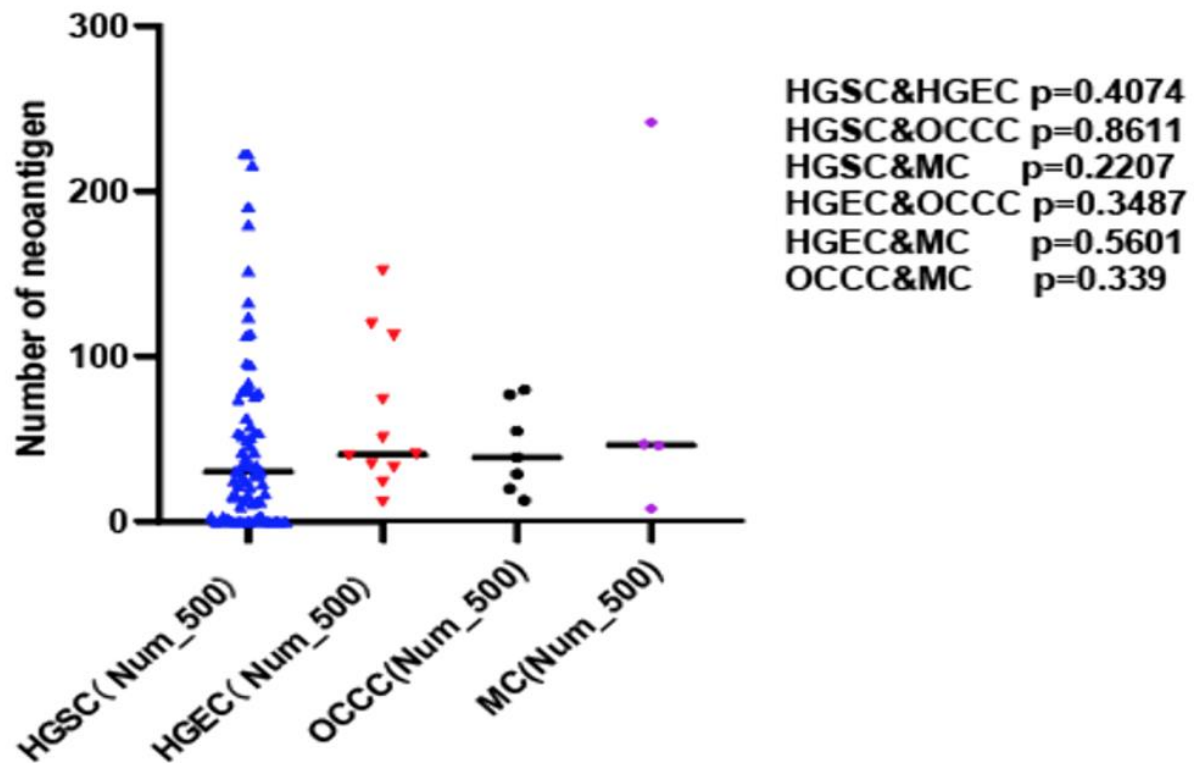
**Introduction:** Neoantigens play a critical role in cancer immunotherapy. Epithelial ovarian cancer (EOC) is a strong heterogeneity tumor, often an immune desert, but immunotherapy is extremely important for intent to cure of cancer. We investigated neoantigen landscape of EOC, tried to select patients who are appropriate to immunotherapy.

**Methods:** 97 patients with EOC from May 2015 to April 2023 were included. Neoantigens were predicted by whole-exome sequencing (WES) and RNA-seq. Mutated peptides with a binding affinity of  $IC_{50} < 500$  nM were regarded as candidate neoantigens. Patient's clinical information were collected and statistical calculations were performed.

**Results:** Of the 97 patients (74 High-grade serous carcinoma (HGSC), 11 Endometrioid carcinoma (EC), 4 Mucinous tumor (MC), 7 Clear cell carcinoma (CCC), and 1 poorly differentiated carcinoma), the detection rate of neoantigens was 85.6%. The number of neoantigens in HGSC, EC, MC, and CCC was 0-223 (30.5), 12-152 (41), 8-242 (39) and 13-80 (46.5), respectively (range, SD). CCC, EC and MC had more neoantigens than HGSC, although the difference was not significant. Among predicted neoantigens, the TP53 gene accounted for the largest proportion at 33%, followed by ARID1A, PIK3CA, PLXNA3 and PPP2R1A genes.







**Conclusion/Implications:** In this study, CCC, EC and MC carried more neoantigens, suggesting that they may benefit more from immunotherapy, however, we should expand the sample size to explore whether the difference is significant. Based on this study findings, future clinical trials of immunotherapy for EOC should consider enrolling more patients with CCC, EC, and MC subtypes, instead of focusing mostly on HGSC patients as in previous trials.

EP240 / #613

**Topic:** AS11. Ovarian Cancer

## **INHERITED LANDSCAPE AND A SPECIFIC RAD51D MUTATION OF CHINESE OVARIAN CANCER PATIENTS**

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**Introduction:** Gene mutations in ovarian cancer demonstrate ethnic differences, and data among Chinese is still insufficient. Here, we elucidated the inherited landscape of Chinese ovarian cancer patients, and further investigated the functional implication of a Chinese-specific enriched RAD51D mutation.

**Methods:** Between 2015 and 2018, 373 consecutive ovarian cancer patients were prospectively enrolled. Mutations of BRCA1/2, other HRR genes and MMR genes were analyzed by next-generation sequencing. A specific pathogenic RAD51D mutation was identified, and its functional implications were investigated by CCK-8 and Colony formation, transwell migration and drug sensitivity assays.

**Results:** Overall, 31.1% (116/373) of patients harbored at least one pathogenic or likely pathogenic germline variant. BRCA1 and BRCA2 accounted for 16.09% and 5.36% respectively, with one patient harboring both mutations. Besides, 32 (8.58%) patients carried other HRR gene mutations, while 3 (0.8%) patients had MMR gene mutations. RAD51D mutation ranked third (8/373, 2.1%) and the rate was much higher compared with other population. Remarkably, all eight patients had a K91fs variant, and presented with satisfactory platinum response and favorable prognoses. This variant conferred enhanced sensitivity to PARP inhibitors in ovarian cancer cells. However, effects on platinum sensitivity were inconsistent among different cell lines. Only under the background of TP53 mutation, RAD51D K91fs mutation could increase the sensitivity to cisplatin.

**Conclusion/Implications:** Our study revealed the inherited landscape of ovarian cancer, and identified a specific enriched RAD51D mutation of Chinese ovarian cancer patients. It can serve as an important reference for ovarian cancer management and provide a potential treatment target.

EP241 / #516

**Topic:** AS11. Ovarian Cancer

## **PATIENT DERIVED ORGANOIDS AS EX-VIVO MODELS FOR HIGH GRADE SEROUS OVARIAN CANCER RESEARCH**

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**Introduction:** Patient-Derived Organoids (PDOs) are in increasing use as ex-vivo models for high-grade serous ovarian cancer (HGSOC) and other cancers, given their genotypic and phenotypic correlations with in vivo tumour. We aimed to characterise inter- and inpatient heterogeneity in PDOs from multiple sites in chemo-naïve HGSOC.

**Methods:** Multi-site tumour samples were collected from HGSOC patients undergoing primary cytoreductive surgery and PDOs grown from extracted tumour cells with/without the Wnt agonist R-spondin. PDOs were trialled against chemotherapies and targeted therapeutics using IC50 and AUC for comparison. Transcriptomic differences between PDOs were explored using RNAseq.

**Results:** PDOs were successfully established ( $\geq 5$  passages) in 8/14 cases (57%), with a mean  $n=5$  sites initially seeded per patient. IC50 and AUC values for platinum compounds and PARP inhibitors varied significantly between patients, and between different sites from the same patient. Cisplatin sensitivity varied 20-fold across 8 different PDO lines ( $p<0.0001$ ), with carboplatin sensitivity differing by almost 10-fold between different tumour sites in one case ( $p<0.0001$ ) highlighting HGSOC inter/inpatient heterogeneity. Rucaparib sensitivity variability was demonstrated between cases and between sites from the same case ( $p<0.001$ ). Resistance was induced in 2 PDO lines through culturing in low dose conditions, with AUC increments were observed for cisplatin ( $p<0.01$ ) and rucaparib ( $p<0.05$ ) compared to controls. Potentially synergistic compounds to overcome platinum and PARPi resistance were trialled.

**Conclusion/Implications:** HGSOC PDOs provide a reliable model for drug screening, incorporating inter and intra-patient heterogeneity. The heterogeneity observed provides rationale for variability in clinical responses and the poor prognosis consistent with advanced HGSOC.

EP242 / #366

**Topic: AS11. Ovarian Cancer**

## **TITLE UNDERSTANDING CURRENT PRACTICES FOR THE MANAGEMENT OF ADVANCED EPITHELIAL HIGH-GRADE OVARIAN CANCER IN THE UK: INTERIM DATA FROM THE OC-NOW SURVEY (2023)**

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**Introduction:** Background Advanced high-grade ovarian cancer (OC) treatment has recently evolved to include novel targeted agents such as PARP-inhibitors. Our survey explores current management of advanced OC in the UK.

**Methods:** Methodology This interim descriptive analysis uses data collected between March-April 2023 from structured interviews with UK-based healthcare professionals (HCPs) involved in secondary care management of advanced OC (OC-NOW).

**Results:** The analysis included 50 OC MDT members. Respondents were mainly based in England (84%; 42/50). Most HCPs (68%; 19/28) used the DESKTOP-III criteria to identify candidates for secondary cytoreduction, with up to 30% of patients considered as eligible in 85% (23/27) of centres. HRD (100%; 41/41) and BRCA1/2 (98%; 40/41) were routinely tested before planning maintenance treatment. Most respondents (90%; 36/40) reported that HRD test results had a turnaround time of 6 weeks. The median number (interquartile range [IQR]) of patients with a BRCA mutation (BRCAmut) was 20.0% (15.0–20.0%), while 25.0% (18.8–30.0%) were HRD (test positive) and BRCA wild type (HRD/BRCAwt), 49.0% (35.0–60.0%) were HRp (test negative) and 10.0% (5.0–11.2%) were HRnd (HR test failure/not determined/inconclusive). Platinum sensitivity was seen as predictive of PARPi maintenance therapy benefit, irrespective of HRD status (Table 1).

**Conclusion/Implications:** Conclusion These results provide an update on UK practice in advanced OC. HRD and BRCA1/2 are now routinely assessed with turnaround times on time for maintenance therapy decision making. For Platinum Sensitive OC, PARPi maintenance is typically considered irrespective of HRD status

EP243 / #883

Topic: *AS11. Ovarian Cancer*

## **INFLUENCING FACTORS AND MANAGEMENT STRATEGIES FOR PERIOPERATIVE COMPLICATIONS OF DIAPHRAGMATIC SURGERY IN OVARIAN CANCER**

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**Introduction:** The diaphragm is a common site of metastasis in advanced ovarian cancer. The development of diaphragm tumor resection surgery is beneficial for achieving complete tumor cell elimination and also poses challenges to the management of perioperative complications. This study aims to explore the influencing factors and prevention and treatment strategies for complications of diaphragm surgery.

**Methods:** This study included advanced ovarian cancer patients who underwent diaphragm tumor resection surgery at Fudan University Shanghai Cancer Center from July 2015 to June 2022. Clinical and pathological characteristics, diaphragm surgical methods, and perioperative complications were retrospectively collected.

**Results:** A total of 396 patients with advanced ovarian cancer were included. 163 patients had perioperative complications, whereas pleural effusion (32.6%), infection (8.3%), and pneumothorax (5.3%) were the most commonly reported. Patients with longer surgery duration (>3 hours) and higher surgical difficulty (Aletti score >5) had a higher incidence of postoperative complications ( $p < 0.01$ ), particularly pleural effusion ( $p < 0.01$ ). Only 60 patients (15.2%) underwent chest tube placement overall, which is not enough to support the routine use of prophylactic chest tube placement in all patients. The incidence of postoperative pleural effusion was significantly higher in patients who underwent diaphragmatic incision surgery (47.8%) than in others (29.5%) ( $p = 0.03$ ).

**Conclusion/Implications:** Pleural effusion is the most common complication of diaphragmatic surgery in ovarian cancer patients. Long surgery duration and high surgical difficulty correlated with postoperative pleural effusions. Routine placement of the prophylactic chest tube is not suitable for all patients. However, for patients who undergo diaphragmatic incision surgery, intraoperative chest tube placement should be considered.

EP244 / #277

Topic: *AS11. Ovarian Cancer*

## **EXAMINING REAL-WORLD TREATMENT BENEFITS OF FIRST-LINE MAINTENANCE NIRAPARIB IN NON-BRCA MUTANT HIGH GRADE SEROUS OVARIAN CANCERS**

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**Introduction:** Maintenance PARP inhibitor therapy after response to first-line chemotherapy is standard of care in advanced high grade serous ovarian cancer (HGSOC). Progression free survival (PFS) benefit for patients on niraparib with non-BRCA mutant (m)/non-homologous recombination deficient (HRD) cancers is limited. This project aims to assess real-world benefits of first-line niraparib in non-BRCAm HGSOC. It investigates, in the absence of funded HRD testing in Canada, surrogate markers of niraparib response such as KELIM score.

**Methods:** Retrospective chart review of patients with non-BRCAm/HRD unknown HGSOC treated with first-line maintenance niraparib at BC Cancer, Canada between 04/2020-06/2022. Demographic and treatment information was collected. PFS was defined as start of niraparib to radiological evidence of disease progression. KELIM score was calculated using validated software.

**Results:** 83 patients were included; 25% had FIGO stage 4 disease. 68% underwent neoadjuvant chemotherapy with optimal cytoreductive rate of whole population of 72%. 60% had disease progression at data cut-off with median follow-up of 15.3 months. Median PFS (mPFS) on niraparib was 12.7 months (range 1.1-29.2). Patients given neoadjuvant chemotherapy with KELIM scores  $\geq 1$  had a trend to longer mPFS (14 months) vs. those with KELIM  $< 1$  (8.8 months) ( $p=0.03$ ). Despite use of individualized starting dose (ISD), 60% required at least 1 dose reduction and 18% experienced grade 3 toxicity.

**Conclusion/Implications:** mPFS on niraparib in this non-BRCAm/HRD unknown HGSOC population was 12.7 months. 60% of patients required a dose reduction due to toxicity despite ISD. KELIM score may be useful to predict PARP inhibitor response and aid clinical decision-making where HRD testing is unfunded.

EP245 / #1396

Topic: *AS11. Ovarian Cancer*

## **HUMAN PERITONEAL FLUID EXERTS OVULATION AND NONOVULATION-SOURCED ONCOGENIC ACTIVITIES TO THE TRANSFORMING FALLOPIAN TUBE EPITHELIAL CELLS**

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**Introduction:** Ovulation is the main cause of oncogenesis of fallopian tube epithelium (FTE), the origin of ovarian high-grade serous carcinoma (HGSC). Previously, we have identified multiple oncogenic activities of the ovulatory follicular fluid (FF), which exerts full-spectrum transforming activities on FTE cells. After ovulation, FF transfuses into the peritoneal fluid (PF) with which the FTE constantly bathes. We wonder whether PF exerts the same spectrum of oncogenic activities as FF and whether they are sourced from FF.

**Methods:** By using a panel of FTE cells with p53 mutation (FT282-V), p53/CCNE1 aberrations (FT282-CCNE1), and after xenograft peritoneal metastasis after spontaneous transformation (FEXT2), we tested the change of different transformation phenotypes after treating with FF and PF collected before and after ovulation.

**Results:** Similar to FF but to a lesser extent, PF generally promoted anchorage-independent growth (AIG), migration, anoikis resistance, and peritoneal attachment and invasion of the transforming FTE cells, and the more transformed cells were more affected. Activities of AIG, invasion, and peritoneal attachment growth were higher in luteal phase PF than proliferative PF, suggesting an ovulation source. In contrast, anoikis resistance and migration activities were indifferent between PF collected before and after ovulation, suggesting an ovulation-independent source. Finally, coinjection of Luc-FEXT2 cells with either FF or luteal phase PF, but not proliferative phase PF, supported early peritoneal implantation in NSG mice.

**Conclusion/Implications:** PF from ovulating women promotes oncogenic phenotypes of FTE cells at different stages of malignant transformation. Other than anoikis resistance and cell migration, a majority of these activities are sourced from ovulation.



EP246 / #164

**Topic: AS11. Ovarian Cancer**

## **HIGH GASDERMIN D EXPRESSION IN OMENTAL ADIPOCYTE PREDICTS POOR PROGNOSIS IN ADVANCED STAGE OVARIAN CANCER**

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**Introduction:** Recently, an inflammatory programmed cell death characterized by gasdermin-mediated inflammatory cell death, pyroptosis, was described. Accumulating evidences indicate that pyroptosis can affect the development of tumors, and especially inflammasomes may serve as positive or negative regulators of tumorigenesis. In this study, based on our previous observation of omental CLS formation in advanced OC, we aimed to investigate the role of pyroptosis in inflammatory adipocytes in the OC tumor microenvironment and explore the possible relationship with patient's prognosis.

**Methods:** Immunohistochemistry: Omental tissue blocks from National Cheng Kung University Hospital were obtained. Informed consents were from each subject before surgery. Statistical analysis: cox proportional hazards model and survival difference were calculated by SPSS as well as GraphPad Prism 8 software to identify significant differences.

**Results:** From 2002 to 2018 , there are 137 serous ovarian cancer patients collected in Cheng Kung University Hospital. The mean age is 56.6 y/o. There are 120 cases in stage III, 17 cases in stage IV. Eighty-six patient (63%) had optimal surgery, while 82 cases (60%) were chemosensitive. For progression free survival analysis through cox proportional hazards model, omental GSDMD (High vs. Low), omental CD68+ CLS (absent vs. present) and omental CD163+ CLS (absent vs. present) showed independent prognostic factors. Patients with high GSDMD expression in omentum tissue carried a poor 5-year survival than those with low GSDMD expression (Hazard ratio 0.56, 95% CI: 0.38-0.82, p=0.003)

**Conclusion/Implications:** High gasdermin D expression in omental adipocytes predicts poor prognosis in advanced stage serous ovarian cancer patients.

EP247 / #480

**Topic: AS11. Ovarian Cancer**

## **LUMICAN ACTIVATES TGFB1-EMT AXIS TO PROMOTE PLATINUM RESISTANCE IN EPITHELIAL OVARIAN CARCINOMA**

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**Introduction:** Platinum resistance seriously affects the survival of patients with epithelial ovarian cancer (EOC). Extracellular matrix play an important role in platinum resistance. Lumican (LUM) is an important proteoglycan in extracellular matrix. We intended to explore the expression of LUM in EOC and its effect on platinum resistance.

**Methods:** Expression profile microarray was used to explore the mechanism of platinum resistance. Immunofluorescence and qRT-PCR was used to detect the expression of LUM in drug-resistant (SKOV3DDP) and wild-type (SKOV3) cells. LUM was detected by immunohistochemistry in tissues. After establishing LUM-overexpressing cells (SKOV3 LUM-OE) and knocked-out LUM cells (SKOV3DDP LUM-KO), the effects of LUM were evaluated. CCK8 was performed to evaluate the effects of cisplatin on EOC cells. Immunofluorescence, western blot and qRT-PCR were performed for determining TGFB1, CDH1, CDH2, ZEB1 and MMP9.

**Results:** The expression of extracellular matrix related genes was significantly enriched in platinum-resistant tissue. The expression of LUM in SKOV3DDP was significantly higher than that in SKOV3, and it was significantly increased after cisplatin treatment of SKOV3. LUM was significantly overexpressed in platinum-resistant tissues (77.78% vs 32.0%,  $P < 0.001$ ), and it's an independent prognostic factor for platinum resistance (OR=8.11,  $P = 0.002$ ). The changes of cisplatin sensitivity were consistent with the changes of LUM after overexpression or knockout it. TGFB1 was positively correlated with LUM expression. CDH2, MMP9, ZEB1 were strongly induced and CDH1 was suppressed in SKOV3 LUM-OE.

**Conclusion/Implications:** High expression of LUM is associated with platinum resistance and poor prognosis in EOC. LUM activates TGF- $\beta$ -EMT signaling pathway to promote platinum resistance in EOC.

EP248 / #551

Topic: AS11. Ovarian Cancer

## A PREDICTIVE VALUE OF CA-125 ELIMINATION OF RATE CONSTANT K(KELIM) ON PROGNOSIS AND DURATION OF BEVACIZUMAB MAINTENANCE THERAPY IN FIRST PLATINUM-SENSITIVE RECURRENCE OF OVARIAN CANCER

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**Introduction:** To evaluate the predictive value of CA-125 ELIMination of Rate Constant K (KELIM) on prognosis and duration of long-term bevacizumab maintenance therapy (BMT) in first platinum-sensitive recurrence of ovarian cancer.

**Methods:** We included patients with platinum-sensitive recurrence of ovarian cancer who underwent six cycles of paclitaxel-carboplatin-bevacizumab chemotherapy followed by BMT between 2015 and 2021. To predict the prognosis and duration of long-term BMT ( $\geq 10$  cycles), we calculated KELIM scores after completion of three cycles of paclitaxel-carboplatin-bevacizumab. Then, we calculated the cut-off value of the KELIM score to predict progression-free interval  $\geq 12$  months.

**Results:** A total of 96 patients were included, who consisted of 28 (29%) treated with secondary cytoreductive surgery (SCS) followed by chemotherapy, and 68 (71%) treated with chemotherapy alone. The cut-off value of the KELIM score for predicting PFI  $\geq 12$  months was 1.08. (AUC 0.82; sensitivity, 0.75; specificity, 0.76). Although SCS did not affect progression-free survival (PFS) and overall survival (OS), high-KELIM demonstrated better prognosis than low-KELIM in patients treated with SCS (PFS, median, 13.7 vs. 15.4 mons;  $p=0.04$ ; OS, 21.7 vs. 28.8;  $p=0.006$ ; Figure 1.), whereas there was no significant difference of PFS and OS according to the KELIM score in those treated with chemotherapy alone. Moreover, high-KELIM score was a favorable factor for long-term BMT in only those treated with SCS (adjusted odd ratio, 15; 95% confidence interval, 1.225-18.363).

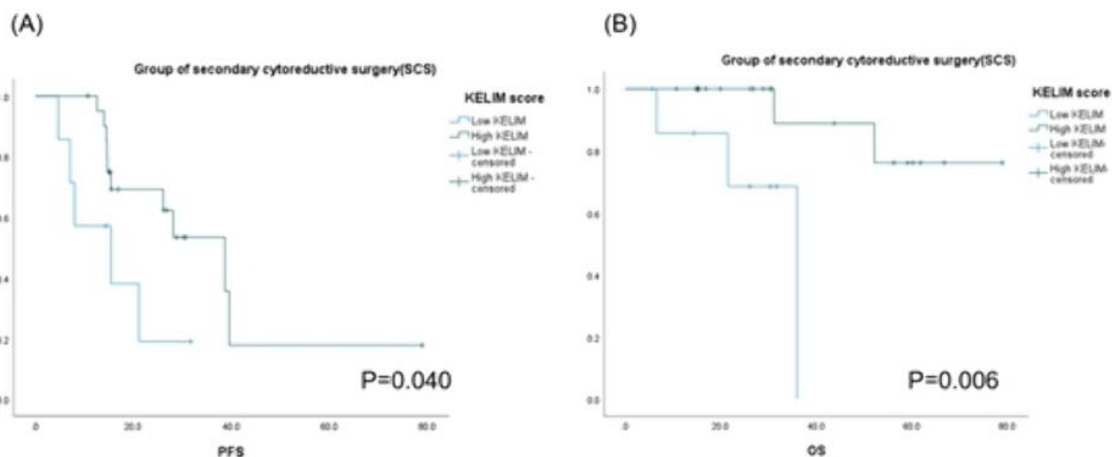


Figure 1. (A) Progression free survival (PFS), (B) overall survival (OS) of secondary cytoreductive surgery followed by paclitaxel-carboplatin-bevacizumab therapy group in the platinum sensitive recurrence of ovarian cancer patients according to KELIM score

**Conclusion/Implications:** High-KELIM had a predictive value for better prognosis and long-term BMT in patients with first platinum-sensitive ovarian cancer who received paclitaxel-carboplatin-bevacizumab followed by BMT after SCS.

EP249 / #705

Topic: *AS11. Ovarian Cancer*

## **PLASMA-ACTIVATED MEDIUM INHIBITS CANCER STEM CELL-LIKE PROPERTIES AND EXHIBITS A SYNERGISTIC EFFECT IN COMBINATION WITH CISPLATIN IN OVARIAN CANCER**

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**Introduction:** Ovarian cancer stem-like cells (CSCs) have been implicated in tumor recurrence, metastasis, and drug resistance. Accumulating evidence has demonstrated the antitumor effect of plasma-activated medium (PAM) in various carcinomas, including ovarian cancer. Thus, PAM represents a novel onco-therapeutic strategy. However, its impact on ovarian CSCs is unclear.

**Methods:** In this study, we assessed whether PAM regulates the stemness properties in a CSC-like spheroid model. Furthermore, we investigated the potential enhanced anti-cancer effects of combination treatment with conventional chemotherapeutic agents and PAM using in vitro and in vivo models.

**Results:** PAM exhibited synergistic cytotoxicity with cisplatin (CDDP) but not with paclitaxel and doxorubicin. In a peritoneal metastasis xenograft model established via intraperitoneal spheroid injection, PAM intraperitoneal therapy significantly suppressed peritoneal carcinomatosis (tumor size and number), with a more significant decrease observed due to the combined effects of PAM and CDDP with no side effects.

**Conclusion/Implications:** We demonstrated the anti-CSC activity of PAM and the synergistic cytotoxic effect of the PAM and CDDP combination therapy on ovarian CSCs. Analysis of intraperitoneal PAM and CDDP combination therapy in a spheroid culture xenograft model of ovarian cancer showed promising results. Further studies are needed to determine the molecular mechanism underlying the synergistic anti-cancer effects of PAM and anti-cancer drugs to enhance their antitumor efficacy against ovarian CSCs and reduce the relevant side effects.

EP250 / #544

Topic: *AS11. Ovarian Cancer*

## **SYNERGISTIC EFFECT OF SHETA2 AND ABEMACICLIB IN OVARIAN CANCER SPHEROIDS AND ASCITES-DERIVED SPHEROIDS**

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**Introduction:** While recent advances in ovarian cancer therapy have improved patient's lives, current therapies are highly toxic. We developed sulfur heteroarotinoid A2 (SHetA2), a non-toxic drug currently in Phase 1 trial. SHetA2 causes cyclin D1 degradation and cyclin-dependent kinases 4 and 6 (CDK4/6) from protection by heat shock cognate 70 protein, causing G1 cell cycle arrest. Abemaciclib is a cyclin-dependent kinase (CDK) 4 and 6 inhibitor used to treat breast cancer. We hypothesized that combination of SHetA2 and abemaciclib synergistically reduces cell lines- and ascites- derived spheroids viability as both drugs target different proteins in the cyclinD1/CDK4/6 complex critical for G1 to S progression.

**Methods:** Ovarian cancer spheroids were developed from ES2 and OVCAR8 ovarian cancer cells lines using ultra-low attachment plates. Ascites-derived spheroids were collected from ovarian cancer patients who were undergoing paracentesis for ascites removal after receiving their informed consent. The half maximal inhibitory concentration (IC<sub>50</sub>) for spheroids or ascites-derived spheroids was determined using CellTiter-Glo® 3D Cell Viability Assay. GraphPad Prism was used to calculate IC<sub>50</sub> for single drugs, while combination indexes were determined using CompuSyn.

**Results:** Ovarian cancer spheroids IC<sub>50</sub> values ranged between 3-10 µM and 10-15 µM for SHetA2 and abemaciclib, respectively. There were synergistic effects when abemaciclib and SHetA2 were combined at doses above IC<sub>50</sub> of both drugs for cell line and ascites-derived spheroids.

**Conclusion/Implications:** Findings from this study support the combination of SHetA2 and abemaciclib as a novel, less toxic therapy for ovarian cancer. Animal models will be carried out to validate these findings.

EP253 / #205

Topic: *AS11. Ovarian Cancer*

## **DISCREPANCY IN DIAGNOSIS OF ADVANCED EPITHELIAL OVARIAN CARCINOMA, TUBAL CARCINOMA AND PRIMARY PERITONEAL CARCINOMA PRIOR TO NEOADJUVANT CHEMOTHERAPY**

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**Introduction:** To evaluate the rate of discrepancy between initial diagnosis and surgico-pathological diagnosis in patients treated with neoadjuvant chemotherapy (NAC) followed by interval debulking surgery (IDS) of advanced epithelial ovarian carcinoma (EOC). The second objective was to determine factors associated with diagnosis discrepancy.

**Methods:** The clinical data, disease status, initial cytology/pathology report and final pathology results were extracted from medical records of selected patients who underwent NAC administration followed by IDS from January 2009 to August 2022. Regression analysis was used to investigate the independent factors associated to diagnosis discrepancy.

**Results:** Overall 229 patients underwent IDS. Of these, 11 patients (4.8%) showed diagnostic differences. Patients with CA125 level <200 U/ml had significantly higher discrepancy rate than the group of CA125 level ≥200 U/ml, with 25.0% vs 2.9% (P<0.001) respectively. Furthermore, patients with CEA level >100 ng/ml has a high discrepancy rate of 100%. The CA125/CEA ratio ≤25 was associated with higher discrepancy than patients with ratio >25, with 75.0% vs 4.1% (P<0.001), respectively. The pretreatment cytology, histology, and cytology plus histology results yielded comparable accuracy rates of 96.8%, 91.8%, and 91.7%, respectively

(P=0.255).

**Summary data of discrepancy patients**

No.	Age	CA-125	CEA	CA125/CEA	EGD&Colonoscopy	Type/site of investigations	Result of pretreatment investigations	Final diagnosis
1	70	21.4	356	0.06	negative finding	Cytology/ ascites	Metastatic adenocarcinoma, mucin producing	LAMN
2	68	118.9	6.86	17.33	negative finding	Cytology/ ascites	Metastatic carcinoma, abundant mucin	LAMN
3	51	842.6	72.96	11.55	-	Cytology/ ascites	Metastatic carcinoma	Poorly differentiated carcinoma of stomach
4	65	111.4	-	-	-	Histology/ omentum biopsy	Metastatic carcinoma, mucous material	LAMN
5	48	365	-	-	-	Histology/ peritoneum biopsy	Metastatic adenocarcinoma	Metastasis mucinous adenocarcinoma from GI origin
6	35	1300	-	-	-	Cytology/ pleural effusion	Metastatic carcinoma	Granulosa cell tumor
7	73	163.4	1.13	144.6	-	Cytology/ ascites	Metastatic carcinoma	Carcinosarcoma of uterus
8	58	1212	0.66	1836.36	-	Histology/ cervical biopsy	High grade serous carcinoma	Carcinosarcoma of uterus
9	46	3387	0.42	8064.29	-	Histology/ pelvic mass biopsy	High grade serous carcinoma	High grade serous carcinoma of endometrium
10	57	1047	29.03	36.07	-	Cytology/ ascites Histology/ endometrial biopsy	Metastatic carcinoma High grade carcinoma	High grade serous carcinoma of endometrium
11	69	91.9	1.64	56.04	-	Cytology/ ascites Histology/ endometrial biopsy	Metastatic carcinoma Endometrioid carcinoma grade2	High grade carcinoma of endometrium

Abbreviations: CA-125, cancer antigen 125; CEA, carcinoma embryonic antigen; EGD, esophagogastroduodenoscopy; GI, gastrointestinal; LAMN, low grade appendiceal mucinous neoplasm

**Conclusion/Implications:** The discrepancy risk for patients with CA125/CEA ratio  $\leq 25$  is unacceptably high, work up for gastro-intestinal malignancies should strongly be recommended. Additionally, either use of cytology or pathology results is reliable for the diagnosis prior to NAC.

EP254 / #645

**Topic: AS11. Ovarian Cancer**

## **THE BCAM-AKT2 FUSION PROTEIN EFFECT ON THE IGF1 SIGNALING PATHWAY IN EPITHELIAL OVARIAN CANCER CELLS**

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**Introduction:** The Insulin Growth Factor1 Receptor (IGF1R) has been identified as a key player in the development of ovarian cancer, making it an appealing target for therapeutic intervention. Fusion genes associated with the IGF1R are good candidates to play this role. Recently, the BCAM-AKT2 fusion protein was identified in ovarian cancer patients. We aim to investigate the BCAM-AKT2 fusion protein involvement in the IGF1 signaling pathway and the mechanism behind the oncogenic effect in epithelial ovarian cancer (EOC).

**Methods:** In-vitro experiments were conducted in EOC cell lines. Protein expression levels of BCAM-AKT2, IGF1R, and the downstream key factors were measured by western blots. In addition, an XTT assay was used to measure the effect of the BCAM-AKT2 fusion protein on proliferation of EOC cell line. Moreover, RNA from SKOV3 and OVCAR4 transfected cells was extracted and RNA-seq was performed to determine the effect of BCAM-AKT2 on gene expression.

**Results:** XTT assays suggest that BCAM-AKT2 induces EOC proliferation. RNA-seq experiment revealed activation of unfolded protein response, and inhibition of viral response, interferon and pyroptosis signaling pathways as a result of BCAM-AKT2 overexpression in SKOV3. However, BCAM-AKT2 did not affect gene expression in OVCAR4. Interestingly, IGF1R protein expression and activation were not affected by the BCAM-AKT2 expression. Moreover, BCAM-AKT2 phosphorylation is independent of IGF1 treatment.

**Conclusion/Implications:** Our results suggest a possible effect of the BCAM-AKT2 fusion protein on key canonical pathways in EOC. We believe that elucidation of the mechanism of the fusion protein will help identify new biomarkers for ovarian cancer.



EP255 / #191

**Topic: AS11. Ovarian Cancer**

## **CORRELATION BETWEEN PREOPERATIVE PCI IMAGING, INTRAOPERATIVE PCI MEASUREMENT, AND OVERALL SURVIVAL IN PERITONEAL CARCINOMATOSIS SECONDARY TO OVARIAN, TUBAL, AND PRIMARY PERITONEAL CARCINOMA.**

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**Introduction:** PCI is widely used to evaluate peritoneal carcinomatosis. This study aims to assess the correlation between preoperative and intraoperative PCI. The secondary objectives were determining whether PCI could predict surgical oncologic outcomes and overall survival.

**Methods:** In a retrospective cohort study, women with advanced-stage epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer who underwent primary cytoreductive surgery or interval debulking were included. The preoperative CT scan findings and intraoperative measurement of the peritoneal carcinomatosis were evaluated using PCI, and their correlation was determined using the Spearman coefficient. The overall survival was calculated using the Kaplan-Meier method.

**Results:** 55 women were enrolled, and 52 patients were eligible and analyzed. Mean preoperative and intraoperative PCI were 5.04 and 7.27, orderly. Twenty-nine patients achieved optimal surgery (55.8%). A moderate correlation exists between the PCI obtained from the CT image and surgical findings ( $r= 0.510$ ,  $P< 0.001$ ). The significant cutoff values of preoperative PCI and intraoperative PCI to predict optimal surgical outcomes could be 7 and 8, respectively. In multivariate analysis, preoperative CA125  $< 416$  U/mL and intraoperative PCI  $< 8$  were the only independent factors for optimal surgery. The overall survival was significantly improved in patients with an intraoperative PCI score of less than 8 (14 to 36 months,  $p=0.015$ ).

**Conclusion/Implications:** The lesser PCI that would predict the optimal surgical outcome, the preoperative PCI from practical imaging would be beneficial as a predictive method to assess the possibility of optimal cytoreduction and the optimal time for surgery.

EP256 / #833

Topic: *AS11. Ovarian Cancer*

## **RETROSPECTIVE ANALYSIS COMPARING THE SURVIVAL OUTCOME OF NIRAPARIB AND OLAPARIB IN ADVANCED OVARIAN CANCER PATIENTS**

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**Introduction:** Targeted therapy has become the mainstay maintenance treatment for patients with advanced ovarian cancer, including those with BRCA1 or BRCA2 mutations. Poly ADP ribose polymerase (PARP) inhibitors, including Niraparib and Olaparib, have demonstrated effectiveness in treating patients in complete or partial remission. However, there is a lack of research comparing the survival outcomes between these two agents. We aimed to compare the survival outcomes associated with niraparib and olaparib in patients with advanced ovarian cancer.

**Methods:** We conducted a single institution, retrospective study on patients with stage III and IV ovarian cancer who had received either Niraparib or Olaparib from November 2019 to February 2023. Patients were stratified according to which PARP inhibitor they received. Our primary objective was to assess the progression-free survival (PFS) and overall survival (OS).

**Results:** A total of 104 patients received a PARP inhibitor during the study timeframe. Thirty-four (32.7%) of patients received niraparib and 70 (67.3%) of patients received olaparib. Median age of patients was 56.8±7.5 years in niraparib group and 57.2±8.8 years in olaparib group. Median PFS was 31.8 months (28.8-34.9) for the olaparib group and 24.8 months (23.095-26.409) for the niraparib group ( $p=0.247$ ). The median OS was 36.5 months (34.638-38.459) for olaparib group and 25.5 months (24.448-26.476) for the niraparib group ( $p=0.599$ ), with no significant difference.

**Conclusion/Implications:** This study compared the survival outcomes of two most commonly prescribed PARP inhibitors. Our results show that olaparib and niraparib were comparable in terms of survival outcome in patients with advanced ovarian cancer.

EP257 / #596

Topic: *AS11. Ovarian Cancer*

## **THE ROLE OF ITERATIVE CYTOREDUCTIVE SURGERY IN RECURRENT OVARIAN CANCER: SURVIVAL OUTCOMES : BEYOND SECONDARY CYTOREDUCTIVE SURGERY**

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**Introduction:** The optimal timing and number of cytoreductive surgery (CRS) procedures in patients with multiple recurrences are still under debate. The aim of study is to evaluate the outcomes and safety of tertiary cytoreductive surgery in secondary relapsed ovarian cancer patients.

**Methods:** We retrospectively reviewed the medical records of secondary relapsed recurrent ovarian cancer patients between January 2000 and March 2023.

**Results:** A total of 123 patients (26 patients who underwent tertiary cytoreductive surgery (TCS) followed by chemotherapy vs. 97 patients who received chemotherapy alone after secondary relapse) were included. The median age was 46.8 years, and the median follow-up time was 64.8 months. Among the patients with TCS, 5 (19.2%) and 1 (3.8%) patients received quaternary and quinary CRS, respectively. 24(92.3%) patients received complete resection in TCS, and post operative adjuvant chemotherapy was administered to 22(84.6%) patients. Out of 26 patients, 18(69.2%) experienced recurrence after TCS, with a median time to recurrence of 22.1 months. Patients with complete tertiary cytoreductive surgery had a significantly longer overall survival (median overall survival (OS): 93 months,  $p = 0.001$ ) compared to those with chemotherapy alone group. (median OS: 47 months, 95% CI 39.0 – 54.9).

**Conclusion/Implications:** Our study suggests that third or more CRS in recurrent ovarian cancer is associated with survival benefit. The outcomes of third or more CRS are influenced by the extent of CRS, with complete CRS associated with better outcomes. The decision to offer third or more CRS should be individualized based on patient factors, including overall health status and extent of disease.

EP258 / #917

Topic: *AS11. Ovarian Cancer*

## **RECURRENCE-FREE SURVIVAL AND OVERALL SURVIVAL IN EARLY-STAGE OVARIAN CANCER CONSIDERING HOMOLOGOUS RECOMBINATION DEFICIENCY(HRD) STATUS.**

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**Introduction:** We aimed to determine the recurrence rate and survival outcome among early-stage epithelial ovarian cancer cases in relationship1 to homologous recombination deficiency (HRD) status.

**Methods:** We conducted single institution retrospective study of stage I/II EOC patients from 2008 to 2022. HRD was defined as evidence of germline or somatic BRCA mutation. Kaplan-Meier analyses were performed.

**Results:** A total of 456 stage I/II patients were included. 22/456 (4.8%) had a germline or somatic BRCA1 mutation 46/456 (10.0%) had a BRCA2 mutation; These 68/456(14.9%) patients comprised the HRD group. The remaining cases were confirmed homologous recombination proficient (HRP, 388/ 456, 85.1%). The overall recurrence rate was 90/456 (19.7%). The recurrence rate was 68/388 (17.5%) in HRP group and 22/68 (32.4%) in HRD group. Median Recurrence-Free Survival (RFS) was 81 months for HRD group and 109 months for HRP group (p=0.145). Median overall survival was not reached for the HRP group and 147 months (95% CI: 129.6-158.8) for the HRD group (p=0.231), with no significant difference.

**Conclusion/Implications:** In this early-stage cohort, despite a high rate of complete surgical staging and adjuvant chemotherapy, recurrence rate was high. The proportion of relapsed patients was higher in the HRD group than in the HRP group, but there was no statistically significant difference. There was no significant difference in RFS and OS between HRD group and HRP group.

EP259 / #509

**Topic: AS11. Ovarian Cancer**

## **GENETIC COUNSELING AND TESTING FOR EPITHELIAL OVARIAN CANCER IN A DIVERSE PATIENT POPULATION**

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**Introduction:** Genetic testing is recommended for women diagnosed with epithelial ovarian cancer. Results inform surveillance, familial testing, and treatment. We report genetic counseling and testing rates at a tertiary care center with a large minority population.

**Methods:** Retrospective cohort study of patients with newly diagnosed epithelial ovarian, fallopian tube, peritoneal cancer between January 2014 and June 2022 at the NewYork-Presbyterian Brooklyn Methodist Hospital.

**Results:** 144 patients identified. Mean age at diagnosis was 63 years (SD:13). 51% identified as white, 36% black, 3.5% Asian, 9% other/unknown; 9% were Hispanic and 26% were non-English speaking. 104 (72%) patients received genetic counseling and 99 (69%) received subsequent genetic testing. 95% of those that underwent genetic counseling underwent testing. The genetic counseling and testing rates were not influenced by race, ethnicity, language, insurance type, BMI, family history of cancer. It was associated with significant difference by cancer stage ( $p<0.01$ ). There was a significant upward trend of proportion of patients that received genetic counseling from 47% in 2015 to 100% in 2022 ( $p<0.01$ ). Most genetic counseling was performed by a gynecologic oncologist (93%) as opposed to a genetic counselor (6.7%). Overall, 12 (8.3%) patients were BRCA+.

**Conclusion/Implications:** Genetic counseling and testing rates within this diverse study population proved to be at least twice as high as the national average of 10-30%, with an increasing year-to-year trend. There were no disparities observed, in contrast to previously published data. BRCA mutation detection was in line with established prevalence within ovarian cancer, indicating adequate screening. © 2023 American Society of Clinical Oncology, Inc. Reused with permission. This abstract was accepted and previously presented at the 2023 ASCO Annual Meeting. All rights reserved."

EP260 / #470

Topic: *AS11. Ovarian Cancer*

## **EFFECT OF DOSE-DENSE PACLITAXEL PLUS CARBOPLATIN WITH OR WITHOUT BEVACIZUMAB FOR JAPANESE EPITHELIAL OVARIAN CANCER: A SINGLE-CENTER RETROSPECTIVE STUDY**

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**Introduction:** There is still controversy or a lack of evidence regarding the efficacy of dose-dense paclitaxel plus carboplatin (ddTC) and bevacizumab (BEV) for epithelial ovarian cancer (EOC) among Japanese and Westerners. We aimed to compare the survival outcomes between conventional paclitaxel plus carboplatin (TC) with BEV and ddTC with or without BEV among Japanese.

**Methods:** We retrospectively analyzed the data from patients newly diagnosed with EOC between 2012 and 2021 at our institutions. The target population was patients with stage III and IV EOC except for poly (adenosine diphosphate–ribose) polymerase inhibitors users. Overall survival (OS) and progression-free survival (PFS) of patients treated with ddTC and ddTC with BEV (ddTC+BEV) were compared to those of patients treated with TC with BEV (TC+BEV). We used Cox proportional hazard models adjusted for patients' backgrounds.

**Results:** There were 75, 259, and 117 patients treated with TC+BEV, ddTC, and ddTC+BEV, respectively. The three groups had similar backgrounds such as histopathology and staging. For PFS, adjusted hazard ratios (aHRs) [95% confidence intervals (95%CI)] were 1.09 [0.79, 1.50] in ddTC and 0.74 [0.52, 1.08] in ddTC+BEV compared to TC+BEV. For OS, aHRs (95%CI) were 0.89 [0.59, 1.34] in ddTC and 0.73 [0.50, 1.05] in ddTC+BEV compared to TC+BEV.

**Conclusion/Implications:** We previously confirmed that ddTC was associated with favorable PFS and OS, and BEV could prolong PFS using the data from 1333 EOC patients at our institution. The present study further suggested that ddTC+BEV had favorable survival outcomes and might be a candidate for a clinical trial.

EP261 / #266

**Topic:** AS11. Ovarian Cancer

## **INFLAMMATION-RELATED BIOMARKERS FOR THE PREDICTION OF PROGNOSIS IN OVARIAN CANCER PATIENTS**

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**Introduction:** Most ovarian cancer patients are diagnosed in an advanced stage, and the recurrence rate is also high. But Ovarian cancer is more sensitive to chemotherapy than other carcinomas, therefore many patients receive multiple regimens of chemotherapy. Repeated chemotherapy eventually becomes palliative, however, there are no accurate indicators about whether to continue chemotherapy or not. The clinical usefulness of inflammation-related prognostic biomarkers available from routine blood examination has been reported, e.g., neutrophil-lymphocyte ratio (NLR), lymphocyte-monocyte ratio (LMR), Leukocyte and C-reactive protein score (Prognostic Index, PI) and so on. Moreover, some scoring systems based on circulating blood cell counts and albumin concentration have been also reported to predict cancer patients' prognosis, such as the Glasgow prognostic score (GPS), and prognostic nutritional index (PNI). The purpose of this study is to evaluate whether these biomarkers can be indicators for chemotherapy policy decisions.

**Methods:** We conducted a retrospective study of patients with ovarian cancer that died after receiving final chemotherapy at our institution from 2007 through 2020. Clinical variables included blood examination data on the day1 of the last chemotherapy.

**Results:** We identified 1,405 women treated for ovarian cancer, and 140 patients with ovarian cancer that died after receiving final chemotherapy at our institution. 87.8% were diagnosed with stage III or IV disease. In multivariable analysis, GPS (HR 3.74,  $p=0.02$ ) and PI (HR 2.75,  $p=0.04$ ) were independently associated with overall survival.

**Conclusion/Implications:** GPS and PI may be useful prognostic predictors for ovarian cancer patients who received multiple chemotherapy regimens.

EP262 / #530

Topic: AS11. Ovarian Cancer

## IS THERE A ROLE FOR INTRAPERITONEAL CHEMOTHERAPY IN EARLY STAGE PELVIC HIGH-GRADE SEROUS CARCINOMA?

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**Introduction:** Previous studies have demonstrated an overall survival benefit with intraperitoneal chemotherapy in Stage III pelvic high-grade serous carcinoma (HGSC), but no studies have evaluated this treatment in early stage disease. We offered IP chemotherapy (IP/IV) to patients with Stage I-II HGSC from 2009-2022. The objectives are to evaluate time to recurrence (TTR), progression-free survival (PFS), and overall survival (OS) associated with IP/IV compared to standard intravenous (IV) chemotherapy.

**Methods:** This is a retrospective population-based cohort study of patients with stage I-II pelvic HGSC, who underwent primary surgery and adjuvant chemotherapy between 2009-2022. Statistical Analysis included Pearson's Chi-square, Kaplan-Meier survival analysis, and Cox regression model to adjust for covariates.

**Results:** 77 and 60 patients received IP/IV and IV chemotherapy, respectively. Those who received IP/IV were significantly younger. Stage distribution was similar between treatment groups. There were 24.7% and 5% confirmed BRCA mutation carriers, but 13% and 26.7% with unknown BRCA status in the IP/IV and IV groups, respectively.

	Chemotherapy				p value
	IP (n=77)		IV (n=60)		
	n	%	n	%	
<b>Age, median (IQR)</b>	58 (51-65)		64 (56-71)		0.0016
<b>Stage</b>					
I	33	42.9%	27	45.0%	0.8
II	44	57.1%	33	55.0%	
<b>BRCA status</b>					
Negative	46	59.7%	39	65.0%	0.0039
Positive	19	24.7%	3	5.0%	
VUS	2	2.6%	2	3.3%	
Unknown	10	13.0%	16	26.7%	

Five-year kaplan-meier outcomes were 77.7% vs. 67.7% TTR (p=0.49), 77.7% vs. 64.9% PFS (p=0.44), and 93.4% vs. 85.1% OS (p=0.29) in the IP/IV and IV groups, respectively. In multivariate analysis, IV chemotherapy trended towards shorter TTR, and worse PFS and OS. Those with unknown BRCA status had significantly better outcomes than confirmed BRCA negative (see



table).

Parameter		Hazard Ratio (95% CI, P value)		
		Overall Survival	Progression Free Survival	Time to Recurrence
<b>Age at diagnosis</b>	1 year	1.01 (0.98-1.05, 0.51)	1.02 (0.98-1.05, 0.36)	1.01 (0.98-1.04, 0.56)
<b>Chemo</b>	IV vs IP	1.45 (0.65-3.24, 0.37)	1.48 (0.76-2.89, 0.24)	1.47 (0.74-2.92, 0.27)
<b>Stage</b>	II vs I	2.11 (0.91-4.89, 0.08)		
<b>BRCA status</b>	+ vs -	0.75 (0.23-2.39, 0.11)	1.03 (0.42-2.55, 0.06)	0.87 (0.33-2.26, 0.05)
	Unk vs -	<b>0.37 (0.14-0.93, 0.03)</b>	<b>0.36 (0.15-0.85, 0.02)</b>	<b>0.30 (0.11-0.81, 0.01)</b>

**Conclusion/Implications:** There are improved outcomes for patients with early stage HGSC who received IP/IV chemotherapy, although not statistically significant. The unknown BRCA status group could have unrecognized BRCA mutation carriers, possibly accounting for better outcomes than those without BRCA mutations.

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## **ACCURACY OF INTRAOPERATIVE FROZEN SECTION DIAGNOSIS IN OVARIAN TUMORS**

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**Introduction:** Diagnosis of ovarian tumors are challenging and requires a pathologist expertise in its diagnosis process. Intraoperative frozen section serves as an important diagnostic tool for intraoperative settings. However, accuracy remains an important factor in frozen section diagnosis. This study is comparing frozen section diagnosis to paraffin block as the gold standard in Prof. Dr. R.D. Kandou Regional Hospital.

**Methods:** This cross-sectional study is conducted in Prof. Dr. R.D. Kandou Regional Hospital during June 2021 to June 2022 obtained by medical records of all patients undergoing intraoperative frozen section and will be compared with paraffin block. Data are then analyzed in IBM Statistics SPSS 25.

**Results:** Comparison of each category between frozen section and paraffin block revealed sensitivity of 83.5%, 100.0%, and 76.9% with specificity of 90.4%, 90.0%, and 95.5% for benign, borderline, and malignant diagnosis respectively. A 100% sensitivity for borderline diagnosis is the result of no false negative results in all 13 borderline cases. All results are found to be significant ( $p < 0.001$ ). Among 28 patients who were diagnosed with borderline cases by frozen section, the final pathological diagnosis was upgraded to malignant 14.3%, 46.4% remained borderline diagnosis and 39.3% diagnosed benign.

**Conclusion/Implications:** Intraoperative frozen section is an important tool that can help manage the patient. But intraoperative frozen section must be calibrate to ensure the accuracy.

EP264 / #775

Topic: **AS11. Ovarian Cancer**

## **GENOMIC ALTERATION BEFORE AND AFTER PROGRESSION ON FIRST EXPOSURE TO PARP INHIBITOR (PARPi) AMONG OVARIAN CANCER PATIENTS**

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**Introduction:** Nowadays, PARP inhibitor(PARPi) is frequently used as maintainace treatment in ovarian cancer patients. Due to the DNA repair defect, BRCA1/2 deficient tumor cells are more sensitive to PARP inhibitors (PARPi) through the mechanism of synthetic lethality. When progressed after using the parp inhibitor, the genomic alteration of the tumor and the reuse of the parp inhibitor were not considered.

**Methods:** A slide was produced for patients who started 1st parp inhibitor from February 2018 to May 2022, and for patients with tissues before and after 1st parpinhibitor treatment. We analyzed 20 matched tissue samples before and after progression on first exposure to PARPi among patients undergoing re-treatment with PARPi to understand the genomic changes, potential implication in resistance mechanism and response to PARPi re-treatment.

**Results:** 10 patients were platinum sensitive and 10 patients were platinum resistant. The histological type was identified as High grade serous carcinoma at 90% and endometrioid carcinoma at 10%.

LOH score increased in 15 patients (88%). TMB increased in 13 patients (76%). The average PARP inhibitor usage period in the platinum sensitive group was 14.65 months which is longer than that of platinum resistant group 6.15months. Analyzing the period of use, the shorter the first PARP inhibitor, the shorter the period of use of the 2nd PARP inhibitor. The most frequently detected gene was MYC amplification and RAD 21 amplification. (n=2)

**Conclusion/Implications:** Post-specific mutations occur and LOH and TMB increase upon progression with PARP inhibitor. Further research on resistance mechanism in case of recurrence using PARP inhibitor is needed.

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## **TIMP3 ATTENUATES AGGRESSIVENESS OF OVARIAN CANCER CELLS AND ENHANCES THE SENSITIVITY TO PACLITAXEL**

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**Introduction:** Epithelial ovarian cancer (EOC) frequently recurs and develops chemo-resistance, resulting in cancer mortality. TIMP3 has been described as a tumor suppressor in several human malignancies, but limited scientific literature focus on the role of TIMP3 in regulating EOC progression or chemoresistance.

**Methods:** Both progression-free survival (PFS) and overall survival (OS), stratified by TIMP3 level were estimated using the Kaplan–Meier method and compared using log-rank tests. To increase the expression level of TIMP3 in A2780CP70 cells, the cells were transfected with the TIMP3 expression vector. The migration and invasion abilities of the transfected cells were estimated using transwell assay. The sensitivity of transfected cells to paclitaxel and apoptotic population were evaluated by MTT assay and flow cytometry assay, respectively. A human apoptotic array was used to screen for changes in apoptosis-related proteins.

**Results:** Patients with TIMP3-overexpressed tumor had favorable long-term PFS ( $p < 0.001$ ) and OS ( $p < 0.001$ ) (Fig 1A). A significant reduction in cell migration and invasion capacities was observed in TIMP3-overexpressed A2780CP70 cells (Fig 1B and 1C). TIMP3 contributed to affect sensitivity of A2780CP70 cells to paclitaxel (Fig 2A), rather than cisplatin. Representative apoptotic profiles showed that increased apoptotic cell populations were more apparent in TIMP3-overexpressed A2780CP70 cells, treated with paclitaxel for 48 hours when compared to its parental cells which is possibly related t

Figure 1.

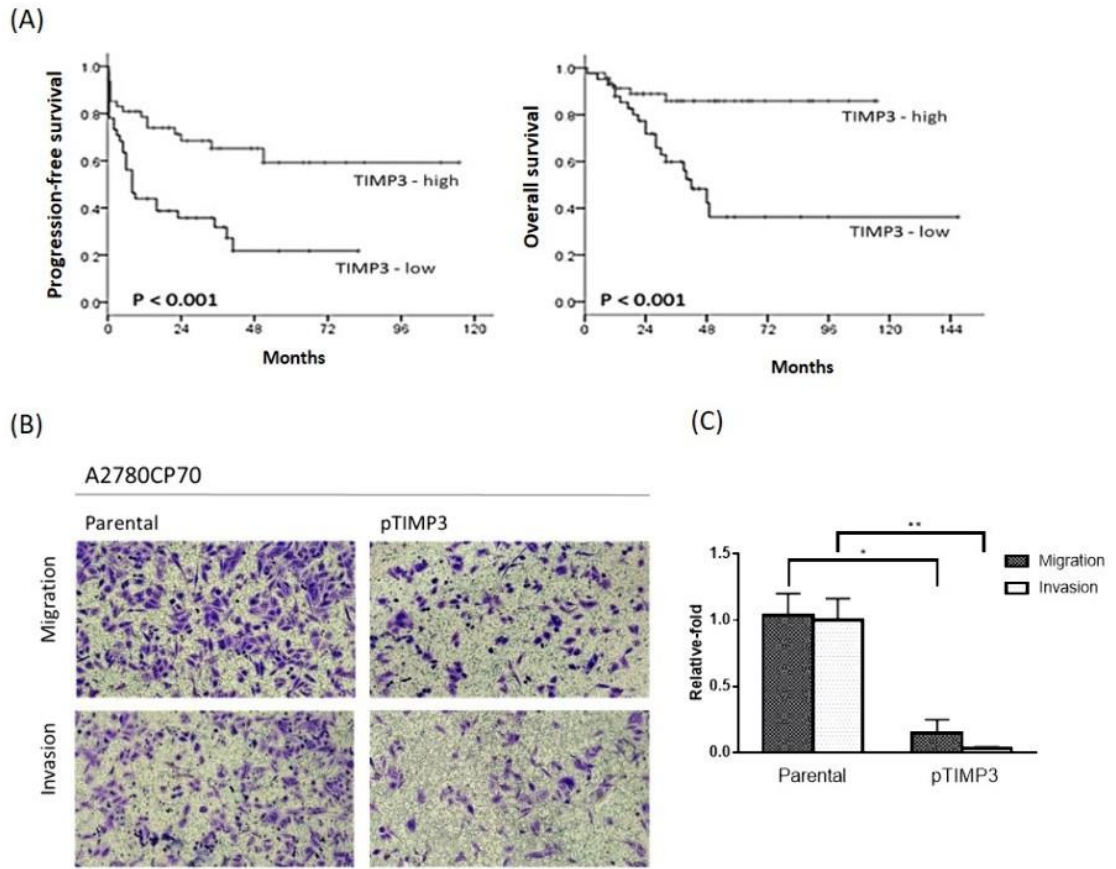
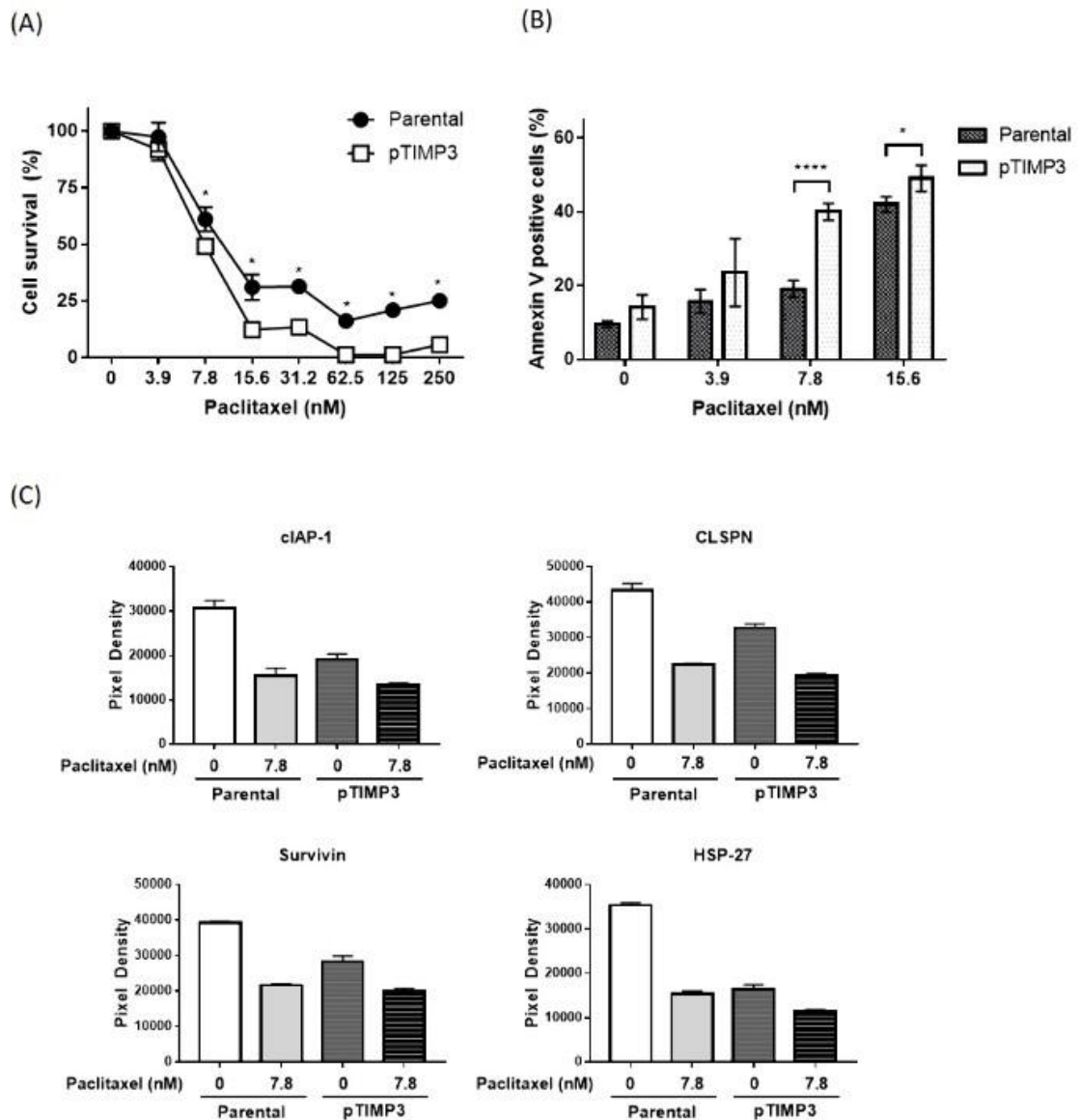


Figure 2.



o down-regulation of cIAP-1, survivin, CLSPN, and HSP-27 (Fig 2B and 2C).

**Conclusion/Implications:** Overexpression of TIMP3 inhibited EOC aggressiveness of A2780CP70, and increased paclitaxel sensitivity. TIMP3 might be a potential target for EOC treatment.

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Topic: *AS11. Ovarian Cancer*

## **RELATIONSHIP OF IMMUNE-RELATED DIABETES MELLITUS WITH EFFICACY OF IMMUNE CHECKPOINT INHIBITORS IN PATIENTS WITH GYNECOLOGIC CANCERS**

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**Introduction:** Immune checkpoint inhibitors (ICIs) have been used in patients with gynecologic cancers, but their efficacy is modest around 10~30% despite occurrence of a wide range of immune-related adverse events (irAEs). Several studies reported a correlation between the development of irAEs and the efficacy of ICIs in patients with various tumors. In this study, we aimed to investigate the relationship of immune-related diabetes mellitus (irDM) with efficacy of ICIs in patients with gynecologic cancers.

**Methods:** We conducted a retrospective review of electronic medical records of 131 patients with gynecologic cancers who received different types of ICIs, such as pembrolizumab, durvalumab, and atezolizumab, on more than once, between 2018 and 2022. We evaluated progression free survival (PFS) and best objective response rate (ORR).

**Results:** Five patients who received ICI treatment were identified to have developed irDM (ovarian cancer, n=3; cervical cancer, n=2). All patients received various types of ICIs, four receiving anti-PD1 inhibitors and one receiving both anti-PD-L1 inhibitor and anti-CTLA-4 inhibitors. The median PFS was 33 months (range 17-41), with an ORR of 100% including two patients with complete response and three with partial response. Only one patient experienced recurrence, with a PFS of 17 months. Four patients required hospitalization due to diabetic ketoacidosis but eventually recovered.

**Conclusion/Implications:** Our findings suggest that there may be a relationship between the development of irDM and the efficacy of ICIs in patients with gynecologic cancer. However, further studies are needed to confirm this association and evaluate its underlying mechanisms.

EP267 / #913

**Topic: AS11. Ovarian Cancer**

## **MONITORING OF MINIMAL RESIDUAL DISEASE WITH CIRCULATING TUMOR DNA IN PATIENTS WITH EPITHELIAL OVARIAN CANCER ON LONG-TERM PARP INHIBITOR MAINTENANCE THERAPY**

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**Introduction:** Epithelial ovarian cancer (EOC) is a lethal gynecologic cancer, with high recurrence rate despite the use of target therapy such as poly ADP-ribose polymerase inhibitor (PARPi). Circulating tumor DNA (ctDNA) is a promising biomarker for detecting minimal residual disease (MRD) in solid tumors. We aimed to investigate the use of ctDNA to detect MRD in patients with EOC who underwent long-term PARPi maintenance treatment.

**Methods:** We prospectively identified 21 patients with EOC who had received PARPi maintenance for over two years. Tissue testing for individual mutation marker was performed with TruSight Oncology panel from Illumina and follow-up ctDNA testing was performed with Pan100 panel from Dxome or small custom panel with high-depth sequencing.

**Results:** A total of 21 patients received different types of PARPi (olaparib, n=12; niraparib, n=7; rucaparib, n=1; and talazoparib, n=1) for a median of 27 months. Twelve patients had germline BRCA mutation, two had somatic BRCA mutation, and one had loss of heterozygosity. MRD was only detected in one patient, who experienced recurrence 3 months after ctDNA evaluation. Among them, two patients experienced recurrence. The other patient had recurrence 7 weeks after ctDNA evaluation without evidence of MRD, suggesting a negative predictive value of 0.905, and a positive predictive value of 1.00.

**Conclusion/Implications:** Our findings suggest that ctDNA can be used to monitor MRD in EOC patients undergoing long-term PARPi maintenance treatment, allowing clinicians to tailor the duration of PARP inhibitor based on patient-specific molecular findings. Further data with additional patients and survival maturation will be presented at the conference.



EP268 / #152

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## **EXPLORING THE IMPACT OF SURGICAL INTERVENTIONS AND IDENTIFYING RISK FACTORS FOR RECURRENCE IN BORDERLINE OVARIAN TUMORS**

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**Introduction:** Despite the low incidence and favorable prognosis of borderline ovarian tumors (BOTs), standardized surgical treatments and risk factors remain debated. This study aimed to evaluate the influence of different surgical interventions on the outcomes of BOTs and to identify risk factors that contribute to their recurrence.

**Methods:** BOT patients at Korea University Anam Hospital from March 2006 and March 2023 were grouped based on recurrence. Therapeutic surgical interventions were classified as conservative, comprehensive, or staging surgeries. Each group's characteristics, clinicopathological factors, surgical interventions, disease-free survival (DFS), overall survival (OS), and recurrence risk factors were compared and analysed. Statistical analyses included student's t-test, chi-square test, Fisher's exact test, Kaplan-Meier analysis, and Cox regression analysing using SPSS.

**Results:** Of 177 patients, 170 were in the non-recurrence group and 7 in the recurrence group, with an average follow-up of 54.7 months. Among relapsed patients, 4 had borderline recurrence and 3 had malignant transformation, with respective DFS of 43 and 18 months. There were no significant differences in DFS and OS on surgical interventions (Figure). Increased risk of BOT recurrence was observed with positive washing cytology and intraoperative iatrogenic rupture (Table), but no significant OS risk factors were

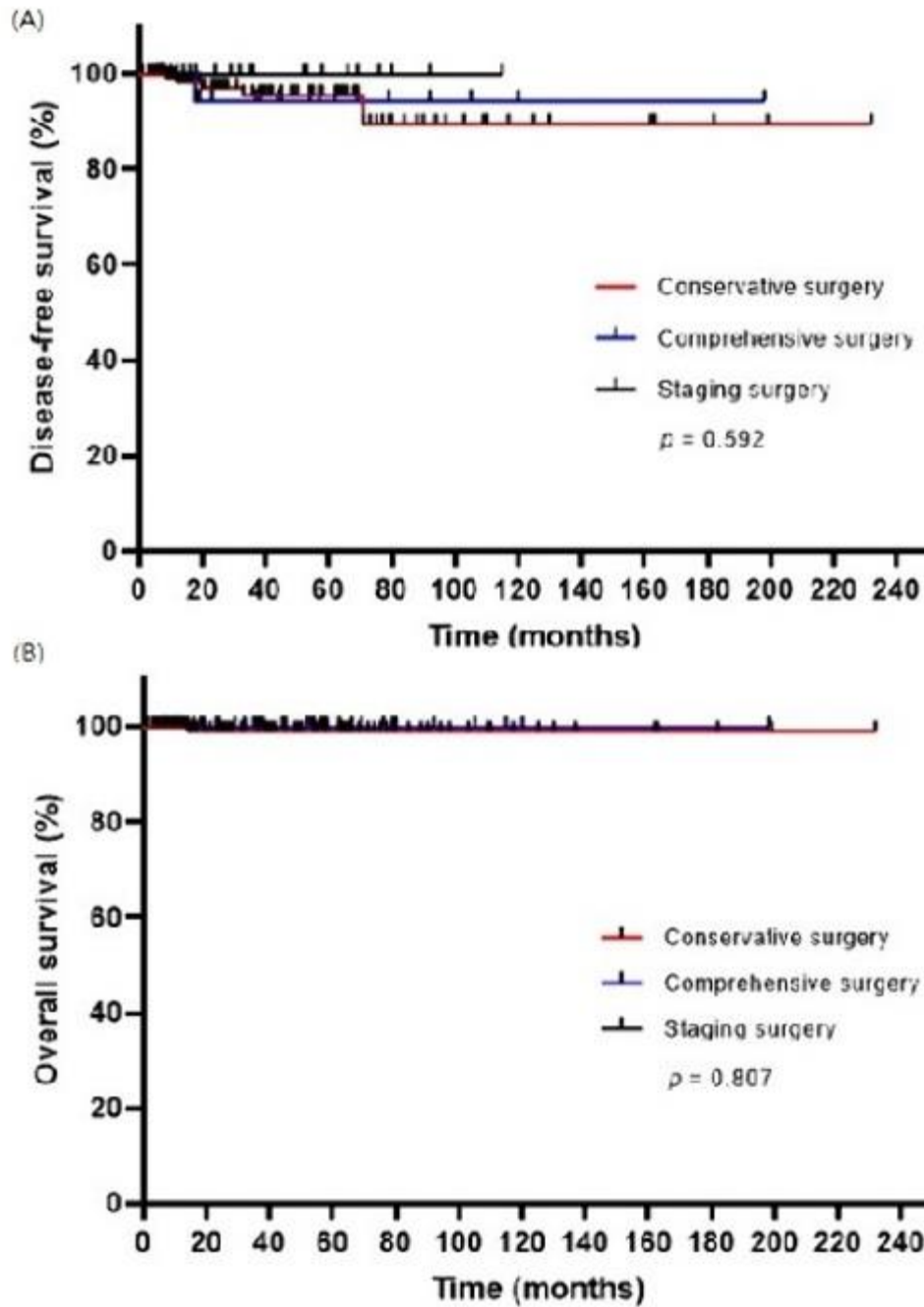


Figure. Survival plot by type of surgical interventions according to Cox proportional hazard model. (A) Disease free survival plot and (B) overall survival plot.

identified.

Table. Cox proportional hazards of disease-free survival in a univariate analysis

	Risk factors for DFS		
	HR	95% CI	p-Value
Age	0.98	(0.928, 1.033)	0.433
Stage			
I	1.00	Reference	
II	0.00	(0.000, 0.000)	
III	0.00	(0.000, 0.000)	
IV	0.00	(0.000, 0.000)	
Histology			
Serous	1.00	Reference	
Mucinous	20.28	(1.254, 327.726)	0.034
Endometrioid	2.52	(0.292, 21.800)	0.400
Seromucinous	0.00	(0.000, 0.000)	0.991
Clear cell	0.00	(0.000, 0.000)	0.998
Surgical approach			
LESS	1.00	Reference	
Laparoscopy	1.07	(0.209, 5.446)	0.939
Robot	0.00	(0.000, 0.000)	0.987
Open	0.30	(0.030, 2.885)	0.295
Surgical intervention			
Conservative surgery	1.00	Reference	
Comprehensive surgery	0.84	(0.101, 7.013)	0.874
Staging surgery	0.00	(0.000, 0.000)	0.986
Washing cytology			
Negative	1.00	Reference	
Positive	30.02	(3.084, 292.210)	0.003
Intraoperative iatrogenic rupture			
No	1.00	Reference	
Yes	5.19	(1.006, 26.765)	0.049
Endometriosis			
No	1.00	Reference	
Yes	1.23	(0.146, 10.392)	0.847
Microinvasion			
No	1.00	Reference	
Yes	3.54	(0.789, 15.846)	0.099
Ovarian surface involvement			
No	1.00	Reference	
Yes	0.05	(0.000, 1.924)	0.692

Note: LESS, laparoscopic single site.

**Conclusion/Implications:** In BOT treatment, surgical intervention differences didn't affect outcomes or DFS and OS. Conservative, comprehensive, and staging surgeries are variable options based on patient age and fertility preservation. To reduce BOT recurrence risk, it is crucial to avoid rupture during surgery and closely monitor postoperative patients with positive washing cytology.

EP269 / #163

Topic: *AS11. Ovarian Cancer*

## **CD8 AND VIMENTIN WAS ASSOCIATED WITH OVERALL SURVIVAL IN PATIENTS WITH OVARIAN CANCER TREATED WITH INTRAPERITONEAL CHEMOTHERAPY**

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**Introduction:** To identify immunohistochemistry markers associated with progression-free or overall survival in patients with ovarian cancer having received intraperitoneal chemotherapy.

**Methods:** By retrospective medical record review, 24 patients with newly diagnosed, stage 3 or 4, high grade serous ovarian cancer having received intraperitoneal chemotherapy more than 3 cycles in Yonsei cancer center from 1990 to 2013 were identified. Immunohistochemical staining of tumor tissue for CD8, FOXP3, PDL1, E-cad and vimentin was performed. The level of expression was measured using established protocols of each marker and was dichotomized (high vs. low) using median value. The association of level of expression of each marker with progression-free or overall survival were examined.

**Results:** The mean age was 61.5 years (range 48 to 79) and 23 patients were stage 3. The median progression-free survival (PFS) was 458 days (range 13 to 4450) and that of overall survival (OS) was 1900 days (range 13 to 4890+). None of 5 markers were associated with progression-free survival (PFS). However, CD8 ( $p=0.2$ ) and vimentin ( $p=0.1$ ) were marginally associated with overall survival (OS). Patients with high expression of CD8 or vimentin had numerically longer PFS than those with low expression in both CD8 and vimentin (median 592d vs 390d,  $p=0.073$ ). Additionally, patients with high expression of CD8 or vimentin had significantly longer OS than those with low expression in both CD8 and vimentin (median 2834d vs 761d,  $p=0.008$ ).

**Conclusion/Implications:** CD8 and vimentin expression was associated with overall survival in patients with ovarian cancer having received intraperitoneal chemotherapy.

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## **CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) FOR RECURRENT HIGH GRADE SEROUS OVARIAN CANCER**

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**Introduction:** Our objective was to compare the differences between the group of recurrent ovarian cancer patients who underwent secondary cytoreductive surgery with HIPEC and without HIPEC, focused on recurrent pattern after surgery and survival outcomes.

**Methods:** From January 2014 to April 2023 at Ajou university hospital, ovarian cancer patients who underwent secondary cytoreductive surgery were included in this study. Various clinicopathological features, progression free survival and overall survival were evaluated.

**Results:** Total 29 patients (18 patients without HIPEC, 11 with HIPEC during secondary cytoreductive surgery) were identified, and 19 patients experienced recurrence. The groups without HIPEC had a higher incidence of extra-abdominal recurrence compared to the group with HIPEC (63.6% versus 0%,  $p=0.013$ ). The mean overall survival of patients with extra-abdominal recurrence was 54.9 months, whereas patients without extra-abdominal recurrence was 94.4 months( $p=0.028$ ). The median hospitalization duration, estimated blood loss during surgery, complications after surgery (except ileus) has no statistically significant difference between two groups.

**Conclusion/Implications:** Although longer follow-up period and larger population may be necessary, there was higher incidence of extra-abdominal recurrence after secondary cytoreductive surgery without HIPEC than with HIPEC. In the case of recurrent ovarian cancer amenable to surgical intervention, performing HIPEC during cytoreductive surgery may influence the survival rates without significant adverse effect.

EP271 / #204

**Topic: AS11. Ovarian Cancer**

## **THE ANTI-CANCER EFFECTS OF AZD4547 ON OVARIAN CANCER CELLS: DIFFERENTIAL RESPONSES BASED ON FGF19 AND C-MET EXPRESSIONS**

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**Introduction:** The FGF/FGFR signaling pathway is known to have a critical role in physiological and pathological processes in human cancers. We analyzed the anti-tumor effect of AZD4547, an inhibitor targeting the FGF/FGFR pathway in epithelial ovarian cancer (EOC).

**Methods:** We treated EOC cells with AZD4547 to evaluate its effects on cell viability and migration. In vivo experiments in orthotopic xenografts using EOC cells and a patient derived xenograft (PDX) model were also performed. Combination effect of AZD4547 and either SU11274, a c-Met-specific inhibitor, or FGF19-specific siRNA was evaluated by MTT assay.

**Results:** AZD4547 significantly decreased cell survival and migration in EOC cells except for A2780-CP20 and SKOV3-TR cells. AZD4547 significantly decreased tumor weight in xenograft models of EOC cells and in a PDX model established with platinum-sensitive tumors but not in A2780-CP20 and SKOV3-TR. Expression of c-Met in SKOV3-TR cells was higher than other cells and combination of SU11274 and AZD4547 increased cell death. Although FGFR1-3 proteins were relatively highly expressed in EOC cells used in this study, FGFR4 was strongly expressed only in A2780 and A2780-CP20. In addition, FGF19 expression, a ligand for FGFR4, was exclusively high in A2780-CP20 cells. Combining AZD4547 with FGF19 siRNA or with a selective FGFR4 inhibitor led to significantly reduced cell proliferation in A2780-CP20.

**Conclusion/Implications:** We suggest that expression level of c-Met or FGF19 can be a predictive biomarker for AZD4547 treatment and that combination therapy of drugs targeting c-Met or FGF19 with AZD4547 can be an effective therapeutic strategy for treating resistant EOCs.

EP272 / #891

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## **IMPACT OF CLINICAL TRIAL PARTICIPATION ON THE SURVIVAL OF PATIENTS WITH NEWLY DIAGNOSED ADVANCED-STAGE OVARIAN CANCER**

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**Introduction:** Clinical trials provide access to novel treatment strategies, which may offer survival benefits to ovarian cancer patients. We sought to determine if participation in any clinical trial is associated with a survival benefit in patients with newly diagnosed advanced-stage ovarian cancer.

**Methods:** We retrospectively investigated the patients who treated for newly diagnosed advanced-stage ovarian cancer at Yonsei Cancer Hospital between 2019 and 2021. This study included 202 patients with stage III-IV, 82 patients who participated in clinical trials and 120 participants receiving standard-of-care therapy (SOC).

**Results:** The median follow-up duration was 31.5 months. Disease recurrence occurred in 123 (60.9%) patients and 45 (22.3%) patients died. Among the patients in both groups, there were no significant differences in age, histologic type, stage, median CA-125 level, comorbidities, and BRCA 1/2 status. There were also no differences in the incorporation of hyperthermic intraperitoneal chemotherapy, neoadjuvant chemotherapy, residual disease after cytoreductive surgery. The patients involved in clinical trials were associated with significantly improvement in progression-free survival (PFS) (31.4 vs. 19.2 months; HR, 0.67; 95% CI, 0.46 to 0.97;  $p = 0.034$ ) compared to SOC. There was no difference in overall survival between two groups ( $P = 0.164$ ).

**Conclusion/Implications:** Clinical trial participation was associated with improved PFS in patients with newly diagnosed advanced-stage ovarian cancer. Clinical trial participation is considered to be beneficial to patients with newly diagnosed advanced-stage ovarian cancer.

EP274 / #837

**Topic:** AS11. Ovarian Cancer

## **CHARACTERIZATION OF A THREE-DIMENSIONAL CULTURE SYSTEM REPRESENTATIVE OF DISEASE PROGRESSION IN HIGH-GRADE SEROUS OVARIAN CANCER**

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**Introduction:** PEO1, PEO4 and PEO6 are cell lines derived from a single patient with high-grade serous ovarian cancer, the most common disease subtype, which illustrate disease progression. In cell culture-treated flat-bottom flasks, PEO1 and PEO4 form two-dimensional cellular aggregates and PEO6 form three-dimensional structures. This project aims to determine if differences in morphology, viability, proliferation, and metabolic activity exist between the three cell lines when grown in an ultra-low attachment plate more representative of in-vivo conditions.

**Methods:** PEO1, PEO4 and PEO6 cells were grown in ultra-low attachment plates. Live/dead cell imaging, apoptosis and proliferation detection as well as ATP quantitation assays were performed using microscope imaging, cytometry and spectrophotometry methods.

**Results:** The cell lines were morphologically different, mimicked the multilayered structure of in-vivo tumors and had a similar proliferation pattern. PEO1 displayed the highest aggregation level, PEO6 the highest compaction level, and PEO4 the lowest aggregation and compaction levels. All three cell lines were found to mimic poorly vascularized tumors by forming a multilayered structure with an outer layer of live cells and an inner core of apoptotic cells, but at different times. It was observed that PEO1, PEO4 and PEO6 cells proliferate mostly in the cell masses' periphery. PEO6 cells produced a higher amount of ATP followed by PEO4 and then PEO1 cells after 4 and 7 days.

**Conclusion/Implications:** Three-dimensional cell culture of established ovarian cancer cell lines in such environment likely will serve as a preclinical model of disease to provide experimental responses to therapeutic agents.



EP276 / #634

Topic: AS11. Ovarian Cancer

## THE IMPACT OF HISTOLOGIC SUBTYPES ON SURVIVAL OUTCOMES IN PRIMARY MUCINOUS OVARIAN CANCER

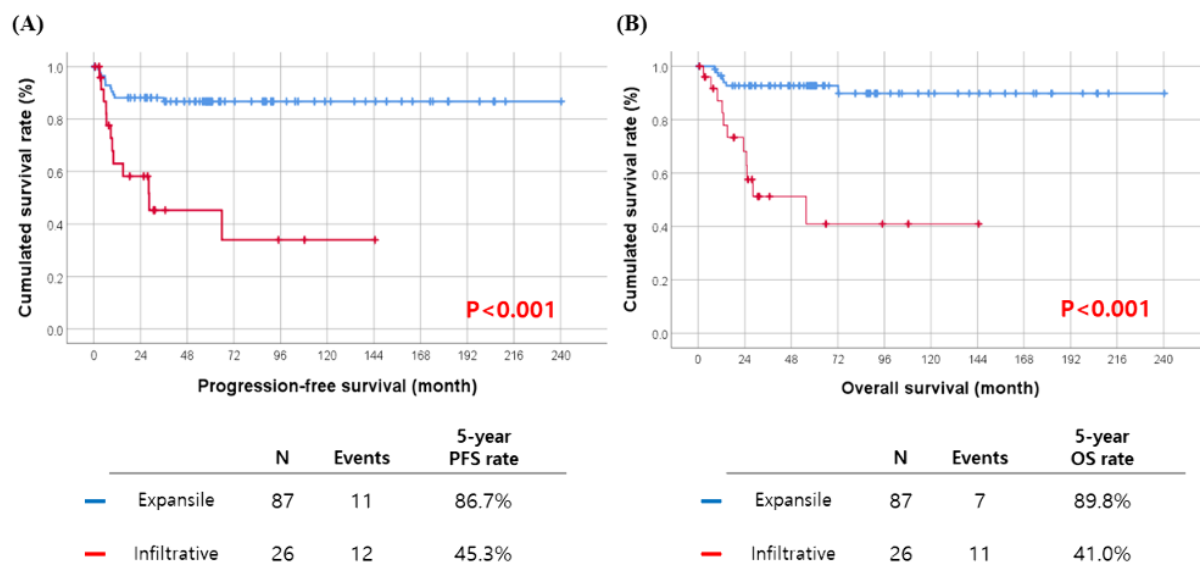
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**Introduction:** Primary mucinous ovarian cancer (PMOC) is a unique and rare subtype of ovarian cancer. In 2014, the World Health Organization introduced a new histologic classification by dividing PMOC into two subtypes: expansile or infiltrative. In this study, we investigated the clinical implications of their histological subtypes on survival outcomes.

**Methods:** We identified patients with PMOC who had undergone primary surgery between 2003 and 2021. Patients with other types of ovarian cancer or severe comorbidities were excluded. We collected patients' baseline characteristics, surgical details, and pathological information. Progression-free survival and overall survival were calculated, while prognostic factors were also investigated.

**Results:** We included 131 patients in total. The median age was 50 years, and 103(78.6%) patients had stage I disease. During 55.9 months of median follow-up, there were 27 recurrences and 20 deaths. Among them, 113 patients were classified into 87(77%) expansile and 26(23%) infiltrative subtypes after the slide review. Advanced stage, lymph node involvement, and residual tumors after surgery were more common in the infiltrative subtype. The infiltrative group showed worse 5-year progression-free and overall survival rates (Figure1). In multivariate analyses, advanced stage and residual tumor after surgery were associated with worse prognosis, while the infiltrative subtype showed no statistical significance (Table1). In the subgroup analysis of stage I disease, there was no difference in survival between the two groups.

Figure 1. (A) PFS (B) OS according to histologic classification among all patients



**Table 1.** Univariate and multivariate analysis of PFS and OS in the study population

Variables	PFS				OS			
	Univariate		Multivariate		Univariate		Multivariate	
	HR [95% CI]	P-value	HR [95% CI]	P-value	HR [95% CI]	P-value	HR [95% CI]	P-value
Age								
>50 vs. ≤50	1.494 [0.698 – 3.195]	0.301	-	-	2.185 [0.871 – 5.481]	0.096	-	-
Stage								
≥ II vs. I	24.548 [10.139 – 59.436]	<0.001	6.506 [1.681 – 25.178]	0.007	58.835 [13.551 – 255.441]	<0.001	16.762 [2.455 – 114.427]	0.004
Initial serum CA-125								
>40 IU/mL vs. ≤40 IU/mL	3.192 [1.391 – 7.326]	0.006	1.847 [0.673 – 5.073]	0.234	3.969 [1.435 – 10.975]	0.008	1.080 [0.342 – 3.415]	0.895
Residual tumor after surgery								
Present vs. absent	29.536 [12.429 – 70.188]	<0.001	4.892 [1.386 – 17.271]	0.014	37.691 [13.968 – 101.704]	<0.001	5.982 [1.246 – 28.716]	0.025
Incomplete staging operation								
Yes vs. no	1.532 [0.688 – 3.411]	0.296	-	-	1.168 [0.477 – 2.858]	0.735	-	-
Histologic subtype								
Infiltrative vs. Expansile	5.452 [2.382 – 12.479]	<0.001	1.586 [0.609 – 4.126]	0.345	7.878 [3.017 – 20.573]	<0.001	1.377 [0.427 – 4.437]	0.592

Abbreviation: PFS, progression free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; CA, cancer antigen

**Conclusion/Implications:** In PMOC, the infiltrative histological subtype showed worse prognosis than the expansile subtype, with a higher proportion of advanced-stage tumors. However, it remains uncertain whether infiltrative subtype is an independent prognostic factor.

EP277 / #794

Topic: *AS11. Ovarian Cancer*

## **STING INHIBITORS REVERSE PLATINUM RESISTANCE IN OVARIAN CANCER BY INHIBITING THE CGAS-STING PATHWAY IN CANCER-ASSOCIATED FIBROBLASTS**

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**Introduction:** Chemoresistance is a key factor limiting the cure rate of ovarian cancer. Cancer-associated fibroblasts (CAFs) have been shown to be actively involved in cancer progression and chemoresistance. Intratumoral inflammatory environments affect many therapeutic responses, but the underlying mechanisms by which CAF participates in chemoresistance by modulating the tumor's inflammatory environment are largely unknown.

**Methods:** We cultured primary ovarian cancer-associated fibroblasts, using indirect co-culture to study how ovarian cancer cells activate CAF to participate in ovarian cancer platinum-resistant. WB shows activation of the cGAS-STING pathway in CAF, and IHC shows differential expression of STING in cisplatin-sensitive/resistant patients. Cell viability or apoptosis using CCK8 or apoptosis kits, respectively. The STING antagonist H-151 and the STING agonist MSA-2 investigated the contribution of the cGAS-STING pathway to the chemoresistance of ovarian cancer.

**Results:** After treatment with cisplatin for ovarian cancer cells, the supernatant was indirectly co-cultured with CAFs, and mRNA sequencing showed that the cGAS-STING-IFNB1 pathway was activated in CAFs. We found that IFNB1 can promote platinum resistance in cancer cells by inhibiting cisplatin-induced DNA damage and promoting HRR. Anti-IFNB1 restores platinum sensitivity. In addition, the expression of STING in the tumor stroma is associated with poor prognosis in patients. In vivo experiments showed that inhibition of STING expression could restore platinum sensitivity, while activating STING could not significantly enhance immune killing ability.

**Conclusion/Implications:** Our study shows that activation of the cGAS-STING pathway in CAFs is involved in platinum resistance in ovarian cancer, and STING inhibitors are able to restore ovarian cancer chemotherapy sensitivity.

EP279 / #598

**Topic:** AS11. Ovarian Cancer

## **OSBPL10-APOE PATHWAY INCREASES RESISTANCE OF PLATINUM AND PARPI BY REGULATING CHOLESTEROL METABOLISM AND DNA DAMAGE REPAIR IN PDX MODEL OF HRD-POSITIVE HGSOC**

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**Introduction:** Compared with HRD-negative ovarian cancer patients, HRD-positive patients are more sensitive to platinum-based chemotherapy and benefit from PARPi is more significant. However, there are still some HRD-positive patients with platinum and PARPi resistance, resulting in a poor prognosis.

**Methods:** In this study, a key differential gene, Oxysterol binding protein like 10 (OSBPL10), was identified by bioinformatics analysis of platinum-resistant and platinum-sensitive HRD-positive ovarian cancer patients after first-line chemotherapy in TCGA database. Western Blot and Immunohistochemistry were performed on tumor tissues from Qilu Hospital of Shandong university to verify the differential expression of OSBPL10. Target genes of OSBPL10 were identified by RNA-seq and validated by RIP. In addition, we established PDX models for high-grade serous ovarian cancer (HGSOC) patients to validate the efficacy of targeting OSBPL10.

**Results:** The expression of OSBPL10 in platinum-resistant HRD-positive ovarian cancer patients were significantly higher than that in platinum-sensitive patients. Inhibiting OSBPL10 enhanced the sensitivity to cisplatin and Niraparib of ovarian cancer cells. Apolipoprotein E (APOE), as a target gene of OSBPL10, was involved in lipid transport and lipoprotein metabolism. Overexpression of OSBPL10 could activate the expression of APOE, enhance DNA damage repair function, and up-regulate cholesterol levels in intracellular, extracellular and tumor microenvironment, leading to increased exhaustion of CD8<sup>+</sup> T cells, and further promoting resistance to cisplatin and Niraparib. Combined with Niraparib, OSBPL10 adenovirus (shRNA- OSBPL10) was more effective in repressing tumor growth of PDX models than Niraparib monotherapy.

**Conclusion/Implications:** OSBPL10-APOE pathway regulated DNA damage repair and cholesterol metabolism, leading to cisplatin and Niraparib resistance of HRD-positive HGSOC.

EP280 / #231

Topic: *AS11. Ovarian Cancer*

## **RESPONSE TO SUBSEQUENT PLATINUM-BASED CHEMOTHERAPY POST PARP INHIBITOR IN RECURRENT EPITHELIAL OVARIAN CANCER**

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**Introduction:** Maintenance therapy with PARP inhibitors (PARPi) can increase progression free survival (PFS) in recurrent or metastatic platinum-sensitive epithelial ovarian cancer (EOC), though some evidence suggests a decreased response to subsequent platinum-based chemotherapy. This study assessed real-world response rates to platinum-based chemotherapy for recurrent high grade EOC following treatment with a PARPi.

**Methods:** Single center retrospective cohort study of patients prescribed a PARPi as maintenance therapy for recurrent or metastatic EOC, including 54 patients on niraparib and 36 patients on olaparib. Median duration of follow-up after PARPi initiation was 16.3 months.

**Results:** Of the 91 patients included in the analysis, 54 (59.3%) experienced disease progression after PARPi therapy, including 10 (11.0%) who progressed within 6 months of their penultimate therapy. Of the 44 patients with disease progression more than 6 months following penultimate therapy, 32 (72.7%) were rechallenged with platinum-based chemotherapy. Of these, 14 (43.8%) further progressed within 6 months of their platinum rechallenge. Median PFS following platinum rechallenge was 4.4 months. Incidence of platinum resistance was 26.4% in the overall population and 44.4% in those with disease progression after initiation of PARPi therapy.

**Conclusion/Implications:** Disease progression following PARPi therapy showed a poor response to subsequent platinum-based chemotherapy, even when progression occurred more than 6 months after the penultimate platinum-based chemotherapy. This supports the theory that PARPi resistance correlates with platinum resistance and raises concern for possible contribution of PARPi in the induction of platinum resistance in recurrent EOC.

EP282 / #263

Topic: *AS11. Ovarian Cancer*

## **ONCOLOGIC OUTCOME OF PRIMARY TREATMENT IN PATIENTS DIAGNOSED WITH EPITHELIAL OVARIAN/TUBAL/PERITONEAL CARCINOMA WHOM UNDERWENT SUBOPTIMAL SURGERY.**

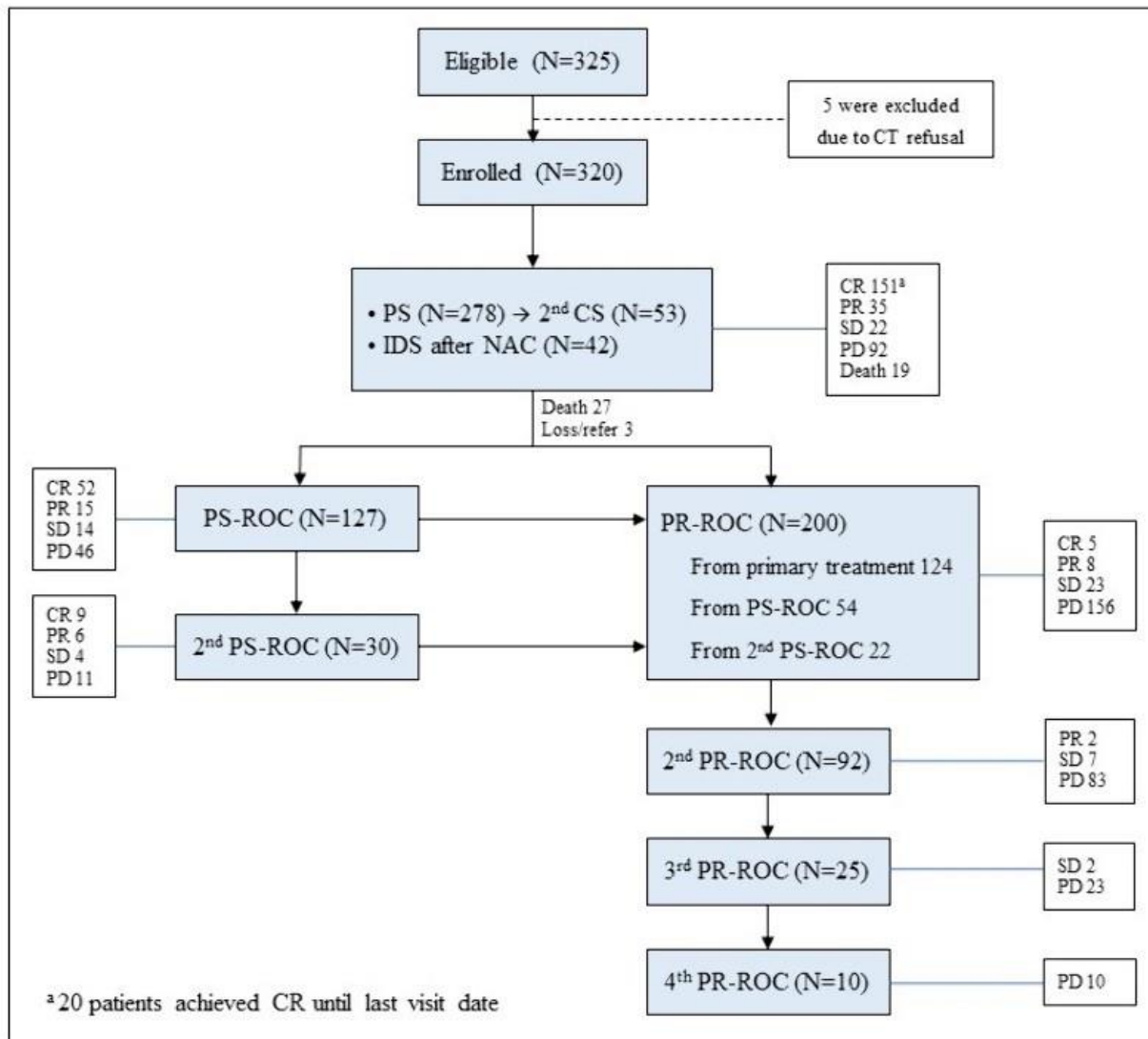
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**Introduction:** To evaluate the response rate of primary treatment, its predicting factors, and to analyze survival outcomes in patients with epithelial ovarian/tubal/primary peritoneal carcinoma whom underwent suboptimal surgery.

**Methods:** This study included women whom received suboptimal surgery between May 2006 and December 2020. The data of patient's clinical information, histopathology, tumor stage, surgical methods and outcomes, adjuvant treatment, and primary treatment outcomes were collected. Follow-up data was documented until 31 March 2023. The oncologic outcomes were analyzed.

**Results:** Total of 320 study patients, overall response rate was 58.1%. The median progression free survival (PFS) duration was 13.167 months [6.675-20.583], and the median overall survival (OS) was 32.850 months [15.008-53.642]. The factors significantly associated with response were received neoadjuvant chemotherapy (NAC) with adjusted odd ratio (aOR) 3.342 (95% CI 1.619-6.900, P=0.001), and high-grade serous carcinoma (HGSC) (aOR 0.153, 95% CI 0.092-0.255, P<0.001). HGSC associated with longer median PFS (15.9 months vs 7.2 months, P<0.001) and median OS (35.221 months vs 11.994 months, P<0.001) compared to non-HGSC.



**Abbreviations:** CR, complete response; 2<sup>nd</sup> CS, secondary cytoreductive surgery; CT, chemotherapy; IDS, interval debulking surgery; NAC, neoadjuvant chemotherapy; PD, progressive disease; PR, partial response; PR-ROC, platinum resistant recurrent ovarian cancer; PS-ROC, platinum sensitive recurrent ovarian cancer; PS, primary surgery; SD, stable disease

Table 2 Regression analysis of 320 patients for associated factors to response of primary treatment

Variables	Overall response rate (%)	Univariate analysis	P-value
<b>Age, years</b>			
≤55, n=158	85 (53.8)		
>55, n=162	101 (62.3)	0.703 [0.450-1.098]	0.121
<b>Body Mass Index, kg/m<sup>2</sup></b>			
<18.5, n=50	25 (50.0)		
18.5-24.9, n=186	114 (61.3)	0.632 [0.337-1.183]	0.152
25.0-29.9, n=57	32 (56.1)	0.781 [0.365-1.674]	0.526
≥30.0, n=27	15 (55.6)	0.800 [0.313-2.048]	0.642
<b>Received NAC</b>			
No, n=278	169 (60.8)		
Yes, n=42	17 (40.5)	2.280 [1.177-4.418]	<b>0.013</b>
<b>Histopathology types</b>			
Others, n=122	40 (32.8)		
High-grade serous, n=198	146 (73.7)	0.174 [0.106-0.284]	<b>&lt;0.001</b>
<b>FIGO stages</b>			
IIB-IIIB, n=34	16 (47.1)		
IIIC-IVB-advanced, n=286	170 (59.4)	0.607 [0.297-1.238]	0.167

Abbreviations: FIGO, The International Federation of Gynecology and Obstetrics; HGSC, high-grade serous carcinoma; NAC, neoadjuvant chemotherapy

**Conclusion/Implications:** The oncologic outcomes of study patients were comparable to the landmark trials. HGSC has higher response rate, longer PFS and OS than non-HGSC.



EP283 / #752

Topic: *AS11. Ovarian Cancer*

## **REAL-WORLD EFFECTIVENESS OF PEGYLATED LIPOSOMAL DOXORUBICIN VERSUS GEMCITABINE IN PLATINUM-RESISTANT/REFRACTORY RECURRENT OVARIAN CANCER**

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**Introduction:** Non-platinum chemotherapy agents are often given in platinum-resistant/refractory recurrent ovarian cancer (PRROC) treatment. This large cohort study aimed to compare the effectiveness between pegylated liposomal doxorubicin (PLD) and gemcitabine, which are 2 most common second-line chemotherapy agents in Thailand.

**Methods:** All epithelial ovarian cancer (EOC) patients treated at two tertiary cancer centers during 2009-2018 were enrolled. PRROC patients were included and their treatments were reviewed. The effectiveness of PLD and gemcitabine was compared using the treatment-effect model.

**Results:** Of 1,708 EOC patients, 954 patients developed recurrence and 530 patients (55.6%) diagnosed as PRROC. The most common second-line chemotherapy regimen was PLD (251 patients, 47.4%), followed by gemcitabine (217 patients, 40.1%), and other (62 patients, 12.5%). After applying the treatment effect model by Inverse Probability Weighting with Regression Adjustment (IPWRA), the median time of disease progression after treatment with PLD, and gemcitabine was 6.3 months (5.4 to 7.1), and 6.7 months (5.2 to 8.2), respectively. The average treatment effect (ATE) or the difference of median time of disease progression between both agents was not statistically significant. Whereas the median time from PRROC diagnosis until death after treatment with PLD and gemcitabine was 22.5 months (17.7 to 27.4), and 17.6 months (15.0 to 20.3), respectively. The ATE indicated that PLD had 4.9 months (-0.5 to 10.4) longer than gemcitabine, although there was no statistical significance.

**Conclusion/Implications:** PLD and gemcitabine had comparable effectiveness for PRROC treatment. The median time from PRROC diagnosis until death after treatment with PLD tended to be 4.9 months longer than gemcitabine.

EP284 / #194

**Topic:** AS11. Ovarian Cancer

## **SURVIVAL RATE, RECURRENCE RATE AND COMPLICATION RATE OF ROUTINE APPENDECTOMY FOR PATIENTS WITH BORDERLINE AND MALIGNANT MUCINOUS OVARIAN TUMOR: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Introduction:** To this day, performing routine appendectomy for borderline and malignant mucinous ovarian tumors still remains a dilemma. This study aims to determine the survival rate, recurrence rate and complication rate among patients diagnosed with borderline and malignant mucinous ovarian tumor who underwent complete surgical staging with appendectomy.

**Methods:** All studies retrospective studies with histopathologic diagnosis of borderline or malignant MOT with subjects who underwent appendectomy during primary surgery including encompassing data on survival rate, recurrence rate and/or complication rate that matched the terms set by the researchers were retrieved. Review Manager Version 5.3 (Revman 5.4.1) was used by the researcher to perform the systematic review and meta-analysis of included studies.

**Results:** The random interval for survival rate is 64.9 to 99.7% with a P-value of <0.1. The prediction interval for recurrence rate is 0 to 100% with 95% confidence interval. The odds of complications occurring is less than 0.69 to 2.99 times with 95% confidence interval with mean effect size is 0.083 with a 95% confidence interval of 0.027 to 0.23.

**Conclusion/Implications:** The mean prevalence of abnormal histology of the appendix in patients diagnosed with borderline and malignant MOT and underwent routine appendectomy is 3-13%. There is no statistically significant difference in survival rate of patients who were diagnosed with borderline and malignant MOT with or without appendectomy during primary surgery. The prediction interval for recurrence rate is 0 to 100% with 95% confidence interval. There is no significant difference between the rate of complications in patients who underwent appendectomy and those without.

EP285 / #976

Topic: **AS11. Ovarian Cancer**

## **BORDERLINE OVARIAN TUMOUR AUDIT AT AN AUSTRALIAN TERTIARY CENTRE**

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**Introduction:** Borderline ovarian tumors represent 10-20% of all epithelial ovarian tumors and one third of patients present younger than 40. We present an updated audit at the Royal Womens' Hospital, reviewing all cases since 1982, with particular focus on outcomes in patients who undergo fertility preserving management; rates, timing and detection of recurrence; duration and frequency of follow-up and rates of progression to cancer.

**Methods:** Single (tertiary) institution retrospective audit. Data were collected from the GEMMA and EPIC databases. Archived pathology reports were re-reviewed in cases where recurrence occurred. Ethics approval was obtained AQA21/15.

**Results:** Mean age at diagnosis was 46. Correlation of frozen section results to final pathology was correct or at least queried in 109/151 cases (72%), 54 (62%) in MBOT and 55 (92%) in SBOT.

Recurrence and Surgical Procedure		
	All Cases (555)	SBOT (229)
Recurrence 1 2 3 As a cancer	31 (6%) 22 (4%) 6 (1%) 3 (<1%) 5 (1%)	22 (10%) 16 (7%) 5 (2%) 2 (1%)
Average time to recurrence (months) [SD]	58 [54]	67 [59]
First Procedure		
Cystectomy	10 (16%)	7 (23%)
USO (or tube or ovary only)	17 (11%)	13 (21%)
BSO only	0%	0%
Hyst + BSO	3 (2%)	2 (2%)

**Conclusion/Implications:** Our work contributes to existing published data.

EP286 / #514

Topic: *AS11. Ovarian Cancer*

## REAL WORLD MANAGEMENT OF ENDOMETRIOSIS: HOW CAN WE PREVENT ENDOMETRIOSIS ASSOCIATED OVARIAN CANCER?

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**Introduction:** Endometriosis treatment is individualized and varies among patients. Studies suggest that hormonal suppression is protective against re-intervention and malignant transformation, however, they are largely based on self-reported diagnoses of endometriosis. We investigated patients with pathology proven endometriosis to characterize current management and determine whether hormone therapy reduces the risk of malignancy.

**Methods:** Patients included had pathologically confirmed endometriosis diagnosed in British Columbia from 2000-2008 (n=4411). Data was linked to health administration holdings through Popdata BC.

**Results:** After surgery, 475 (10.8%) patients received unopposed estrogen, 1567 (35.5%) estrogen and progesterone and 423 (9.6%) progesterone alone ( $p < 0.001$ ). 408 (9.3%) used GnRH agonists or antagonists. 194 (4.4%) patients were diagnosed with ovarian cancer; 68 (1.6%) with endometrioid and 58 (1.3%) with clear cell histology. There were 30 cancers diagnosed more than 6 months following index surgery. Those with ovarian cancer were less likely to have a prior physician visit coded for endometriosis (11% versus 34%;  $p < 0.001$ ) and were more likely asymptomatic (34.6% with prior visits for pelvic pain versus 51.4% ;  $p < 0.001$ ). Patients with malignancy were less likely to have been prescribed hormonal suppression prior to surgery, 13% with OCP use and 1.9% with GnRH agonist use compared to 36% and 10% respectively in benign endometriosis ( $p < 0.001$  for both medications).

**Conclusion/Implications:** The majority of patients in our cohort were not placed on hormonal suppression after a pathology proven diagnosis of endometriosis. This study suggests early diagnosis and treatment of endometriosis may be protective against malignant transformation however a larger study is required.

EP287 / #748

**Topic: AS11. Ovarian Cancer**

## **THE PROGNOSTIC IMPACT OF LIMITED-STAGING SURGERY IN PATIENTS WITH STAGE IA EPITHELIAL OVARIAN CANCER: A MULTI-CENTER STUDY WITH A PROPENSITY SCORE-ADJUSTED ANALYSIS.**

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**Introduction:** Complete-staging surgery is recommended for stage IA ovarian cancer (OC), but may be omitted for various reasons, including the preservation of fertility and an advanced age. We herein investigated the prognostic impact of limited-staging surgery in patients with stage IA epithelial OC.

**Methods:** We retrospectively collected data on 4,730 patients with malignant ovarian tumors from the databases of multiple institutions and ultimately included 293 with stage IA epithelial OC. Limited-staging surgery was defined as one that did not involve hysterectomy, systematic retroperitoneal lymphadenectomy, or the collection of ascites cytology. We used an inverse probability of treatment weighting analysis with propensity scores and estimated the hazard ratios of recurrence and death with limited-staging surgery.

**Results:** In total, 176 out of 293 patients (39.9%) were assigned to the limited-staging surgery group. After propensity score (PS) adjustments, no significant differences were observed in recurrence-free survival (RFS) or overall survival (OS) between the limited- and complete-staging surgery groups (P-value=0.651 and 0.469, respectively). Even in the subgroup analysis with age stratification, RFS and OS were similar in the limited- and complete-staging surgery groups.

**Conclusion/Implications:** The present results indicate the limited prognostic impact of limited-staging surgery for stage IA epithelial OC.

EP289 / #884

Topic: *AS11. Ovarian Cancer*

## **LIPID MOLECULES IDENTIFIED BY METABOLOME ANALYSIS PROMOTE THE CELL PROLIFERATION OF EPITHELIAL OVARIAN CANCER**

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**Introduction:** Previously we reported that lipolysis-stimulated lipoprotein receptor (LSR) mediates the cell proliferation via lipid metabolism in epithelial ovarian cancer (EOC). We newly developed anti-LSR antibody. Anti-LSR antibody showed stronger anti-tumor effect against LSR positive EOC cells, especially in High-Fat Diet (HFD) fed mouse compared to Normal-Diet (ND) fed mouse. That suggests lipid molecules in HFD might contribute to cell proliferation via LSR. In this study, we performed metabolome analysis using each serum of HFD and ND fed mouse. We analyzed the metabolomic profile of lipid molecules.

**Methods:** We established HFD and ND fed mouse and obtained each serum to perform metabolome analysis. We compared the metabolomic profile of HFD and ND fed mouse serum and identified the lipid metabolites which might associate with the cell proliferation. We evaluated the effect on promoting cell proliferation by the lipid molecules and signaling pathway mediated through LSR.

**Results:** Metabolome analysis detected 210 metabolites, and PCA showed obviously different metabolic profiles of HFD serum compared to ND serum. PLS-DA also revealed cholesterol, oleic acid and arachidonic acid as lipid molecules with high VIP score. These molecules significantly promoted the cell proliferation through MAPK signaling pathway ( $p < 0.05$ ).

**Conclusion/Implications:** Metabolome analysis showed that certain lipid molecules contribute cell proliferation of LSR positive EOC.

EP290 / #820

Topic: *AS11. Ovarian Cancer*

## **INTERMITTENT PARP INHIBITOR REGIMEN IN OVARIAN CANCER (IPIROC): ORIGIN AND FEASIBILITY OF IMPLEMENTING A PROOF-OF-CONCEPT EXPLORATORY STUDY**

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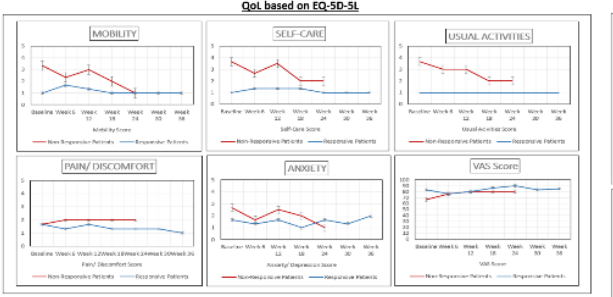
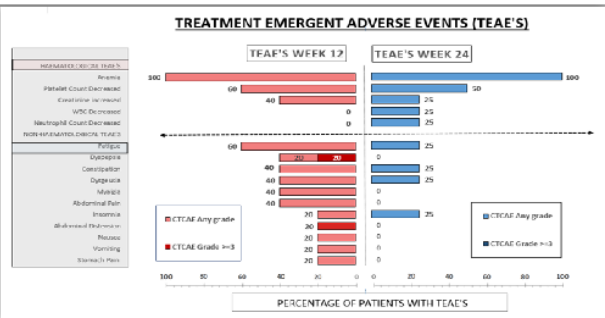
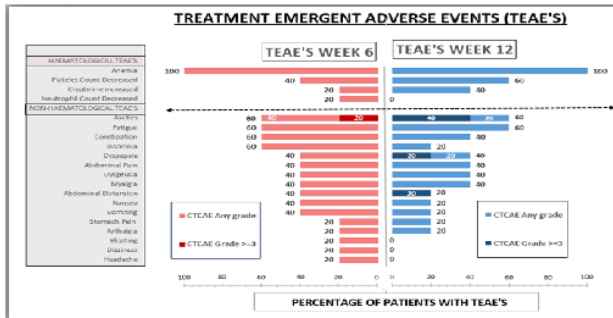
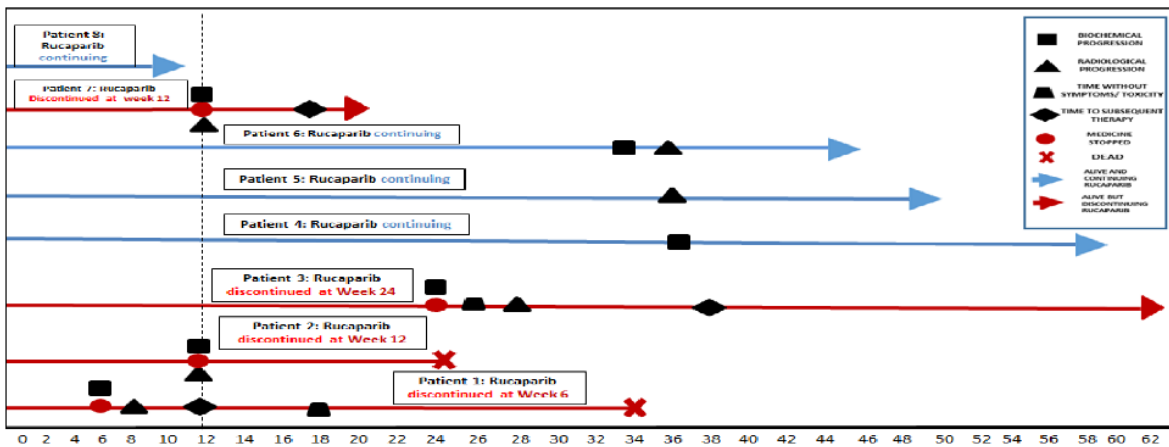
**Introduction:** Availability/affordability and toxicity of PARP inhibitors (PARPi) for ovarian cancer treatment represent an unmet clinical need in LMICs, especially in women with anaemia/low-BMI. Through a CRUK/DBT-India-funded project, we generated proof-of-concept preclinical data showing durable parp inhibitory action after single dose rucaparib >72 hours. An academic/exploratory clinical feasibility study was planned for de-escalation/optimal scheduling, under GCIG mentorship (Sponsor: KoIGOTRG).

**Methods:** Institutional ethical approval was obtained. Patient-public-involvement workshops were held for assessing consumer preference/acceptance and willingness-to-pay. Platinum-sensitive (>3 months PFI) recurrent HGSC ovarian cancer patients were invited to participate, if deemed eligible for PARPi treatment. Bi-weekly rucaparib-generic (1200 mg, 2 days/week, 72hours apart) was administered orally for 12 weeks. Tolerability/toxicity/QOL and response-rate was assessed, followed by physician's-choice of treatment/patients'-preference for continuation of intermittent regimen. PBMC was extracted and stored at 0/24/72/168 hours after the 1st rucaparib dose for future PK/PD studies. Barrier identification for implementing a dose de-escalation study was conducted using EASE model.

**Results:** Of the 8 patients enrolled till April 2023, 3 women with large volume disease/ascites progressed at 12 weeks. 4 women continued till 24 weeks: 3 of them expressing willingness for continuing at 58, 52 and 48 weeks respectively due to favourable tolerability/QOL/response. No grade-3 haematological toxicity was recorded. Further 3 women on daily PARPi maintenance therapy, requiring dose de-escalation due to toxicity/affordability, opted for this regimen (outside study) and remain disease/toxicity free at >6months.

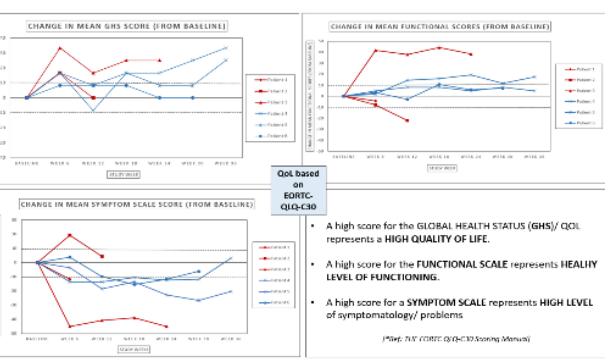
**KPI for successful implementation: EASE**

	How to implement, process and measures	Lessons learned (Example: breast cancer study, phase II vs I study)
Ethical	Right questions adapted to the specific setting	Involve patients: SPI-vision on accepting detriment in efficacy to adjust for feasibility plan to spend time on patient and provider advocacy, develop awareness and IAP Plan to tackle hard parts Patient – randomization consent design
Feasible	Select key endpoints	Select key of relevant and relevant endpoints/ outcome measures Select recruitment time frame and intervals for measurement
Acceptable/Adaptable	Resource adaptive guidelines for conduct and design including sample size estimation- what is acceptable versus deliverable	Pilot phase (population sensitive specific and systematic) start to finish and then PAUSE adaptable study designs to allow for variation of populations (7 endpoints) Allow time to adapt to good quality treatment and study conduct standards
Affordable	Cost effective study designs and conduct strategies to reduce cost of running studies (RCT approach)	Single arm studies ( historical control/ Bayesian models) include economic analysis Virtual, Remote technologies/ electronic storage/ AI
Sustainable	Select sites	Careful selection of PI/ study sites in phase- single site may not cope with large numbers
scalable	quantity versus quality	continuous education and training/ back up plans
Effective/Equipose/Encourage	Innovative study/statistical designs - How to reduce sample size - How to include more subjects rather than designing multiple studies	Right choice of endpoints Additional weightage if biomarkers/translational endpoints included - lesser numbers may achieve the goal Careful selection of PI/ study sites- single site may not cope with large numbers provider advocacy/ incentives ( developing clinical academic programs)
Early diagnosis	Early diagnosis of complications in conduct and robust risk management strategy/ trouble shooting	Go slow with regulatory process and recruitment ( NPT)- build the road on go! Plan a pilot / exploratory rehearsal and pause ( can't waste limited resource)



Each dimension in the EQ 5D has five response levels: No problems (Score 1), Slight problem (Score 2), Moderate problem (Score 3), Severe problem (Score 4) and Extreme Problem (Score 5), thus a higher response level represents a LOW HRQoL.

Also, it includes a Visual Analogue Scale (VAS) which records the respondent's self-rated health status on a graduated [0-100] scale, with higher scores for HIGHER HRQoL.



A high score for the GLOBAL HEALTH STATUS (GHS)/ QoL represents a HIGH QUALITY OF LIFE.

A high score for the FUNCTIONAL SCORE represents HEALTHY LEVEL OF FUNCTIONING.

A high score for a SYMPTOM SCALE represents HIGH LEVEL of symptomatology/ problems

(Page: 115-117/CRQ: EQ-5D-5L Scoring Manual)



**Conclusion/Implications:** Provider/referral bias mitigation and advocacy, incorporation of patients' preference and involving policymakers are important in designing future novel efficacy studies for dose de-escalation in LMICs.

EP291 / #959

**Topic: AS11. Ovarian Cancer**

## **DYING UNDIAGNOSED: CHALLENGES OF MANAGEMENT OF PELVIC MASSES IN A RESOURCE-POOR SETTING IN NORTHWESTERN NIGERIA**

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**Introduction:** Ovarian cancer is the second most prevalent but most lethal gynaecologic malignancy in our institution. The study aimed at determining the rate of non-diagnosis in patients with pelvic masses suspicious for ovarian malignancy while reviewing the management challenges

**Methods:** A three-year review of patient records was carried out. Cases with high indices of suspicion for ovarian cancer were identified by criteria including pelvic masses with malignant radiographic features, ascites, pleural effusion, cachexia, anemia, or metastatic disease. This multidisciplinary study was done in collaboration with consultants from radiology, radiation oncology, pathology, and gynaecologic oncology

**Results:** One hundred and twenty-two cases highly suspicious for ovarian malignancy were identified with a mean age of 40.6 years. Of these, 28 (23%) had surgery and 77% did not have any form of histological diagnosis. Of those that had surgery, 13 (46.4%) had upfront surgery and 15 (53.6%) neoadjuvant chemotherapy followed by interval debulking surgery. Only two cases had documented complete (R<sub>0</sub>) debulking. Among those that had upfront surgery, one case was an ovarian fibroid and one was a fibrosarcoma while two cases (15.4%) were borderline tumours. Chemotherapy was commenced based on malignant cells on ascitic or pleural fluid cytology in three cases. Epithelial carcinomas accounted for 48% of cancers. Challenges include late presentation, insufficient funding, unavailable interventional radiology, immunohistochemistry, genetic testing, and maintenance therapies, high cost of chemotherapy, inadequate skill, unaffordable/erratic imaging et cetera

**Conclusion/Implications:** Based upon our data, most patients with tumours highly suspicious for ovarian cancers probably die undiagnosed. Management of ovarian cancer remains a challenge despite advances in surgical and chemotherapeutic options

EP292 / #701

Topic: *AS11. Ovarian Cancer*

## **REVISITING THE ROLE OF INTERVAL CYTOREDUCTIVE SURGERY (ICS) FOLLOWING NEOADJUVANT CHEMOTHERAPY (NACT) FOR PATIENTS WITH ADVANCED STAGE EPITHELIAL OVARIAN CANCER; A MULTICENTER DATABASE ANALYSIS.**

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**Introduction:** Investigate the role ICS for ovarian cancer patients receiving NACT.

**Methods:** Patients diagnosed between 2010-2015 with stage III-IV ovarian carcinoma who received NACT and ICS with known status of residual disease were identified in the National Cancer Database. Median overall survival was compared with the log-rank test while Cox models were constructed to control for confounders (aHR).

**Results:** A total of 5055 patients were identified; after controlling for confounders those with gross residual disease (n=2366) had worse OS compared to patients with complete gross resection, CGR (n=2689) (aHR 1.36, 95% CI: 1.26, 1.47). Patients with gross disease  $\geq$  1 cm (n=1050) had comparable OS to those with < 1cm (n=1316) (33.84 vs 33.08 months, p=0.27; aHR 1.06, 95% CI: 0.95, 1.18). Patients who underwent high-complexity ICS and achieved CGR (n=570) did not have better OS compared to those who had low-complexity ICS and gross residual disease (n=724) (38.28 vs 35.84 months, p=0.11; aHR: 1.08, 95% CI: 0.93, 1.26). However, they had higher rates of prolonged hospital stay (11.8% vs 4.1%, p<0.001), and unplanned re-admission (3.5% vs 1.8%, p=0.056). CGR was associated with borderline survival benefit for high-risk patients (defined as those aged  $\geq$ 80 years or those aged 75-79 years with at least other risk factor (stage IV disease, comorbidity index score 2+, or complex surgery)) (33.25 vs 30.46 months, p=0.035; aHR: 1.22, 95% CI: 1.02, 1.47).

**Conclusion/Implications:** While CGR following ICS is associated with improved OS, elderly patients, those with comorbidities or those requiring extensive surgical procedures appear to benefit the least.

EP293 / #283

Topic: *AS11. Ovarian Cancer*

## **POST-OPERATIVE COGNITIVE DECLINE IN PATIENTS UNDERGOING MAJOR GYNECOLOGIC ONCOLOGY SURGERY: A PRELIMINARY PROSPECTIVE STUDY**

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**Introduction:** Postoperative cognitive decline (POCD) can occur in up to 60% of patients in the first month after surgery. POCD has been linked to poorer quality of life and increased mortality. It has not yet been thoroughly explored in Gynecologic Oncology. Studying its incidence may inform future efforts to mitigate functional decline after surgery.

**Methods:** This observational cohort study involved twenty-four patients aged  $\geq$  fifty-five undergoing surgery for a gynecologic malignancy from February to July 2022. Semi-structured interviews and the Mini Mental State Exam were administered before and one- and three-months after surgery. Assessments were delivered virtually and in-person owing to the COVID-19 pandemic. Using previous literature, POCD was defined as  $\geq$  two-point decline from baseline.

**Results:** Eighteen participants completed the one-month follow-up, and fifteen completed the three-month follow-up. Average age was 64, three patients underwent surgery for endometrial cancer, and thirteen for ovarian cancer. Two patients received chemotherapy before surgery; six received it after. No patients experienced postoperative delirium. Mean baseline MMSE virtual and in-person scores were 16.6 out of 17 and 12.9 out of 13, respectively. Two patients had a one-point decline at one month; both recovered by three-months. One patient had a one-point decline at three-months. Semi-structured interviews revealed common themes of “brain fog” at one-month and mild, persistent attention and word-finding deficits at three-months.

**Conclusion/Implications:** This study captured subtle qualitative themes suggestive of potential POCD. Larger studies and more extensive neuropsychological batteries may further characterize the POCD in Gynecologic Oncology, and elicit subtle findings not clearly reflected on MMSE scores.

EP294 / #363

Topic: **AS11. Ovarian Cancer**

## **PHASE 1/2 STUDY OF GALINPEPIMUT-S PLUS PEMBROLIZUMAB COMBINATION IN PATIENTS WITH WT1+ PLATINUM-RESISTANT OVARIAN CANCER IN 2ND/3RD LINE OF THERAPY**

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**Introduction:** Galinpepimut-S (GPS) is an HLA-unrestricted heteroclitic peptide vaccine against Wilms Tumor-1 (WT1), an antigen highly expressed in ovarian cancer (OC). GPS has shown promising activity as maintenance therapy in combination with checkpoint blockade in patients with OC in 2nd/3rd remission. We investigated GPS plus pembrolizumab in patients with measurable WT1+ platinum-resistant OC relapsed after or refractory to 1st/2nd -or later- line of therapy.

**Methods:** GPS (800 mcg)/GM-CSF (70 mcg) were administered subcutaneously Q3Weeks on D1CycleX, Cycles 1-2, followed by GPS/GM-CSF plus pembrolizumab 200 mg intravenously Q3Weeks Cycles 3-6. After an unpaired pembrolizumab administration at Week 18, the combination resumed Q3Weeks Cycles 7-12, per protocol. Primary endpoints were safety and overall response rate (ORR). Exploratory endpoints were PFS, OS and immune response.

**Results:** Safety: N=25, GPS alone=8 (due to disease progression); >1 dose of combination =17. Median age: 64-yrs; median number of prior lines: 2. Five patients experienced 11 SAEs, one of which was drug related. No DLTs. Only known toxicities of either drug were observed. Efficacy: N=16: ORR=6.3% (versus 11.5% in comparable patients given pembrolizumab alone in KEYNOTE-028); disease control rate (ORR + stable disease) was 50% with a 14.4-month median follow-up. Median PFS and OS were 2.8 and 18.4 months, respectively versus 1.9 and 13.8 months in KEYNOTE-028, correspondingly. Immune response: N=14: post-GPS increments in WT1-reactive CD8/CD4 cell frequencies in 42.8%/85.7% of patients.

**Conclusion/Implications:** GPS/pembrolizumab combination was safe & highly immunogenic and showed modest clinical benefit in patients with measurable advanced platinum-resistant OC, warranting further investigation.

EP296 / #849

**Topic: AS11. Ovarian Cancer**

## **EVALUATION OF CA 125, PHYSICAL AND RADIOLOGICAL FINDINGS IN RECURRENT EPITHELIAL OVARIAN CANCER ELIGIBLE FOR SECONDARY CYTOREDUCTION**

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**Introduction:** There is insufficient evidence regarding appropriate follow-up investigations to detect secondary cytoreductive surgery (SCS) eligible recurrences in epithelial ovarian carcinoma (EOC). We aimed to evaluate the role of CA 125, physical examination, and radiological findings in a cohort of recurrent EOC treated with SCS.

**Methods:** In this retrospective study clinical information of all women who had undergone SCS for the first recurrence of EOC at Tata Medical Center between January 2013 and December 2022 was extracted from electronic medical records. Relevant descriptive statistics were used in the analysis.

**Results:** A total of 53 women underwent SCS and all had histopathology-proven relapse on surgical specimens. The median age was 54 years (IQR 46-61). The mean CA 125 value at recurrence was 172 U/mL (IQR 16.5-88.5). The sensitivity of CA 125 value to detect recurrences with a cut-off of 35 U/mL (upper level of normal) and 70 U/mL were 58.4% and 28.3% respectively. Physical examination alone had a sensitivity of 24.5% in detecting recurrence. Computed tomography (CT) detected recurrence with 94.3% sensitivity. Pelvis (24.5%) was the most common location of recurrence on imaging, followed by spleen (20.8%). There was moderate agreement between the CT scan detected location of recurrence and histopathologic findings (kappa 0.505,  $p < .001$ ). CT scan could predict complete resection (CC0) in 84.9% of cases.

**Conclusion/Implications:** Physical examination and CA 125 have low sensitivity in detecting SCS-eligible recurrences. Prospective studies of periodic cross-sectional imaging are warranted in the follow-up of EOC in the era of SCS.

EP297 / #848

**Topic:** AS11. Ovarian Cancer

## **FERTILITY-SPARING SURGERY IN STAGE I UNILATERAL BORDERLINE OVARIAN TUMOR: IS OVARIAN CYSTECTOMY SAFE?**

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**Introduction:** To evaluate the long-term safety of ovarian cystectomy in patients with stage I unilateral borderline ovarian tumors (BOTs) who desire preserved fertility.

**Methods:** This retrospective study included 309 patients with stage I unilateral BOTs who underwent fertility-sparing surgery between 1990 and 2015. Patients were divided into two groups according to the type of adnexal surgery: unilateral oophorectomy or salpingo-oophorectomy (USO group) and unilateral ovarian cystectomy (UOC group). Surgical, oncological, and reproductive outcomes were compared.

**Results:** A total of 263 patients (85.1%) underwent USO and 46 (14.9%) underwent UOC. After a median of 53 months of follow-up (range: 6–249), 13 patients in the USO group (4.9%) and 4 patients in the UOC group (8.9%), respectively, had recurrent disease ( $P = 0.288$ ), and three (1.1%) and none (0%), respectively, died of disease ( $P > 0.999$ ). Two patients from the UOC group had recurrence on the same side of the ovary, and two had recurrence in the opposite ovary. All patients underwent a successful salvage operation.

**Conclusion/Implications:** The recurrence rate after UOC in women with stage I unilateral BOTs was higher than that after USO. However, the difference was not significant, and all recurrences were successfully salvaged by secondary surgery. Overall survival was not compromised after UOC. Therefore, UOC can be considered in patients with stage I unilateral BOT who do not have other options for fertility preservation.

EP299 / #684

Topic: AS11. Ovarian Cancer

## PHARMACOKINETICS, TOXICITIES, AND TISSUE CONCENTRATIONS OF GEMCITABINE SPRAYED BY ROTATIONAL INTRAPERITONEAL PRESSURIZED AEROSOL CHEMOTHERAPY IN A PIG MODEL

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**Introduction:** We evaluated the pharmacokinetics, tissue concentrations, and toxicities of gemcitabine during rotational intraperitoneal pressurized aerosol chemotherapy (RIPAC) in pigs.

**Methods:** We sprayed gemcitabine of 10% and 30% of doses for intravenous chemotherapy in six pigs (cohort 1, n=3, 300 mg/m<sup>2</sup>; cohort 2, n=3, 1,000 mg/m<sup>2</sup>). We evaluated the time-dependent plasma concentrations of gemcitabine before RIPAC to 120 hr for the pharmacokinetics, tissue concentrations in twelve peritoneal regions, and hepatic and renal functions before RIPAC to 120 hr in the two cohorts.

**Results:** Mean values of the peak plasma concentration ( $C_{max}$ ), the time to  $C_{max}$  ( $T_{max}$ ), the time taken for  $C_{max}$  to drop in half ( $T_{1/2}$ ), and the area under the curve from time zero to the time of last quantifiable concentration ( $AUC_{last}$ ) were 1,320 and 7,476 ng/ml, 1.92 and 1.83 hr, 1.52 and 1.96 hr, and 4,718 and 26,347 ng·hr/ml in cohorts 1 and 2, respectively. Mean values of tissue concentrations were 1.3 to 11.2 times higher than in cohort 2 and in cohort 1 despite the similar ratio of tissue to plasma concentration, and tissue concentrations in the two cohorts were higher in the parietal peritoneum than in the visceral peritoneum. Cohort 2 showed the change of hepatic function after RIPAC, whereas there were no changes of hepatic and renal functions in cohort 1.

**Conclusion/Implications:** Considering the change of hepatic function in gemcitabine of 1,000 mg/m<sup>2</sup>, gemcitabine of 300 mg/m<sup>2</sup> can be considered as the starting dose for RIPAC in a phase 1 trial.



EP301 / #199

**Topic: AS11. Ovarian Cancer**

## **A STUDY OF SURGICO-PATHOLOGICAL SPECTRUM AND LYMPH NODE EVALUATION IN EPITHELIAL OVARIAN CANCERS: AN AMBISPECTIVE STUDY**

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**Introduction:** Consensus regarding lymph node evaluation in epithelial ovarian cancer is emerging. The objective of the present study was to evaluate surgico-pathological findings, lymph node (LN) involvement, and prediction of LN metastasis by preoperative imaging and intraoperative assessment in women with epithelial ovarian cancer (EOC).

**Methods:** Women with EOCs who underwent cytoreductive surgery (CRS) between Jan 2019 to April 2022 were included. Distribution of histology, stage and LN metastasis was studied. Predictive value of radiologic and surgically enlarged LNs with final histopathology was studied.

**Results:** A total of 101 women with EOCs underwent CRS, of which 5 (4.95%) with co-existent endometrial cancer were excluded. Fifty women (52%) underwent primary and 46 women (48%) interval CRS. HGSC was commonest (n=66, 68.75%), followed by mucinous (n=15, 15.63%), endometrioid (n=6, 6.25%), LGSC (n=4, 4.17%) and carcinosarcoma (n=2, 2.08%). Majority of women, 69 (71.88%) were stage III and IV at presentation. Complete cytoreduction was achieved in 75 (78.12%) cases. Seventy-five women (78.13%) of EOC underwent pelvic and/or para-aortic lymphadenectomy, out of which 23 (30.67%) were histologically positive. Both radiologically and surgically enlarged LNs significantly predicted LN metastasis on histopathology (p=0.02 and 0.006 respectively). The combined sensitivity, specificity, PPV, and NPV of both CECT and surgically enlarged LNs was 78.26%, 57.69%, 45%, and 85.71%, respectively

**Conclusion/Implications:** Serous histology, high-grade tumors and suspicious LNs in CECT and during surgery are significantly associated with LN metastasis.

EP303 / #621

Topic: *AS11. Ovarian Cancer*

## **LOW DOSE LENVATINIB PLUS TORIPALIMAB IN PATIENTS WITH HEAVILY PRETREATED GYNECOLOGICAL SOLID TUMORS: A PILOT STUDY**

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**Introduction:** Patients with heavily pretreated gynecological solid tumors have extremely limited treatment options. Lenvatinib combined therapy has efficacy in treating advanced endometrial carcinoma (including non-endometrioid), but nearly half of patients were intolerable toxicity of the recommended doses. Accordingly, we performed this pilot study to evaluate the efficacy and safety of low dose lenvatinib plus toripalimab in patients with heavily pretreated gynecological solid tumors.

**Methods:** Lenvatinib was administered with a starting dose of 8 or 12 mg orally once daily based on patient's body weight and an intravenous infusion of toripalimab was received at a dose of 240 mg every 3 weeks. Patients received therapy for up to 24 months until disease progression or unacceptable toxicity. The primary endpoint was progression free survival (PFS).

**Results:** Twenty-one patients (ovarian, n=14; endometrial, n=6; vulvar, n=1), who experienced disease progression after prior median 3 lines of systemic therapy, were enrolled and treated from September 2021 to April 2023. In the 21 patients, the median PFS was 5.0 months, the median duration of response (DOR) was 5.2 months, and disease control rate(DCR) was 38.1%. The most common grade 3 treatment-related adverse events(TRAEs) were hypertension (33.3%) and proteinuria (9.5%), respectively. No grade 4 TRAEs occurred.

**Conclusion/Implications:** This study, to our knowledge, is the first to explore the effects of low-dose lenvatinib plus Toripalimab in gynecological solid tumors. The encouraging efficacy and safety of this pilot study strongly support the further investigation of low-dose Lenvatinib plus Toripalimab in patients with heavily pretreated gynecological solid tumors.

EP304 / #430

Topic: *AS11. Ovarian Cancer*

## **AUTOPHAGY DEFECT AND ITS CLINICAL SIGNIFICANCE IN SEROUS OVARIAN CARCINOMA**

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**Introduction:** Autophagy is a physiological cellular process for degradation and recycle of useless proteins, however it maintains survival of cancer cells with defects in apoptosis. This study aimed to evaluate autophagy status and the clinical significance in serous ovarian carcinoma (SOC).

**Methods:** Tissue microarray including 72 SOC, 10 serous adenoma, and 13 borderline serous tumors was used for immunohistochemical analysis. Immunoreactivity of LC3, Beclin-1, p62 and TFEB were semi-quantitatively scored. Clinicopathological parameters were obtained from medical records. Kaplan-Meier estimate and the Cox regression were used for survival analysis.

**Results:** LC3 and TFEB were present in 31.9% and 20.8% of SOC. Beclin-1 and p62 were significantly upregulated in SOC compared with controls (70.8% and 95.8%;  $p = 0.03$  and  $p < 0.001$ , respectively). Significant correlation was observed among LC3, Beclin-1 and p62. A simultaneous accumulation of Beclin-1 and p62 represents coexistence of induction and last stage of autophagy, suggesting autophagy activation with impairment of autophagy flux. In univariate analysis, the presence of TFEB, suboptimality, advanced FIGO stage, and chemoresistance were significantly associated with worse disease-free survival and overall survival (OS). Multivariate analysis showed that surgical optimality and chemoresistance were independent predictor for OS. The expressions of p62 and TFEB were positively correlated with FIGO stage ( $p = 0.017$  and  $p = 0.015$ , respectively) and Beclin-1 expression was lower in high-grade tumor than low-grade tumor ( $p = 0.001$ ).

**Conclusion/Implications:** A dysregulation of autophagy was found in SOC. Beclin-1, p62 and TFEB were associated with aggressiveness and poor prognosis of SOC.

EP305 / #401

**Topic: AS11. Ovarian Cancer**

## **NEUTROPHIL LYMPHOCYTE RATIO AND PLATELET LYMPHOCYTE RATIO AS PROGNOSTIC MARKERS IN OVARIAN CANCER**

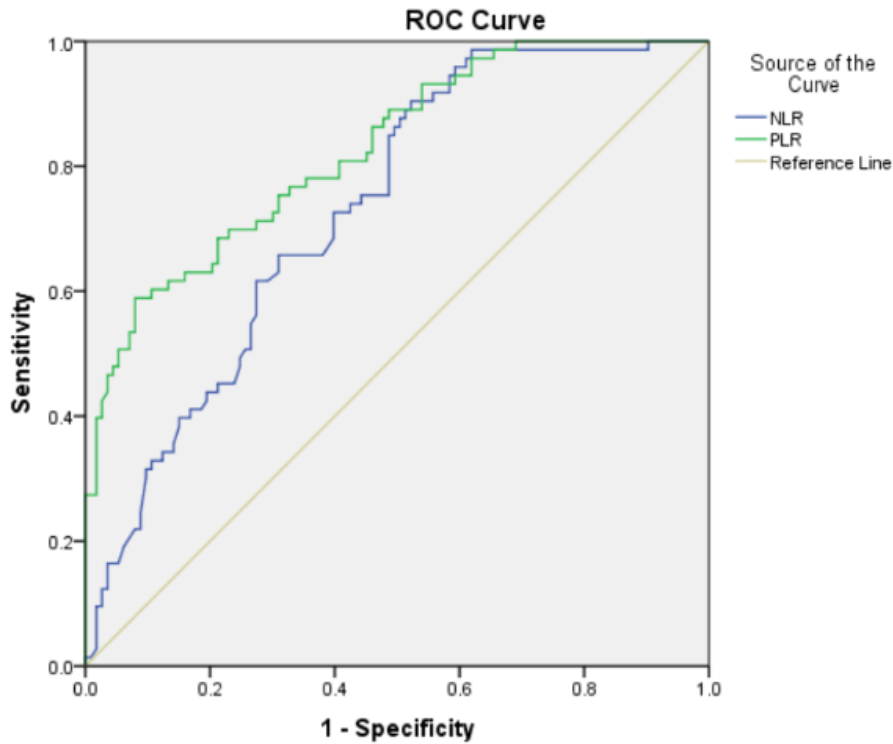
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**Introduction:** Inflammation plays an essential role in tumour development in cancer initiation, progression and metastasis. Immune cell components of blood count offer an attractive measure of inflammation being part of routine clinical care at minimal cost and inconvenience to the patient. It is hypothesised that raised Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) are two such markers associated with poor prognosis in ovarian cancer. Hence, this study was conducted to find association NLR and PLR with survival outcome in ovarian cancer.

**Methods:** This study was conducted in a tertiary care teaching hospital after ethical clearance from Institutional ethics committee and written informed consent from all patients recruited. Records of 260 ovarian cancer cases admitted over five years were retrospectively searched for pretreatment neutrophil, lymphocyte and platelet counts to calculate NLR and PLR. Details of demography, disease characteristics, treatment and recurrence were recorded. Survival outcomes were correlated with the NLR and PLR. Statistical analysis was performed on SPSS version 21 using ROC curves and correlation analysis.

**Results:** NLR and PLR had negative correlation with 5-year overall survival rate. ROC analysis showed that NLR below 2.8 was associated with 5 year OS of 72.2% while NLR above 2.8 was associated with OS of 27.8 %. PLR below 204 was associated with 5 year OS of 77.7% while that above 204 was associated with 5 year OS of

22.3%.



Parameter	Area under curve	SE	'p'	95% CI	
				Lower bound	Upper bound
NLR	0.732	0.036	<0.001	0.662	0.803
PLR	0.826	0.030	<0.001	0.767	0.886

**Conclusion/Implications:** Both Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio are independent prognostic inflammatory markers for survival of ovarian cancer.

EP306 / #96

Topic: *AS11. Ovarian Cancer*

## **IMPACT OF OBESITY ON TREATMENT AND SURVIVAL OUTCOME IN EPITHELIAL OVARIAN CANCER PATIENT: A 10-YEAR RETROSPECTIVE STUDY**

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**Introduction:** To evaluate the impact of obesity on surgical outcomes, adverse effects of chemotherapy, and survival outcomes among patients with epithelial ovarian cancer in the Thai population.

**Methods:** We retrospectively reviewed the medical records of epithelial ovarian cancer patients who underwent staging laparotomy at Siriraj Hospital from January 2008 to December 2018. Patient characteristics, surgical outcomes, chemotherapy-related complications, and survival were compared between non-obese (BMI < 25.0) and obese (BMI ≥ 25) patients using the Western Pacific Regional Office (WPRO) BMI cut-off criteria.

**Results:** Of the 444 patients initially included, 18 were excluded, leaving 426 patients for analysis, with 21.9% (n=93) in the obesity group and 78.1% (n=333) in the non-obesity group. The obesity group had a higher incidence of diabetes mellitus (P < 0.0001), hypertension (P = 0.003), and dyslipidemia (P = 0.027) than the non-obesity group. Obesity was independently associated with postoperative complications, including wound problems (adjusted OR: 6.175; 95% CI: 1.891-13.191; P<0.001) and venous thromboembolism (adjusted OR: 5.991; 95% CI: 2.848-12.605; P<0.001), but fewer event of neutropenia (P=0.002) and delays in chemotherapy administration (P=0.015). The two groups had no significant difference in progression-free survival (P = 0.135) or five-year overall survival (P = 0.923).

**Conclusion/Implications:** Obesity does not affect survival outcomes in patients with epithelial ovarian cancer but increases the risk of postoperative complications, including wound complications and venous thromboembolism.

EP307 / #763

Topic: **AS11. Ovarian Cancer**

## **CLINICOPATHOLOGIC FACTORS ASSOCIATED WITH LONG-TERM SURVIVAL IN ADVANCED EPITHELIAL OVARIAN CANCER**

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**Introduction:** The 5-year survival rate for patients with advanced epithelial ovarian cancer remains poor. Given the high mortality associated with this disease, it is important to analyze the factors associated with long-term survival beyond 5 years.

**Methods:** We retrospectively analyzed data from patients with stage III or IV epithelial ovarian cancer diagnosed from 2013 to 2019. Characteristics of women who survived  $\geq 5$  years after diagnosis were compared to those who survived fewer than 5 years of diagnosis using chi-square tests and multivariable logistic regression.

**Results:** Of the 345 patients who survived more than 5 years, 214 (62%) experienced recurrence, and 43 (12.5%) died with disease during a median f/u time of 78 (60-144) months. The long-term survivors were more likely to receive the primary cytoreductive surgery (85.0% in  $\geq 5$ year group, 68.9% in  $< 5$ year group,  $p < 0.001$ ) and had higher ratio of no gross residual disease (78.3% in  $\geq 5$ year group, 60.4% in  $< 5$ year group,  $p < 0.001$ ). They had a higher rate of BRCA mutation ( $p = 0.001$ ), longer progression-free survival (median 44.5 vs. 18.0 months in  $\geq 5$ year group vs.  $< 5$ year group,  $p < 0.001$ ). In addition, when the disease recurred, they received more aggressive surgical treatments after disease recurrence (24.6% in  $\geq 5$ year group, 8.3% in  $< 5$ year group,  $p < 0.001$ ).

**Conclusion/Implications:** Long-term survival is not common in patients with epithelial ovarian cancer, even in advanced cases. Although several prognostic factors are well known, there is a need to follow up on the current state of knowledge of relevant factors in long-term survivors. These findings are important for patient counselling.

EP308 / #1547

Topic: *AS11. Ovarian Cancer*

## **THE IMPACT OF LYMPH NODE DISSECTION ON SURVIVAL IN PATIENTS WITH STAGE I OVARIAN ENDOMETRIOID CARCINOMA**

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**Introduction:** Compared with other pathological types, the prognosis of ovarian endometrioid carcinoma (OEC) is better. The treatment of OEC follows the general principles of epithelial ovarian cancer treatment, with comprehensive staging surgery and tumor reduction surgery. However, patients underwent lymphadenectomy may affect their quality of life. This study investigated the value of lymph node dissection in improving the prognosis of early stage OEC patients and sought the optimal number of lymph node resections.

**Methods:** We collected and organized the clinical and pathological materials of 2717 postoperative patients with stage I OEC in the SEER database from 2004 to 2018. Uni- and multi- Cox regression models were used to screen for the independent risk factors and divide patients into subgroups. Kaplan-Meier was used for survival analysis in subgroups to explore the relationship between lymph node dissection and survival in stage I OEC patients. We used Cox regression combined with restricted cubic spline (RCS) function to analyze the optimal number of lymph node dissections (LNN).

**Results:** Age, marital status, tumor size, histological grade, and lymphadenectomy are independent risk factors affecting the overall survival (OS) of stage I OEC patients. Patients who underwent lymphadenectomy had an improved OS compared to those who did not. Cox regression analysis and restrictive cubic spline function analysis suggests that when LNN is 21, patients receive the best survival benefit.

**Conclusion/Implications:** Lymphectomy can improve the prognosis of stage I OEC patients, and we recommend 21 LNNs as the entry point for evaluating the stratification of prognosis in stage I OEC patients.



EP309 / #597

**Topic: AS11. Ovarian Cancer**

## **HISTONE LACTYLATION INDUCES CISPLATIN RESISTANCE IN OVARIAN CANCER VIA IMPROVING HOMOLOGOUS RECOMBINATION REPAIR**

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**Introduction:** Ovarian cancer is a fatal tumor in the female, majorly associated with chemotherapy resistance. Lactylation, a novel post-translational modification, is proven to be involved in multiple biological processes. This study aims to unravel the role of histone lactylation in the development of chemoresistance in ovarian cancer.

**Methods:** We utilized GSEA to investigate alterations in glycolysis in cisplatin sensitive/resistant patients. Differential expression of H3K9la was demonstrated using WB and IHC. Cell viability or apoptosis were measured using CCK8 or apoptosis kit, respectively. Then ChiP-seq and ChiP-qPCR were performed to identify downstream targets of H3K9la. GCN5, the potential regulator of H3K9la, was validated using protein-protein interactions and cell experiments. And IP-mass spectrometry was used to identify lactylation sites for non-histone. Lastly, we established ovarian cancer PDX models to validate the therapeutic effects of GCN5.

**Results:** Cisplatin-resistant ovarian cancer is characterized by increased glycolysis and H3K9la expression. Inhibiting glycolysis decreased H3K9la levels and made ovarian cancer cells more sensitive to cisplatin. RAD50 were targets of H3K9la, which facilitated HR repair and conferred cisplatin resistance. Our study also found that lactylation of RAD50 enhanced HR repair. Additionally, GCN5 was identified as an upregulator of H3K9la. When combined with cisplatin, CPTH2 was effective in repressing tumor growth and burden of PDX models.

**Conclusion/Implications:** Our study demonstrates the crucial importance of histone lactylation in regulating cisplatin response of ovarian cancer. Additionally, we identified novel potential therapy targets to overcome chemotherapy resistance, improving prognosis for patients.

EP310 / #537

Topic: *AS11. Ovarian Cancer*

## **SPATIAL HETEROGENEITY OF THE ACTIONABLE GENOMIC ALTERATIONS IN OVARIAN CLEAR CELL CARCINOMA**

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**Introduction:** Spatial heterogeneity in malignant tumors (heterogenous distribution of genetically diverse tumor subpopulations across different sites) is associated with resistance to treatment. The current study aimed to identify the spatial heterogeneity of the actionable genomic alterations (AGAs) in ovarian clear cell carcinoma (OCCC).

**Methods:** Advanced OCCCs with four or more metastatic lesions resected at primary debulking surgery were included. Genomic DNA extracted from the formalin-fixed paraffin-embedded blocks of multiple cancerous lesions was analyzed by targeted deep sequencing with the custom panel including 84 OCCC-related genes. The genomic profiles of multiple cancerous lesions were compared to identify the spatial heterogeneity of the AGAs in individual cases.

**Results:** Fifty cancerous lesions obtained from eight OCCCs were analyzed, and seventy-six potentially pathogenic variants (sixteen types of AGAs in six genes) were identified in five of eight OCCCs. Fifteen of sixteen AGAs in six genes, including ARID1A, PIK3CA, CTNNB1, TP53, PIK3R1, and KRAS, were shared across the primary and all metastatic lesions. However, in one case, the AGA of PIK3CA was only detected in the omental dissemination in which KRAS mutations were shown in all cancerous lesions.

**Conclusion/Implications:** One AGA in PIK3CA showed spatial heterogeneity in advanced OCCC, suggesting that therapeutic strategies considering the spatial heterogeneity of the AGAs may be required in OCCC.

EP311 / #691

Topic: *AS11. Ovarian Cancer*

## **EFFICACY OF THE PORCUPINE INHIBITOR ETC-1922159 (ETC-159) PLUS PEMBROLIZUMAB IN MICROSATELLITE STABLE (MSS) OR PROFICIENT MISMATCH REPAIR (pMMR) PLATINUM RESISTANT OVARIAN CARCINOMAS (PROC)**

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**Introduction:** PD-(L1) inhibitors have limited efficacy in MSS/pMMR recurrent ovarian cancers. Upregulation of the Wnt pathway has been associated with immune exclusion in the tumour microenvironment. ETC-159 is a small molecule porcupine inhibitor that suppresses WNT secretion. Ph1B trial explored the combination of ETC-159 with PD-1 inhibition in PROC.

**Methods:** In a Phase 1B open label study patients  $\geq 18$  years, with adequate organ function and MSS/pMMR PROC were eligible. ETC-159 was dosed orally QOD in combination with 200 mg pembrolizumab IV every 21 days. Responses were evaluated via RECIST1.1 and iRECIST. PK, PD and tumour profiling were assessed at multiple time points throughout the trial.

**Results:** Six PROC patients were treated with the combination in dose escalation & expansion. The majority (66%) were high- grade serous ovarian carcinomas with a median 4 lines (2-7) of previous treatments. SAEs were pneumonitis and erythema with fever (8 mg, 1 patient). No fractures or other skeletal SAEs were observed. Of 6 evaluable patients, two patients had a PR. 1 harbouring a SUFU-1 mutation (on treatment for 27 weeks) and another with BRCA2 mutant who had progressed on PARPi and immunotherapy. Two others achieved SD as best response for 12 and 18 weeks, respectively, with 1 more currently ongoing. A disease control rate (SD/PR/CR  $\geq 12$  weeks) of 67% was observed.

**Conclusion/Implications:** Preliminary data suggest Wnt signalling inhibition with ETC-159 in combination with pembrolizumab is tolerable with no unexpected safety signals and may provide clinical benefit for platinum resistant MSS/pMMR ovarian cancer patients.

EP312 / #540

Topic: *AS11. Ovarian Cancer*

## **INTRAPERITONEAL CHEMOTHERAPY WITHOUT BEVACIZUMAB VERSUS INTRAVENOUS CHEMOTHERAPY PLUS BEVACIZUMAB AS FRONTLINE THERAPY IN ADVANCED OVARIAN CANCER**

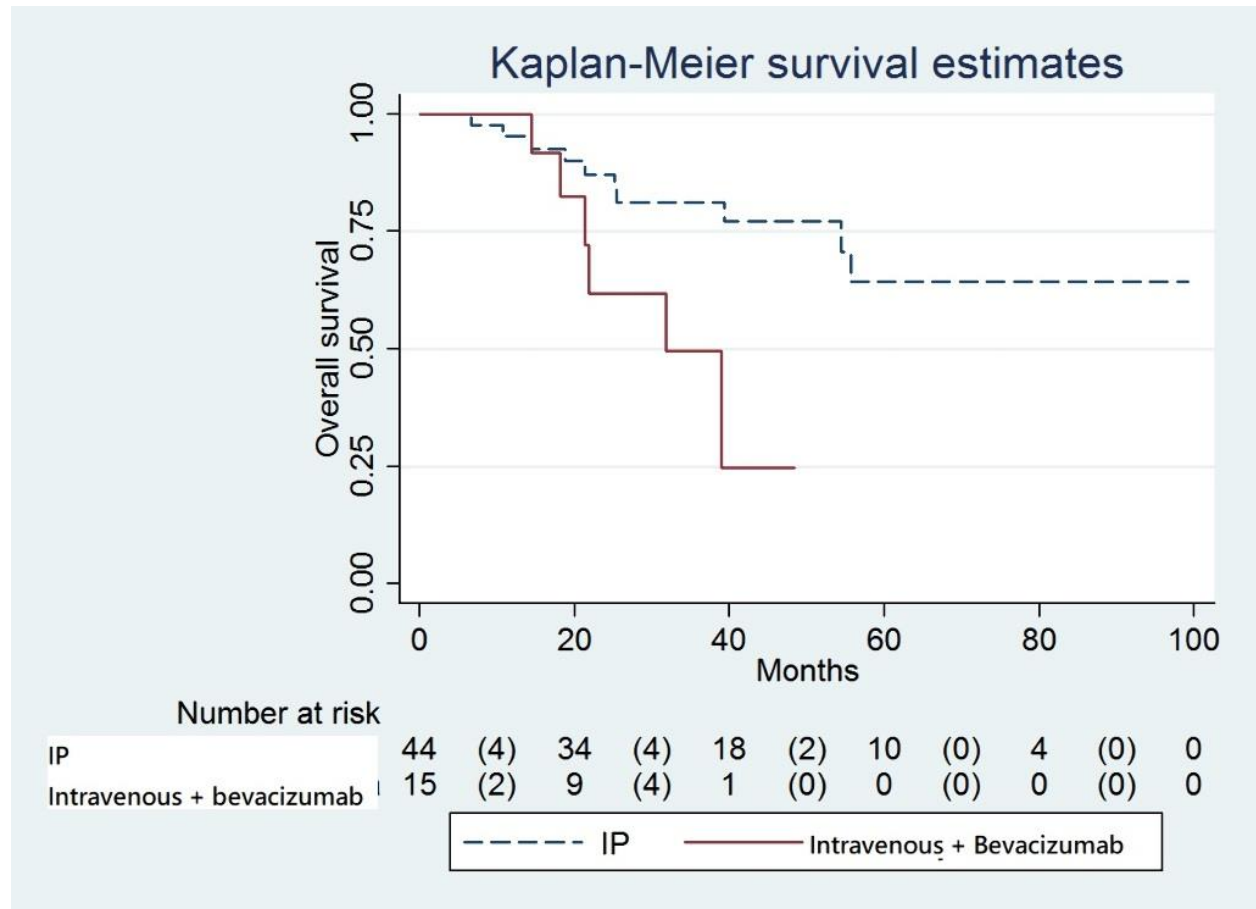
Wan Hua Stella Ting, Hsiao-Feng Wang, Hui-Hua Chen, Hsu-Dong Sun, Ming-Chow Wei, Sheng-Mou Hsiao

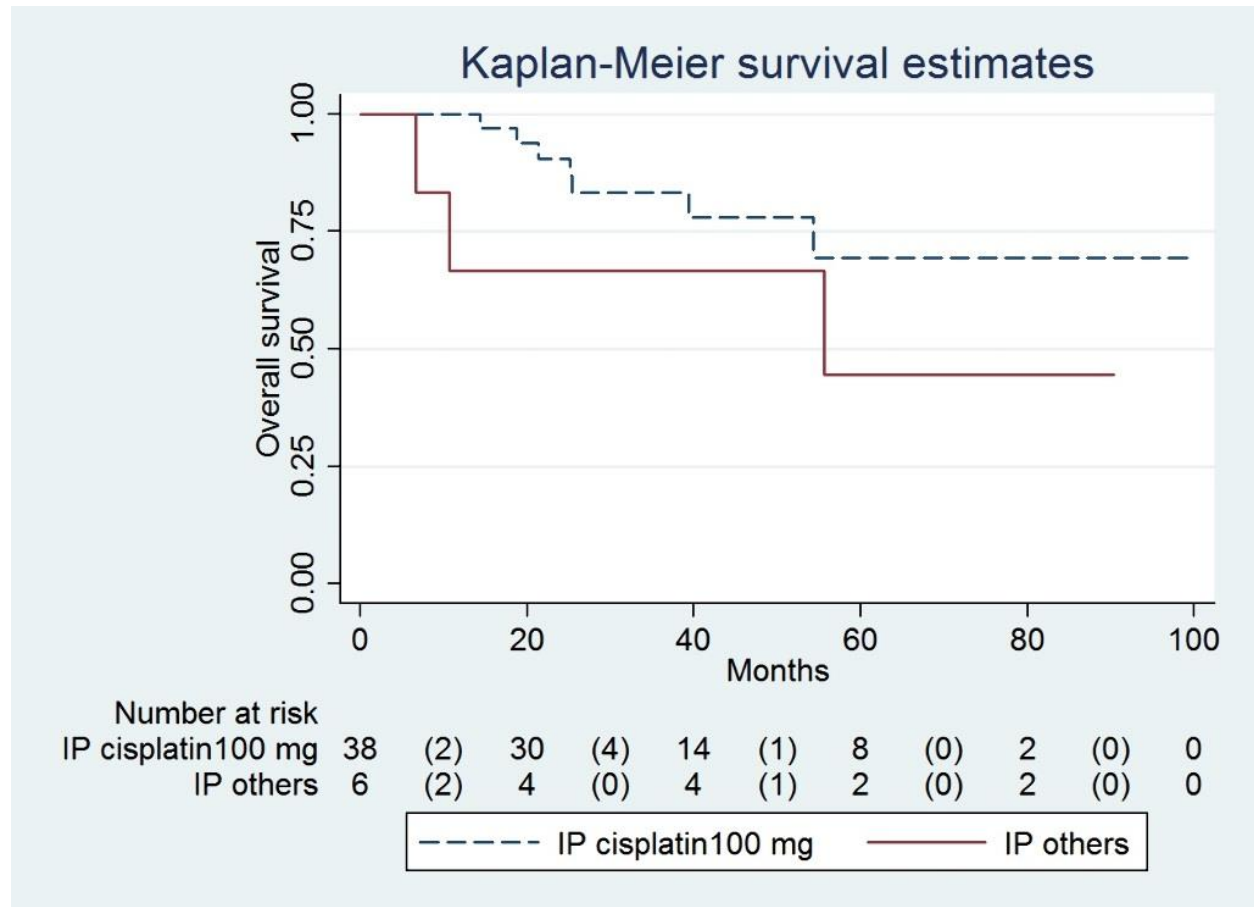
Far Eastern Memorial Hospital, Department Of Obstetrics And Gynecology, New Taipei City, Taiwan

**Introduction:** To compare the clinical outcomes between intravenous carboplatin/paclitaxel chemotherapy plus bevacizumab versus intraperitoneal cisplatin/paclitaxel chemotherapy without bevacizumab as the frontline treatment in women with advanced ovarian, fallopian tube and primary peritoneal cancer.

**Methods:** All consecutive women with stage II~IV cancer treated with either frontline intraperitoneal cisplatin/paclitaxel without bevacizumab (IP group) or intravenous carboplatin/paclitaxel with bevacizumab (IVB group) at a tertiary referral center were reviewed.

**Results:** A total of 59 women (IP group, n=44; IVB group, n=15) were reviewed. There was no significant difference in the progression-free survival (median: 33.6 versus 14.8 months, p=0.13). However, overall survival (OS) was significantly higher in the IP group, compared with the IVB group (median: not reached versus 31.7 months, p=0.02; adjusted hazard ratio (HR)=0.35, 95% confidence interval (CI)=0.10 to 1.07, p=0.065, Figure 1). Additional predictors for OS include cancer stage and the number of chemotherapy cycles. Besides, the standard dose of 100 mg/m<sup>2</sup> cisplatin was a predictor for OS, compared with other intraperitoneal regimens (adjusted HR=0.14, 95% CI=0.02 to 0.87, p=0.03, Figure 2).





**Conclusion/Implications:** Intraperitoneal cisplatin/paclitaxel chemotherapy without bevacizumab seems to be better in OS, compared to intravenous carboplatin/paclitaxel chemotherapy with bevacizumab in the frontline treatment of women with advanced ovarian cancer.

EP313 / #916

Topic: *AS11. Ovarian Cancer*

## LIMITATION OF CA125 IN PREDICTING COMPLETE RESECTION AFTER NEOADJUVANT CHEMOTHERAPY IN ADVANCED OVARIAN CANCER

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**Introduction:** The optimal timing of interval debulking surgery (IDS) after neoadjuvant chemotherapy (NACT) in advanced epithelial ovarian cancer (EOC) is uncertain. Hence, there is a need to have a reliable test that can predict the feasibility of CC0.

**Methods:** Patients with stage III/IV EOC, fallopian tube, or primary peritoneal cancer treated in 2016-2021 were identified from a single institution. Their clinical parameters and surgical records reviewed retrospectively.

**Results:** 260 eligible patients were identified. 125 patients (54.3%) received NACT, among which 2 (1.6%) had non-evaluable CA125 (i.e., baseline is <2x upper normal limit), and 14 (11.2%) could not undergo IDS due to disease burden. Finally, 100 patients with documentation on the CC0 were included in the analysis (Table 1). CC0 rate was 67%. Univariate analysis showed that the presence of ascites, diaphragmatic and mesenteric masses, median change of CA125 level, median Fagotti's score based on pre-operative imaging, were significantly associated with CC0. Multivariate analysis showed that the change of CA125 level was not significant ( $p=0.069$ , odds ratio (OR) 0.968; 95% confidence interval (CI) 0.934–1.003), and the only significant parameter was pre-operative radiological Fagotti's score ( $p=0.008$ ; OR 1.521; 95% CI 1.117–2.071). Receiver operating characteristics (ROC) curve analysis showed that the area under the curve (AUC) of CA125 in predicting CC0 was 0.678 and 0.740 respectively (Figure 1), and the estimated sensitivity of CA125 was 0.53 only.

**Conclusion/Implications:** 260 eligible patients were identified. 125 patients (54.3%) received NACT, among which 2 (1.6%) had non-evaluable CA125 (i.e., baseline is <2x upper normal limit), and 14 (11.2%) could not undergo IDS due to disease burden. Finally, 100 patients with documentation on the CC0 were included in the analysis (Table 1). CC0 rate was 67%. Univariate analysis showed that the presence of ascites, diaphragmatic and mesenteric masses, median change of CA125 level, median Fagotti's score based on pre-operative imaging, were significantly associated with CC0. Multivariate analysis showed that the change of CA125 level was not significant ( $p=0.069$ , odds ratio (OR) 0.968; 95% confidence interval (CI) 0.934–1.003), and the only significant parameter was pre-operative radiological Fagotti's score ( $p=0.008$ ; OR 1.521; 95% CI 1.117–2.071). Receiver operating characteristics (ROC) curve analysis showed that the area under the curve (AUC) of CA125 in predicting CC0 was 0.678 and 0.740 respectively (Figure 1), and the estimated sensitivity of CA125 was 0.53 only. We estimated the Youden index and the point closest to-(0,1) corner in the ROC curve of CA125, and the sensitivity was 0.53 from the latter.

The result highlighted the insufficiency of CA125 in predicting CC0. More simple and novel markers are needed to predict the feasibility of CC0.

Parameters	Demographic data		Univariate analysis		
	n = 100		p value	OR	95% CI of OR
Age (years, range)	59.5 (11 - 75)		0.355	0.983	0.948 - 1.019
Body mass index (kg/m <sup>2</sup> , range)	22.0 (15.3 - 32.5)		0.171	0.917	0.81 - 1.038
Diagnosis					
CA ovary	68 (68.0%)				
CA fallopian tube	8 (8.0%)				
CA peritoneum	24 (24.0%)				
Stage					
3a	3 (3.0%)				
3b	5 (5.0%)				
3c	37 (37.0%)				
4	55 (55.0%)				
Histology		0.674	0.772	0.231	2.577
high-grade serous	66 (66.9%)				
clear cell	3 (3.0%)				
endometrioid	4 (4.0%)				
mucinous	5 (5.1%)				
dedifferentiated	1 (1.0%)				
non-specific	1				
BRCA status		0.769	1.176	0.398	3.477
germline / somatic wild-type	43 (58.9%)				
germline / somatic mutant	27 (37.0%)				
VUS	3 (4.1%)				
not done or missing	27				
Presence of metastasis at diagnosis					
ascites	29/92 (31.5%)	0.008	0.279	0.108	0.72
diaphragmatic lesion (mass or plaque)	28/87 (32.2%)	0.031	0.34	0.128	0.908
mesenteric mass (mass or retraction)	27/87 (31.0%)	0.001	0.186	0.067	0.513
spleen metastasis	6/92 (6.5%)	0.059	0.183	0.031	1.064
lung metastasis	4/92 (4.3%)	0.366	0.397	0.053	2.973
pleural metastasis (nodule or pathologically proven)	3/92 (3.3%)	0.19	0.195	0.017	2.251
distant lymph node metastasis	3/92 (3.3%)	0.19	0.195	0.017	2.251
Median number of cycles of neoadjuvant chemotherapy (n, range)	4 (3 - 9)	0.1	1.312	0.95	1.813
3 - 4 cycles	77 (77.0%)				
≥ 6 cycles	23 (23.0%)				
Use of avastin	6 (6.0%)	0.381	2.1	0.4	11.026
Use of HIPEC	21 (21.0%)				
Median CA125 change (from baseline to time of IDS)(%, range)	96.0% (-26.7 - 100.0%)	0.026	0.964	0.933	0.995
Median radiological Fagotti's score before IDS	2 (0 - 8)	<.0.001	1.607	1.25	2.065
Residual disease					
CC0	67 (67.0%)				
CC1-3	33 (33.0%)				
Chemotherapy response score					
1	14 (22.6%)				
2	29 (46.8%)				
3	19 (30.6%)				
missing	38				
Median progression-free survival (months, range)	20.0 (16.2 - 23.6)				
Median overall survival (months, range)	47.0 (35.6 - 58.4)				



Table 1 Demographic data of patients receiving neoadjuvant chemotherapy and univariate analysis of different parameters predictive of complete resection (CC0, no residual disease; CC1, residual disease <2.5 mm; CC2, residual 2.5 – 25 mm; CC3, residual disease > 25 mm; IDS, interval debulking surgery)

## Change of CA125 from baseline to time at IDS

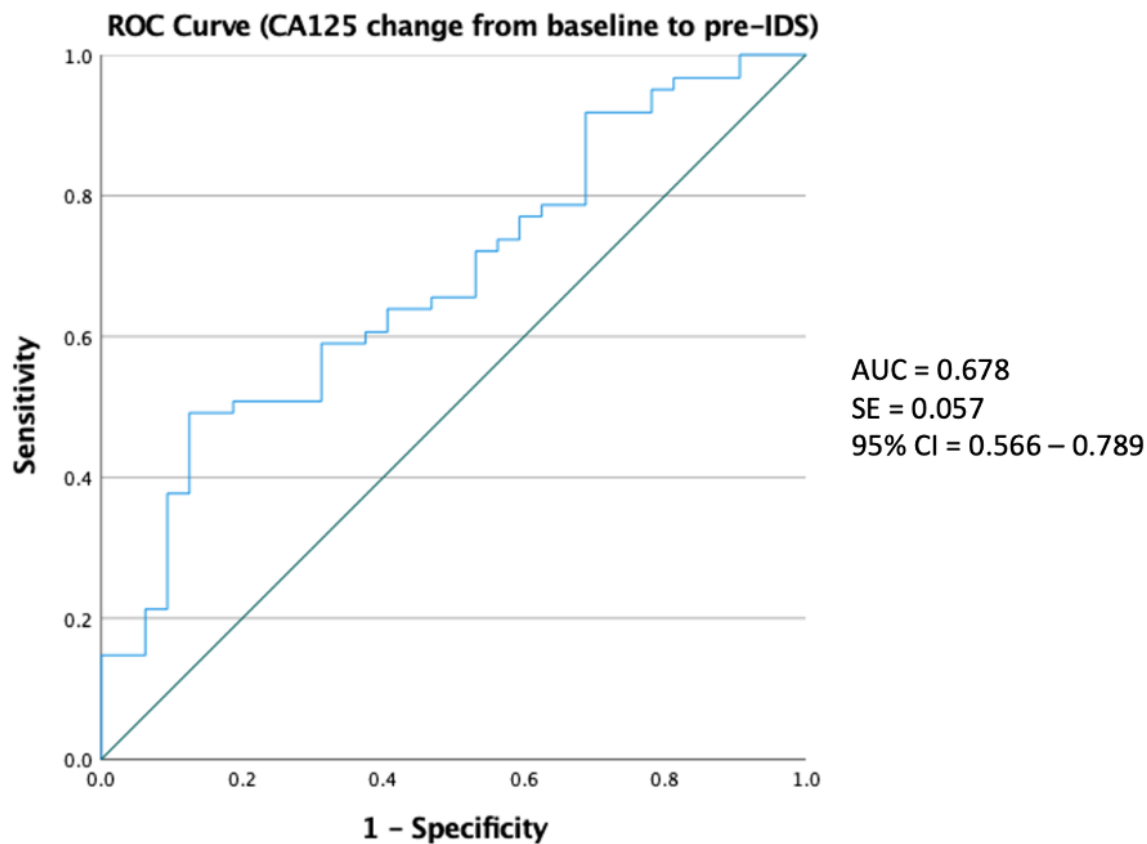


Figure 1 Area under the curve (AUC) for CA125 change and radiological Fagotti's score in predicting complete resection (CC0) in our cohort

EP314 / #349

**Topic: AS11. Ovarian Cancer**

## **FYN EXPRESSION IS ASSOCIATED WITH SENSITIVITY TO PLATINUM-BASED CHEMOTHERAPY FOR OVARIAN SEROUS CARCINOMA**

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**Introduction:** We examined the correlation between Fyn expression and the sensitivity to platinum-based chemotherapy for ovarian serous carcinoma.

**Methods:** We reviewed 64 cases of ovarian serous carcinoma stage III-IV from 2005 to 2014. Cases were divided into two groups one group in which maximum debulking surgery followed by platinum-based chemotherapy was performed and did not recur within 6 months after initialization of chemotherapy (group A; n=32), and another group in which maximum debulking surgery followed by platinum-based chemotherapy was performed and recur within 6 months (group B; n=32). Fyn expression was examined immunohistochemically in paraffin-embedded sections using the avidin-biotin peroxidase complex method. This study was approved by the institutional review board in our facility.

**Results:** The expression of Fyn was significantly higher in the group B than in the group A ( $p < 0.01$ ). Cases were divided into two groups according to a cutoff value of 6 which was calculated using a receiver operating characteristic curve: one group in which Fyn expression was low level (weighted score  $\leq 6$ , n=32), and another group in which Fyn expression was high level (weighted score  $\geq 8$ , n=32). Low Fyn expression group might be sensitive to platinum-based chemotherapy than high expression group ( $p = 0.04$ ). There was no significant difference in overall survival between two groups ( $P = 0.05$ ).

**Conclusion/Implications:** Expression of Fyn might be associated with sensitivity to platinum-based chemotherapy for advanced ovarian serous carcinoma.

EP315 / #771

**Topic: AS11. Ovarian Cancer**

## **HYPERSPECTRAL IMAGING FOR THE IN VIVO DETECTION OF OVARIAN CANCER**

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**Introduction:** For women diagnosed with advanced-stage epithelial ovarian cancer, complete cytoreductive surgery (CRS) is the most powerful independent parameter for prolonged survival. An intraoperative imaging technique to detect tumor deposits could help achieve complete CRS. Hyperspectral imaging (HSI) provides information on tissue composition, including tissue oxygenation, hemoglobin-, and tissue water and fat indices. In an earlier ex-vivo study it was shown that HSI can be used for ex-vivo tumor detection. Currently, we are evaluating whether HSI can be used in-vivo to distinguish tumor from healthy tissue.

**Methods:** HSI data of healthy and tumorous peritoneum, omentum, ovary, and mesentery were obtained in-vivo and preprocessed by image calibration and glare removal. The data were correlated to histopathology and used to train classifiers. The ability to delineate tumorous from healthy tissues was determined using leave-one-out cross-validation.

**Results:** A total of 18 images from 12 patients were included. In total 302.258 data points were extracted based on the knowledge of the surgeons and histopathological information. Our data shows that different organs that are affected by ovarian cancer yield different spectra. Additionally, we observe a difference in the spe

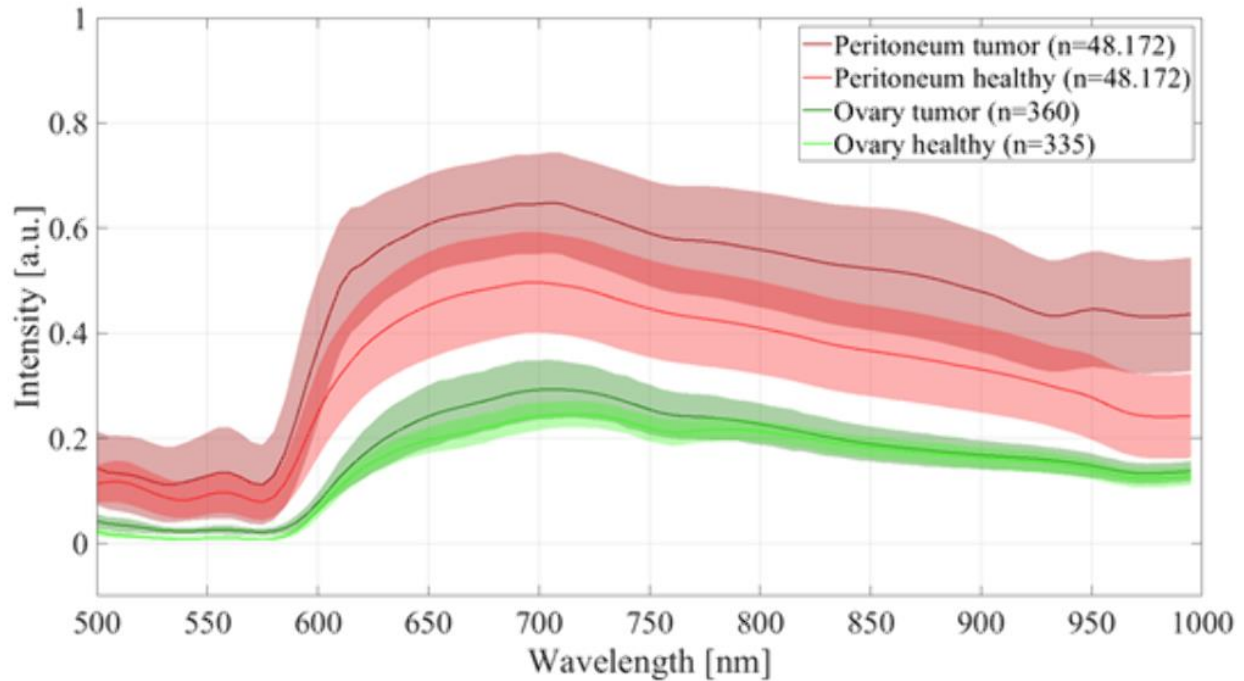


Figure 1: Mean spectra of tumorous and non-tumorous samples of the peritoneum and ovaries with the shaded areas representing the interquartile range, and n the number of datapoints.

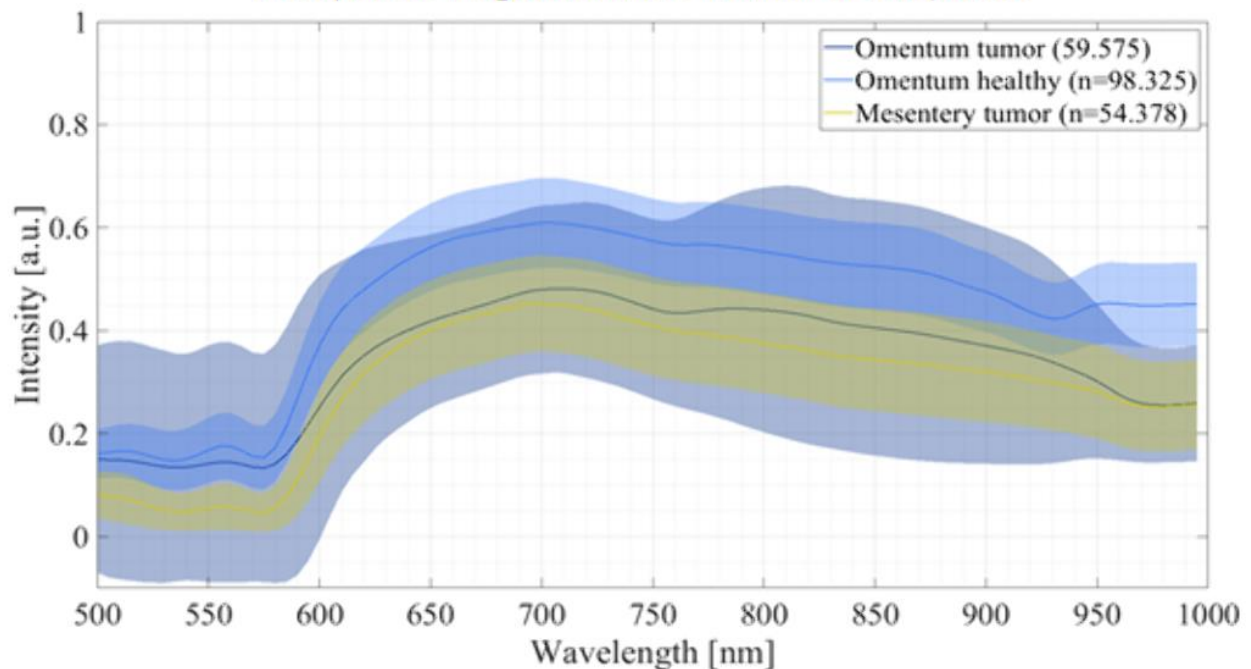


Figure 2: Mean spectra of tumorous and non-tumorous samples of the omentum and the mesentery with the shaded areas representing the interquartile range, and n the number of datapoints.

tra of tumor and non-tumor tissue.

**Conclusion/Implications:** HSI enables the classification of various tissue types, including tumor and non-tumor tissue. To improve classification outcomes, it is crucial to obtain more data and to make separate groups of healthy and tumorous tissues for each of these tissue types. HSI is a promising technique to differentiate between healthy tissue and ovarian cancer lesions and eventually help surgeons to achieve complete CRS.

EP316 / #618

**Topic: AS11. Ovarian Cancer**

## **IMPACT OF PERITONECTOMY ON MORBIDITY AND MORTALITY AND ONCOLOGICAL OUTCOME DURING CYTO-REDUCTIVE SURGERY (CRS) FOR EPITHELIAL OVARIAN CANCER**

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**Introduction:** Cytoreductive surgery (CRS) provides a survival benefit when achieved without residual disease. Total peritoneal peritonectomy (TPP) is a surgical procedure used for complete resection of microscopic peritoneal dissemination.

**Methods:** To assess the impact of peritonectomy on cytoreduction completeness, oncological outcomes, morbidity and mortality in epithelial ovarian cancers. The retrospective analysis of peri and post operative outcome following peritonectomy during CRS was carried out from December 2020 - May 2022 (18 months) All peri and post operative data were analysed with focus on morbidity, mortality and oncological outcomes.

**Results:** From the 46 patients analysed, 27, 17 & 2 were primary debulking, interval debulking & secondary CRS respectively. The Median patients age was 39.5 years. Total peritonectomy was performed in 34 patients and 12 underwent partial peritonectomy. Of the 46 cases, pelvic peritonectomy (31), Right diaphragm peritonectomy (16), lesser omentectomy (38), left diaphragm peritonectomy (8), parietal peritonectomy (41) were performed, respectively. Total of 46 cases, 10 had bowel surgeries, 4 cases had splenectomy, 6 cases had liver deposits/capsule resection. TPP group had longer duration of surgery, higher PCI (median 19.5), higher surgical complexity score (SCS), more blood loss and increased hospital stay. TPP group had increased pulmonary complications, intra-pleural & intra-abdominal collections. There were 4 deaths within 30 days of post operative period.

**Conclusion/Implications:** Performing TPP reduces the chance of missing the microscopic disease, therefore can minimize local recurrence, and better oncological outcomes. TPP can be performed with acceptable morbidity and mortality, at the cost of prolong duration of surgery and higher blood loss.

EP317 / #772

**Topic: AS11. Ovarian Cancer**

## **A TARGETED HOMOGENOUS RECOMBINATION GENE PANEL FOR EPITHELIAL OVARIAN CARCINOMAS WITH DIFFERENT HISTOLOGICAL SUBTYPES AND CLINICAL OUTCOMES**

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**Introduction:** In recent years, promising survival benefits from maintenance therapy with poly (ADP-ribose) polymerase (PARP) inhibitor (PARPi) has changed the management of epithelial ovarian cancer (EOC) in newly diagnosed and recurrent disease. Identification of BRCA and/or homologous recombination (HR) gene mutation is critical for selecting patients for PARPi treatment and as a prognostic and predictive biomarker in high-grade serous carcinoma (HGSOC), yet its role in other histology remains controversial. Our study aims to retrospectively analyze the correlation of BRCA/HR gene mutation with the clinical outcomes of EOC patients.

**Methods:** 318 women diagnosed with EOC who had received debulking surgery and platinum-based adjuvant chemotherapy at NTUH were retrospectively reviewed. The tumor tissue was sent for genetic analysis for somatic mutation of genes in HR gene panel, including BRCA 1/2. Clinical data were obtained from medical records.

**Results:** 25.4% of patients with HGSOC (n = 177) had BRCA/HR mutation and showed better sensitivity to platinum-based chemotherapy (83.9% vs. 69.5%, P=0.029) and longer progression-free survival (PFS) (P=0.004 and <0.001, respectively). However, only 7.8% of patients with non-serous histology had BRCA/HR mutation and showed no correlation with platinum sensitivity, PFS, or overall survival. Through the multivariate analysis, we confirmed the protective effect of BRCA/HR mutation with disease recurrence and death in patients with HGSOC yet no effect was found on non-serous histologic type.

**Conclusion/Implications:** BRCA/HR mutation is a prognostic biomarker in HGSOC yet not in non-serous patients. Further study is needed to follow up on the clinical response to PARPi in these patients and find out other proper prognostic biomarkers.

EP318 / #571

Topic: *AS11. Ovarian Cancer*

## **CIRCULATING TUMOR DNA-BASED MOLECULAR RESIDUAL DISEASE DETECTION FOR THE MONITORING OF HIGH-GRADE SEROUS OVARIAN CANCER**

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**Introduction:** Standard treatment for epithelial ovarian cancer involves surgery and platinum-based chemotherapy, but recurrence or disease progression still occurs in over 70% of patients. CtDNA-based MRD testing may be a potential biomarker for disease surveillance.

**Methods:** Primary ovarian cancer with stage II-IV of HGOC patients was recruited in this study. Tumor sample was collected for whole exome sequencing (300x). Proprietary algorithm was used to select 30-40 single nucleotide variants for each patient. Blood was collected and MRD was detected by multiplex PCR-based sequencing (OriMIRACLE S<sup>TM</sup>, 100,000x) using the customized panel (NCT05027828).

**Results:** As of the summary submission, we have completed WES sequencing for 20 patients, of which 11 carry HRR pathway mutations. Among the 13 patients who underwent pre- and post-operative ctDNA monitoring, 11 were ctDNA positive before surgery. We found a significant decrease in ctDNA variant allele frequency (VAF) before and after surgery (before: median VAF 0.95%, after: median VAF 0.04%,  $p=0.0054$ ). Additionally, Pearson correlation analysis showed a positive correlation between pre-treatment ctDNA VAF and CA125 levels ( $R=0.685$ ,  $p=0.017$ ). The median VAF of ctDNA in stage IV patients was higher than that in stage I-III patients (2.14% vs. 0.56%,  $p=0.69$ ). All the 13 patients were negative for MRD after completion of chemotherapy. Follow-up is ongoing.

**Conclusion/Implications:** MRD testing is feasible for monitoring epithelial ovarian cancer patients, with over 80% of HGSOc patients being MRD-positive at baseline. The MRD status was generally consistent with the clinical status of the patients. The performance of MRD in predicting recurrence of HGSOc is still under investigation.



EP319 / #1479

Topic: AS11. Ovarian Cancer

## OVULATION RELEASES FIBRONECTIN TO PROMOTE PERITONEAL SEEDING OF PRECANCEROUS AND CANCEROUS HIGH-GRADE SEROUS CARCINOMA CELLS ORIGINATING FROM THE FALLOPIAN TUBE EPITHELIUM THROUGH INTEGRIN B1 SIGNALING

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**Introduction:** Previously, we have discovered ovulatory follicular fluid (FF) carries transforming signals to promote full-course carcinogenesis of fallopian tube epithelium (FTE), the origin of ovarian high-grade serous carcinoma[<https://pubmed.ncbi.nlm.nih.gov/33530497/>]. This study investigated FF-fibronectin(FN) in peritoneal seeding of transforming FTE cells.

**Methods:** Partially and fully transformed FTE cells were treated with FF, paired peritoneal fluid (PF), or recombinant FN. Transformation phenotypes were evaluated in FTE cells with/without ITGB1 knock-down. Peritoneal seeding was evaluated by IVIS after i.p. xenograft together with FF in NSG mice.

**Results:** Cell migration-promoting activity was observed after treating with >100-KDa FF or FN protein which was three times higher in FF than in the paired PF. Compared to the full-transformation activity of FF, FN specifically promoted cell proliferation, migration, or invasion. ITGB1- KD caused lower cell proliferation, peritoneal attachment, and AIG. It also reduced the migration-and proliferation-promoting effects of FF and FN. Compared to FF treatment which generally increased p-FAK, p-SRC, p-ERK, and p-AKT, FN treatment increased p-FAK and p-SRC. Looking into the changes in FF- and FN-treated cells, ITGB1-KD resulted in a decrease of p-ERK, p-SRC, or p-FAK and an increase of p-AKT. In the mouse i.p. xenograft tumorigenesis model, depletion of FN from FF showed in a marked reduction of intraperitoneal seedings at week 7, and ITGB1-KD resulted in a decrease at day 12.

**Conclusion/Implications:** The results disclose proliferation-, migration- and invasion-promoting activities of FN abundantly present in ovulatory FF, which promotes peritoneal seedings of transformed FTE cells. Integrin  $\beta$ 1 primarily mediates this activity.

EP321 / #854

**Topic: AS11. Ovarian Cancer**

## **LNCRNA PART1 AUGMENTS PARPI SENSITIVITY IN OVARIAN CANCER**

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**Introduction:** The inhibitor of PARP (PARPi) is one of the most concerned drugs recently. Since both PARPi and platinum act through DNA damage, we intend to find targets for overcoming PARPi resistance through the differences of gene expression between platinum-resistant and platinum-sensitive ovarian patients in TCGA.

**Methods:** We divided ovarian cancer patients in TCGA into platinum-sensitive and platinum-resistant groups and conducted differential gene analysis on them. MTT assay was used to draw the drug concentration tolerance curve of ovarian cancer cells. The effect of PART1 on cell growth was detected by EdU and CCK8 assays. Western blot was used to detect the effect of PART1 on DNA damage repair pathway. The effect of PART1 on PARPi sensitivity in vivo was verified by subcutaneous tumor formation in nude mice. RNA-seq was conducted to analyse the changes of gene and pathways.

**Results:** LncRNA PART1 was significantly down-regulated in platinum-resistant patients in TCGA. CCK8 assays indicated knockdown of PART1 could confer resistance of cisplatin and olaparib on ovarian cancer cells. Cell proliferation was restricted after PART1 knockdown. Western blot experiments showed that PART1 played a role by inactivating the DNA damage response pathway. Subcutaneous tumor formation experiments verified that PART1 can enhance the sensitivity of cells to olaparib and promote proliferation in vivo. The RNA-seq results showed that DNA damage response pathway was significantly activated by PART1 knockdown.

**Conclusion/Implications:** LncRNA PART1 augments PARPi sensitivity in ovarian cancer by inactivating DNA damage response pathway.

EP322 / #101

**Topic: AS11. Ovarian Cancer**

## **COL4A6 PROMOTES TUMOR PROGRESSION AND PREDICTS POOR CLINICAL OUTCOME IN OVARIAN CANCER**

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<sup>1</sup>Chi Mei Medical Center, Liouying Campus, Department Of Medical Research, Tainan, Taiwan, <sup>2</sup>National Cheng Kung University, Department Of Obstetrics And Gynecology, Tainan, Taiwan, <sup>3</sup>Chi Mei Medical Center, Liouying Campus, Department Of Obstetrics And Gynecology, Tainan, Taiwan

**Introduction:** Biomarkers that predict disease progression might assist the development of better therapeutic strategies for aggressive cancers, such as ovarian cancer. Here, we investigated the role of collagen type IV alpha 6 (COL4A6) in cell invasiveness and tumor formation and the prognostic impact of COL4A6 expression in ovarian cancer.

**Methods:** A2780CP70 and OVCAR8 cells transfected with a small interference RNA of COL4A6 (shCOL4A6) and A2780 and OVCAR4 cells transfected with a COL4A6 expression plasmid. Site-directed mutagenesis assay, luciferase assay, chromatin immunoprecipitation assay, invasion assay and xenograft animal study were performed in this study. COL4A6 mRNA expression levels of 160 ovarian tumors were determined by real-time RT-PCR.

**Results:** Small interference RNA-mediated specific reduction in COL4A6 protein levels suppressed the invasive ability and oncogenic potential of ovarian cancer cells and decreased tumor formation. A combination of experimental approaches, including real-time RT-PCR, casein zymography and chromatin immunoprecipitation assays, showed that COL4A6 knockdown attenuated discoidin domain receptors /p-DDR1 expression and suppressed binding of E2F to its putative DDR1 promoter binding site, suggesting that the E2F-DDR1 axis is upregulated by COL4A6. Pharmacological inhibition of DDR1 abrogated the COL4A6-dependent cell invasiveness. Analysis of 160 ovarian cancer patients indicated that high COL4A6 mRNA levels are associated with advanced disease stage. The 5-year recurrence-free and overall survival rates were significantly lower ( $p=0.001$  and  $p=0.001$ , respectively) among patients with high expression levels of tissue COL4A6 mRNA compared to those with low expression.

**Conclusion/Implications:** COL4A6 may promote tumor aggressiveness via the E2F/DDR1 axis and that COL4A6 expression can predict clinical outcome in ovarian cancer patients.

EP323 / #463

Topic: *AS11. Ovarian Cancer*

## **EFFICACY AND SAFETY OF MIRVETUXIMAB SORAVTANSINE IN CHINESE PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER WITH HIGH FOLATE RECEPTOR ALPHA EXPRESSION: RESULTS FROM IMGN853-301 (SORAYA CHINA) STUDY**

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<sup>1</sup>Hangzhou Zhongmei Huadong Pharmaceutical Co.,Ltd, Global Development Center, Hangzhou, China, <sup>2</sup>Fudan University Shanghai Cancer Center, Department Of Gynecologic Oncology, Shanghai, China, <sup>3</sup>Shandong Cancer Hospital, Gynecologic Oncology, Jinan, China, <sup>4</sup>Zhejiang Cancer Hospital, Gynecologic Oncology, Hangzhou, China, <sup>5</sup>Fujian Cancer Hospital, Gynecologic Oncology, Fuzhou, China, <sup>6</sup>Union Hospital Tongji Medical College Huazhong University of Science and Technology, Gynecologic Oncology, Wuhan, China, <sup>7</sup>Hubei Cancer Hospital, Gynecologic Oncology, Wuhan, China, <sup>8</sup>Hunan Cancer Hospital, Gynecologic Oncology, Changsha, China, <sup>9</sup>Cancer Hospital of Guangxi Medical University, Gynecologic Oncology, Nanning, China, <sup>10</sup>West China Second University Hospital, Sichuan University, Obstetrics And Gynecology, Chengdu, China, <sup>11</sup>The Second Hospital of Anhui Medical University, Gynecologic Oncology, Hefei, China, <sup>12</sup>Sun Yat-sen University Cancer Center, Gynecologic Oncology, Guangzhou, China, <sup>13</sup>Shanxi Provincial People's Hospital, Gynecologic Oncology, Xian, China, <sup>14</sup>The First Affiliated Hospital of USTC, University of Science and Technology of China, Gynecologic Oncology, Hefei, China, <sup>15</sup>The Second Affiliated Hospital of Zhengzhou University, Gynecologic Oncology, Zhengzhou, China

**Introduction:** Current therapies for platinum-resistant ovarian cancer (PROC) are primarily non-platinum chemotherapies with limited response and an important unmet clinical need. Mirvetuximab soravtansine (MIRV) is a folate receptor  $\alpha$  (FR $\alpha$ )-directed antibody-drug conjugate which had been approved by FDA in Nov-2022 for FR $\alpha$  positive PROC. IMGN853-301 is a single-arm registration study to evaluate the efficacy and safety of MIRV in Chinese PROC patients.

**Methods:** 35 PROC patients were enrolled with 51% of patients with three lines of prior therapy. All patients received prior bevacizumab; 77% of patients received a prior PARP inhibitor. Eligible patients had FR $\alpha$ -high tumor according to PS2+ methodology from Ventana FOLR1 assay. All patients received single-agent MIRV at 6 mg/kg using adjusted ideal body weight on Day 1 Q3W until progressive disease or intolerable toxicity.

**Results:** As of the data cutoff of 25-April-2023, median follow-up was 4.5 months. In all of 35 evaluable patients by investigator per RECIST 1.1, confirmed and unconfirmed ORR was 31.4% (95% CI: 16.85%, 49.29%), and 3-month PFS rate was estimated as 73.5%(95% CI: 55.30%, 85.25%). The most common ( $\geq 20\%$ ) treatment-related adverse events (all grade and grade 3-4) were Keratopathy (57.1% and 14.3%), Aspartate aminotransferase increased (45.7% and 0%), White blood cell count decreased (37.1% and 2.9%), Alanine aminotransferase increased (37.1% and 0%), Vision blurred (37.1% and 17.1%), Platelet count decreased (37.1% and 5.7%), Neutrophil count decreased (37.1% and 5.7%), and Xerophthalmia (20.0% and 14.3%).

**Conclusion/Implications:** MIRV demonstrated consistent clinically meaningful antitumor activity and favorable tolerability and safety in Chinese patients with FR $\alpha$ -high PROC.

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Topic: *AS11. Ovarian Cancer*

## **FIBROBLAST GROWTH FACTOR 11 (FGF11) PROMOTES PROGRESSION AND CISPLATIN CHEMORESISTANCE THROUGH THE HIF-1A/FGF11 SIGNALING AXIS IN OVARIAN CLEAR CELL CARCINOMA**

Min Yin, Huimei Zhou, Jiaxin Yang

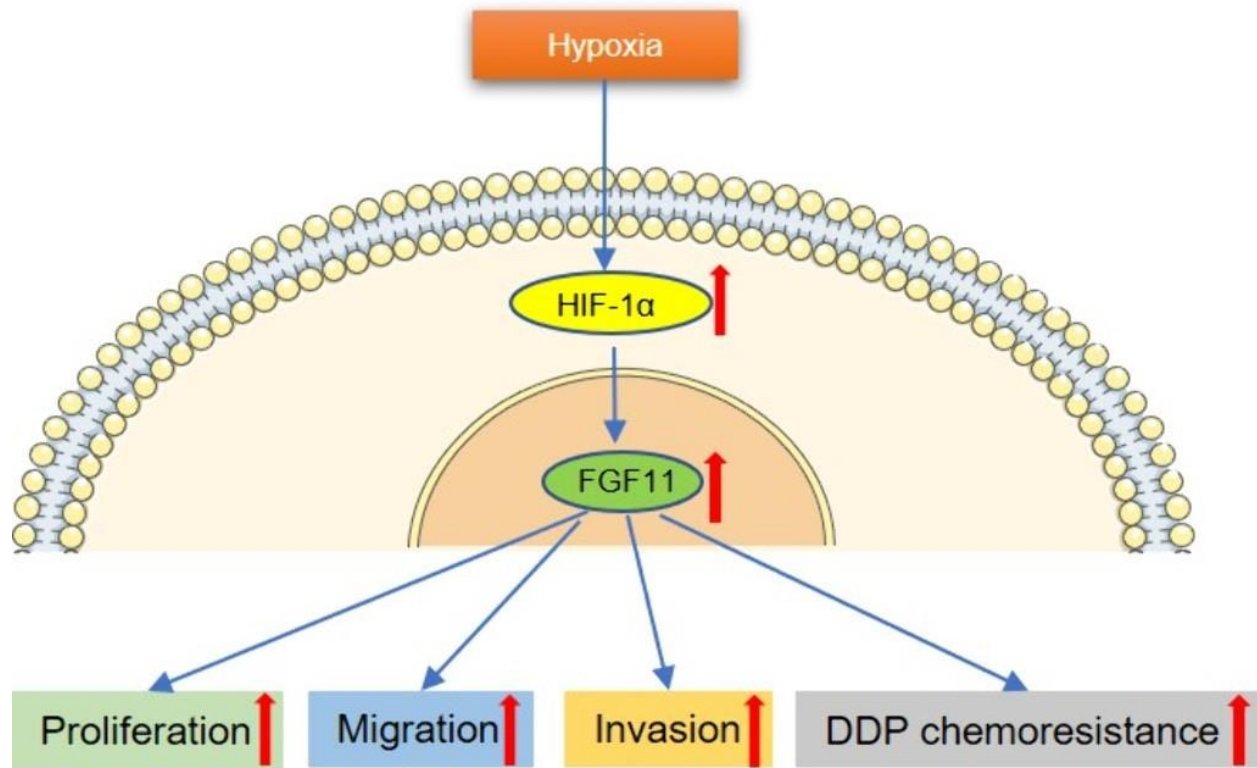
Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Obstetrics And Gynecology, Beijing, China

**Introduction:** Ovarian clear cell carcinoma (OCCC) is relatively resistant to platinum-based chemotherapy, which is associated with a poor prognosis. Evidence is mounting that fibroblast growth factors (FGFs) play key roles in human malignancies. However, the impact of FGF11 on OCCC is not completely understood.

**Methods:** Twenty-four patients who were diagnosed with OCCC in FIGO stage II-IV were included. According to their response to first-line platinum-based chemotherapy, patients were classified into two groups: the chemoresistant (CR) group and the chemosensitive (CS) group. Nanostring nCounter PanCancer Pathway panel was performed to explore expression profiles in OCCC showing different chemosensitivity. shRNA targeting FGF11 was utilized to knock down the expression of FGF11 in OCCC cell lines. Colony formation assay, CCK-8 assay, wound healing, transwell invasion assay and flow cytometric analysis were subsequently performed to detect the effect of FGF11 on OCCC cell progression and cisplatin (DDP) chemoresistance. Western blot assays and rescue experiments were employed to examine the mechanism of FGF11 in OCCC.

**Results:** Expression and bioinformatic analysis verified that FGF11 was significantly upregulated in chemoresistant OCCC tissues and higher expression of FGF11 was related to poorer survival. Downregulation of FGF11 inhibited cancer progression and DDP chemoresistance of OCCC cells. Mechanistically, FGF11 was regulated by the HIF-1 $\alpha$ /FGF11 signaling axis. Inhibition of cancer cell progression and DDP chemoresistance caused by HIF-1 $\alpha$  knockdown can be rescued by the overexpression of FGF11.

**Conclusion/Implications:**



FGF11 promoted cancer progression and DDP chemoresistance via the HIF-1 $\alpha$ /FGF11 signaling axis in OCCC, suggesting the potential of HIF-1 $\alpha$ /FGF11 signaling axis as a therapeutic target for OCCC.

EP326 / #380

Topic: AS11. Ovarian Cancer

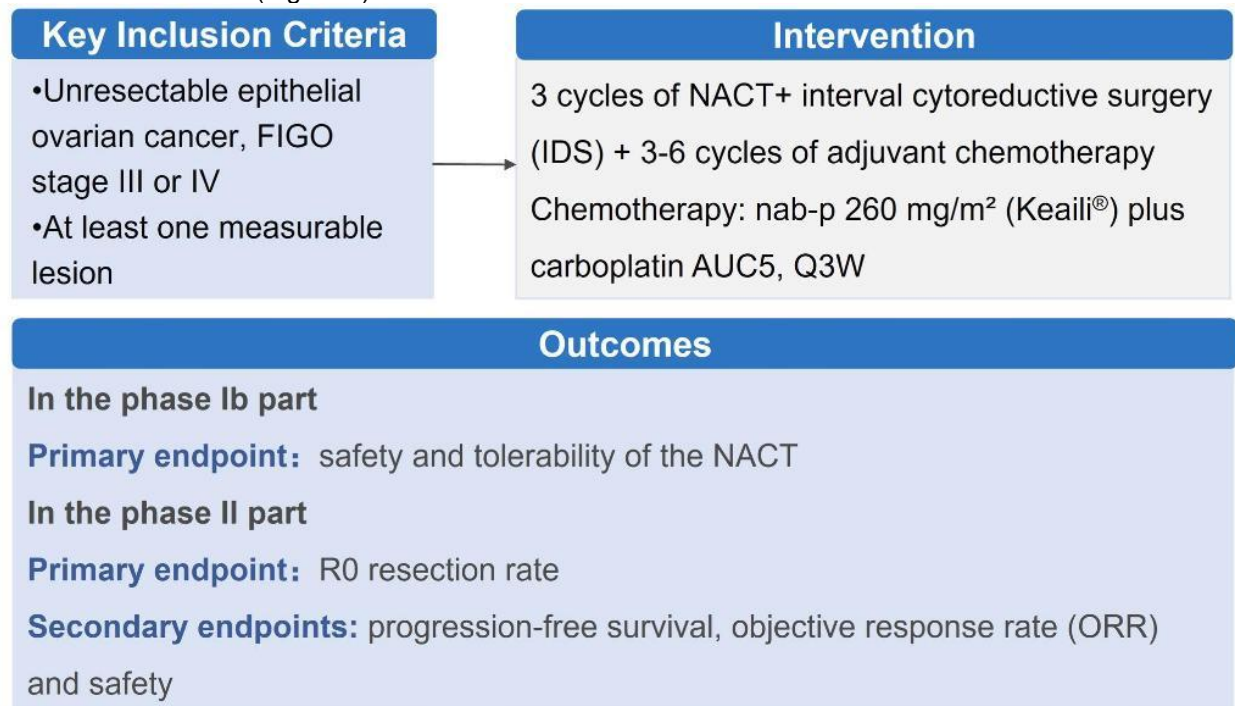
## EFFICACY AND SAFETY OF NANOPARTICLE ALBUMIN-BOUND PACLITAXEL PLUS CARBOPLATIN AS NEOADJUVANT CHEMOTHERAPY FOR WOMEN WITH UNRESECTABLE OVARIAN CANCER: A SINGLE-CENTER, OPEN PHASE IB/II CLINICAL TRIAL

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<sup>1</sup>Fudan University Shanghai Cancer Center, Gynecologic Oncology, Shanghai, China, <sup>2</sup>Fudan University Shanghai Cancer Center, Gynecologic Oncology, Shanghai, China

**Introduction:** This study aimed to explore the efficacy and safety of nanoparticle albumin-bound paclitaxel (nab-p) combined with carboplatin as a neoadjuvant chemotherapy (NACT) regimen for patients with ovarian cancer (OC).

**Methods:** This is a single-center, open phase Ib/II Clinical Trial (ChiCTR1900026893). We enrolled women with unresectable epithelial OC, FIGO stage III or IV. Patients received 3 cycles of NACT, then interval debulking surgery (IDS), followed by 3-6 cycles of adjuvant chemotherapy. Each 3-week cycle consisted of carboplatin AUC5 plus nab-p 260 mg/m<sup>2</sup>(Keaili®). In the phase II part, the primary objective was R0 resection rate(Figure 1).



FIGO: International Federation of Gynecology and Obstetrics, NACT: neoadjuvant chemotherapy, Nab-p: nanoparticle albumin-bound paclitaxel.

### Figure 1. Study design

**Results:** Phase Ib results showed the NACT was safe and tolerable, so the study proceeded to phase II. A total of 50 patients were included in this analysis, 10 patients in the phase Ib and 40 patients in the phase II. Twenty-nine (58%) patients had stage IV. All patients completed planned NACT and 8 (16%)

patients experienced delayed chemotherapy due to adverse events (AE). After NACT, the objective response rate was 81.3% (95%CI: 67.4%-91.1%) in 48 patients who had at least one tumor assessment. Among the 45 patients who underwent IDS, 5 patients (11.1%) had surgery delayed due to AE, all patients achieved optimal debulking and 77.8% (95%CI: 62.9%-88.8%) achieved R0 resection. During NACT, the most common grade 3/4 AEs were hematologic toxicities, including neutropenia (78%), leucopenia (48%) and thrombocytopenia (24%). All AEs returned to normal or acceptable levels after receiving appropriate treatment.

**Conclusion/Implications:** Nab-p plus carboplatin as a NACT regimen was effective and tolerable for unresectable epithelial OC.



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Topic: **AS11. Ovarian Cancer**

## **PREDICTIVE MODELS FOR DIFFERENTIATION OF EPITHELIAL OVARIAN CANCER FROM BENIGN OVARIAN MASS**

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**Introduction:** Although there have been advancements in triaging women with pelvic masses using multimodal laboratory assays like ROMA and CPH-I, there is still a need for more cost-effective and efficient models. Additionally, there is a need for a reliable model that can detect EOC in premenopausal women at an early stage.

**Methods:** The study analyzed data from 122 EOC patients and 820 patients with BOMs. Pearson's correlation coefficient, the Mann-Whitney U test, the area under the curve (AUC) were used for analysis.

**Results:** 39.3% of the 122 EOC patients had stage I-II cancer, and 60.7% had stage III-IV cancer. Multivariate logistic regression analysis revealed that human epididymal secretory protein 4 (HE4) and red cell distribution width (RDW) were significant predictors of EOC and constituted the full model (FM). The AUCs of FM for predicting EOC were comparable to those of ROMA or CPH-I, regardless of tumor stage or menopausal status. However, the sensitivity of FM at a set specificity of 75% was significantly higher than that of ROMA in predicting EOC in premenopausal women.

**Conclusion/Implications:** The AUCs of FM were comparable to those of ROMA or CPH-I in terms of predicting EOC, regardless of the tumor stage or menopausal status; however, the FM was more sensitive than ROMA in predicting EOC in premenopausal women at a set specificity of 75%. Additionally, FM has the advantage of being less expensive than ROMA or CPH-I. Further prospective studies are required to validate these results of present study.

EP330 / #1472

Topic: *AS11. Ovarian Cancer*

## **ARTIFICIAL INTELLIGENCE-BASED MODEL ENABLES ACCURATE DIAGNOSIS OF OVARIAN CANCER USING LABORATORY TESTS: A MULTICENTER, RETROSPECTIVE STUDY**

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**Introduction:** Early diagnosis of ovarian cancer (OC) is difficult due to the lack of effective biomarkers. Laboratory tests are necessarily applied in clinical routine practice and some tests have shown diagnostic and prognostic relevance to OC.

**Methods:** In this multicenter, retrospective study, we collected 98 laboratory tests and the age of women with or without OC admitted to three hospitals during 2012 and 2021. A risk prediction fusion framework (MCF model) that combined estimations from twenty artificial intelligence classification models was developed for OC diagnosis. It was evaluated on an internal validation set (3,007 individuals) and two external validation sets (5,641 and 2,344 individuals), respectively. The performance of MCF model was compared with the classic OC biomarker CA125 and HE-4, as well as seven competing state-of-the-arts methods.

**Results:** Based on 52 features (51 laboratory tests and age), the MCF achieved an AUC of 0.949 (95% CI 0.948-0.950), 0.882 (0.880-0.885), and 0.884 (0.882-0.887) . Most features were significantly associated with accuracy of OC diagnosis according to univariate logistic regression. The MCF model showed higher AUC and sensitivity compared with CA125 and HE4 in identifying OC patients. The MCF also tolerated with input laboratory tests exclusive of CA125 or other tumor markers and yield acceptable prediction accuracy, and outperformed state-of-the-arts models. The MCF was wrapped as an OC prediction tool publicly available at <https://github.com/xinzhen-lab/OC-prediction>.

**Conclusion/Implications:** MCF model using laboratory tests achieved satisfactory and consistent performance in OC diagnosis from three validation sets. The included laboratory tests besides CA125 and HE4 contributed to diagnosis of ovarian cancer.

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**Topic: AS11. Ovarian Cancer**

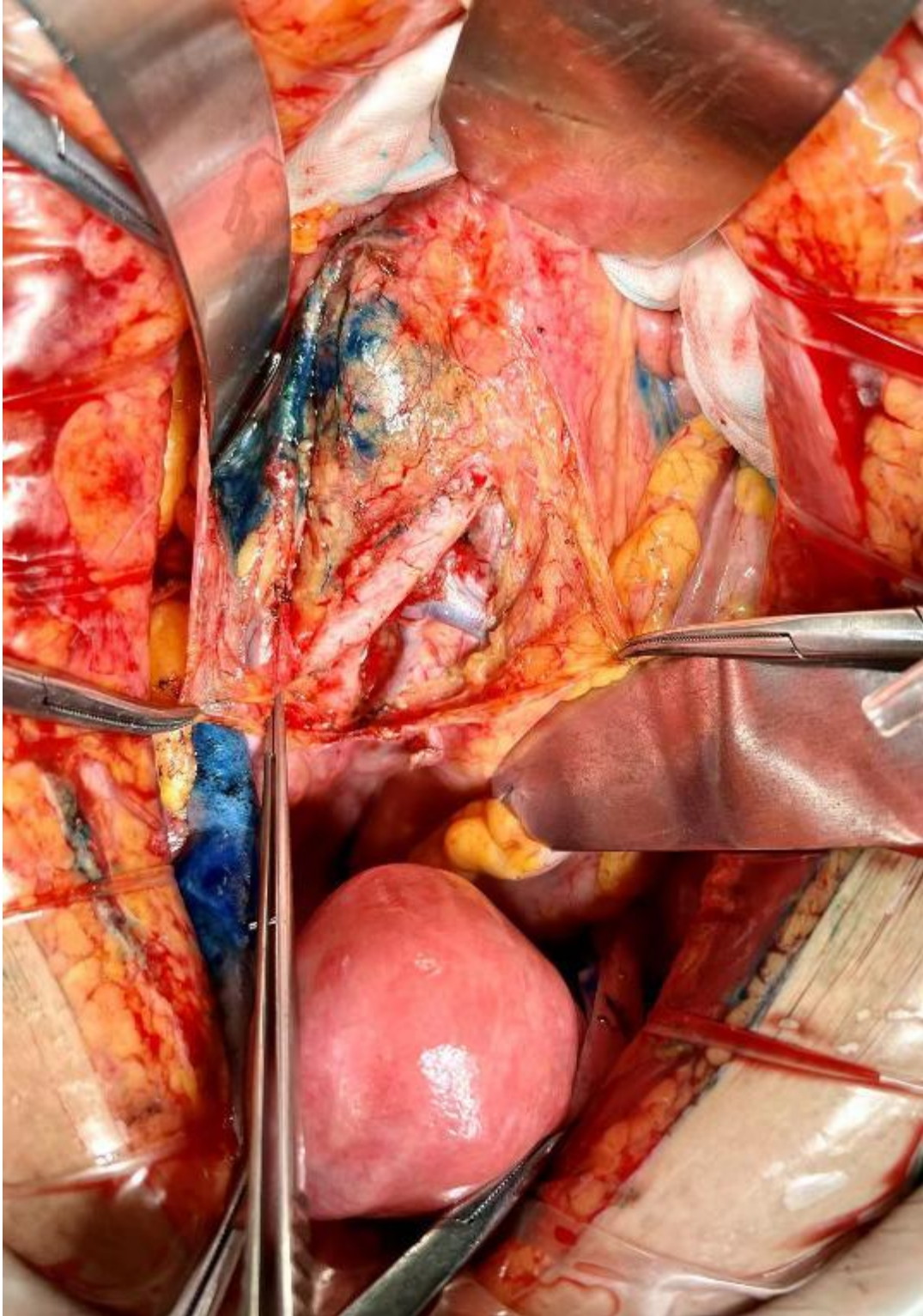
## **SENTINEL LYMPH NODES MAPPING IN OVARIAN CANCER- PRELIMINARY RESULTS FROM SINGLE CANCER CENTER STUDY**

Zhengmao Zhang, Hongxia Wang

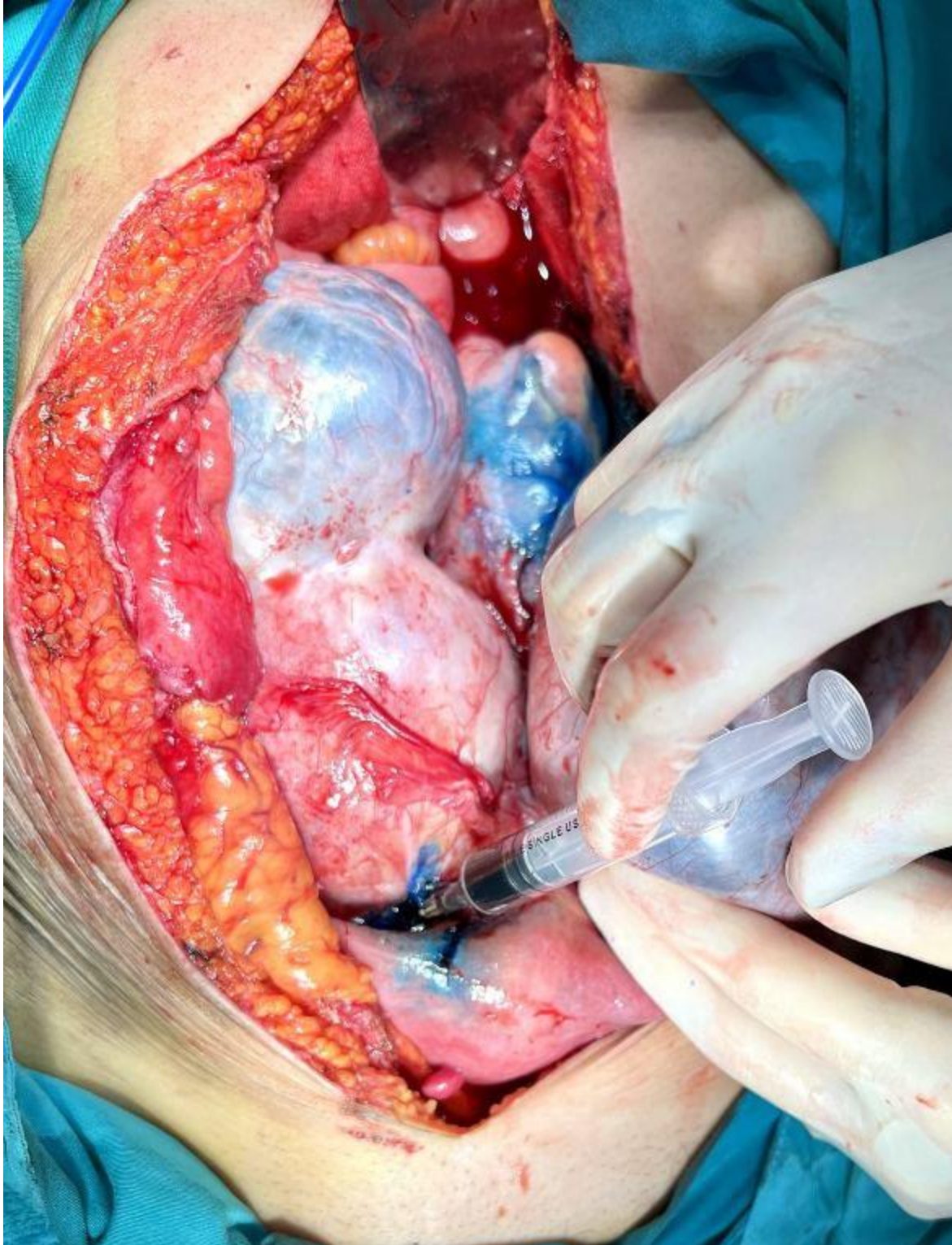
Fourth Hospital of Hebei Medical University, Gyn, Shijiazhuang, China

**Introduction:** Objective: To analyze the distribution, detection rate, false negative rate, sensitivity and negative predictive value of the Sentinel Lymph nodes (SLN) and explore the value of SLN mapping in predicting the LNs metastasis in ovarian cancer.

**Methods:** It is a prospective single arm trial at one cancer center. 29 cases of ovarian cancer patients were enrolled from May 1, 2020 to Dec. 31, 2022. All the patients were injected with methylene blue into the ovarian cortex, uterine horns and infundibulopelvic ligaments by the same surgeon who once learned SLN mapping technique at Memorial Sloan-Kettering Cancer Center, SLNs biopsy was performed followed by systematic pelvic and para-aortic lymphadenectomy. The negative SLNs on HE staining were detected by immunohistochemistry cytokeratin staining (AE1/AE3) for low-volume metastasis.



**Results:**



The overall detection rate of SLN in ovarian cancer was 100% , sensitivity was 85.7%, false negative rate was 14.3%, and negative predictive value was 95.7%. The average of 31 LN and 9 SLNs were dissected for each person. SLN of ovarian cancer was mainly distributed in the supermesenteric and inferomesenteric Para-cava(34.8%, 33.3%). 7 cases of LNs metastasis were found among all 29 cases, there were 12

SLNs metastasis and 45 NSLNs metastasis. 1 SLN was found to be isolated tumor cells (ITC). Metastatic SLNs mainly distributed in the Para-caval region(91.2%).25 cases were PDS and 9 were IDS.

**Conclusion/Implications:** Intraoperative SLN mapping by injecting methylene blue is safe, feasible for predicting the LNs metastases, and pathological ultra-staging for SLNs could improved the detection rate of LNs metastasis in ovarian cancer.

EP332 / #492

**Topic:** AS11. Ovarian Cancer

## **EXOSOMAL MIR-148A-3P SERVES AS TUMOR SUPPRESSOR FOR OVARIAN CANCER**

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**Introduction:** Exosome is associated with chemoresistance in various cancers, whereas such a role in OVCA is not yet clear.

**Methods:** The exosomes were extracted by ultracentrifugation. High-Throughput sequencing was used to measure miRNA levels in exosomes isolated by A2780 and A2780-DDP. Integrated with public databases, exosomal miRNAs associated with cisplatin-resistance, prognosis were identified using computational studies. The crucial miR-148a-3p were selected for further investigation. Gain- or loss-functional assays were performed to define the function of miR-148a-3p. The plasma exosomes and surgical tissues were collected to detect the expression level.

**Results:** The exosomes were characterized by measuring protein markers, performing nanoparticle tracking analyses and transmission electron microscopy. 126 differentially expressed and 12 prognostic exosomal miRNAs were observed. The prognostic exosomal miRNAs-related cluster and signature were established and validated, indicating their clinical and biological significance. Comprehensive bioinformatics approaches demonstrated crucial role of miR-148a-3p in prognosis and cisplatin-resistance. Low expression of miR-148a-3p was observed in cell and tissues, especially cisplatin-resistant samples. Nevertheless, miR-148a-3p was overexpressed in plasma exosome and cisplatin-resistant cell exosomes. We confirmed the findings in both publicly available expression profiling and the samples we collected. We found that miR-148a-3p suppressed proliferation, migration, invasion, cisplatin-resistance, and induced apoptosis, indicating the role of tumor suppressor for miR-148a-3p. Ulteriorly, the inhibition of exosome release induced miR-148a-3p intracellular accumulation, the opposite was observed in the stimulative of exosome.

**Conclusion/Implications:** Our data elucidated an unappreciated mechanism of miR-148a-3p in tumor suppressing and cisplatin resistance for OVCA. We uncovered that exosome exclusion of miR-148a-3p to promotes malignancy and cisplatin resistance of OVCA.

EP333 / #110

**Topic: AS11. Ovarian Cancer**

## **STAGE IVB EPITHELIAL OVARIAN CANCER WITH ISOLATED DISTANT LYMPH NODE METASTASES: SHOULD A NEW SUBSTAGE BE CREATED? A MULTI-INSTITUTIONAL ANALYSIS.**

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**Introduction:** We aimed to evaluate the prognostic impact in patients with the isolated distant lymph node metastases for stage IVB epithelial ovarian cancer.

**Methods:** We conducted a multi-institutional retrospective analysis of patients with stage IV ovarian cancer. We compare OS in women with lymph node as only distant metastatic site to those with pleural metastases only and to patients with other/multiple stage IV ovarian cancer.

**Results:** All 618 eligible patients were screened. These patients were diagnosed with stage IVA (n =135, 21.8%), stage IVB only due to distant lymph node metastases (stage IVB-LN) (n = 163, 26.4%), stage IVB with other/multiple sites of distant metastases (stage IVB-other/multiple) (n =320, 51.8%). The age, histological type, cell differentiation, performance status, postoperative residual tumor, first line chemotherapy among the different stages were balanced (each, P > 0.05). The median OS for patients with stage IVB-LN was 48.62 months (95% CI: 31.25 - 54.29) compared to 29.82 months (95% CI: 23.24-34.48) for those with stage IVA (p < 0.001) and 21.27 months (95% CI: 15.43 - 28.46) for those with stage IVB-other/multiple (p < 0.001). Multivariable analysis revealed that stage IVB-other/multiple was an independent indicator of increased risk of mortality compared with stage IVB-LN (HR: 2.15, 95% CI: 1.67 - 2.23, p < 0.001); Patients with stage stage IVA had a worse survival compared to those with stage IVB-LN (HR: 1.68, 95% CI: 1.25 -1.84, p=0.019 ).

**Conclusion/Implications:** Stage IVB-LN is associated with better survival compared to stage IVB-other/multiple and stage IVA.



EP334 / #226

Topic: *AS11. Ovarian Cancer*

## **BEVACIZUMAB COMBINED WITH CHEMOTHERAPY IS SUPERIOR TO CHEMOTHERAPY IN OVARIAN CANCER AFTER PARPI: EVIDENCE FROM A RETROSPECTIVE ANALYSIS**

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**Introduction:** With the increasing use of PARPi, clinical cases of PARPi resistance and recurrence among OC patients have become more common. Traditional chemotherapy has proven effective in cases of OC recurrence after PARPi treatment. However, the effectiveness of combining bevacizumab with chemotherapy for this purpose remains uncertain, as comparative trials of the two treatments have yet to be widely published. In this study, we conducted a retrospective evaluation of both treatment strategies.

**Methods:** The study enrolled 41 OC patients who experienced relapse after PARPi treatment and subsequently received chemotherapy, with or without Bevacizumab, at a single institution. Baseline levels were found to be balanced between the two groups. Kaplan-Meier analysis and Cox regression were

employed to compare progression-free survival (PFS) and overall survival (OS) for both

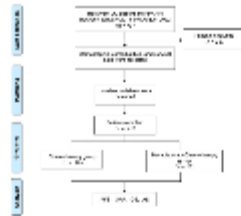


Fig 1. Patient disposition and adverse events.

Table 1. Demographic characteristics and clinical data of the patients

Abbreviations: PS, Performance score; CTT, Cytotoxic chemotherapy; OS, Overall survival; PFS, Progression-free survival

HR, Hazard ratio; 95% CI, 95% confidence interval; SD, Standard deviation

Parameter	CTT (n=50)	Bevacizumab (n=50)	P-value
<b>Demographic</b>			
Age (yr)	52.5	51.5	0.347
ECOG stage			
0	2 (4%)	1 (2%)	
1	13 (26%)	13 (26%)	0.457
2	13 (26%)	13 (26%)	
3	9 (18%)	11 (22%)	
4	9 (18%)	12 (24%)	
BRCA status			
+	10 (20%)	10 (20%)	0.227
-	13 (26%)	13 (26%)	
CA125 (U/ml)	129.000.000	87.000.000	0.291
CA150 (ng/ml)	25.000	25.000	0.529
ECOG performance			
0	9 (18%)	11 (22%)	
1	13 (26%)	10 (20%)	0.172
2	13 (26%)	13 (26%)	
3	9 (18%)	11 (22%)	
4	9 (18%)	13 (26%)	
CTT (days)			
N/A	3 (6%)	1 (2%)	0.777
<b>OS (months)</b>	5 (9.8%)	10 (20%)	0.001
<b>PFS (months)</b>			
0	5 (9.8%)	1 (2%)	0.001
1	10 (19.6%)	11 (22%)	
2	10 (19.6%)	11 (22%)	
3	8 (15.8%)	7 (14%)	

a) Stage 0-1 only

b) All patients

c) Mean ± standard deviation

d) Fisher's exact test

treatments.

**Results:** Both groups were well matched in all parameters. The hazard ratio (HR) for PFS events in patients was 0.482 (95% CI, 0.247 to 0.942; unstratified log-rank P=0.020). The median PFS was 11 months for the bevacizumab arm vs. 5 months for chemotherapy alone. Median OS was 11 months with

chemotherapy alone versus 15 months with bevacizumab-containing therapy, and the OS HR was 0.573 (95% CI, 0.292 to 1.126). Grade  $\geq 2$  hypertension (1/23) and thrombosis (2/23) were more common with bevacizumab, while GI perforation occurred in 4.3% (1/23) of bevacizumab-treated

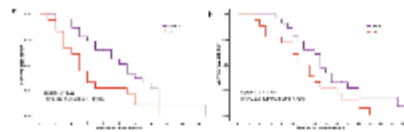


Fig 1. Primary endpoint: overall survival (OS) (Kaplan-Meier plot). BEV+CT (n=23) vs CT (n=23).

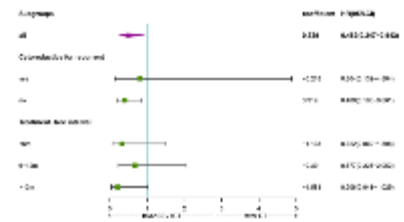


Fig 3. Subgroup analysis

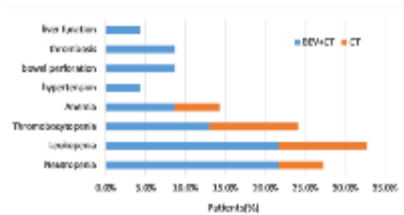


Fig 4. Other grade  $\geq 2$  adverse events (Medical Dictionary for Regulatory Activities-preferred terms). BEV: bevacizumab; CT: chemotherapy; AE: adverse event.

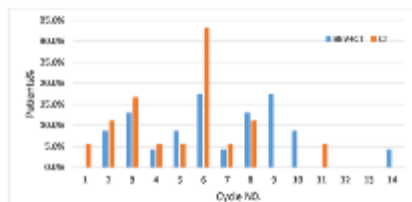


Fig 5. Summary of treatment exposure. BEV: bevacizumab; CT: chemotherapy.

patients.

**Conclusion/Implications:** This study found that in patients who relapsed after PARPi, chemotherapy combined with Bevacizumab led to better survival outcomes, and the side effects were well tolerated. Further randomized controlled trials are needed to confirm these results.

EP335 / #563

Topic: *AS11. Ovarian Cancer*

## **NEUTROPHIL-TO-LYMPHOCYTE RATIO AND PLATELETS-LYMPHOCYTES RATIO AS RESPONSE MARKERS IN OVARIAN CANCER PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY**

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**Introduction:** Systemic inflammatory responses are closely associated with cancer initiation, progression and metastasis, consequently, inflammatory markers, including the neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR), have been studied in many cancers. The objective of this study was to evaluate the impact of the NLR and PLR as a response indicator to the neoadjuvant chemotherapy (NACT) in high grade serous localized ovarian cancer (HGSOC)

**Methods:** A total of 30 patients who had received NACT followed by interval debulking surgery were eligible for retrospective analysis. The pretreatment and post-treatment PLR, NLR in all patients were calculated based on complete blood counts

**Results:** The median age of our patient was  $50 \pm 9$  years, 10 % were stage II and 90% were stage III the pretreatment NLR and PLR were correlated with response to NACT, Patients with lower  $NLR < 2.5$  and  $PLR < 185$  had a significantly better response rate to NACT versus those with a higher NLR and PLR. the decrease in NLR and PLR rates after chemotherapy can be considered as an early prediction of response to treatment. PLR and NLR are high in the presence of residual tumor after surgery.  $PLR > 200$  and  $NLR > 2.6$  were biomarkers of suboptimal surgery. PLR and NLR levels are well correlated with serum CA125 levels.

**Conclusion/Implications:** Our results suggested that NLR and PLR were well-connected with response to NACT in patients with HGSOC. As a response indicator, NLR and PLR may predict benefit from chemotherapy. Relationship between NLR, PLR and CA125 may provide new information about the pathogenesis of ovarian cancer.

EP336 / #874

Topic: AS12. Palliative Care

## **SEMIQUANTITATIVE LYMPHOSCINTIGRAPHY IN GYNECOLOGIC CANCER PATIENTS WITH LOWER EXTREMITY LYMPHEDEMA: PREDICTION OF SHORT-TERM OUTCOME AFTER LYMPHATICOVENOUS ANASTOMOSIS.**

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<sup>1</sup>Yeouido St. Mary's Hospital, Obstetrics And Gynecology, Seoul, Korea, Republic of, <sup>2</sup>Yonsei University Wonju College of Medicine, Republic of Korea, (South), Obstetrics And Gynecology, Wonju, Korea, Republic of, <sup>3</sup>Yeouido St. Mary's Hospital, Colledge of Medicine, The Catholic University of Korea, Nuclear Medicine, Seoul, Korea, Republic of

**Introduction:** We aimed to evaluate the predictive value of semiquantitative lymphoscintigraphy in patients who underwent lymphovenous anastomosis (LVA) for lower extremity lymphedema (LEL).

**Methods:** We retrospectively reviewed patients with LEL who underwent preoperative lymphoscintigraphy and LVA. From the lymphoscintigraphy, the transport index in 120 min (TI<sub>120</sub>) and 240 min (TI<sub>240</sub>) were respectively calculated by visual assessment of 5 criteria: lymphatic transport kinetics, distribution pattern, time to appearance of lymph nodes, visualization of lymph nodes, and visualization of vessels. The volume differential (VD) between the affected and the contralateral unaffected lower extremities (LEs) was calculated and the volume differential reduction at 1 (VDR<sub>1</sub>), 3 (VDR<sub>3</sub>), and 6 months (VDR<sub>6</sub>) were respectively calculated to evaluate the postoperative outcome.

**Results:** In total, 46 patients were included. According to Campisi's stage, the majority of patients (76%) had stage III disease. In the lymphoscintigraphy, the mean TI<sub>120</sub> and TI<sub>240</sub> of 46 affected LEs were 26.8±11.4 and 25.9±11.3, respectively. The mean preoperative VD was 26±14% (range, 2-59). Campisi's stage increased with BMI, TI, and preoperative VD. There were significant positive correlations of TI with BMI and preoperative VD, respectively (p<0.05). In postoperative assessment, the mean VDR<sub>1</sub>, VDR<sub>3</sub>, and VDR<sub>6</sub> were 60±99% (range, -9-526), 78±121% (range, 5-572), and 74±116% (range, -92-499), respectively. There was significant negative correlation between preoperative VD and each VDR (p<0.05). Both TI<sub>120</sub> and TI<sub>240</sub> showed significant negative correlation with VDR<sub>3</sub> and VDR<sub>6</sub> (p<0.05), although not VDR<sub>1</sub>.

**Conclusion/Implications:** This study suggests that semiquantitative lymphoscintigraphy using TI can be valuable as an effective tool for assessment of preoperative severity.

EP338 / #147

Topic: *AS12. Palliative Care*

## **A PROSPECTIVE COHORT STUDY OF NINJIN-YO'EITOU FOR FATIGUE, MALAISE, ANOREXIA AND ANEMIA IN OLAPARIB TREATMENT FOR THE PATIENTS WITH OVARIAN CANCER; KCOG-G1904 STUDY**

Satou Fujiwara<sup>1</sup>, Ruri Nishie<sup>1</sup>, Fuminori Ito<sup>2</sup>, Makiko Taniguchi<sup>2</sup>, Masato Aoki<sup>3</sup>, Hidekatsu Nakai<sup>3</sup>, Kazuto Tasaki<sup>4</sup>, Emi Yoshioka<sup>5</sup>, Kensuke Hori<sup>5</sup>, Atsushi Arakawa<sup>6</sup>, Taiger Koike<sup>7</sup>, Yoshimasa Bomoto<sup>7</sup>, Takashi Motohashi<sup>8</sup>, Kimihiko Ito<sup>5</sup>

<sup>1</sup>Osaka Medical and Pharmaceutical University, Department Of Obstetrics And Gynecology, Takatsuki, Japan, <sup>2</sup>Nara Prefecture General Medical Center, Department Of Obstetrics And Gynecology, Nara, Japan, <sup>3</sup>Kindai University, Department Of Obstetrics And Gynecology, Osakasayama, Japan, <sup>4</sup>Kurume University, Department Of Obstetrics And Gynecology, Kurume, Japan, <sup>5</sup>Kansai Rosai Hospital, Department Of Obstetrics And Gynecology, Amagasaki, Japan, <sup>6</sup>Nagoya City University West Medical Center, Department Of Obstetrics And Gynecology, Nagoya, Japan, <sup>7</sup>Gifu University, Department Of Obstetrics And Gynecology, Gifu, Japan, <sup>8</sup>Tokyo Women's Medical University, Department Of Obstetrics And Gynecology, Tokyo, Japan

**Introduction:** Olaparib is an oral poly (ADP-ribose) polymerase inhibitor that has shown antitumor activity in patients with advance or recurrent ovarian cancer. It is associated with adverse side effects, including fatigue, malaise, anorexia and anemia, which may force its discontinuation. Ninjin'yoeitou (NYT) is a herbal medicine that can effectively treat these adverse events. However, the efficacy of NYT in reducing these side effects with Olaparib is not clear.

**Methods:** The present study included 45 patients who received Olaparib for newly diagnosed advanced or platinum sensitive recurrent ovarian cancer at eight Kansai Clinical Oncology Group (KCOG)-related institutions. Treatment-related adverse events were graded with use of the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0. Quality of life was assessed with the Functional Assessment of Cancer Therapy-Ovarian Cancer (FACT-O) questionnaire (completed at baseline and every month until 6 months had passed or disease progression), the FACT/NCCN Ovarian Symptom Index (FOSI), and the Trial Outcome Index (TOI).

**Results:** Grade 3 or higher anemia occurred in 13 of 45 patients (29%), Grade 2 or higher fatigue in 6 (13%), and anorexia in 2 (4%). The incidence of discontinuation due to side effects was 15% (7/45). Moreover, NYT could maintain quality of life under all measures: FACT-O, TOI, and FOCl. NYT also significantly improved fatigue after the start of Olaparib administration (p=0.017).

**Conclusion/Implications:** NYT could maintain quality of life by suppressing Olaparib-induced fatigue and help the long-term maintenance therapy of Olaparib in patients with ovarian cancer by reducing these adverse events.

EP339 / #372

Topic: *AS13. Patient Advocacy*

## **LYMPHEDEMA IN GYNECOLOGICAL CANCER SURVIVOR; A NATIONWIDE COHORT STUDY**

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**Introduction:** Leg lymphedema after gynecological cancer treatment is common and negatively affects the quality of life and function of patients. This study investigated the cumulative incidence and risk factors of lymphedema in gynecological cancer patients, as well as utilization of health care resources for post-treatment lymphedema.

**Methods:** Using the Korean National Health Insurance Service(NHIS) database, we conducted a nationwide, retrospective cohort study of patients with gynecological cancer treatment. We analyze the incidence and risk factors of lymphedema by using cox proportional hazards regression models. We also analyzed diagnostic and treatment claim codes to find out trend or costs of utilization of health care resources for lymphedema treatment.

**Results:** A total of 93,218 patients with gynecological cancer were evaluated between January 2004 and December 2017. Among them, total 10,451(11.2%) developed lymphedema. Incidences of lymphedema were 11.4%, 13.1%, and 9.16% in cervical cancer, endometrial cancer and ovarian cancer respectively. Age and multimodal treatment are considered to be possible risk factors for lymphedema in patients with gynecological cancer ( $p < 0.001$ ), while residence and income quartile were not associated with lymphedema in gynecologic cancer patients. The expands of health care resources for the treatment of lymphedema has increased over the years.

**Conclusion/Implications:** Lymphedema is a common complication affecting women with gynecological cancer. This is the first population-based the first population-based study to identify risk factors for lymphedema in gynecological cancer patients. National healthcare costs for lymphedema treatment are increasing in Korean society. Health care providers should give attentions for high-risk lymphedema group during and after cancer-related treatment.



EP340 / #681

**Topic:** *AS13. Patient Advocacy*

## **CONTRACEPTION COUNSELLING AND PREGNANCY SCREENING PRACTICE WITHIN AN ONCOLOGIC DEPARTMENT; AN INSTITUTION EXPERIENCE**

Jade Desilets, Marie-Catherine Viau, Megan Schneiderman, Luisa Luciani Castiglio, Selda Elmas, Shuk On Annie Leung  
Cancer Research Program RI-MUHC, Gynecologic Oncology, Montreal, Canada

**Introduction:** The goal of this study is to describe the pregnancy screening and contraception counselling practice within the Departments of Oncology at McGill University Health Center as part of a needs assessment to develop a referral pathway to a complex contraception clinic.

**Methods:** An electronic survey comprising 21 questions was delivered via email to 187 clinicians of the oncology departments providing care to patients with cancer. The survey assessed counselling practice and level of comfort regarding contraception while patients are undergoing oncologic treatment. Descriptive statistics were used for analysis.

**Results:** Of the 187 members of the oncologic department, 70 responded to the survey including oncologist, nurses, pharmacist and radiation technologists. Forty-seven percent (47%, n =33) reported always advising female patients to avoid pregnancy while on active treatment and only 36% (n=22) felt comfortable providing contraception counselling. The most common reasons identified by respondents for lack of comfort with contraception counseling was lack required knowledge (36%, n=25). Amongst oncologists (n=22), 68% (n=15) reported rarely ordering a pregnancy test prior to initiation of cancer treatment. All respondents would refer their patients to complex contraception clinic pre-treatment should it be available. Based on these results a referral pathway to a complex contraception clinic was developed.

**Conclusion/Implications:** This survey shows a low rate of pre-treatment pregnancy screening and contraception counselling through the oncology department with lack of knowledge identified as the main barrier. This highlights an opportunity for improvement with the introduction of systematic pregnancy testing and contraception counselling via the implementation of a referral pathway to contraception specialist.

EP341 / #890

Topic: *AS13. Patient Advocacy*

## **THE NEED OF A BETTER DISCUSSION BETWEEN DOCTORS AND PATIENTS WITH REGARDS OF FERTILITY PRESERVATION AFTER ANTI CERVICAL CANCER TREATMENTS**

Bar Levy

HaBait Shel Bar - Israel Women's Cancer Association (RA), Management, Tel Aviv, Israel

**Introduction:** According to studies, the age range of cervical cancer patients usually ranges between the age 35 to 39 or 60 to 64 years old and is relatively younger than other gynecological cancers' age range. In this young age range, a patient might want to give birth after treatments.

**Methods:** A call for answers to a survey was published in the Israeli Cervical Cancer Facebook Community, and community members were invited to respond voluntarily and anonymously through a coded and encrypted web form.

**Results:** 67 women between the ages of 21 and 45 responded to the survey (median age 37 years). 55.22% were diagnosed with CIN 3, 19.4% were diagnosed with stage 1 Cervical Cancer, 5.97% with stage 2, 5.97% were diagnosed with stages 3-4, 13.43% did not know how to answer this question. 77.61% are sexually active with a singular known partner. 58.2% recall having a discussion with their attending physician regarding fertility preservation, before the beginning of the treatments. 32.83% recall such a discussion afterward treatments. 11.94% give birth after illness or had a child thanks to a surrogate mother.

**Conclusion/Implications:** This study underscores the need for greater attention to patients' fertility preservation aspects before and after completion of treatments and the need in coordinate patients' expectations regarding birth planning with regards of the ability to do so after treatments. Research involving a larger sample size may help to better support the information needs of survivors.

EP342 / #659

Topic: *AS13. Patient Advocacy*

## **BUREAUCRATICAL DIFFICULTIES OF CANCER PATIENTS IN ISRAEL – A PRELIMINARY STUDY**

Bar Levy

HaBait Shel Bar - Israel Women's Cancer Association (RA), Management, Tel Aviv, Israel

**Introduction:** Cancer patients need to navigate their path in their journey and take into consideration many medical disciplines and other such as legal or social, hence having difficulties in their disease management.

**Methods:** Personal interviews were performed with 57 women cancer patients, treated in main medical centers in Israel, aged 32 to 82 years old (median 63 years old). 59.65% of patients have breast cancer, 28.07% have ovarian cancer, 14.04% have uterine cancer and 3.51% have cervical cancer. 5.26% of the patients have double malignancies. 61.4% of patients have an advanced disease. 87.72% of the patients under systemic treatment.

**Results:** 84.21% of the patients had any actionable recommendation from the oncologist. 36.84% of the patients thought they needed help with executing oncologist's recommendations or achieving legal rights. 38.6% of the patients were seeking for help. 45.45% of patients seeking help, needed help with performing genetic or molecular testing, 40.91% needed help with booking appointments for doctors, imaging, or procedures. 18.18% needed help with claiming rights, 9.09% needed help with enrolling to a study, 4.55% needed help with possess drugs prescribed off label and in 4.55% needed help with booking a second opinion consultation.

**Conclusion/Implications:** This preliminary study suggests that many patients need assistance in disease management to perform better in their patient journey. Thus, oncology institutes should offer assistance in executing oncologist's recommendations, enrolling in studies or achieving legal rights.

EP343 / #352

Topic: *AS14. Pre-Invasive Disease*

## **COMPARISON BETWEEN MOBILE COLPOSCOPY AND CONVENTIONAL COLPOSCOPY IN DETECTING HIGH GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA**

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**Introduction:** The detection of high grade cervical intraepithelial neoplasia is traditionally done by conventional colposcopy. However, this procedure requires special equipment and needs to be performed by a specialist. Data on the performance of mobile colposcopy are still limited, so we aimed to evaluate the performance of mobile colposcopy in detecting high grade cervical intraepithelial neoplasia comparing with conventional colposcopy.

**Methods:** Patients with abnormal cervical cancer screening tests were included in the study. Mobile colposcopy and conventional colposcopy were performed in all patients then biopsy was done following the standard recommendation. Images from mobile colposcopy were assessed by two independent doctors. The diagnostic performance was evaluated and the colposcopic results were compared between mobile colposcopy and conventional colposcopy.

**Results:** Ninety-one patients were enrolled in the study. There were poor-quality mobile colposcopic images in 3 patients. The accuracy in detecting high grade cervical intraepithelial neoplasia were 76.14% using mobile colposcopy, and 79.12% using conventional colposcopy. The sensitivity, specificity, positive predictive value, and negative predictive value were 52.94%, 81.82%, 40.91%, and 87.88% in mobile colposcopy, and 61.11%, 83.56%, 47.83%, and 89.71% in conventional colposcopy, respectively. The concordance rate between mobile colposcopy and conventional colposcopy was 72.73%. There was a fair agreement between mobile colposcopy and conventional colposcopy (Kappa = 0.273, 95%CI 0.048-0.497).

**Conclusion/Implications:** The diagnostic performance of mobile colposcopy was comparable to conventional colposcopy with a fair agreement between the two procedures. Mobile colposcopy may be an alternative option in the diagnosis of high grade cervical intraepithelial neoplasia.

EP344 / #385

Topic: *AS14. Pre-Invasive Disease*

## **CLINICAL WORKUP AND TREATMENT FOR LOBULAR ENDOCERVICAL GLANDULAR HYPERPLASIA IN A REGIONAL GYNAEONCOLOGY CENTRE IN HONG KONG.**

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**Introduction:** Lobular endocervical glandular hyperplasia (LEGH) is a rare benign disorder of the uterine cervix but it has the potential to develop into minimal deviation adenocarcinoma, which is a well differentiated form of gastric-type mucinous carcinoma. The differential diagnosis includes multiple cervical cystic lesions such as Nabothian cysts. A detailed workup for multiple cervical cystic lesions could help identify patients with the precursor lesions and treat accordingly before it transforms into a malignancy. An individualized preoperative workup and counselling was important to guide an appropriate management.

**Methods:** A retrospective review in a regional tertiary gynaecology centre in Hong Kong was conducted between 2019 to 2020. Total of 797 case records were included. Three women were diagnosed to have lobular endocervical glandular hyperplasia after hysterectomy. Their clinical characteristics and preoperative imaging findings were analysed.

**Results:** The mean age at diagnosis was between the range of 47-57 years old. One was pre-menopausal and two were menopausal. One woman presented with intermenstrual bleeding, one woman presented with watery vaginal discharge and one woman was diagnosed LEGH after hysterectomy for leiomyomas. Preoperative workups included physical examination, ultrasonography and MRI.

**Conclusion/Implications:** Lobular endocervical glandular hyperplasia is a rare benign condition of the endocervix. The presentation ranged from asymptomatic to troublesome watery vaginal discharge and abnormal vaginal bleeding. It is crucial to have a systematic workup and detailed counselling for appropriate management before it transforms into the malignant condition of a minimal deviation adenocarcinoma.

EP346 / #1537

Topic: *AS14. Pre-Invasive Disease*

## **INVESTIGATING VULVAR LICHEN SCLEROSUS AND HIGH-RISK ONCOGENIC HPV ASSOCIATION**

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**Introduction:** This prospective study aims to explore the potential connection between vulvar lichen sclerosis (LS) and the prevalence of high-risk oncogenic HPV infection.

**Methods:** Conducted at Hacettepe University Hospital from January to July 2023, the study included LS-confirmed biopsy and benign/nonspecific groups. Inclusion criteria encompassed women aged 30 to 40, single, 1-4 partners, non-smokers, and no diseases/condylomas. The Chi-square test assessed significance.

**Results:** Out of 198 vulvar biopsies, 173 had complete data. LS group (76 patients) & control (97 patients) were analyzed. LS: 34.2% (26/76) HPV-positive, 65.8% (50/76) negative. Control: 19.5% (19/97) HPV-positive, 80.5% (78/97) negative ( $P < 0.05$ ).

**Conclusion/Implications:** The study concludes that due to the premalignant nature of vulvar lichen sclerosis, vigilant monitoring of vulvar lesions is crucial. Notably, a significant elevation in high-risk oncogenic HPV prevalence was observed among LS patients. The calculated Odds Ratio (OR) of approximately 2.84 (95% CI: [2.829, 6.235]) underscores this association's importance. Therefore, thorough cervical pathology follow-up is advised for individuals diagnosed with vulvar LS. Larger studies can provide a deeper understanding of the complex relationship. This study contributes to the growing knowledge on vulvar LS and its potential implications on cervical health, emphasizing the need for comprehensive patient care and further research. By shedding light on this link, clinicians can better tailor their approach to LS patients, ensuring early detection and management of associated risks.

EP348 / #653

Topic: *AS14. Pre-Invasive Disease*

## **AGE-STRATIFIED HISTOPATHOLOGICAL RESULTS IN CERVICAL INTRAEPITHELIAL NEOPLASIA 2 PATIENTS TREATED WITH CERVICAL EXCISION**

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**Introduction:** This study analyzed the clinical outcomes of cervical intraepithelial neoplasia 2 (CIN2) patients according to age by histologically reviewing the cervical excision specimen to help in personalized treatment plan for CIN2.

**Methods:** This retrospective cohort study included CIN2 patients who immediately underwent LEEP for the treatment and were followed up for 2 years with cervical cytology and HPV test. Medical records regarding clinical characteristics and histopathologic results were reviewed. We analyzed pathological and clinical outcomes according to age.

**Results:** A total of 164 CIN2 patients were included. The mean age of the patients was 38.5 years. Histological results of cervical excision specimen were: 13 (7.9%) cases in no residual lesion, 31 (18.9%) cases in CIN I, 44 (26.8%) cases in CIN II, 75 (45.7%) cases in CIN III and 1 (0.6%) cases in micro-invasive carcinoma. There were no significant differences in the pathological grade, rates of positive surgical margins and more advanced lesions of the specimens between the age groups. Ten patients (6.1%) had recurrence with cervical dysplasia (8 cases in LSIL, 2 cases in HSIL). The rate of recurrence was not differ between the age groups.

**Conclusion/Implications:** Regardless of age, the proportion of more advanced lesions of cervical excision specimen in CIN2 is relatively high (44.4% to 51.6%). The risk of recurrence of HSIL after conization in CIN2 is very low (1.2%). Therefore, balanced information on the benefits and harms of different treatment options should be provided when an expectant management is adopted in CIN 2 patients.

EP349 / #850

Topic: *AS14. Pre-Invasive Disease*

## **CLINICAL IMPLICATION OF CERVICAL LENGTH CHANGE AFTER LOOP ELECTROSURGICAL EXCISION PROCEDURE IN CHILDBEARING WOMEN WITH CERVICAL INTRAEPITHELIAL NEOPLASIA**

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**Introduction:** Cervical shortening and its' possible impact on obstetrical outcomes are one of the primary concerns for women who need loop electrosurgical excision procedure (LEEP). Persistent HPV infection after LEEP is a surrogate prognostic marker guiding post-treatment surveillance. This study aims to investigate the clinical impact of cervical length change after LEEP regarding HPV clearance.

**Methods:** Patients under 40 who underwent LEEP by a single surgeon for their cervical intraepithelial neoplasia (CIN2+) from March 2019 to December 2022 were retrospectively enrolled in this study. Cervical lengths were measured pre-procedure and three months after LEEP. The operator tried not to make fragmentation of specimen. The depth of the main ectocervical specimen was measured. Cervical length change was analyzed with the depth of the specimen and HPV clearance.

**Results:** A total of 109 women were analyzed. The median (range) of age, initial cervical length, and ectocervical specimen depth was 31 (21~39) years, 8(1~1.8)mm, and 3(1.5~5.0)cm, respectively. CLs at post-procedure three months were obtained in 89 women (81.6%). The median(range) CL change was 3 (-10~20)mm. There was no statistical correlation between CL change and ectocervical specimen depth. HPV clearance at 3 months after LEEP was more prevalent in the thicker ectocervical specimen depth group (dichotomized by the median value, 53.2% vs. 81.1%,  $p=0.005$ ). In multivariate analysis adjusting clinicopathologic factors, only ectocervical specimen depth was an independent predictive factor for HPV clearance.

**Conclusion/Implications:** Cone depth can be individualized if CL is measured preoperatively. Standardization of CL measurement in nonpregnant women should be preceded.



EP350 / #408

Topic: *AS14. Pre-Invasive Disease*

## **COMPLETE VISUALIZATION OF TRANSFORMATION ZONE IN COLPOSCOPY USING ESTRADIOL OR MISOPROSTOL: A CLINICAL TRIAL**

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**Introduction:** Both estradiol and misoprostol have been used for complete visualization of the transformation zone (TZ) in colposcopy. However, no consensus has been reached on the priority of one medication over the other. This study aimed to compare the efficacy of estradiol and misoprostol for complete visualization of TZ in colposcopy of premenopausal and postmenopausal women.

**Methods:** In this clinical trial, 78 patients with unsatisfactory colposcopy were randomly divided into three groups using a block randomization software package. Group 1 (n=25) received 25 µg of vaginal estradiol for 14 days prior to colposcopy. Group 2 (n=27) received 400 µg of misoprostol 12 h prior to colposcopy. Group 3 (n=26) served as the control group and did not receive any medication. TZ visibility, age, BMI, history of vaginal delivery or sexually transmitted diseases or human papillomavirus (HPV) and drug-related side effects were compared among the three groups and also between premenopausal and postmenopausal women. Data were analyzed using analysis of variance (ANOVA), Kruskal-Wallis, Chi-square, and Fisher's exact tests.

**Results:** The percentage of complete TZ visualization was 72%, 55.6%, and 26.9% in the estradiol, misoprostol, and control groups, respectively (P=0.005). These values were 70%, 33.3%, and 0%, respectively, in postmenopausal women (P=0.043) and 60%, 72.7%, and 33.3%, respectively, in premenopausal women (P=0.152). With regard to drug-related side effects, there was no statistically significant difference between the three groups (P=0.374).

**Conclusion/Implications:** Estradiol was significantly superior to misoprostol for complete visualization of TZ, particularly in postmenopausal women, with no difference in side effects.

EP351 / #229

Topic: *AS15. Rare Tumors*

## CLINICAL FACTORS RELEVANT TO INTER-OBSERVER REPRODUCIBILITY IN PATHOLOGICAL DIAGNOSIS OF IMMATURE TERATOMA OF THE OVARY: A RETROSPECTIVE STUDY OF 148 CASES

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**Introduction:** Mature teratomas with diminutive foci of immature neural epithelium should not be diagnosed as immature teratomas. Inter-observer reproducibility in pathological diagnosis of immature teratoma and its association with clinical factors are unclear.

**Methods:** This retrospective study aimed to identify biomarkers that predict the malignant potential of immature ovarian teratomas (UMIN000046404). A total of 148 cases diagnosed as immature teratomas from 21 institutions were included. A pathologist, blinded to clinical information, performed the central pathological review. Out of 148 cases, 102 were diagnosed as immature teratomas (Immature Group), 44 as mature teratomas (Mature Group), and 2 were excluded as they did not fulfill the inclusion criteria of the study. Clinical information of the cases was analyzed.

**Results:** Age was lower in the immature group (median, 22.5 years, range 2–44) than in the mature group (28, 11–48) ( $p=0.01$ , Student's t-test). Salpingo-oophorectomy of the affected adnexa was performed in 90 (88%) and 17 (39%) cases in the immature and mature groups, respectively ( $p<0.01$ , Fisher Exact test); while the remaining underwent tumor resection, preserving the affected ovary. Three (2.9%) and 22 (50%) cases in the immature and mature groups, respectively, underwent laparoscopy ( $p<0.01$ , Fisher's Exact test).

**Conclusion/Implications:** Patients misdiagnosed with immature teratoma at primary institutions but centrally diagnosed with mature teratoma tended to be older, had undergone laparoscopy, and had the affected ovary preserved. Cases with a preoperative clinical diagnosis of mature teratoma and a postoperative pathological diagnosis of immature teratoma warrant further consultation from expert pathologists.

EP352 / #1291

Topic: *AS15. Rare Tumors*

## **CASE SERIES OF HUGE GENITAL WARTS REQUIRING GYNECOLOGIC ONCOLOGISTS SKINNING VULVECTOMY FROM,SPHMMC,ADDIS ABABA, ETHIOPIA**

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**Introduction:** Human papilloma virus is the commonest sexually transmitted infection among young adult, fortunately enough most of the individuals infected with human papilloma virus are asymptomatic and able to clear the virus so long as they have no innate or acquired immune deficiency. Though it is not uncommon to see genital warts of small-medium sized, it is very rare to find giant genital warts which cannot be managed with topical ablative therapy. Human immune-deficiency virus (HIV) co-infection is the most important contributor for locally aggressive vulvar condyloma acuminatas (Buschke Lowenstein tumor).

**Methods:**





Here I report a case series of giant vulvar condyloma accuminata (vulvar wart) of three cases with two of the cases of Sero-positive for HIV on HAART (highly active anti-retroviral therapy) CD4 counts of all of them under 500 cells/ul , including a ten year old pre-menarche female who had also a giant wart which was not amenable for local ablative treatments. referred from regional hospitals for possible vulvectomy in our teaching hospital.

**Results:** The surgeries were skinning vulvectomy with huge tumor bleeding at the base with no major intra-operative complications. All of the cases had superficial wound infections and improved significantly with a local wound care.

**Conclusion/Implications:** HPV associated vulvar genital condyloma accuminata, in HIV seropositive patients can be beyond local ablative treatments and delay in referral and care for these cases can cause significant impact in their quality of life. The surgical care of giant warts needs gynecologic oncologist surgical expertise.

EP354 / #665

Topic: *AS15. Rare Tumors*

## **HISTOPATHOLOGIC AND ONCOLOGICAL CHARACTERISTICS OF OVARIAN BORDERLINE TUMOURS WITH POSITIVE PERITONEAL CYTOLOGY: A CASE SERIES**

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**Introduction:** Borderline ovarian tumors (BOTs) of the ovary, also called tumors of low malignant potential, are a heterogeneous group of lesions defined histologically by atypical epithelial proliferation without stromal invasion. Recurrence rates can approach 20%. The impact of positive peritoneal cytology is not known.

**Methods:** This retrospective cohort study identified all patients who underwent primary surgical resection of BOTs at a tertiary referral center between February 2017 and March 2023, and who were found to have positive peritoneal cytology at the time of surgery. Demographics and outcome measures were obtained from the medical records.

**Results:** Overall, 13 patients were identified. Median age was 48 (range 22-81). Eleven patients (11/13, 84.6%) had elevated ca-125 at time of diagnosis, with a median of 300 U/mL (range 9-1834 U/mL). In total, 12 patients had a serous borderline tumour, and 1 had a mucinous tumour. Five patients had stage 1 disease, and 8 patients were upstaged to stage III due to the presence of desmoplastic non-invasive implants. Micropapillary pattern was observed in four cases. Median follow-up was 39 months (range 3-75 months). No patient received adjuvant treatment, and no recurrence was reported.

**Conclusion/Implications:** Little is known about the clinical significance of positive peritoneal cytology in BOTs. Our case series may indicate that the presence of neoplastic cells in pelvic washing cytology is not associated with a high rate of recurrence, with the limitations of a small sample size. Positive cytology appears to be correlated with the presence of non-invasive peritoneal implants.

EP355 / #365

Topic: *AS15. Rare Tumors*

## **MULTIOMICS PROFILING OF CHINESE PATIENTS WITH SMALL CELL CARCINOMA OF THE OVARY, HYPERCALCEMIC TYPE**

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**Introduction:** Small cell carcinoma of the ovary, hypercalcemia type (SCCOHT) is a rare and lethal malignancy that occurs most frequently in young women. Studies have shown that mutations in the SMARCA4 gene are one of the factors driving the development of SCCOHT. However, little has been reported about the molecular characteristics in Asian patients. This study aims to reveal the genetic and expression profiles of an independent cohort of Chinese SCCOHT cases by Whole Exome Sequencing (WES) and RNA sequencing.

**Methods:** We enrolled a total of 12 patients with SCCOHT. WES was conducted in 10 of them and 4 were matched with blood samples. We also obtained fresh tumor tissue from 5 patients and performed RNA sequencing.

**Results:** Among the 12 SCCOHT patients, 10 carried SMARCA4 mutations accompanied by loss of protein expression and 1 had a deletion of exon 1-6 in SMARCB1. Somatic variations affecting Notch and Hippo signaling pathway were detected in 60.0% of SCCOHT. Through gene set variation analysis (GSVA), the following pathways were up-regulated in SCCOHT compared with benign ovarian tissue: oxidative phosphorylation, MYC targets, E2F targets, G2M checkpoint, etc. While Notch and WNT signaling pathways were down-regulated.

**Conclusion/Implications:** Here we report the molecular profile of SCCOHT in the Chinese population for the first time. These findings contribute to the further exploration of the pathogenesis of SCCOHT and the development of new targeted therapies.



EP356 / #37

Topic: *AS15. Rare Tumors*

## **THE ROLE OF ADJUVANT PLATINUM-BASED CHEMOTHERAPY IN EARLY ADULT GRANULOSA CELL TUMOR OF THE OVARIES: A META-ANALYSIS OF COMPARATIVE STUDIES**

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**Introduction:** Adult granulosa cell tumors (AGCT) are the most common type of malignant ovarian sex chord stromal tumors but only comprise 2 to 5 percent of all malignant ovarian neoplasms. Most have an indolent growth pattern, but their tendency for late relapses is well documented. Despite the lack of supporting data, NCCN recommends platinum-based adjuvant chemotherapy (AC) for Stage I with intermediate and high-risk features. Therefore, we conducted this meta-analysis to evaluate the impact of AC on disease recurrence in a stage I enriched AGCT.

**Methods:** A review of the medical literature was conducted using online databases. Inclusion criteria consisted of English language, diagnosis of AGCT, studies with a preponderance of stage I, comparative studies of AC versus none, and studies that reported recurrence rates. Studies that had a preponderance of advanced stages or juvenile variants were excluded. A meta-analysis using the fixed effects and random effects models was conducted.

**Results:** Seven retrospective comparative studies with 500 patients were included. The average median age was 47, and the average median follow-up was 58 months. Around 79% were stage I, and 79% of stage I were IC. Most AC were BEP and EP. Platinum-based AC in early-stage AGCT didn't impact recurrence rates (HR=1.39, 95%CI 0.86-2.25, I<sup>2</sup>=48%, p=0.18).

**Conclusion/Implications:** This is the first meta-analysis to show platinum-based AC does not improve the recurrence rate in early AGCT. In the absence of evidence supporting any benefit, recommendations to use platinum-based AC with or without Bleomycin should be re-evaluated since its risk is well-documented and carry potentially serious side effects.

EP357 / #863

Topic: *AS15. Rare Tumors*

## **INVESTIGATION OF PROGNOSTIC FACTORS IN NEUROENDOCRINE CARCINOMA OF THE UTERINE CERVIX**

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**Introduction:** Neuroendocrine carcinoma of the cervix (NECC) is a rare, aggressive histologic type of cervical cancer. This study aimed to investigate prognostic factors of NECC and compare survival outcomes according to the treatment methods.

**Methods:** NECC patients who received primary treatment at our institution between 2000 and 2020 were retrospectively identified. We collected patients' clinicopathologic and survival data, including age at diagnosis, histologic subtype, stage, immunohistochemical staining results, and detailed treatment methods. Multivariate analyses were conducted to identify prognostic factors for progression-free survival (PFS) and overall survival (OS).

**Results:** In total, 47 NECC patients were included in this analysis. The mean age at diagnosis was 46.9 years. In related to histologic subtypes, 23 (48.9%) and 7 (14.9%) were diagnosed with small cell and large cell NECCs, respectively, while 17 (36.2%) had NECC combined with other carcinomas. Patients with early-stage (2009 FIGO stage IB1), locally advanced-stage (IB2-III A), and distant metastasis (IVB) showed 15.6, 17.7, and 7.0 months of the median PFS, respectively, and 94.7%, 92.3%, and 15.6% of 18-month OS rates, respectively. In terms of primary treatment, 32 (68.1%) received surgical treatment. In multivariate analysis, small cell NECC (aHR, 0.297; 95% CI, 0.133-0.663; P=0.003) was identified as a favorable prognostic factors for PFS. In a subgroup of patients with stage IVB NECC, no differences in PFS and OS were observed between the chemotherapy-only and multimodal therapy groups.

**Conclusion/Implications:** Initial FIGO stage and histologic subtypes were significant prognostic factors for survival. For patients with stage IVB disease, chemotherapy only might be preferable rather than combined therapy.

EP358 / #615

Topic: *AS15. Rare Tumors*

## **METHYLATION PROFILING IDENTIFIES TWO DISTINCT CLUSTERS OF SMALL CELL CARCINOMA OF THE OVARY HYPERCALCEMIC TYPE (SCCOHT)**

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**Introduction:** Small cell carcinoma of the ovary hypercalcemic type (SCCOHT) is a highly aggressive ovarian malignancy that occurs in young women and is defined by inactivating mutations in SMARCA4. While current treatment modalities only show limited success, emerging evidence suggests that a subset of patients may respond to immunotherapy. Here we set out to assess if methylation profiling can stratify SCCOHT into clinically meaningful subgroups.

**Methods:** We collected a multicenter series of clinically annotated SCCOHT. Tumor samples were analysed using the Illumina EPIC and 450k BeadChip. Focal copy number score (FCS) was computed from segmented array data using CNApp. Statistical analyses included the Chi-Squared tests and one-way ANOVA.

**Results:** Our cohort included 27 SCCOHT. The age at diagnosis ranged from 7 – 47 years (n=25, median of 25 years) and 45 % of tumors where this information was available (n=20) presented with low stage disease. Clustering analysis of DNA methylation data identified two distinct tumor clusters (C1, n=15 and C2, n=12). C1 was associated with a trend towards younger patient age when compared to C2 (23.7 years vs. 30.2 years). Tumors assigned to C1 also showed a trend towards a lower mean FCS as compared to tumors from C2 (7.4 vs. 12.75). There was no difference in clinical stage between the two clusters.

**Conclusion/Implications:** Based on a small series our data suggests that there are two distinct DNA methylation clusters of SCCOHT. Analyses of larger cohorts of SCCOHT are warranted to understand, if the clusters identified correlate with patient survival and/or response to (immuno-)therapy.

EP359 / #860

Topic: *AS15. Rare Tumors*

## **A RETROSPECTIVE STUDY OF 11 CASES FROM A SINGLE INSTITUTION: MALIGNANT TRANSFORMATION ARISING FROM MATURE CYSTIC TERATOMA.**

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**Introduction:** Malignant transformation arising from ovarian mature cystic teratoma(MT-MCT) is very rare and has a poor prognosis. This study investigated clinical characteristics and prognosis of MT-MCT in a single institution.

**Methods:** A retrospective chart review was performed. Patients diagnosed with MT-MCT at Haeundae Paik Hospital between 2010 and 2022 were identified.

**Results:** Among 718 cases of ovarian MCT, malignant transformations were found in 11 patients (1.5%). The median age was 49 (range, 22-86) years. The mean size of MT-MCT was 11 (range, 4-22) cm. The most common symptom was abdominal discomfort, reported in seven(63.6%) cases, followed by urinary dysfunction in two(18.1%) cases. Tumor markers were elevated in preoperative examination and mainly included CA125(63.6%),CA19-9(36.3%),and SCCag(18.1%). Three patients underwent staging surgery, while eight patients underwent cystectomy or salpingo-oophorectomy without staging surgery. Five patients had squamous cell carcinoma, three had carcinoid, and three had other histological subtypes. Seven cases were in FIGO stage I, four cases were in stage II-IV. Patients in stage IC to IV received adjuvant chemotherapy and the overall 1-year survival rate was 33.3%. All the patients in stage IA survived until the period of follow up (mean survival time 51 months) except for one patient who died of old age.

**Conclusion/Implications:** The possibility of MT-MCT was associated with large tumor size or advanced age. In cases of stage 1C or higher, the prognosis was worse compared to other types of ovarian cancer. Therefore, when encountering large tumor size or advanced age, it is important to consider the possibility of malignancy.

EP360 / #693

Topic: *AS15. Rare Tumors*

## **PROGNOSTIC FACTORS FOR SURVIVAL IN PATIENTS WITH RARE PERITONEAL SURFACE MALIGNANCY: DIFFUSE MALIGNANT PERITONEAL MESOTHELIOMA- A SINGLE INSTITUTION EXPERIENCE**

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**Introduction:** Diffuse malignant peritoneal mesothelioma (DMPM) is a rare and aggressive cancer that originates in the peritoneum. Due to its poor prognosis, a better understanding of its clinical characteristics and prognostic factors is needed. This study aimed to investigate such factors and their association with survival in patients with DMPM.

**Methods:** We conducted a retrospective analysis of patients diagnosed with DMPM at Ajou University Hospital from February 2000 to June 2022. Various clinical characteristics and potential risk factors that may influence survival were evaluated.

**Results:** We identified a total of 22 patients (6 male, 16 female) with DMPM. The median age of the patients was 57.5 years (range 20-80). The overall median survival was 31.1 months (95% CI 15.8-46.4), with a 5-year survival rate of 25.3%. Of the patients, 2 received cytoreductive surgery and followed by adjuvant chemotherapy, 4 received cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy (CRS+HIPEC). Survival analysis revealed that cytoreductive surgery ( $p=0.014$ ) and intraperitoneal chemotherapy ( $p=0.008$ ) were significantly associated with overall survival.

**Conclusion/Implications:** Our findings suggest that cytoreductive surgery and intraperitoneal chemotherapy are important treatment options for improving survival in patients with DMPM. Further research is needed to better understand the optimal treatment approach for this rare and aggressive cancer.

EP361 / #722

Topic: *AS15. Rare Tumors*

## **CLINICOPATHOLOGICAL FEATURES AND SURGICAL PROCEDURE OF ADNEXAL MASSES WITH ABDOMINAL PAIN IN PEDIATRIC AND ADOLESCENT PATIENTS**

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**Introduction:** This study investigated the clinicopathological features and surgical procedures of adnexal masses with abdominal pain in pediatric and adolescent patients.

**Methods:** Retrospective cohort study of 212 pediatric and adolescent patients was performed who admitted for abdominal pain and presenting with an adnexal mass between March 2012 to December 2019

**Results:** The proportion of patients presented with acute onset pain, persistent or recurrent pain, and duration of pain less than 3 months was significantly higher in the TO group than in the non-TO group ( $P < 0.001$ ). 69.2% of patients with torsion had fixed pain sites, compared with 42.2% in patients without torsion ( $P < 0.001$ ). The symptom of nausea and vomiting was more common among girls with torsion ( $P < 0.0001$ ). 88.5% of girls with torsion had an ovarian cyst/mass  $\geq 5$  cm, compared with 75.0% in girls without torsion ( $P = 0.038$ ). 66.7% of girls underwent ovary-preserving surgery, compared with 92.2% in patients without torsion. The most common pathologic types were mature teratoma and simple cyst, accounting for 29.4% and 25.6%, respectively. The multivariate analyses confirmed that mass size greater than 5 cm, acute onset pain, persistent or recurrent pain were significantly associated with increased risk of torsion.

**Conclusion/Implications:** Most pediatric or adolescent patients with adnexal torsion present with acute onset of persistent, recurrent pain and had fixed pain sites. Thus, a strategy of earlier and liberal use of Diagnostic Laparoscopy (DL), particularly with a pelvic mass size greater than 5 cm, acute onset pain, persistent or recurrent pain, may improve ovarian salvage.

EP362 / #696

Topic: *AS15. Rare Tumors*

## **NEW PATIENT-DERIVED MODELS AND THERAPY SCREENING IN MUCINOUS OVARIAN CARCINOMA**

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**Introduction:** Mucinous ovarian carcinoma (MOC) is a rare cancer with poor outcomes when advanced due to innate resistance to standard of care platinum-taxane chemotherapy regimens. There is a lack of evidence to support different chemotherapy choices due to poor clinical trial recruitment and a scarcity of suitable pre-clinical models. Our objective was to develop new patient-derived models of MOC and use them to test therapies.

**Methods:** We collected tissue samples with consent from women undergoing surgery for primary or recurrent MOC. We optimised culture conditions for growing tumour cells as 3D organoids in Matrigel, which included specific growth factors and processing conditions. Successful cultures were characterised by immunohistochemistry (CK7, CK20, PAS, PAX8, p53, HER2) and DNA and RNA sequencing for comparison to the original tumour. Organoids were tested with 14 therapeutic agents and evaluated using CellTiter-Glo, brightfield imaging and Hoechst staining.

**Results:** We successfully cultured eight MOC as organoid lines that showed strong concordance with tumour genetic and protein characteristics. Drug screening showed little response to platinum-based chemotherapies. Variable responses were seen with paclitaxel, mitomycin C and gemcitabine, with the strongest responses observed with topoisomerase I inhibitors irinotecan and topotecan.

**Conclusion/Implications:** This is the first cohort of organoid models for MOC tested across a wide range of chemotherapeutic agents. Results support clinical observations of limited response to platinum chemotherapy, while other therapies show some promise as alternatives. Future work will explore combinations of agents as well as correlation back to genetic and gene expression characteristics to assess biomarkers of response.

EP363 / #213

Topic: *AS15. Rare Tumors*

## **THE ROLE OF SURGEON SPECIALTY IN MANAGEMENT AND SURVIVAL OF MALIGNANT OVARIAN GERM CELL TUMORS: A POPULATION-BASED STUDY**

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**Introduction:** The aim of this study is to describe treatment and survival outcomes in patients with malignant ovarian germ cell tumors (MOGCT) who had surgery by general gynecologists (GG) versus gynecologic oncologists (GO).

**Methods:** A population-based retrospective cohort study, including adult patients with MOGCT identified in the provincial cancer registry (1996-2020). Baseline characteristics, surgical and chemotherapy treatment were compared between those with surgery by GG or GO. Cox proportional hazards (CPH) model was used to determine if surgeon specialty was associated with overall survival (OS).

**Results:** Overall, 363 patients were included. One-hundred and sixty (44%) patients underwent surgery by GO and 203 (56%) by GG. There were higher rates of stage II-IV in the GO group (27.5% vs 3.9%,  $p < 0.001$ ) (table). Multivariable logistic regression with age, histologic type, and socioeconomic status showed stage of disease was the only factor associated with having surgery by a GO (OR 6.79, 95% CI 2.83-16.30,  $p < 0.001$ ). 5-year OS was 90% vs 93% in the GO vs GG ( $p = 0.39$ ). CPH model showed factors associated with increased rate of death were age at diagnosis (HR 1.09, 95% CI 1.07-1.12) and chemotherapy (HR 3.12, 95% CI 1.44-6.75). Surgeon specialty was not independently associated with all-cause death (HR 1.04, 95% CI 0.51-2.15).



p=0.91).

**Table 1 – Baseline characteristics and surgical management stratified by surgeon’s specialty**

Variable	Gynecologic oncology n= 160	General gynecology n=203	P value
Age, years, median	29 (23-38)	31 (24-38)	0.280
Stage: n(%)			<.0001
I	48 (30.0%)	56 (27.6%)	
II-IV	44 (27.5%)	8 (3.9%)	
Hysterectomy, n(%)	42 (26.3%)	37 (18.2%)	0.065
Oophorectomy: n(%)			0.015
Unilateral	106 (66.3%)	151 (74.4%)	
Bilateral	45 (28.1%)	33 (16.3%)	
Staging surgery, n(%)	48 (30)	19 (9.3)	<.0001
Chemotherapy, n(%)	103 (64.4%)	76 (37.4%)	<.0001
Time-to-chemotherapy, days, median	36 (24-59)	47 (28-78)	0.056

**Conclusion/Implications:** In this group of MOGCT, the difference in 5-year OS was not statistically significant between patients having surgery by GO compared to GG, although survival rates were lower than expected in the GG group despite their low-risk features. Patients with confirmed/suspected MOGCT should be referred to GOs for optimal management.

EP368 / #235

**Topic: AS16. Screening/Early Detection**

## **IS CYTOLOGICAL EVALUATION IN THE CERVICAL CANCER SCREENING PROGRAM IN JAPAN INDEPENDENT OF THE TEST RESULTS FOR HPV? NILM VS. ASC-US IN HPV-POSITIVE CASES**

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**Introduction:** Japan is considering introducing “HPV test primary cytology triage” for cervical cancer screening. Among HPV-positive cases, NILM is considered as negative, and ASC-US or higher as positive for triage result. Since cytology is based on cell morphology, the results of cytological evaluation, whether for triage or screening, should be consistent. However, cytologists not blinded to the results of HPV testing might provide biased results. Therefore, we attempted to confirm if the results of cytological evaluation could be influenced by the results of HPV testing.

**Methods:** From the Usefulness Study on Combined Cytology and HPV Testing, we listed the laboratories conducting cytological evaluation and HPV testing, respectively. We asked cytology laboratories if they could refer to the HPV test results while providing cytology decisions, and if they might change their decisions in cases with positive HPV test results.

**Results:** A total of 52 each of HPV testing laboratories and cytological laboratories were included; 31 of these conducted both HPV testing and cytological evaluations. In all, 6 cytological laboratories had access to the HPV test results, and in 5, the results of cytology could be changed from NILM to ASC-US depending on the HPV test results.

**Conclusion/Implications:** About 10% of cytological laboratories have access to the HPV test results, which often influences the results of their cytology evaluation. In order to ensure accuracy of cytology triage, laboratories should be discouraged from changing their evaluation results based on the HPV test results, and to monitor the distribution of the triage results.

EP369 / #581

Topic: AS16. Screening/Early Detection

## IMPACT OF FOCUSED INTERVENTIONS TO ENHANCE CERVICAL CANCER SCREENING UPTAKE AT TERTIARY CARE HOSPITALS IN INDIA: A MULTICENTRIC STUDY

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**Introduction:** Cervical cancer screening coverage does not meet WHO elimination targets even at tertiary institutes in India. This interventional study assessed the impact of simple quality improvement (QI) tools in five tertiary care institutes where a situational analysis was previously done.

**Methods:** This WHO-SEARO supported multicentric study was conducted between August 2021 and May 2022. Root cause analysis using Fishbone (4Ps) and seven PDSA (Plan-Do-Study-Act) cycles were undertaken.

**Results:** Root-cause analysis showed that despite Policy, Procedure- and People-related factors were barriers to adequate screening (Figure 1).

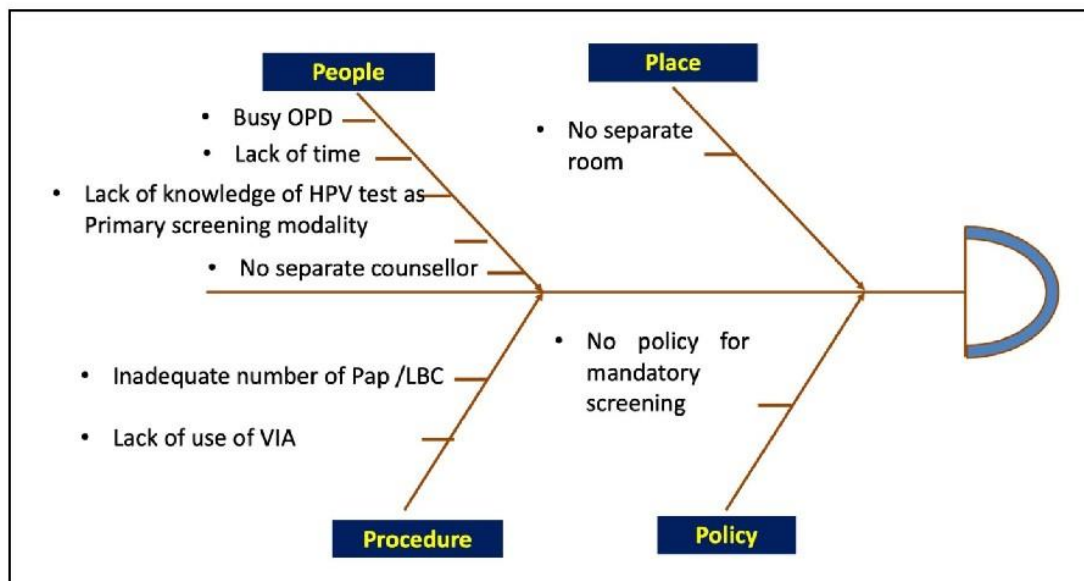


Fig 1: Root Cause Analysis: FISH BONE CHART (4Ps)

PDSA-1 (training of healthcare professionals) increased the mean screening rate from baseline 24.8% to

28.8% (range 16.8-33.0%). PDSA-2 (poster display in clinics) had no impact (28.1%; range 16.4-36.2%). PDSA-3 (instant reminders using tags over cards) led to marginal improvement (31.0%; range 26.9-70%). PDSA-4 (facilitating VIA in each room) actually reduced screening rate (22.7%; range 17.3-30.9%) due to poor compliance in busy clinics. PDSA-5 (creation of a dedicated screening facility by paramedical workers (PMWs) further increased the screening rate to 43.6% (range 25-47.7%). PDSA-6 (daily WhatsApp reminders to HCPs) had variable impact (43%; range 17.9-90%). However, sustenance was not feasible, as PMWs were posted for other clinical services and also separate facility interrupted the patient's flow. PDSA-7 (increased supply of kits along with counselling at entry point and stamp application on card) could increase the rates to 52.8% (range 35-98%). (Figure 2)

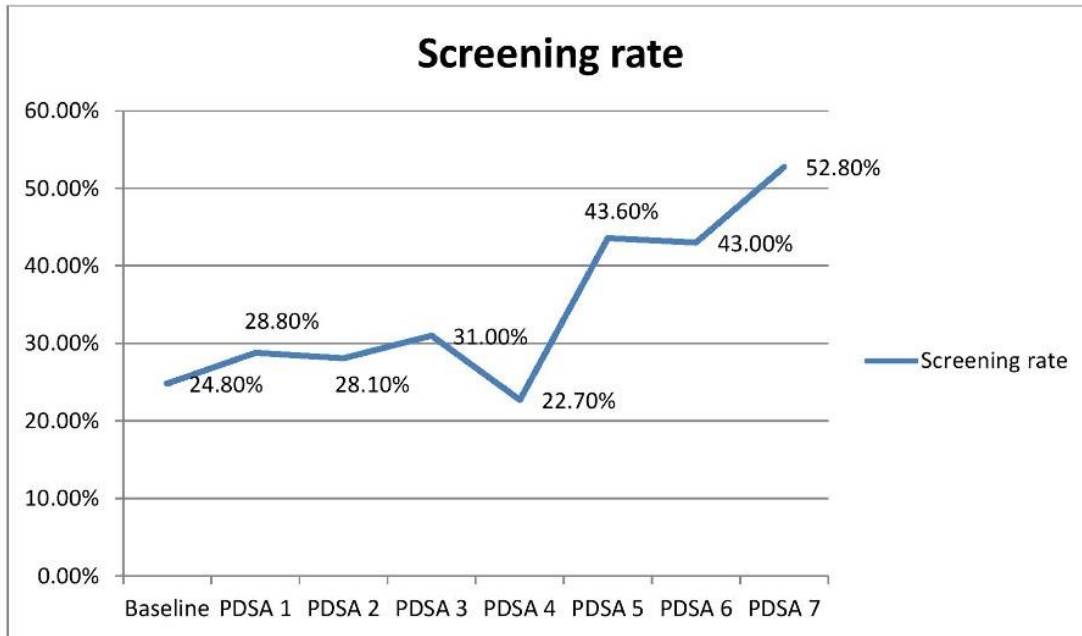


Fig 2: Mean screening rates after each focused intervention

**Conclusion/Implications:** Sensitization and training of healthcare professionals and paramedical workers is essential. Novel, contextual interventions can improve screening uptake even in tertiary hospitals in developing countries.

EP370 / #835

**Topic: AS16. Screening/Early Detection**

## **DIAGNOSTIC ACCURACY OF CYTOLOGY TEST IN HPV-INDEPENDENT CERVICAL ADENOCARCINOMA**

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**Introduction:** Human papillomavirus (HPV)-independent cervical cancer account for approximately 5% of cervical cancer, especially in adenocarcinomas. These subtypes have poorer prognosis and require clinical attention. Recent guidelines on cervical cancer screening recommend primary HPV screening rather than conventional cytology test. This study evaluated the accuracy of cytology test in HPV-independent (HPVI) cervical adenocarcinoma and compared it to HPV-associated (HPVA) cervical adenocarcinoma.

**Methods:** Medical records of 94 patients with HPVI cervical adenocarcinoma were collected after pathologic review. Patients with HPVA cervical adenocarcinoma from January 2019 to November 2021 were set as a control group. Patients who had not performed cytology test before diagnosis were excluded. Pathologic report of cervical biopsy and the results of most recent cytology test prior to diagnosis were investigated. Histologic subtype of cervical cancer was divided according to 2020 WHO Female Genital Tumors classification.

**Results:** Eighty-one patients in HPVI group and 110 patients in HPVA group were included in final analysis. Among HPV-associated adenocarcinoma, usual-type was the most common type (80.9%, 89/110). In HPV-independent adenocarcinoma, there were 59 (72.8%) cases of gastric-type, 10 (12.3%) cases of clear cell-type, 5(6.2%) cases of endometrioid-type, and 3(3.7%) cases of mesonephric-type adenocarcinoma. Patients with HPV-associated cancer had abnormal cytology test result in 79.1% (87/110), with false-negative rate of 20.9% (23/110). In patients with HPV-independent adenocarcinoma, 63.0% (51/81) had abnormal cytology test result, with false-negative rate of 37.0% (30/81).

**Conclusion/Implications:** The false-negative rate of cytology test was higher in HPV-independent adenocarcinoma than in HPV-associated adenocarcinoma. Cervical cytology test is not accurate for screening HPV-independent adenocarcinoma.

EP371 / #384

**Topic: AS16. Screening/Early Detection**

## **NATIONAL MAMMOGRAPHIC SCREENING PROGRAM FOR BREAST CANCER IN UZBEKISTAN: FIRST RESULTS**

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**Introduction:** A state level national screening program was designed and decided to implement through a pilot in the Bukhara region, in age group of women from 45-65 years (incidence rate about 80 per 100 000 population).

**Methods:** Bukhara region has 13 subdivisions. Every subdivision was equipped with a digital mammograph (13 fixed and 2 mobile units) with centralized real-time system of registration and reporting using specialized software (Uzfujirunlek). All mammograms were sent to central reading center based at National Cancer Center in Tashkent in real time. Standard BIRADS scoring is used. Here we report data from the beginning of screening program (May 2021) to January 2023.

**Results:** A total of 137 245 women were screened. Out of this group 398 (0.3%) were found to have BIRADs 5, 4 998 women (3.6 %) were found to have BIRADs 4 and BIRADS 1-2 category was reported in 126 859 women (92.4%). All patients with BIRADs 0-4-5 (10 903) results were sent for the further examination. Breast cancer were detected in 377 (3.5% from BIRADs 0-4-5) women. 81 cases were diagnosed in stage I (22.4%), 214 in stage II (58.5%), 42 in stage III (8.5%) and 40 in stage IV (10.6%). The highest number of patients were between the age of 55-65 (51.4%), and 48.6% were in age 45-55.

**Conclusion/Implications:** Screening at the population level in Uzbekistan proved to be feasible. Almost 80% of women were diagnosed at the early stages. It becomes possible to decrease mortality and increase survival rate of breast cancer patients in Uzbekistan.

EP372 / #735

**Topic: AS16. Screening/Early Detection**

## **HUMAN PAPILLOMAVIRUS INFECTIONS AMONG WOMEN WITH CERVICAL LESIONS IN UZBEKISTAN**

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**Introduction:** The prevalence of HPV types 16 and 18 was studied in healthy women, patients with concomitant and precancerous diseases of the cervix and cervical cancer women from Tashkent city.

**Methods:** Totally 787 (100%) women were examined, and 79 (10%) of them were with cervical lesions and 21 (2.7%) - healthy. Out of the patients with cervical lesions, morphologically eroded ectropion, endocervicosis, polyps were registered in 26 (32.9%) women, CIN - 19 (24%) patients and cervical cancer - 24 (30.4%). The age of women ranged from 18 to 62 years. The material for the study was smears and biopsies from the cervix. HPV DNA detection with Genotyping was performed by PCR.

**Results:** In 26.9% of women with concomitant cervical lesions, there was revealed HPV types 16 and 18. Out of CIN patients it was detected HPV DNA in 73.7% cases; out of cervical cancer patients - HPV was detected in 95.6% cases. Moreover, out of healthy women, without visual pathology of the cervix, HPV was detected in 19%. It was performed cervical conization by an electrosurgical method with systemic antiviral therapy for patients with concomitant diseases and CIN. Patients were monitored every 6 months by using HPV test of cervical smears. After treatment HPV DNA was present in 49.9% of smear samples.

**Conclusion/Implications:** HPV has the ability to eliminate from the human body on its own, however, the results of the study showed that even after local and systemic therapy, HPV can persist in the body, finally lead to invasive cervical cancer.

EP373 / #787

**Topic:** AS16. *Screening/Early Detection*

## **TITLE: ELIMINATION OF CERVICAL CANCER: DOES COLPOSCOPY REALLY MATTER IN LOW RESOURCE SETTING?**

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**Introduction:** Cervical cancer (CC) is the second most common malignancy among women in Bangladesh which is preceded by a precancerous phase called CIN. This facilitates early detection of CIN and thereby making CC preventable. Colposcopic scoring systems can select patients who require treatment. This study was performed to compare between two colposcopic scoring system for selecting the patients with cervical pre-cancer for treatment as a single visit approach.

**Methods:** This prospective study enrolled 300 women aged 18 years or over with abnormal cervical screening test. All women underwent colposcopy by both Reid colposcopic index and Swede score. Biopsy was taken in all cases. The performance of both scores was assessed.

**Results:** A total of 54 (18%) CIN2+ lesions were detected. Reid colposcopic index at a cutoff of 5 had sensitivity, specificity, positive predictive value, and negative predictive value for detecting CIN2+ was 87.62%, 94.71%, 87.62%, and 94.71%, respectively. Using Swede score at a cutoff 5 sensitivity, specificity, positive predictive value, and negative predictive value were 96.59%, 89.58%, 77.27%, and 98.62%, respectively and at cutoff 8 were 68%, 98.03%, 94.44%, and 86.2%, respectively. The strength of correlation between the two scores was 0.603.

**Conclusion/Implications:** There was a good association between two colposcopic scoring. Swede score at cut off 5 can be used for screening, whereas cut off 8 can be used for treatment purpose as single visit approach. Thus colposcopy really matters in eliminating cervical cancer in low resource setting where the high performance test for the screening are still evolving.



EP374 / #148

Topic: *AS16. Screening/Early Detection*

## **PREVALENCE OF HIGH-GRADE LESIONS OR CANCER AND THEIR ASSOCIATED FACTORS AMONG WOMEN AGED > 60 YEARS WITH ABNORMAL CERVICAL CANCER SCREENING**

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**Introduction:** This study was to explore the prevalence and associated factors with high-grade lesions or cancer in women aged > 60 years with abnormal cervical cancer screening.

**Methods:** Medical records of women aged > 60 years who had abnormal cervical cancer screening from 8 Thai cancer centers during 2009-2021 were retrospectively reviewed. Baseline characteristics, prior and current cervical cancer screening and subsequent histopathology were collected. Logistic regression analysis was performed to identify associated factors with high-grade lesions or cancer.

**Results:** A total of 1,622 women were included. The mean age was 68.2±7.2 (range 60-100). Twenty one percent (251/1,175) were immunocompromised, 10% (55/511) still had sexual activity. Forty percent (527/1,293) had never had screening test. History of high-grade lesions or cancer were reported in 48.9% (128/262). The current abnormal screening results were normal cytology with positive high-risk HPV 0.9%, ASCUS 38%, LSIL 11.8%, ASC-H 11.9%, HSIL 12.6%, AGC 19.7%, SCCA 4.7% and adenocarcinoma 0.3%. Subsequent histopathology revealed high-grade lesions and cancer in 12.6% and 14.4% respectively. By univariable analysis, factors associated with high-grade lesions and cancer were older age, immunocompromised women, never had screening, and prior high-grade lesions or cancer. By multivariable analysis, the only independent significant factor was prior high-grade lesions or cancer (adjusted OR = 5.04, p<0.001).

**Conclusion/Implications:** The risk of high-grade lesions and cancer in elderly women with abnormal cervical cancer screening was substantial. Continuing cervical cancer screening at age beyond screening recommendation should be considered especially in women with history of high-grade lesions or cancer.

EP377 / #1514

**Topic: AS16. Screening/Early Detection**

## **FIRST IMPLEMENTATION OF HPV SELF-SAMPLING IN VIETNAM: AN ASSESSMENT OF ACCURACY AND FEASIBILITY**

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**Introduction:** WHO recommends HPV self-sampling as a safe and highly accepted additional strategy in cervical cancer screening for women aged 30-60 years [1]. Currently, no research on HPV self-sampling has been conducted in Vietnam. This study aims to evaluate the accuracy, acceptability, and women's experience of HPV self-sampling compared to healthcare provider collection at Da Nang Oncology Hospital.

**Methods:** A cross-sectional study was conducted at Da Nang Oncology Hospital from April to June 2023 for women aged 30–65 years. HPV self-sampling was performed using Copan Self Vaginal FLOQSwabs prior to physician-collected HPV on the same day. Samples were preserved in Thinprep PreservCyt and analysed by Roche Cobas 4800.

**Results:** The study included 108 cases, for which the sample-inadequacy rate was 4.6% (5/108 cases). Patient's mean age was  $44.0 \pm 8.1$  with 75.0% aged 30-49 years. Among 103 qualified cases, positive rates for HPV16, HPV18 and 12 other high-risk HPV types were 0.97%, 0% and 2.91% respectively in self-collected versus 0.97%, 0.97% and 2.91% in physician-collected samples. The accuracy of HPV self-sampling was 99.0% when using physician-sampling as a reference (102/103 cases). 50.0% of women preferred self-collection, 44.4% preferred physician-collection, and 5.6% had no preference. 77.8% believed healthcare provider-sampling was more accurate than self-sampling. Only 8.3% reported painful experience and 9.3% encountered difficulty with self-sampling. The majority (91.7%) would choose HPV self-sampling at home for next screening and 96.3% would recommend it to other women.

**Conclusion/Implications:** HPV self-sampling is an accurate and highly acceptable approach for Vietnamese women to improve the cervical cancer screening rate.

EP378 / #519

**Topic: AS16. Screening/Early Detection**

## **CERVICAL CANCER PREVENTION PROGRAM IN NEPAL: A COMPREHENSIVE 'TRAIN THE TRAINER' APPROACH**

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**Introduction:** Cervical cancer is a leading cancer in Nepal. Lack of access to screening and trained health professionals to manage preinvasive and invasive cervical disease contributes to high cancer incidence and mortality.

**Methods:** Cancer Care Nepal (CCN) and MD Anderson Cancer Center (MD Anderson) partnered to implement a 'train the trainer' (TOT) program to teach cervical cancer screening and management. TOT courses were held for specialists from five institutions throughout Nepal to learn how to deliver these trainings. Each participating institution then held local courses for nurses and doctors. The training was complemented with monthly Project ECHO® (Extension for Community Healthcare Outcomes) telementoring videoconferences.

**Results:** Two TOT and five local training courses were held for providers from 20 centers from November 2021 to October 2022. During COVID-19 pandemic travel restrictions, the MD Anderson faculty joined the courses and provided didactics virtually. In-person, hands-on training using simulation models to teach VIA, colposcopy, ablation and LEEP were led by the Nepalese faculty. The 173 participants included 28 gynecologists, 4 gynecologic oncologists, 1 medical oncologist, 22 general practitioners, and 118 nurses. 126 (73%) completed the pre- and post-course surveys with 86% of respondents expressing their desire to make changes in their practice as a result of the courses. In 2022, CCN became a Project ECHO hub and has held 12 sessions with approximately 20 participants from 11 centers per session.

**Conclusion/Implications:** Our TOT and local training courses have increased the reach of training, with the goal of decreasing the burden of cervical cancer in Nepal.

EP379 / #991

Topic: *AS16. Screening/Early Detection*

## **PILOT IMPLEMENTATION OF HPV SELF-COLLECTION FOR CERVICAL CANCER SCREENING IN COLOMBIA: CHALLENGES OF NON-ORGANIZED PROGRAMS**

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**Introduction:** Objective: to assess acceptability and adherence to cervical cancer screening algorithms based on self-collected HPV testing among hard-to-reach women in Colombia

**Methods:** a randomized trial with three arms included: 1) HPV and pap-smear samples collected by clinicians in one visit and followed by colposcopy/biopsy and treatment; 2) HPV self-collection followed by colposcopy/biopsy and treatment; and 3) HPV self-collected followed by ablative treatment. Women 30 to 65 years without history of cervical cancer screening in the previous 3-years were invited to participate. Invitation and sample collection were planned by home visits and by mail. Acceptability was defined as percentage of women tested among invited, and adherence as percentage of women compliant with the diagnostic and treatment workup among HPV-positive women

**Results:** No women could be recruited as planned given the low efficacy for home visits and mail/post. Alternative strategies were implemented including invitation by phone call, in-person invitation in health centers, and screening campaigns. Two hundred and fifteen women were included. The patients recruited in arms 1, 2 and 3 were 68, 72, and 75, respectively. 4.7% of women of the target population were reached by call, and 21.1% of women attending the screening campaigns were eligible. Acceptability was 74.4%, 94.7%, and 92.8% with the phone calls, in-person invitation, and screening campaigns respectively. the compliance with the diagnostic work-up was 100.0% and 53.3% in arms 1 and 2. Treatment compliance was not assessable

**Conclusion/Implications:** HPV self-collection is highly acceptable; however, coverage of hard-to-reach populations is challenging for scenarios without organized programs

EP380 / #723

Topic: *AS16. Screening/Early Detection*

## **IS IT NECESSARY TO EXPAND THE SCREENING AGE MARGIN FOR DIAGNOSIS OF CERVICAL CANCER AT A REGIONAL LEVEL? THIRD REGION, CHILE**

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**Introduction:** Current WHO recommendation remarks screening with high-performance tests of women with ages between 35-45 years to accelerate the elimination of cervical cancer. Our local cervical cancer screening program recommends PAP screening for women between 25 and 64 years of age.

**Methods:** Retrospective review with statistical database analysis using clinical records, protocols, and biopsies of the gynecology oncology committee of diagnosed patients with cervical cancer between November 2020-April 2023. A bleeding, friable, exophytic lesion in the cervix was considered clinical suspicion.

**Results:** Total of 95 patients with diagnosis of cervical cancer; 19 patients (20%) outside the recommended screening range for age: 17 patients >64 years and 2 patients <25 years. 2 patients referred with atypical pap smear results (unknown reason why PAP was done) and 17 due to clinical suspicion. On the physical examination 95% (18) had an obvious lesion. 3 patients were in stage Figo I (IA2, IB2 and IB3), 6 in stage II (2 IIA2, 4 IIB), 5 in stage III (1 III B, 4 IIIc1) and 4 in stage IV B, 1 in non-specific stage (lymphoma). Histological type: 74% (14) squamous, 21% (4) adenocarcinomas and 5% (1) lymphoma.

**Conclusion/Implications:** We believe this to be an important finding to promote change on the prevention strategy at the regional level regarding the age of screening, since 20% of the population in approximately 3 years demonstrated to have a fatal pathology that is clearly preventable as the studies say due to timely and adequate screening.

EP382 / #190

**Topic:** AS16. *Screening/Early Detection*

## **LIMITATIONS OF CERVICAL CYTOLOGY AS A SCREENING TEST IN THE DIAGNOSIS OF CERVICAL CANCER**

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**Introduction:** In Japan's Cervical Cancer Screening Guidelines (2020), the cervical cytology alone method is recommended to be performed every 2 years as a cervical cancer screening. On the other hand, its sensitivity and specificity are varied, respectively, and approximately 6% of the results are false-negative. In this study, we investigated the status of cervical cancer screening in the 2 years prior to diagnosis in our cervical cancer cases, and examined risk factor(s) for underestimation by screening.

**Methods:** Cervical cancer patients who underwent initial treatment at our hospital between January 2012 and February 2022 were included in the study. Patient backgrounds (age at diagnosis, previous history, history of vaginal delivery, menstrual history, etc.) and cervical cancer screening status and results in the two years prior to diagnosis were extracted from medical records, and statistical analyses were conducted for patients whose cytological diagnosis was underestimated.

**Results:** There were 323 cervical cancer cases during the study period. Of these, 22 patients (6.9%) were in the underestimated group who had undergone cervical cytology screening in the 2 years prior to diagnosis and had been diagnosed as normal. A history of cervical conization was found in 3 patients (13.6%) of the underestimated group and in 10 patients (3.3%) of the control group (n=301), which was statistically significant ( $p=0.0175$ ).

**Conclusion/Implications:** It is well known that cervical cancer screening is necessary even after conization for CIN3. Moreover, we hypothesize that results of cervical cytology screening alone may be underestimated in patients with a history of previous cervical conization.

EP383 / #755

**Topic:** AS16. *Screening/Early Detection*

## **THE SIGNIFICANCE OF HPV TEST FOR CERVICAL CANCER SCREENING IN LOW-GRADE ABNORMAL CYTOLOGY GROUP USING SOUTH KOREAN DATA.**

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**Introduction:** This study aimed to evaluate the significance of HPV testing as a screening test for cervical cancer.

**Methods:** Between April 2010 and September 2021, women initially diagnosed with ASCUS or LSIL and having HPV infection were included. They underwent cytology and HPV testing every 6 months until disease progression. Cytology results were categorized as ASCUS/LSIL positive or HSIL positive. HPV infection patterns were divided into high-risk 1 (16, 18, 31, 33, 45, 52, 58), high-risk 2 (35, 39, 51, 56, 59, 66, 68), low-risk 3, and regression 4 (HPV regression within 6 months). Sensitivity for cytology and HPV testing at 1, 2, and 3-year intervals was evaluated, along with Cox analysis for disease progression.

**Results:** Total 1,273 participants were included, and 98 women (7.7%) experienced disease progression. The best AUC for cytology was 0.85 with a sensitivity of 0.735 over 3 years in the HSIL positive group. For HPV testing, the best AUC was 0.778 and sensitivity was 0.765 over 3 years in the high-risk 1 group. Disease progression significantly differed among the HPV groups, with a hazard of 11.4 ( $p=0.001$ ) in the high-risk 1 group. HPV regression showed no disease progression. Among participants under 30, no statistically significant progression was observed as HPV infection pattern.

**Conclusion/Implications:** In women diagnosis for ASCUS/LSIL, HPV test showed slightly higher sensitivity compared to cytology. Considering survival analysis, it is recommended to add HPV test of high-risk 1 for women over 30 years.

EP384 / #667

**Topic:** AS16. *Screening/Early Detection*

## **A SIX MONTH REVIEW OF ALL RAISED CA125 BLOOD TEST REFERRALS TO THE SUSPECTED CANCER PATHWAY IN A UK TRUST**

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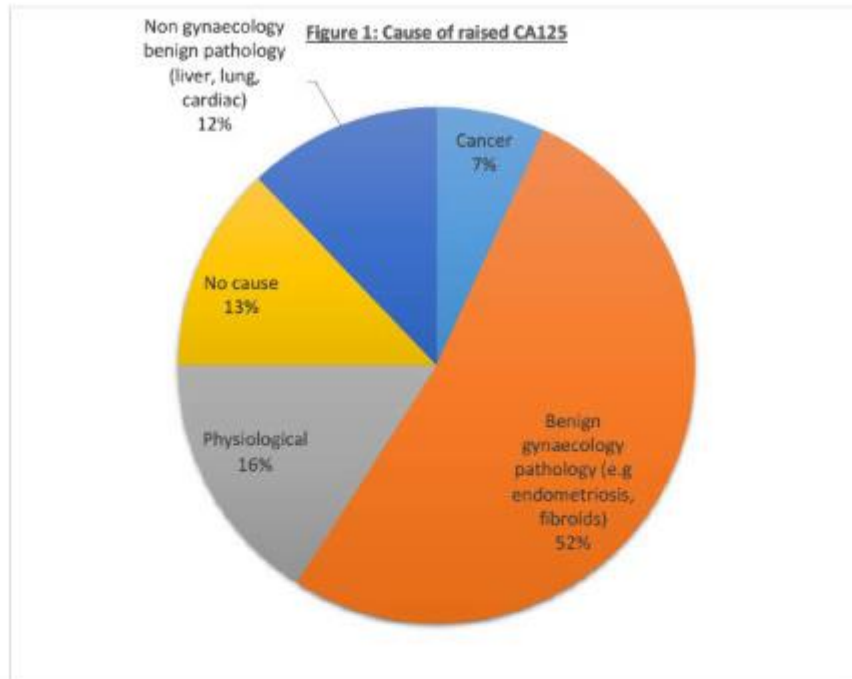
**Introduction:** In the UK, a CA125 blood test is advised for anyone presenting to general practice with symptoms suggestive of ovarian cancer. If raised, they are referred for further investigation. Not all patients with a raised CA125 will have cancer. We have noticed a range of practice in our Trust and this likely relates to the lack of guidance on raised CA125 management in the absence of cancer, particularly in the pre-menopausal population.

**Methods:** Retrospective review of all patients referred on the suspected cancer pathway to Chelsea and Westminster Hospital NHS Foundation Trust, UK between July 1<sup>st</sup> 2022 and 31<sup>st</sup> December 2022, to identify management and outcomes.

**Results:** 134/1895 patients were referred with a raised CA125. Only 5/19 ovarian cancer diagnoses in this time period were referred with a raised CA125. 4 patients had a diagnosis of non-ovarian cancers. Figure 1 shows the remaining causes. All patients who had a CA125 of over 3000 had cancer. No patient with a CA125 less than 60 had cancer. 81 patients were premenopausal. All patients underwent a pelvic ultrasound scan and amongst this group, management varied with only 40 removed from the suspected cancer pathway at first attendance. The remaining 40 underwent further investigation: Repeat CA125



(n=22), MRI



(n=18).

**Conclusion/Implications:** Lack of guidance for the management of raised CA125 reflects there being no level which is diagnostic of ovarian cancer. Raised CA125 may be physiological or due to benign

conditions. Further research is needed to determine whether management pathways should differ depending on menopausal status or age.

EP385 / #290

**Topic:** *AS16. Screening/Early Detection*

## **A COMPARATIVE STUDY OF SELF-COLLECTED VERSUS CLINICIAN-COLLECTED SPECIMENS IN DETECTING HIGH-RISK HPV INFECTION: A PROSPECTIVE CROSS-SECTIONAL STUDY**

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**Introduction:** The primary endpoint of this study aimed to investigate the correlation between self-collected vaginal specimens versus clinician-collected cervical specimens in detecting high-risk HPV infection. Furthermore, the secondary endpoint was the satisfaction of self-collection for HPV testing.

**Methods:** From October 2021 to September 2022, 104 women with HPV16 or HPV18-positive or other 12 high-risk HPV-positive with cytology  $\geq$  ASCUS were enrolled. The primary endpoint of the study was the assessment of the level of agreement and correlation between human papillomavirus (HPV) testing results obtained from self-collected vaginal specimens and those obtained from clinician-collected cervical specimens in detecting high-risk HPV infections, which was accomplished using Cohen's Kappa coefficient ( $k$ ). The secondary endpoint was the satisfaction of women with the vaginal self-collected method. Data analysis was using STATA (StataCorp LLC, College Station, TX), with results considered statistically significant at a P-value of less than 0.05.

**Results:** Paired self-collected and clinician-collected specimens were obtained from 104 women with previous HPV-positive results. The agreement in detecting HPV infection was "substantial" with a kappa coefficient of 0.75. More than 90% of participants rated self-collection as a very good to excellent method because of convenience and safety. For methods of further follow-up, 51% of participants chose self-sampling, the remaining preferred collection by clinicians. There were no complications with the intervention observed.

**Conclusion/Implications:** Self-collected HPV testing is substantially correlated with clinician-collected specimens in detecting cervical high - risk HPV infection. This cell collection method appears to be highly satisfactory and may provide better compliance in the detection of cervical HPV infection.

EP386 / #538

Topic: *AS17. Social Inequities and Impact on Cancer Outcomes*

## **PATIENT REPORTED OUTCOMES (PROS) VARY BY ETHNICITY AND PREFERRED LANGUAGE IN A DIVERSE GROUP OF GYNECOLOGIC CANCER SURVIVORS**

Charlotte Gerrity<sup>1</sup>, Abdulrahman Sinno<sup>2</sup>, Akina Natori<sup>3</sup>, Vandana Sookdeo<sup>4</sup>, Jessica Macintyre<sup>5</sup>, Sophia George<sup>2</sup>, Carmen Calfa<sup>3</sup>, Frank Penedo<sup>6</sup>, Matthew Schlumbrecht<sup>2</sup>

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**Introduction:** Racial and ethnic disparities in PROs among gynecologic cancer survivors are not well studied. We evaluated whether individual-level characteristics were associated with PROs in diverse gynecologic cancer survivors.

**Methods:** Gynecologic cancer patients seen in an ambulatory oncology clinic completed a psychosocial and practical needs assessment prior their appointments through the electronic medical record (EMR) patient portal. Assessments were available in English and Spanish. Fatigue, pain interference, physical function, depression, anxiety, and health-related quality of life were assessed with Patient-Reported Outcomes Measurement Information System (PROMIS<sup>®</sup>) and FACT-G7 computer adaptive tests. Demographic and clinical information was collected from the EMR. Analyses were performed using Chi-square, Kruskal-Wallis, and linear regression with significance set at  $p < 0.05$ .

**Results:** 582 women completed the assessment; 20% ( $n=116$ ) were racial minorities and 54.5% ( $n=310$ ) were Hispanic. 192 (32.8%) completed the assessments in Spanish. There were no differences by race and all scores were poorer in patients who had recurred (all  $p > 0.05$ ). Older age and government insurance coverage were associated with lower physical functioning ( $p < 0.001$ ). Hispanics had lower mean fatigue scores compared to non-Hispanics (49.31 vs 51.74,  $p=0.01$ ). Relative to patients whose preferred language was English, patients whose preferred language was Spanish had lower mean depression (47.63 vs 48.97,  $p=0.05$ ) and fatigue scores (48.27 vs 51.27,  $p < 0.01$ ).

**Conclusion/Implications:** Patient demographics influence PROs among gynecologic oncology survivors, with Hispanic ethnicity and Spanish language preferences associated with lower reported symptoms of depression, anxiety, and fatigue. Further studies should examine potential mechanisms that may account for differences in reported PROs.

EP387 / #852

**Topic: AS17. Social Inequities and Impact on Cancer Outcomes**

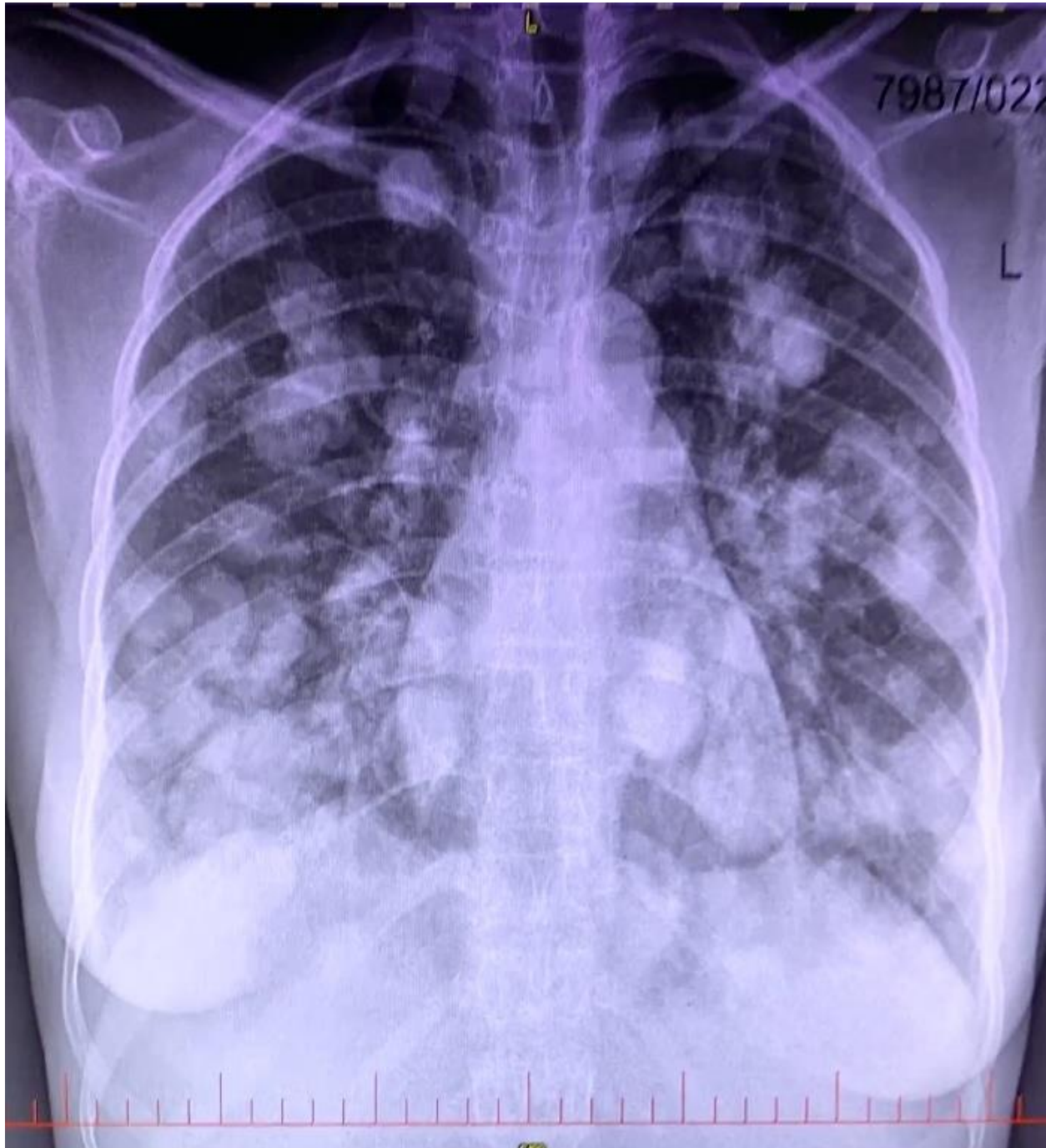
## **GYNECOLOGICAL CANCERS IN SUB-SAHARAN AFRICA: MANAGEMENT OF CHORIOCARCINOMA.**

Valentina Iacobelli<sup>1</sup>, Francesco Taliente<sup>2</sup>, John Bosco Nsubuga<sup>3</sup>, Deusdedit Kateregga<sup>3</sup>, Giovanni Scambia<sup>1</sup>

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**Introduction:** The incidence and mortality of cancer are predicted to rise in sub-Saharan Africa (SSA), with a projected increase in cancer deaths to approximately 1 million per year by 2030. We present the management of an aggressive choriocarcinoma with two main aims: first, to raise the awareness on gynecological cancers in SSA, as clinicians in this context seldom face this diagnosis; second, to highlight the need of expansion of cancer care facilities in these settings.

**Methods:**



Our setting is Matany Hospital, Region of Karamoja, Northern Uganda. A 29-year-old woman presented with intractable vaginal bleeding, dyspnea, and low abdominal pain, ultimately diagnosed with choriocarcinoma after endometrial biopsy. Despite advice for immediate referral for chemotherapy at a cancer institute, the patient refused due to economic reasons and subsequently died from pulmonary embolism.

**Results:** This presentation highlights the frustration associated with cancer management in rural settings in developing countries and emphasizes the need for expansion of cancer care facilities in these regions. Choriocarcinoma is a curable disease; therefore is unacceptable that a young woman could die today because she is not guaranteed access to cancer treatment.

**Conclusion/Implications:** Universal health coverage is advocated to reduce out-of-pocket costs for essential cancer therapy and promote equitable access to screening, diagnosis, and management, ultimately reducing deaths from gynecological cancers in SSA. Paradigmatic shifts in governmental policies and engagement with traditional, complementary, and alternative medical practices are necessary to reduce missed diagnoses and late referrals. Tailored context-based guidelines for cost-effective cancer management algorithms are encouraged to be developed by interdepartmental working groups.

EP389 / #731

**Topic:** AS17. *Social Inequities and Impact on Cancer Outcomes*

## **FRAILITY AS A FACTOR IN SURGICAL DISPARITIES**

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**Introduction:** The objective of this study was to identify sociodemographic factors associated with frailty and impact on postoperative outcomes.

**Methods:** Women undergoing ovarian cancer debulking from 2016-2020 in the National Inpatient Sample were identified. Frailty was defined by a Hospital Frailty Risk Score (HFRS) >5, a weighted index surveying >50 social and medical comorbidities. Mortality and postoperative complications were identified using ICD-10 codes from same admission and classified as medical, surgical or infectious. Social and clinical demographic data were collected. Pearson's chi-squared test and logistic regression analysis were performed. Odds ratios with 95% confidence intervals were calculated.

**Results:** Of 12,926 women undergoing debulking, 1,829 (14%) were frail. Frailty was associated with prolonged hospitalization ( $p < 0.001$ ) and >1 postoperative complication ( $p < 0.001$ ). In univariate analysis, frailty was associated with race/ethnicity, age, income and insurance status ( $p < 0.01$ ). In multivariate analysis, race/ethnicity were no longer associated with frailty (Black: 1.12; 95%CI 0.92-1.36; Hispanic: 0.99; 0.80-1.22) but low income (highest quartile income 0.76; 95%CI 0.7-0.9) and Medicaid as payor (1.3; 1.1-1.6) remained associated. Frail women were more likely to be treated in low ovarian cancer volume centers (high volume center 0.74; 0.64-0.85) and after controlling for frailty, treatment at a low ovarian cancer volume center was independently associated with postoperative complications (high volume treatment center 0.47; 0.41-0.53).

**Conclusion/Implications:** Frailty was associated with adverse financial factors but not race/ethnicity. Frail women are more likely to be treated in low volume centers with independently higher rates of postoperative complications, indicating a disparity in access to care for this at-risk population.



EP390 / #403

**Topic: AS18. Surgical Techniques and Perioperative Management**

## **BASELINE COMPLIANCE WITH ENHANCED RECOVERY AFTER SURGERY (ERAS) IN GYNAECOLOGIC ONCOLOGY IN LOW MIDDLE INCOME COUNTRIES (LMIC), THE SOUTH AFRICAN EXPERIENCE.**

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**Introduction:** Enhanced Recovery After Surgery (ERAS) has significantly reduced complication rates and hospital stay in high income countries. There is a lack of perioperative multi-disciplinary teams, adherence to care guidelines and robust outcomes data in low- and middle- income countries (LMIC). The aim of this prospective cross sectional study was to determine baseline outcomes data, and compliance with guidelines prior to implementation of ERAS in Gynaecologic Oncology at a tertiary hospital in South Africa.

**Methods:** Verbal consent to collect data was obtained from 50 patients, 18 years, and older undergoing elective gynaecological oncology surgery. Anonymised data was entered into the EIAS database by the ERAS Care coordinator. Data was collected on socio-demographic and patient characteristics as well as compliance to the ERAS guidelines in the preoperative, intraoperative, and postoperative period. Outcomes data on length of stay, readmission rates and 30-day follow-up were measured. Ethical approval for this study was obtained from the University of Cape Town Health Research Ethics Committee (HREC ref 068/2022).

**Results:** Among the 50 patients, the overall compliance with ERAS guidelines was 43.9%. ERAS compliance was 16.9% pre-admission; 78.1% pre-operative, 94.2% intra-operatively and 16.9% post-operatively. The average length of stay was 5 days, readmission rate was 4.3% and 30-day complication rate was 21.3%.

**Conclusion/Implications:** Compliance with ERAS guidelines in gynaecologic oncology at our LMIC hospital remains low despite proven benefit of these interventions. This deficit is most pronounced in our pre-admission and post-operative periods. Formal implementation of ERAS will lead to improvement in patient outcomes in LMIC.

EP391 / #83

**Topic: AS18. Surgical Techniques and Perioperative Management**

## **EXPLORING NIPPLE SKIN SPARING MASTECTOMY WITH IMMEDIATE RECONSTRUCTION BY IMPLANTS FEASIBILITY WITH ASSISTANCE OF LAPAROSCOPIC SINGLE PORT-25 FIRST CASES REPORTS**

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**Introduction:** Moving forward from VNOTES techniques in hysterectomy to a concept of No Scar in Breast Surgery and exploring the optimisation of vision in Nipple Skin sparing Mastectomy during prophylactic Mastectomy

**Methods:** this is a continuous series of a single institution and a single surgeons study. 25 patients with fully validate indications of prophylactic mastectomy underwent for assisted total laparoscopic skin sparing mastectomy and immediate reconstruction by a fully train single surgeon in reconstructive surgery and also fully train surgeon with more than 400 procedures of laparoscopic abdominal single port ' myomectomy, borderline ovarian staging, laparoscopic assisted vaginal hysterectomy) We are describing our step by step technics the procedure is first described Dissection of the outer quadrant of the breast with scissors, then we put the single port and then we follow the procedure with endoscopic assistance and bipolar The first 7 patients was done by single port with assistance of an additional 3 mm port the second serie of 7 patients underwent laparoscopic assistance for the dissection of the NAC and inner part of the breast The last and recent serie of 11 patients underwent fully assisted procedure The removal of specimen is done in endobag without morcellation the insertion of the implant is challenging

**Results:** All the patients underwent a complete procedure without a major operative time-No immediate or Late complication occurs due to the technics patient satisfaction is good

**Conclusion/Implications:** The operation is safely feasible more cases are needed to validate that very interesting new technics

EP392 / #415

**Topic: AS18. Surgical Techniques and Perioperative Management**

## **LOW PRESSURE LAPAROSCOPIC PROCEDURES IN OBESE GYNECOLOGICAL PATIENTS USING A NEW SUBCUTANEOUS ABDOMINAL WALL-RETRACTION DEVICE.**

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**Introduction:** Treatment of obese female patients represents a challenge, due to cardiac function and hemodynamic changes during minimally invasive surgery with pneumoperitoneum and steep Trendelenburg position. Main reasons for LPT conversion in obese patients were inadequate exposure due visceral adiposity and an intolerance of Trendelenburg. The aim of this prospective study was to assess conversion to laparotomy and perioperative complications after of low pressure laparoscopy (LPL) surgery using a new subcutaneous abdominal wall-retraction device in morbidly obese patients.

**Methods:**

**Table 2. Type of Surgery**

Measure	Value
Indication for surgery	
Endometrial hyperplasia	6/30 (20%)
Endometrial cancer	18/30 (60%)
Adnexal mass	6/30 (20%)
TLH <sup>+</sup> -BSO <sup>+</sup>	4/30 (13.3%)
TLH <sup>+</sup> -BSO <sup>+</sup> -SNL <sup>‡</sup> biopsy	22/30 (73.3%)
MSO <sup>§</sup>	1/30 (3.3%)
BSO <sup>+</sup> and omentectomy	1/30 (3.3%)
TLH <sup>+</sup> -BSO <sup>+</sup> -SNL <sup>‡</sup> biopsy and complete peritoneal staging	2/30 (6.6%)
Histology	
Endometrial cancer	20/30 (66,6%)
Hiperplasia	4/30 (13.3%)
BOT	2/30 (6.6%)
Other	4/30 (13.3%)

*data are expressed as number (percentage).*

*\*Total Laparoscopic Hysterectomy; †Bilateral Salpingo-Oophorectomy; ‡Sentinel Lymph Node; § Monolateral Salpingo-Oophorectomy*

30 consecutive obese patients (BMI > 35 kg/m<sup>2</sup>) were eligible for the study. 20 patients had endometrial cancer, 4 atypical endometrial hyperplasia and 6 BOT/adnexal mass.

**Results:** The mean age was 69, with a mean BMI of 39 kg/m<sup>2</sup>. The exposure of the operating field was optimal in 28 out 30 cases (93.3%). Laparotomy conversion rate was 6,6% (2/30). One intraoperative complication occurred. An hematoma related to insertion of the subcutaneous needle of the wall lifter occurred. According to the Dindo Classification ≥ a 2, early complications rate was

16%.

**Table 3. Type of surgery**

<b>Measure</b>	<b>Value</b>
Operative time (min)	170 (111 – 249)
Conversion to laparotomy	7/30 (23.3%)
Specimen extraction	3/30 (10%)
Advanced disease	2/30 (6.6%)
Difficult visualization	2/30 (6.6%)
Complete surgical staging	29/30 (96.6%)
Intra-operative complications	1/30 (3.3%)
Hospital stay (days)	4 (3 – 13)
30-days complications	7/30 (23.3%)
Clavien Dindo classification	
grade 1	2/30 (6.6%)
grade 2	5/30 (16.6%)
No complications	23/30 (76.6%)

*data are expressed as median (range) or number (percentage)*

**Conclusion/Implications:** LPL technique using the LaparoTensor device is safe and feasible in obese patients. The subcutaneous retractor is a way to create a large intra-abdominal operative space without the need of intraperitoneal high pressure and offers greater benefit to obese patients with no effect on the hemodynamic and respiratory functions. LPL technique may assist both surgeon and anesthesiologist to reduce conversions rate. Prospective studies could confirm our results.

EP393 / #475

**Topic: AS18. Surgical Techniques and Perioperative Management**

## **POSTERIOR LEAF RESECTION OF THE VESICOUTERINE LIGAMENT IN RADICAL HYSTERECTOMY**

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**Introduction:** Many clinicians aim to perform adequate parametrial resection, considering that severe bladder dysfunction is a frequent complication after radical hysterectomy. There are no standardized guidelines on whether type 2 or type 3 hysterectomies should be performed. In several institutes, the posterior layer of the vesicouterine ligament is not completely resected in nerve-sparing radical hysterectomy, whereas the vesical vein in the posterior layer of the vesicouterine ligament is resected at the root of the deep uterine vein. Therefore, the present study aimed to compare bladder function and relapse-free survival between classic nerve-sparing radical hysterectomy, in which the posterior leaf of the vesicouterine ligament is completely resected, and simplified nerve-sparing radical hysterectomy, in which only the vesical vein of the posterior layer of the vesicouterine ligament are resected.

**Methods:** This was a single-institution historical cohort study. The surgical procedures varied according to age. We performed the classic nerve-sparing radical hysterectomy with complete resection of the posterior leaf of the vesicouterine ligament, up to 2015. After 2016 we resect only vesical vein of the posterior leaf.

**Results:** There was no significant difference in relapse-free survival between the two surgical procedures. Resection of the posterior layer of the vesicouterine limited to the veins was superior in terms of both motor and sensory bladder functions.

**Conclusion/Implications:** Resection of the posterior layer of the vesicouterine ligament, which is a procedure limited to the veins, is an effective and safe method for radical hysterectomy. It may be more useful for preserving the bladder function without leading to unfavorable oncologic outcomes.

EP394 / #888

**Topic: AS18. Surgical Techniques and Perioperative Management**

## **FEASIBILITY AND SAFETY OF ARTISENTIAL FOR MINIMALLY INVASIVE SURGERY IN EARLY STAGE GYNECOLOGIC CANCER: RESULTS FROM THE KGOG 4002/GYANT STUDY**

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**Introduction:** To evaluate the feasibility and safety of ArtiSential for performing minimally invasive surgeries for gynecological cancers.

**Methods:** We conducted a prospective interventional study at eight tertiary institutional hospitals in Korea between November 2021 and April 2022. Eligible patients were 18 years or older and planned to undergo minimally invasive surgery for gynecologic cancer. We collected baseline characteristics, surgical information, and postoperative outcomes. The primary endpoint was to compare the operation time required for gynecologic cancer surgery using ArtiSential with the reported operation time for surgery using conventional laparoscopic instruments or robots. The secondary objectives were to evaluate the surgical outcomes of gynecologic cancer surgery using ArtiSential compared to conventional laparoscopic instruments or robots and collect operator feedback on equipment improvements during surgery.

**Results:** A total of 40 patients were enrolled in the study, with 19 patients having endometrial cancer, 15 patients having cervical cancer, and 6 patients having ovarian cancer. The average duration of all surgeries was  $187.0 \pm 49.2$  minutes, and no complications were encountered during the surgery. During the assessment of lymph nodes, ArtiSential was utilized in 64.7% of cases with an average assessment time of  $40.3 \pm 19.4$  minutes. The majority of surgeons using ArtiSential reported that it performed slightly better compared to conventional laparoscopic instruments, while 47.5% reported that it performed slightly worse compared to da Vinci surgery.

**Conclusion/Implications:** Minimally invasive surgery using ArtiSential is feasible and safe for the surgical management of early stage gynecologic cancer.

EP396 / #252

**Topic: AS18. Surgical Techniques and Perioperative Management**

## **EFFECT OF FASCIA CLOSURE USING BARBED SUTURE ON INCISIONAL HERNIA IN MIDLINE LAPAROTOMY FOR GYNECOLOGICAL DISEASES (BARBER TRIAL, KGOG 4001)**

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**Introduction:** To examine the effect of fascia closure using barbed suture on incisional hernia in patients who underwent midline laparotomy for gynecological disease.

**Methods:** 174 patients undergoing midline laparotomy for gynecologic disease, BMI<35, age>18 years and ECOG performance status 0-2 were 1:1 randomized to case (facial closure using barbed suture) vs. control (facial closure using non-barbed suture) group at 9 institutes in Korea, from February 2021 to December 2021. We compared the incidence of incisional hernia up to 1-year post-surgery between case and control group.

**Results:** Of 174 patients (case 86, control 88), 36 patients were excluded because they were not followed till 1 year (case 19, control 17). No incisional hernia was observed in excluded 36 patients till last visit. Remaining 138 patients (case 67, control 71) were included in this analysis and all patients underwent fascial closure as assigned. Baseline and surgical variables including portion of cancer surgery (51/67 [76.1%] vs. 62/71 [87.3%]; p=0.088), mean wound length (24.3 cm vs. 25.1 cm; p=0.587) and mean surgery time (219.4 minutes vs. 243.2 minutes; p=0.257) were balanced. The incidence of incisional hernia up to 1-year post-surgery was similar between case and control groups (0/67 [0.0%] vs. 1/71 [1.4%]; p>0.999). No treatment-related adverse events other than incisional hernia, pain, wound infection and dehiscence were reported.

**Conclusion/Implications:** Fascia closure using barbed suture showed zero incisional hernia up to 1 year in patients who underwent midline laparotomy for gynecological disease, but fail to reduce incisional hernia compared to conventional method.



EP397 / #420

**Topic: AS18. Surgical Techniques and Perioperative Management**

## **TRANSVAGINAL NATURAL ORIFICE TRANSLUMINAL ENDOSCOPIC SURGERY (VNOTES) FOR EARLY STAGE ENDOMETRIAL CANCER**

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**Introduction:** Transvaginal Natural Orifice Transluminal Endoscopic Surgery (vNOTES) has gained popularity in benign gynaecological conditions. The main advantage of vNOTES is to overcome the limitations of traditional vaginal hysterectomy, particularly on limited exposure and poor visualization. As vNOTES is a relatively new surgical approach, the experience with vNOTES in gynaecological malignancies is still lacking. The aim of this study was to evaluate the feasibility and safety of vNOTES in managing women with early-stage endometrial cancer and to evaluate the short-term oncologic outcome.

**Methods:** A retrospective review was conducted on women who had vNOTES total hysterectomy and bilateral salpingo-oophorectomy (THBSO) for atypical endometrial hyperplasia or early-stage endometrial cancer at a university-affiliated gynaecologic oncology centre from January 2021 to February 2022. Demographics data, perioperative complications and oncologic outcome were reviewed.

**Results:** 13 women had vNOTES THBSO done for atypical endometrial hyperplasia (n=2) and endometrial cancer (n=11). The mean age was 65.7 years [standard deviation (SD) 10.0] and the mean body mass index was 29.0kgm<sup>2</sup> (SD 5.9). The mean blood loss and operative time were 200ml (SD 130.1) and 175 minutes (SD 40) respectively. Two (15.4%) women required conversion to conventional laparoscopy. There were no perioperative complications including visceral injury, re-laparotomy or readmission reported. The mean length of hospital stay was 1.5 days (SD 0.5). The mean follow-up period was 15 months (SD 4.5), and there was no recurrence of endometrial cancer reported.

**Conclusion/Implications:** vNOTES THBSO appeared to be a feasible and safe surgical approach for atypical endometrial hyperplasia and early-stage endometrial cancer.

EP398 / #161

**Topic: AS18. Surgical Techniques and Perioperative Management**

## **AIR TRAVEL AND THROMBOEMBOLISM AMONG POSTOPERATIVE GYNECOLOGIC CANCER PATIENTS: TEN-YEAR SINGLE-CENTRE EXPERIENCE PRIOR TO THE ERA OF POSTOPERATIVE EXTENDED THROMBOPROPHYLAXIS**

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**Introduction:** Air travel and cancer surgery are associated with increased risk of venous thromboembolism (VTE). We sought to investigate the incidence of postoperative VTE in gynecologic oncology patients who flew before and after surgery, prior to the era of routine postoperative extended VTE prophylaxis.

**Methods:** A retrospective cohort study identified 136 patients having travelled by air to and from surgery between 2008-2017. All patients underwent laparoscopy or laparotomy for suspected or confirmed gynecologic malignancy at a single tertiary cancer care centre. Medical records were reviewed for demographic, medical and outcome data, including diagnosis of VTE within 30 days of surgery.

**Results:** The combined incidence of VTE (deep venous thromboembolism or pulmonary embolism) was 1.5%. One patient experienced a pulmonary embolism and one an upper extremity deep vein thrombosis. Both had advanced ovarian cancer and underwent debulking surgery (primary debulking and interval debulking). Only five patients in this cohort were discharged with extended duration anticoagulation due to a history of previous VTE. Sixty-two percent underwent laparotomy, of which 52% were debulking surgeries. Among these patients, 67% received neoadjuvant chemotherapy. Sixteen percent of patients had upper abdominal surgery and 48% a pelvic and/or para-aortic lymph node dissection.

**Conclusion/Implications:** Although extended VTE prophylaxis was not routinely administered, the incidence of postoperative VTE was low. Within the Canadian context, where centralized cancer care often requires patients to travel long-distances to access specialized services, these findings offer additional reassurance that the postoperative risk of VTE is low even in this high-risk population.

EP399 / #1266

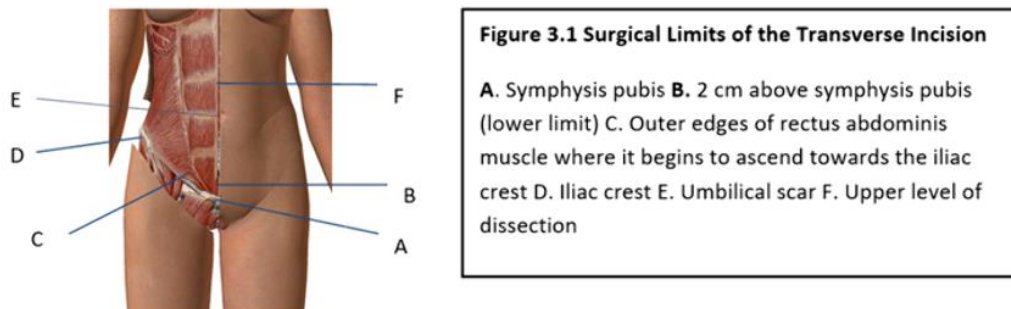
Topic: **AS18. Surgical Techniques and Perioperative Management**

## COMPARATIVE STUDY OF ABDOMINAL SURGICAL APPROACH TRANSVERSE AND VERTICAL INCISION IN PELVIC TUMOR SURGERY

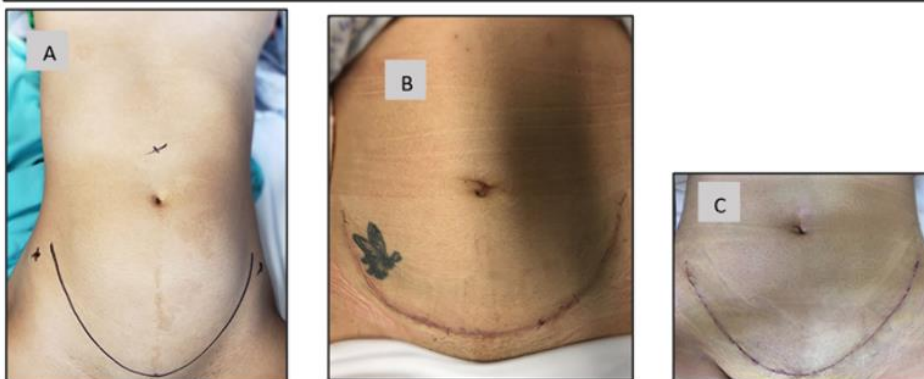
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**Introduction:** To evaluate and compare the results of the transverse incision (TI) and the vertical incision (VI) in postoperative morbidity, resectability, and satisfaction in patients with pelvic tumors suspected of malignancy.

**Methods:** An open, non-randomized, prospective, and longitudinal clinical trial was carried out. Female patients treated at the morning and evening Pelvis clinic service of the Jalisciense Institute of Cancerology were included, with suspicion or confirmation of a malignant pelvic tumor, and were taken to a surgical procedure, in the period from November 1, 2017, to November 31, 2017. December 2018.



**Figure 3.2 Photographs of the transverse incision** A. Marking of the incision to be made and the surgical limits shown in a cross B. Scar 8 days after surgery C. Scar 10 days after surgery



**Results:** 41 patients, two groups, VI (n = 23) and those with a TI (n = 18). The results of surgical exposure, resectability, surgical times, morbidity, pain, and a questionnaire to assess patient satisfaction according to the aesthetic appearance of the incision made were compared. Patients with (VI) were older (p=0.000), weighed more (p= 0.011), and had a higher BMI (p= 0.000). No significant differences were found between the two groups in terms of surgical exposure, resectability, bleeding, surgical margins,

number of pelvic or para-aortic nodes, postoperative complications, or pain. The level of satisfaction reported by the patient for the incision made was higher in the (IT) group ( $p= 0.000$ ).

**Conclusion/Implications:** Due to similar clinical results, the decision to perform a vertical or transverse incision should be made between the surgeon and the patient, taking into account the surgical procedure to be performed, the patient's characteristics, and the assessment of probable post-surgical complications.

EP400 / #284

**Topic:** *AS18. Surgical Techniques and Perioperative Management*

## **THE IMPORTANCE OF DEVELOPING THE CONTENT AND PROGRAM TO IMPROVE THE EFFECTIVENESS OF CADAVER SURGERY TRAINING**

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**Introduction:** With the diversity of surgical techniques, off-the-job-training has also become more diverse. Among them, there have been many reports that cadaver surgery training (CST) is useful for surgical education. However, it is important for surgical education to have a purpose and to receive appropriate education. We report that it was necessary to have the program and content for each physicians' proficiency level.

**Methods:** We have held five CST seminars at our hospital. This time, we analyzed the past CST questionnaires and questions. We examined how effective the program was in each physician proficiency level, with surgeon background as a qualitative factor and anatomical knowledge as a quantitative factor. Forty-five physicians participated in the study, divided by whether they were pre- or post-specialty, oncologist, or certified endoscopist. The number of experienced cases, number of complications, and motivation were also asked, and anatomical questions were answered on the web before and after CST.

**Results:** Multivariate analysis showed that the more cases and complications experienced, the higher the educational effect of CST. In other words, advanced skills programs are effective for physicians who have acquired subspecialties, but there is a need for a general program for trainee physicians.

**Conclusion/Implications:** With the results obtained in this study, I created a CST program for each proficiency level: preparatory training as STEP 1, then implementation as STEP 2, and finally a review program as STEP 3.

EP401 / #21

Topic: *AS19. Survivorship*

## **ASIAN AMERICAN BREAST CANCER SURVIVORS WITH HIGH NEEDS FOR HELP**

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**Introduction:** Asian American breast cancer survivors have been known as a group with high needs for help despite high social support by their families. To provide appropriate and adequate support for this specific group, it is important to decide what are the characteristics of those with high needs. The purpose of this study was to examine the characteristics of Asian American breast cancer survivors with high needs for help during their survivorship transition.

**Methods:** The data from a larger clinical trial among 185 Asian American breast cancer survivors were used for this study. Multiple instruments were used in the larger study, yet only the data collected using the Supportive Care Needs Survey-Short Form 34 (SCNS-SF34) and multiple scales to measure the survivors' characteristics were used. The data analysis was done through decision tree analyses with the algorithm of classification and regression trees.

**Results:** The women with the highest needs had different characteristics depending on the types of needs. Those with the highest psychological needs had high psychological symptom distress (cut point = 1.60), low self-efficacy (cut point = 100.50), high global symptom distress (cut point = 2.21), and low immigration age (cut point = 29.50).

**Conclusion/Implications:** The findings suggest the risk groups of Asian American breast cancer survivors to target in future interventions to reduce their needs for help.

EP402 / #127

**Topic:** AS19. Survivorship

## **ADVERSE EFFECTS AND QUALITY OF LIFE OF PATIENTS WITH CERVICAL CANCER UNDERGOING RADICAL CHEMORADIOTHERAPY**

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**Introduction:** Concurrent chemoradiation is the standard of care for women with locoregionally advanced cancer of the cervix. The disease and treatment can affect the quality of Life (QOL). The study aimed to determine the adverse events and quality of life of these patients.

**Methods:** A prospective longitudinal study was conducted at our institution in patients with histologically confirmed carcinoma cervix undergoing radical concurrent chemoradiotherapy. Patients with severe physical or mental disabilities and those who developed recurrence in the follow-up period were excluded from further formal interviews. Ninety-five patients were enrolled from 1<sup>st</sup> April 2021 to 31<sup>st</sup> April 2022. The NCI Common Terminology Criteria for Adverse Events v 5.0 were completed at weeks 0,1,3, at brachytherapy, at 3 and 6 months. The EORTC QLQ-C30 and QLQ-CX24 questionnaires were administered at week 0, at brachytherapy, at three months, and at six months.

**Results:** The lowest global quality of life scores were recorded during treatment, with the highest scores six months post-treatment. Physical, role and social functioning declined during treatment but improved later, while emotional functioning scales were lowest at the beginning of treatment but improved significantly during treatment and follow-up. Body image declined during radiotherapy, and sexual worries increased with a decline in sexual and vaginal functioning post-treatment. The most common acute toxicities were fatigue, diarrhoea, nausea, anaemia, and leukopenia, while constipation, vaginal dryness, and dyspareunia were the most common late toxicities reported.

**Conclusion/Implications:** These results can help healthcare providers better manage symptoms and improve outcomes for patients with advanced cervical cancer undergoing concurrent chemoradiotherapy.

EP404 / #379

Topic: *AS20. Symptom Management/Supportive Cancer Care*

## **DISCREPANCIES BETWEEN PATIENT AND HEALTHCARE PROFESSIONAL VALUES IN MANAGING SIDE EFFECTS OF GYNECOLOGIC ANTICANCER DRUG THERAPY IN JAPAN**

Masakazu Abe<sup>1</sup>, Hironobu Hashimoto<sup>2</sup>, Azusa Soejima<sup>3</sup>, Yumiko Nishimura<sup>4</sup>, Ami Ike<sup>5</sup>, Michiko Sugawara<sup>5</sup>, Muneaki Shimada<sup>6</sup>

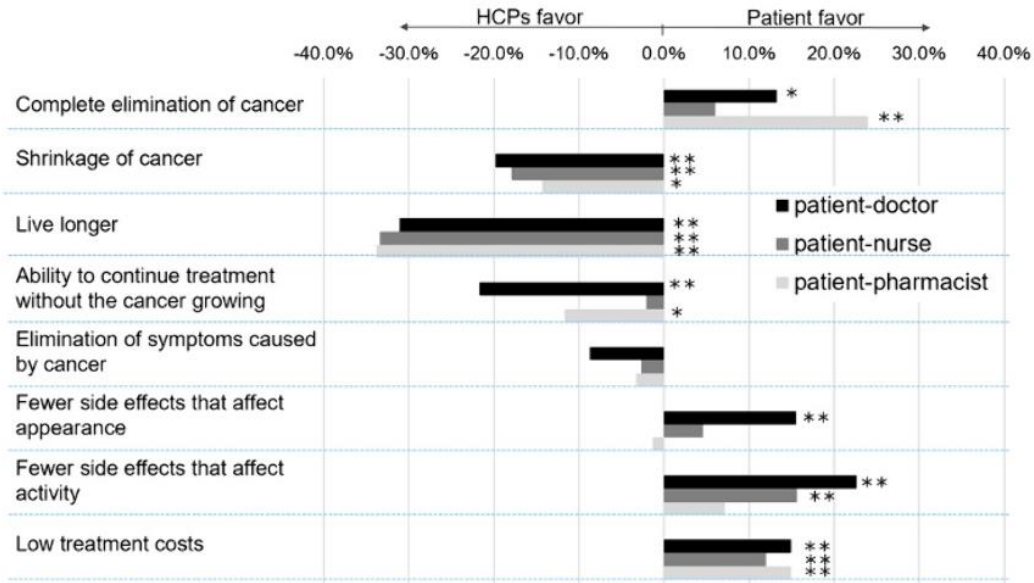
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**Introduction:** It has been reported that physicians tend to underestimate the impact of side effects on their patients. It is important to understand patients' thoughts and values about side effects to provide a patient-centered treatment approach.

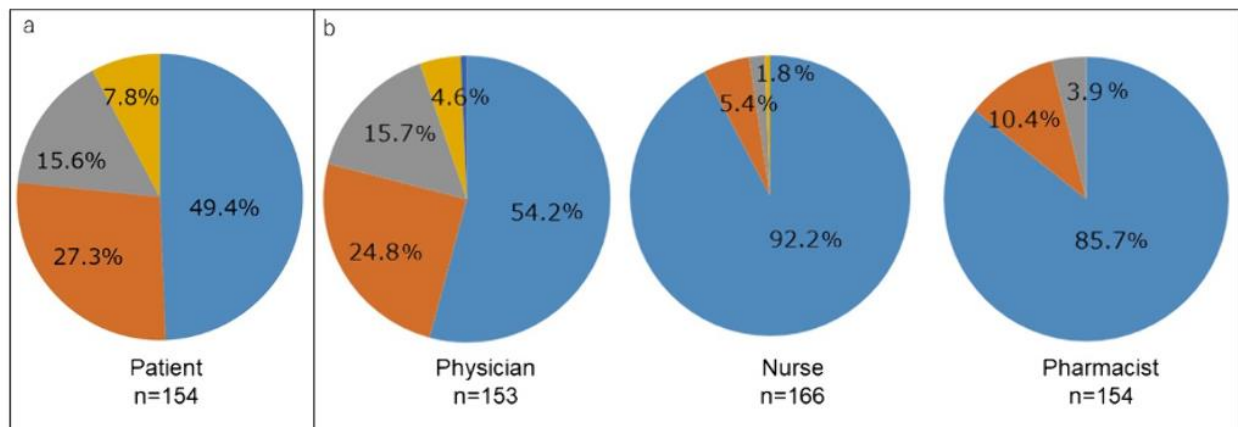
**Methods:** A cross-sectional observational study (web-based questionnaire) was conducted among patients who had received anticancer drug therapy for uterine and ovarian cancer and health care professionals (HCPs), including physicians, nurses, and pharmacists involved in gynecologic cancer care.

**Results:** A survey was performed from November to December 2022, and responses were received from 154 patients, 153 physicians, 166 nurses, and 154 pharmacists. Regarding the differences in anticancer drug preferences, HCPs emphasized OS prolongation and tumor reduction, while patients emphasized safety (fewer side effects affecting activity and appearance) and complete elimination of cancer, with a significant difference between patients and physicians, especially in safety (Fig.1). Regarding the extent of reporting of side effects, 49.4% of patients reported all symptoms, including adverse events and side effects, while 54.2% of physicians, 92.2% of nurses, and 85.7% of pharmacists wanted patients to report all symptoms including adverse events and side effects (Fig. 2).





**Figure 1. Differences in treatment preferences between patients and HCPs**  
The difference was calculated by subtracting the percentage (sum of top 3) of each HCP from that of patients (patients: n=154, physicians: n=154, nurses: n=166, pharmacists: n=154). \*p<0.05, \*\*p<0.01 by Fisher's exact test. Questionnaire for HCPs: what are the top 3 that HCPs believe patients' value?, Questionnaire for patients: what are the top 3 do you think value most?



**Figure 2. Comparison of the levels of communication about symptoms of side effects between patients and health care professionals**

**Conclusion/Implications:** Anticancer drugs must be decided after understanding the patient's preferences through Shared Decision Making. It is important that not only physicians, but also nurses, pharmacists, and other members of the multi-disciplinary team listen to the patient-reported side effects / adverse events and provide support with respect to the patient's values, leading to appropriate management of side effects.

EP408 / #395

Topic: AS20. Symptom Management/Supportive Cancer Care

## A RETROSPECTIVE REVIEW OF THE REAL-WORLD EXPERIENCE OF THE PROPHYLACTIC PEGFILGRASTIM IN PATIENTS WITH GYNECOLOGIC CANCER

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**Introduction:** Patients receiving the myelosuppressive chemotherapy are vulnerable to febrile neutropenia (FN). Granulocyte colony-stimulating factors(G-CSF) is recommended to use for chemotherapy-induced neutropenia. To determine the incidence of chemotherapy-induced FN and evaluate the outcomes in prophylactic use of pegfilgrastim.

**Methods:** This single-center retrospective study evaluated electronic health records of patients with gynecologic cancer treated between January 2018 and December 2022. The primary outcomes were the incidence of grade 3/4 neutropenia and FN after the first and across all chemotherapy cycles. The secondary outcomes were the incidence of additional laboratory tests and hospitalization.

**Results:** A total of 166 patient records were reviewed. FN was not reported in the prophylactic use of pegfilgrastim and only one case of grade4 neutropenia occurred, except when pegfilgrastim was not used prophylactically in the first cycle. In the group of standard-care chemotherapy, 32patients(23.5%) and 355cases(44%) of grade 3/4 neutropenia were respectively reported in the first cycle and in across all cycles. FN was 5(3.7%) in first cycle and 32(23.5%) in across all cycles(Table 1). 7patients were hospitalized in the first cycles and 11 cases were reported in across all cycles. A total 16patients and 74patients experienced additional laboratory tests respectively in the first cycle and across all cycles(Table2).

Table 1. The primary outcomes in the prophylactic use patients and the standard-care patients

number of patients(total) N=166	Pegfilgrastim n=30		Control n=136	
	first cycle(n=30)	all cycles(n=174)	first cycle(n=136)	all cycles(n=806)
Outcome, n(%)				
Febril neutropenia	0 (0.0%)	0 (0.0%)	5 (3.7%)	9 (1.1%)
Grade 3/4 neutropenia	1 (3.3%)	10 (6.0%)	32 (23.5%)	355 (44.0%)
Chemotherapy dose delays	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (0.9%)
Chemotherapy discontinuation	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Hospitalization(total)	1 (3.3%)	1 (0.60%)	7 (5.1%)	11 (1.4%)
due to febril neutropenia	0 (0.0%)	0 (0.0%)	5 (3.7%)	9 (1.1%)
due to neutropenia	1 (3.3%)	0 (0.0%)	2 (1.5%)	2 (0.3%)
due to other cause	0 (0.0%)	1 (0.60%)	0 (0.0%)	0 (0.0%)

Table 2. The secondary outcomes in the prophylactic use patients and the standard-care patients

	Pegfilgrastim		Control	
	first cycle(n=30)	all cycles(n=174)	first cycle (n=136)	all cycles(n=806)
The number of patients who experience additional laboratory test	0 (0.0%)	0 (0.0%)	16 (11.8%)	74 (9.2%)
The number of additional visit to the office	1 (3.3%)	1 (0.60%)	21 (15.4%)	321 (39.8%)
Antibiotics management	0 (0.0%)	0 (0.0%)	5 (3.7%)	11 (1.4%)
The number of patients who received the G-CSF medication	1 (3.3%)	30 (17.2%)	31 (22.8%)	101 (12.5%)

**Conclusion/Implications:** Prophylactic use of pegfilgrastim in patients who received myelosuppressive chemotherapy may be a preferable option to prevent FN and neutropenia. Although the pegfilgrastim costs expensive, the prophylactic use reduces displeased additional laboratory tests and hospitalization.

EP409 / #609

**Topic:** AS21. *Trophoblastic Diseases*

## **DEFECT OF MIS IN PLACENTAL SITE TROPHOBLASTIC TUMORS AND EPITHELIOID TROPHOBLASTIC TUMORS**

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**Introduction:** This study aims to evaluate mismatch repair defect (MMRd) in placental trophoblastic tumors (PSTTs) and epithelial trophoblastic tumors (ETT).

**Methods:** This study was performed in three academic hospitals retrospectively. Serial histology sections from 15 patients diagnosed with a PSTT or ETT were immunohistochemically stained using the MLH1/MSH2/MSH6/PMS2 to test MMRd. MMRd was determined by one pathologist. Less than 10 % of expression in IHC was considered as MMRd.

**Results:** We obtained IHC stain of MLH1/MSH2/MSH6/PMS2 from 15 patients' samples. There were nine PSTT and six ETT patients. Sample from PSTT patients showed one MLH1 defect and one PMS2 defect. Sample from ETT patients showed PMS2 defect in five out of six samples. One sample showed defects in MLH1, MSH6, and PMS6.

**Conclusion/Implications:** Gestational trophoblastic tumors especially in ETT showed high MMRd. This study explains the high response rate in PSTT and ETT to immune checkpoint inhibitors. This type of tumor may be a good target of immune checkpoint inhibitors.

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**Topic: AS21. Trophoblastic Diseases**

## **PROGNOSTIC FACTORS ASSOCIATED WITH ULTRA-HIGH-RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA**

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**Introduction:** The aim of this study was to determine the prognostic factors associated with ultra-high-risk gestational trophoblastic neoplasia (UHR-GTN). Globally, women diagnosed with UHR-GTN have poor outcomes, despite the disease being the most curable gynecological malignancy.

**Methods:** This was a hospital-based retrospective study that was carried out at Moi Teaching and referral hospital from 2017 to 2023. The prognostic factors analyzed included patients, treatment, and disease factors.

**Results:**

**Table 1. Association between Mortality and socio-demographics and clinical characteristics obstetrics (n = 14)**

Variables	Mortality				$\chi^2$	p
	Yes (n = 7)		No (n = 7)			
	No.	%	No.	%		
<b>Age (years)</b>					6.200	0.387
18-24	3	42.9	0	0.0		
25-30	1	14.3	1	14.3		
31-36	1	14.3	2	28.6		
37-42	1	14.3	2	28.6		
43-48	1	14.3	0	0.0		
≥49	0	0.0	2	28.6		
<b>Marital status</b>					0.424	FE p=1.000
Single	2	28.6	1	14.3		
Married	5	71.4	6	85.7		
<b>Education level</b>					0.372	MC p=1.000
Primary	3	42.9	3	42.9		
Secondary	1	14.3	1	14.3		
Tertiary	3	42.9	3	42.9		
<b>Employment status</b>					2.159	MC p=0.551
Employed	0	0.0	2	28.6		
Unemployed	2	28.6	1	14.3		
Housewife	5	71.4	4	57.1		
<b>Health insurance cover</b>					0.424	FE p=1.000
Yes	6	85.7	5	71.4		
No	1	14.3	2	28.6		
<b>Parity</b>					3.450	MC p=0.471
Nulliparous	2	28.6	0	0.0		
Multiparous (≥1 delivery at ≥26 weeks)	3	42.9	2	28.6		
Grand multiparous (≥4 deliveries)	2	28.6	4	57.1		
Not in file	0	0.0	1	14.3		
<b>Pregnancy loss</b>					2.775	MC p=0.287
Yes	5	71.4	2	28.6		
No	2	28.6	4	57.1		
Not in file	0	0.0	1	14.3		
<b>History of molar pregnancy</b>					1.178	MC p=1.000
Yes	2	28.6	2	28.6		
No	5	71.4	4	57.1		
Not in file	0	0.0	1	14.3		
<b>Comorbidities</b>					1.077	FE p=1.000
Hypertension	0	0.0	1	14.3		
BMI >25 Kg/m <sup>2</sup>	2	28.6	2	28.6		
Septicemia	3	42.9	1	14.3		
Venous thromboembolism	1	14.3	0	0.0		
Anemia (Hb <10g/dl)	7	100.0	7	100.0		
<b>Initial B-hCG titer</b>					1.077	FE p=1.000
<1,000,000	1	14.3	7	100.0		
>1,000,000	6	85.7	0	0.0		

$\chi^2$ : Chi square test  
p: p value for comparison between the studied categories

MC: Monte Carlo

FE: Fisher Exact

**Table 2. Association between Mortality with patient, disease, and treatment factors (n=14)**

Variables	Mortality				χ <sup>2</sup>	*p
	Yes (n = 7)		No (n = 7)			
	No.	%	No.	%		
<b>Patients factors</b>						
<b>Patient's age (years old)</b>						
< 40	5	85.7	3	42.9	2.800	0.286
≥ 40	1	14.3	4	57.1		
<b>Comorbidity</b>						
Yes	7	100.0	5	85.7	1.000	1.000
No	0	0.0	1	14.3		
<b>Patient's ECOG performance index</b>						
≤ 3	6	85.7	7	100.0	1.000	1.000
≥ 4	1	14.3	0	0.0		
<b>Weight loss (BMI)</b>						
< 18 kg/m <sup>2</sup>	2	28.6	3	42.9	0.111	1.000
≥ 19 kg/m <sup>2</sup>	5	71.4	4	57.1		
<b>Disease factors</b>						
<b>Liver metastasis</b>	3	42.9	2	28.6	0.111	1.000
<b>Brain metastasis</b>	5	42.9	1	14.3	1.400	0.559
<b>GIT metastasis</b>	1	14.3	0	0.0	1.000	1.000
<b>Spleen metastasis</b>	0	0.0	1	14.3	1.000	1.000
<b>Lung metastasis</b>	7	100.0	7	100.0	-	-
<b>WHO score ≥ 12</b>	7	100.0	7	100.0	-	-
<b>Site of metastasis</b>						
2 sites	2	28.6	7	100.0	2.333	*p=0.462
≥ 3 sites	5	71.4	0	0.0		
<b>Size of the metastatic lesions</b>						
≤ 7 mm	1	14.3	5	71.4	4.667	*p=0.103
≥ 1 cm	6	85.7	2	28.6		
<b>Stage IV disease (FIGO staging)</b>						
Yes	7	100.0	7	100.0	-	-
No	0	0.0	0	0.0		
<b>Histologic type of GTN</b>						
Choriocarcinoma	6	85.7	1	42.9	2.900	*p=0.365
Invasive mole	0	0.0	1	14.3		
Not in file	1	14.3	7	42.9		
<b>Persistent elevated β-hCG titer</b>						
Yes	4	57.1	1	14.3	2.800	*p=0.286
No	3	42.9	5	85.7		
<b>Treatment factors</b>						
<b>Previous chemotherapy</b>	1	14.3	2	28.6	0.121	1.000
<b>Treatment Received</b>						
Chemotherapy only	3	42.9	2	28.6	0.511	1.000
Combined chemotherapy and surgery	4	57.1	5	71.4		
<b>Dexamethasone administration</b>	7	100.0	7	100.0	-	-
<b>Hysterectomy</b>	3	42.9	3	42.9	0.00	1.000
<b>Dilatation and curettage</b>	0	0.0	2	28.6	2.333	0.552
<b>Craniotomy</b>	0	0.0	1	14.3	1.000	1.000
<b>Delay (in days) for initiating treatment</b>						
≥ 7 days	6	85.7	2	28.6	4.667	0.100
< 7 days	1	14.3	5	71.4		
<b>Delay in continuing with treatment initiated</b>						
≥ 7 days	5	71.4	5	71.4	0.000	1.000
< 7 days	2	28.6	2	28.6		
<b>Treatment regimens</b>						
EMA/EP	0	0.0	2	28.6	3.921	0.796
EP/EMA	2	28.6	2	28.6		
TE/TP	1	14.3	0	0.0		
EMACO	2	28.6	2	28.6		
Planned to start EMA/EP	1	14.3	0	0.0		
EP/EMA then TE/TP	1	14.3	1	14.3		
<b>Completed the treatment</b>	0	0.0	4	57.1		
<b>Completed follow-up</b>	0	0.0	3	42.9	3.858	0.192
<b>Dosage of chemo drug correct</b>	7	100.0	7	100.0	-	-
<b>Persistence bleeding</b>	5	85.7	1	14.3	7.143*	0.029*
<b>Drop by 15% of β-hCG titer</b>	3	42.9	5	85.7	2.800	0.286

A total of 14 patients with UHR-GTN had their medical records reviewed. There was a 50% mortality rate. Mortality was higher among patients aged < 40 years old [85.7% vs 14.3%, p=0.23]. A high mortality rate was reported among women with anemia (100%) and septicemia (42.9%). Most patients with an initial β-hCG of > 1,000,000 died from the disease [85.7% vs 14.3%, p=1.00]. Mortality from patients with liver and brain metastases was equally reported as 42.9% [p=0.56]. Death among those with more than 3 site metastases was 71.4% [p=0.46]. Mortality among those with more than 3 cm metastasis lesions size was

85.7% [p=0.10]. The mortality rate among those who received multimodality treatment was high [57.1% vs 42.9%, p=1.0]. A delay of  $\geq 7$  days in initiating and continuing treatment was not statistically associated with mortality [85.7%, p=0.10] and [71.4%, p=1.00], respectively.

**Conclusion/Implications:** The prognosis of UHR-GTN is poor. The age < 40 years old, anemia, septicemia, and initial  $\beta$ -hCG level  $\geq 1$  million, the number and size of metastatic lesions were not statistically associated with mortality; however, there were reported to have high mortality.



EP412 / #446

Topic: *AS21. Trophoblastic Diseases*

## **EFFECT OF PULMONARY RESECTION ON INITIALLY TREATED PATIENTS WITH RESIDUAL LESIONS OF PULMONARY METASTASIS FROM GESTATIONAL TROPHOBLASTIC NEOPLASIA: A CLINICAL RETROSPECTIVE ANALYSIS**

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**Introduction:** To evaluate the prognosis and recurrence in initially treated patients with pulmonary metastasis from gestational trophoblastic neoplasia (GTN), and to explore the clinical significance of pulmonary resection.

**Methods:** Retrospective analysis was performed on 606 GTN patients with pulmonary metastasis who received standardized chemotherapy as initial treatment in Peking Union Medical College Hospital (PUMCH) from January 2002 to December 2018. The patients were divided into the surgery (51 patients) and non-surgery groups (555 patients). The prognosis of these patients was compared. Risk factors affecting recurrence were analyzed to explore the effect of pulmonary resection.

**Results:** Among low-risk patients, CR rate is 100% and recurrence rate is below 1% in both groups .Among high-risk patients, CR rate and recurrence rate are 93.5% and 10.3% in the surgery group and 94.7% and 14.3% in the non-surgery group, respectively. There was no significant difference in all prognosis features between the two groups.(all with  $P > 0.05$ ). No significant difference was found in recurrence rates considering the recurrence risk factors ( $\geq 3.2$  cm residual lung lesions; FIGO score  $\geq 9.0$ ; drug resistance) between the two groups (all with  $P > 0.05$ ).

**Conclusion/Implications:** After standardized chemotherapy, pulmonary resection is not necessary for initially treated stage III GTN patients whose blood  $\beta$ -hCG drop to normal levels and residual lung lesions remain stable . These patients should be closely monitored during the follow-up regardless of the size of residual lung lesions or high/low risk score, especially within 1 year after CR.

EP413 / #15

Topic: *AS21. Trophoblastic Diseases*

## **A CASE SERIES OF EIGHT PATIENTS WITH GESTATIONAL TROPHOBLASTIC NEOPLASIA: CLINICAL AND BIOLOGICAL CHARACTERISTICS AND OUTCOME**

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**Introduction:** Gestational trophoblastic neoplasia (GTN) are a rare group of tumors that arise from the placental villous

**Methods:** We report the presenting features, treatment, and outcomes of patients diagnosed to have GTN over a nine-year period in a single institution. Patients diagnosed to have hydatidiform mole were excluded

**Results:** Between 2013 and 2022, a total of 8 patients were diagnosed to have GTN. Median age was 37 (26-52) years. One patient was diagnosed to have metastatic disease 2 years after menopause. Six patients presented with vaginal bleeding, and one each with dyspnea and headache. Three patients had an antecedent history of hydatidiform mole, while 4 patients had antecedent full-term pregnancy. One patient presented with CNS metastasis, while one had co-incidental atypical meningioma. 05 patients presented with pulmonary metastasis. Splenic artery embolization was employed in one patient to arrest spontaneous retro-peritoneal bleed. Pre-treatment human chorionic gonadotropin ( $\beta$ -HCG) ranged between 4,300 to  $1.29 \times 10^6$  IU/L. According to the FIGO criteria, six patients had high risk disease. These patients received either EMA/CO (etoposide, methotrexate and actinomycin, oncovin cyclophosphamide) (4 patients), or BEP (2 patients). One patient required hysterectomy. Median time to response was 6.8 (04 to 12) weeks. Treatment was continued for 06 weeks after serological remission. All patients are in continuous complete remission

**Conclusion/Implications:** The prevalence of GTN among Omani population is unknown and there is need to collect and report data on consecutive patients. Standard-of-care treatment ensures an excellent prognosis.

EP414 / #1443

**Topic:** AS22. *Vulvar and Vaginal Cancer*

## **TREATMENT OUTCOME IN PATIENTS WITH VULVAR CANCER: AN INSTITUTIONAL EXPERIENCE IN BANGLADESH**

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**Introduction:** Objective: This study evaluated the risk factors, clinical presentation and different modalities of treatment and survival outcome of vulvar cancer patients.

**Methods:** Method: This was a cohort study of 76 cases diagnosed as vulvar cancer in National Institute of Cancer Research & Hospital from July 2015 to June 2020. Risk factors, stage of disease, treatment modalities, disease outcomes and survival were analyzed. Kaplan-Meier curve was used to determine the predictors for progression free survival and overall survival.

**Results:** Mean age of the patients was 54.5 years and 52.6% patients were below 40 years. The percentages of the patients with FIGO stage I, II, III and IV were 14.5%, 34.2%, 28.9%, and 7.9% respectively. About 68% had positive inguinal nodes and 20 (26.3%) were HPV positive. Squamous cell carcinoma (81.6%) was the predominant type. Equal number of patients (21, 27.6%) were treated by Wide Local Excision with Bilateral Groin Node Dissection (BGND) and by Radical Vulvectomy with BGND, 11 (14.5%) received CCRT. Forty-four patients (57.9%) were in irregular follow up. About 13% patients experienced local recurrence, 35 (46.1%) cured, 12 (15.8%) expired, 18 (23.7%) were alive with disease & rest were lost to follow up. Overall survival was 77.1 months. At the end of the five year 63.6, 38.2 and 9.09 percents of patients of Stage I, II and III were alive respectively.

**Conclusion/Implications:** Vulvar cancer can occur below 40 years of age. Surgical treatment is the best option in the early stage of disease (Stage I and II) and gives high survival rates.

EP415 / #186

Topic: *AS22. Vulvar and Vaginal Cancer*

## **IS ROBOTIC-ASSISTED SURGERY A BETTER CHOICE IN VAGINECTOMY OF COMPLICATED VAGINAL HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS THAN CONVENTIONAL LAPAROSCOPIC SURGERY?**

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**Introduction:** The aim of this study was to evaluate the operative outcomes of robotic-assisted laparoscopic vaginectomy (RALV) and conventional laparoscopic vaginectomy (CLV) for patients with complicated vaginal high-grade squamous intraepithelial lesions (HSIL).

**Methods:** an analysis of one hundred and nine patients with complicated vaginal HSIL (32 patients in the RALV group and 77 patients in the CLV group) who underwent minimally invasive vaginectomy was conducted retrospectively.

**Results:** Compared with the CLV group, patients in the RALV group demonstrated less estimated blood loss, a lower rate of intraoperative complications and shorter durations of paralytic ileus time, urinary catheter indwelling time and postoperative hospitalization time (all  $P < 0.05$ ). However, the RALV group had significantly higher hospital costs than the CLV group ( $P < 0.05$ ). The total operative time, postoperative complications, positive surgical margins, pathology upgrading or treatment outcomes did not significantly differ between the two groups (all  $P > 0.05$ ).

**Conclusion/Implications:** Our results demonstrated that both RALV and CLV can achieve satisfactory treatment outcomes, while RALV has the advantages of less intraoperative blood loss, fewer intraoperative complications and faster postoperative recovery. RALV has the potential to become a better choice for vaginectomy without regard to the burden of hospital costs.

EP416 / #595

**Topic:** AS22. *Vulvar and Vaginal Cancer*

## **PREDICTIVE FACTORS OF LYMPH NODE INVOLVEMENT IN VULVAR CANCER**

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**Introduction:** The aim of this study was to identify histological factors associated to lymph node metastasis (LNM) in vulvar cancer (VC).

**Methods:** We retrospectively included 192 patients treated for VC at the Salah Azaiez Institute between 1994 and 2022. We analyzed the clinical and histological factors correlated with LN invasion.

**Results:** The mean age was  $64.93 \pm 13.817$  years (range, 24-104 years). Surgery consisted on a radical vulvectomy, hemivulvectomy, and pelvic exenteration in respectively 96.4%, 2.1%, and 1.6% of cases. Lymph node (LN) dissection was bilateral 88.5% of cases. The mean tumor size was  $42.21 \pm 24.018$  mm. Tumors were classified as stage FIGO I, II, III and IV in 55.2%, 9.4%, 32.8% and 2.6% of cases. Perineural invasion (PNI) and lymphovascular space invasion (LVSI) were detected in 13.5 and 2.7% of cases. LNM was assessed in 67 patients (34.9%) with bilateral groin metastasis in 24 cases (35.8%). On univariate analysis, LN invasion was significantly correlated to the age < 70 years (41.8 vs 26.2% in patients aged more than 70 years,  $p=0.027$ ), the presence of LVSI (100% vs 39.8%,  $p=0.037$ ) and PNI (80% vs 35.4%,  $p=0.001$ ) and the tumor size exceeding 40mm (45.8% vs 28.8%,  $p=0.017$ ). On multivariate analysis, independent factors of LN metastasis were the presence of PNI (OR=0.298, 95%CI=0.174-0.686;  $p=0.001$ ) and the tumor size (OR=0.199; 95%CI=0.021-0.379,  $p=0.029$ ).

**Conclusion/Implications:** Since LNM represent an independent prognostic factor for survival, a nomogram based on histological and clinical characteristics could lead to better detection of patients with a high risk of LN metastasis.

EP417 / #599

**Topic:** AS22. *Vulvar and Vaginal Cancer*

## **PROGNOSTIC FACTORS OF SURVIVAL AND RECURRENCE IN VULVAR CANCER: A TUNISIAN RETROSPECTIVE STUDY OF 192 PATIENTS**

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**Introduction:** To identify the prognostic factors correlated to the overall survival (OS) and recurrence-free survival (RFS) in vulvar cancer (VC).

**Methods:** We retrospectively included 192 patients treated for VC at the Salah Azaiez Institute between 1994 and 2022. Clinical, pathological, and evolutionary data were reported. Survival curves were generated by the Kaplan-Meier method and predictive factors of outcome were analyzed using Cox proportional hazards models.

**Results:** The mean age was  $64.93 \pm 13.817$  years. Surgery consisted of a radical vulvectomy, hemivulvectomy, and pelvic exenteration in respectively 96.4%, 2.1%, and 1.6% of cases followed by adjuvant radiotherapy in 38.5% of cases. Lymph node (LN) dissection was bilateral in 88.5% of cases. The mean tumor size was  $42.21 \pm 24.018$  mm. LN metastasis was assessed in 67 patients (34.9%). Lymph node ratio LNR=0, LNR0-0.2, and LNR $\geq$ 0.2 were recorded in respectively 64.7%, 22.1%, and 13.2% of cases. Tumors were classified as stage FIGO I, II, III, and IV in 55.2%, 9.4%, 32.8%, and 2.6% of cases respectively. With a mean follow-up time of  $35.48 \pm 35.48$  months, the 5-year OS was 52.5% and the 5-year RFS was 55.8%. On multivariate analysis, the independent prognostic factor of OS was the LNR (HR=5.702; 95% CI= 2.282-14.245; p<0.0001), FIGO stage (HR=2.089; 95% CI=1.028-4.277; p=0.042) and free margins R0 (HR=2.247; 95% CI=1.215-4.155; p=0.01). Recurrence was recorded in 37.5% of cases. Independent prognostic factor of RFS were the LNR (HR=2.911; 95% CI=1.468-5.779; p=0.002), FIGO stage (HR=1.835; 95% CI=1.071-3.141; p=0.027) and free margins (HR=2.091; 95% CI=1.286-3.999; p=0.003).

**Conclusion/Implications:** LNR, FIGO stage, and complete resection were the independent prognostic factors of survival and recurrence in VC.

EP418 / #626

**Topic:** AS22. *Vulvar and Vaginal Cancer*

## **WHAT IS THE IMPACT OF THE NUMBER OF RETRIEVED LYMPH NODE IN THE RECURRENCE FREE SURVIVAL OF VULVAR CANCER?**

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**Introduction:** To investigate the impact of the number of retrieved lymph nodes (NRLN) in the recurrence-free survival (RFS) of patients with vulvar cancer (VC).

**Methods:** We retrospectively included 192 patients treated for VC at the Salah Azaiez Institute between 1994 and 2022. The NRLN was stratified into 2 groups: NRLN <12 and NRLN ≥ 12. We analyzed the impact of the NRLN on RFS according to clinical and pathological factors.

**Results:** The mean age was 64.93± 13.817 years (range, 24-104 years). Surgery consisted of a radical vulvectomy, hemivulvectomy, and pelvic exenteration in respectively 96.4%, 2.1%, and 1.6% of cases. Lymph node (LN) dissection was bilateral in 88.5% of cases and the mean number of retrieved lymph LN was 14. LN metastasis (LNM) was assessed in 67 patients (34.9%). NRLN<12 and ≥12 were recorded in respectively 31.8% and 68.2% of cases. After a mean follow-up time of 35.48±35.48 months, the 5-year RFS in patients with NRLN<12 and NRLN≥12 was 38.2% and 64.9% respectively (p=0.092). The subgroup analysis revealed that a NRLN≥12 was significantly associated with a better 5 years RFS compared to NRLN<12 in stage pT1 (70.1% vs 38.9%, p=0.016), patients staged without LNM (81% vs 46.5%, p=0.032), patients with 3 or more LNM (33.6% vs 0%, p=0.027), in case of R0 resection (74.8% vs 36.6%, p=0.005) and in the absence of lymphovascular space invasion (64.9% vs 28.7%, p=0.046)

**Conclusion/Implications:** The removal of more than 12 LN improves VC outcomes in patients with node-positive and negative disease, pT1 stage, and complete resection.

EP419 / #629

**Topic:** AS22. *Vulvar and Vaginal Cancer*

## **PROGNOSTIC ANALYSIS OF FIGO STAGE I AND II OF VULVAR CANCER: A RETROSPECTIVE STUDY OF 123 CASES**

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**Introduction:** To identify clinical, pathological features and survival predictors of vulvar cancer in patients with no lymph node metastasis.

**Methods:** A retrospective study of 123 patients who were diagnosed and treated for vulvar cancer staged I and II at the Salah Azaiez Institute of Oncology between 1994 and 2022

**Results:** Mean age was  $65.61 \pm 14.081$  years (range, 30-104 years) and median follow-up was  $37.84 \pm 40.221$  months. Surgery was a radical vulvectomy, hemivulvectomy, and pelvic exenteration in respectively 96.7%, 2.4%, and 0.8% of cases. Inguinal Sentinel lymph node (LN) biopsy was performed in 10 cases (8.1%), bilateral inguinofemoral lymphadenectomy (ILND) in 101 cases (81.1%), and unilateral (ILND) in 14 cases (11.4%). The mean tumor size was  $38.04 \pm 20.45$  mm. Tumors were classified as stage pT1a, pT1b, pT2, and pT3 in respectively 4.9%, 81.3%, 13%, and 0.8% of cases. The 5 years overall survival was 64.2% and decreased with advanced age  $\geq 70$  years (45% vs 74% in patients younger than 70 years,  $p = 0.014$ ) and with the presence of perineural invasion (PNI) (0% vs 70.7%,  $p = 0.028$ ). The 5-year recurrence-free survival was 65.8% and decreased with a number of retrieved LN less than 12 (0% vs 45.3% in case of 12 or more LN;  $p = 0.001$ ), and the presence of PNI (33.3% vs 71.4%,  $p = 0.002$ ). Moreover, the rate of recurrence increased with the pT stage (0%, 26%, and 52% respectively in stages pT1a, pT1b, and pT2-3;  $p = 0.021$ ).

**Conclusion/Implications:** The survival of patients with stage I and II of vulvar cancer is correlated to the number of retrieved LN and the presence of PNI.



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## **PROGNOSTIC VALUE OF PERINEURAL INVASION IN VULVAR CANCER**

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**Introduction:** Perineural invasion (PNI) is considered a poor prognostic factor in various malignant tumors, however, its predictive value in vulvar (VC) cancer remains unclear. This study aimed to determine the prognostic significance of PNI in patients with VC.

**Methods:** We retrospectively analyzed clinicopathological data on 192 patients with VC treated surgically at the Salah Azaiez Institute of Tunisia between 1994 and 2022.

**Results:** The mean age was  $64.93 \pm 13.817$  years (range, 24-104 years). Surgery consisted of a radical vulvectomy, hemi vulvectomy, and pelvic exenteration in respectively 96.4%, 2.1%, and 1.6% of cases. Lymph node (LN) dissection was bilateral in 88.5% of cases. The mean tumor size was  $42.21 \pm 24.018$  mm. Tumors were classified as stage FIGO I, II, III, and IV in 55.2%, 9.4%, 32.8%, and 2.6% of cases. LN metastasis was recorded in 34.9%. Perineural invasion (PNI) and lymphovascular space invasion (LVSI) were detected respectively in 13.5% (n=15) and 2.7% (n=3) of cases. The presence of PNI was associated with young age  $\leq 50$  years (46.7% vs 18.8%), advanced stage III-VI (80% vs 35.4%,  $p=0.001$ ), stage LN metastasis (80% vs 35.4%,  $p=0.001$ ) with a LN ratio  $\geq 0.2$  (46.7% vs 12.5%,  $p=0.01$ ) and bilateral groin metastasis (33.3% vs 13.5%,  $p=0.005$ ), the presence of LVSI (20% vs 0%,  $p<0.0001$ ), a decreased 5 years overall survival (OS) (12.8% vs 56.9%,  $p<0.0001$ ) and decreased 5 years recurrence-free survival (RFS) (20.8% vs 60%,  $p=0.001$ ).

**Conclusion/Implications:** The presence of PNI in vulvar cancer is correlated to aggressive tumors and decreased OS and RFS

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## **CHEMORADIATION FOR ADVANCED PRIMARY VULVAR CANCER – A RETROSPECTIVE SINGLE INSTITUTION ANALYSIS**

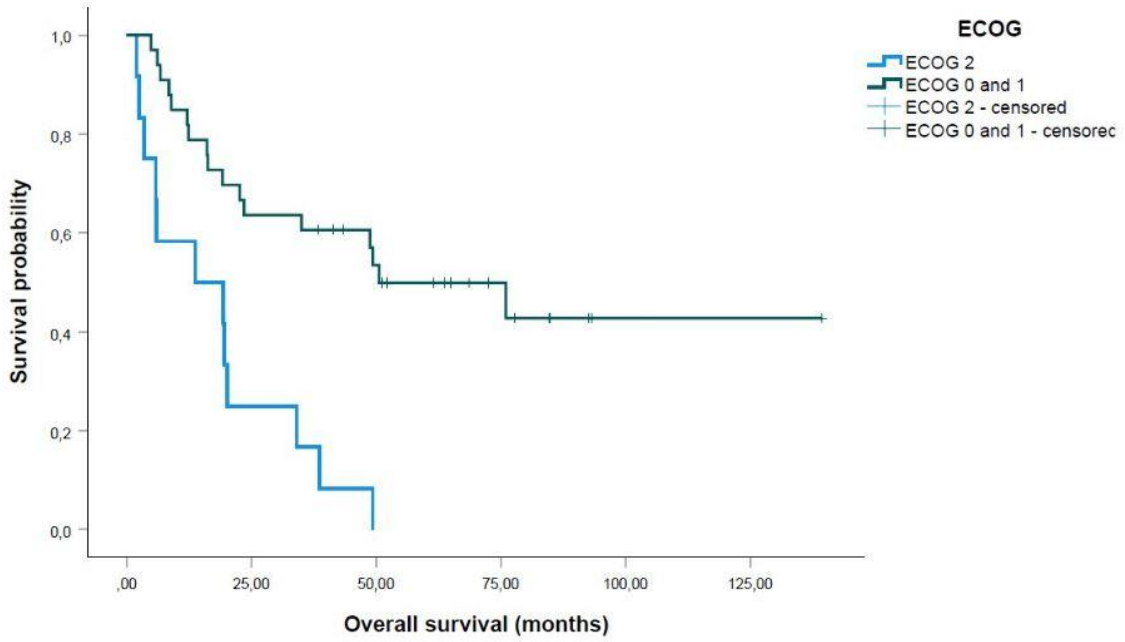
Esten Nakken, Silje Os

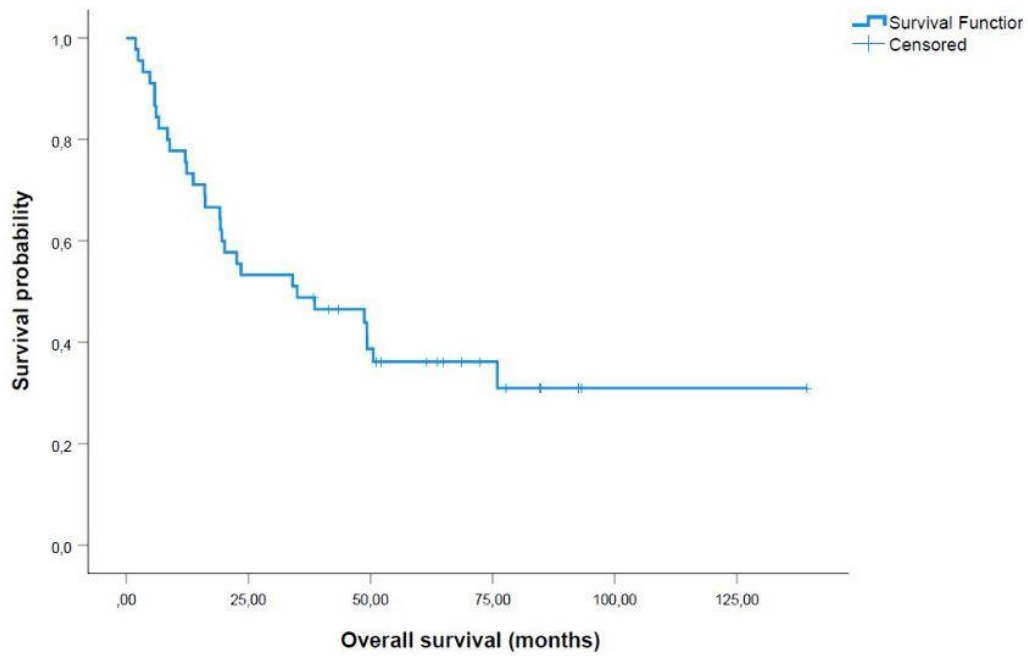
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**Introduction:** Patients with advanced vulvar cancer that are considered inoperable can be cured with (chemo)radiation. We present a single institution experience with treatment outcomes and factors associated with survival.

**Methods:** A retrospective cohort study of patients with proven carcinoma of the vulva diagnosed from 2011 to 2020 at Oslo University Hospital (Norway) is presented. Data were collected from the hospital radiation registry and medical records.

**Results:** A total of 45 patients with inoperable vulvar cancer were included. Median age at diagnosis was 75 years (range 30-91). Forty-four patients were diagnosed with squamous cell carcinoma, one patient had adenocarcinoma. Equal number of cases belonged to stage II and III (40% each) of the FIGO 2021 classification. Fourteen patients (31.1%) had verified lymph node metastases. Fourteen patients also received cisplatin. Thirty-one patients (68.9%) received external beam radiotherapy only, the remaining received a combination of external beam and brachytherapy. Median total tumor dose (EQD2) was 70.1 Gy (range 58.9-80.6). Thirty-three patients presented with ECOG 0-1 at start of radiotherapy, the remaining 12 had ECOG 2. Twenty-one patients (46.7%) experienced recurrence of the cancer, of these 19 recurred in the vulvar region. Median time to progression was 6.0 months. Median overall survival for the whole cohort was 35.0 months (range 1.9-139.3). ECOG 0-1, concomitant cisplatin and use of brachytherapy was significantly associated with improved survival.





**Conclusion/Implications:** Carefully selected patients with good performance status can experience long-term survival after chemoradiation for vulvar cancer. Quality of life should be monitored in future prospective studies.

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## **EXTRAMAMMARY PAGET'S DISEASE (EMPD) OF THE VULVA: OUTCOMES OF 22 PATIENTS TREATED WITH IMIQUIMOD CREAM.**

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**Introduction:** Extramammary Paget's disease (EMPD) of the vulva is a rare form of intra epithelial adenocarcinoma, which is most common in postmenopausal women. The gold standard treatment for non-invasive EMPD vulva is wide local excision. Surgery is challenging in elderly women with multiple comorbidities. Imiquimod, a topical immune response modifier is a new treatment modality with encouraging results.

**Methods:** Retrospective analysis Objective is to retrospectively investigate the efficacy of 5% imiquimod cream in patients with non-invasive vulvar Paget disease both primary and recurrent.

**Current Trial Status:** Results IRB permission and individual consent for photo documentation was available for all patients. Data were available for 22 patients with complete clinical, histological and photo documentation. Thirteen patients (59%) were treated for primary EMPD, and 9 patients (44.4%) were treated for recurrent EMPD. A complete response was reported in 11 patients (50%), and 11 patients (50%) had a partial response. A histologic complete response was observed in 5 of the 11 patients with a complete response. Duration of use of imiquimod was 12 to 28 weeks. No systemic side effects noted in any patient. Local irritation was noted and documented in 6 patients. Lesion size was noted less than 8 cm in patients with complete clinical response. Extensive lesions extending to groin folds and perinium responded partially. conclusion Topical 5% imiquimod cream can be an effective and safe treatment alternative for small volume non-invasive vulvar EMPD.

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## **PROGNOSTIC FACTORS AND CLINICAL OUTCOMES IN PATIENTS WITH VULVAR CANCER: A 15-YEAR RETROSPECTIVE STUDY**

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**Introduction:** The primary objective was to determine the prognostic factors affecting progression-free and overall survival. The secondary objective was to determine the progression-free survival (PFS) and overall survival (OS) in vulvar cancer patients.

**Methods:** We retrospectively reviewed the medical records of vulvar cancer patients at Siriraj Hospital between 2006 and 2020. Patient characteristics, surgical outcomes, pathological characteristics, and immunohistochemical (IHC) results: p16, p53, and PD-L1 were analyzed to predict the survival outcomes.

**Results:** Of 104 vulvar cancer patients, prognostic factors that significantly correlated with worsening PFS were coexisting vulvar lesions, such as sclerosis and extramammary Paget's disease ( $p=0.008$ ), positive lymphovascular invasion (LVSI) ( $p=0.011$ ), positive pelvic or paraaortic node metastases ( $p=0.042$ ), and positive p53 status ( $p=0.046$ ). Tumor size over 4 cm in diameter was significantly associated with worsening OS ( $p=0.001$ ). The median PFS was 26.3 months, and the median OS was 44.7 months. The patients with positive p16 and negative p53 IHC had significantly better PFS and OS,  $p=0.004$  and  $0.025$ , respectively.

**Conclusion/Implications:** Coexisting vulvar lesions, LVSI status, pelvic or paraaortic node metastases, and p53 status significantly affect PFS in vulvar cancer patients. Tumor size over 4 cm is negatively associated with OS.