IGCS 2023
Annual Global Meeting
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IGCS 2023 Abstracts:
Featured Printed Poster Presentations
(Poster Rounds with the Professors)

Featured printed posters will be presented in Poster Rounds with the Professors' sessions during the 30-minute coffee breaks on all three days of the meeting as per the interactive program. The printed posters will be displayed in the Poster Area next to Registration at the meeting venue.

Featured poster presenters were requested to submit an ePoster and a short audio file as well. 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. Submitted audio files will be available together with their ePosters within the ePoster Stations onsite and the IGCS 360 Educational Portal.

PR001 / #687 / Poster Board #: 11

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

PAN-GYNECOLOGIC CANCER ANALYSIS OF SOMATIC HOMOLOGOUS RECOMBINATION DEFICIENCY PATHOGENIC GENE VARIANTS: MORE PREVALENT THAN WE THINK?

Muhammad Danyal Ahsan[1], Emily Webster[1], Murtaza Qazi[2], Xuan Li[1], Sarah Levi[1], Evelyn Cantillo[1], Eloise Chapman-Davis[1], Kevin Holcomb[1], Ravi Sharaf[3], Melissa Frey[1]
[1]Weill Cornell Medicine, Gynecologic Oncology, New York, United States of America, [2]Lankenau Medical Center, Internal Medicine, Wynnewood, United States of America, [3]Weill Cornell Medicine, Gastroenterology, New York, United States of America

Introduction: We conducted a pan-gynecologic cancer analysis of the prevalence of somatic pathogenic gene variants (PGVs) in homologous recombination deficiency (HRD) genes.

Methods: The American Association for Cancer Research's (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE) database version 13.1 was queried via cBioPortal (http://genie.cbioportal.org) for the following gynecologic tumors: epithelial ovarian, sex-cord stromal, germ cell, endometrial, uterine sarcoma, cervical and vulvar/vaginal tumors. PGV frequencies of 27 HRD genes were descriptively reported among these tumors: ATM, ARID1A, ATRX, BRCA1, BRCA2, BARD1, BRIP1, BLM, BAP1, CHEK1, CHEK2, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCL, MRE11, NBN, PALB2, RAD50, RAD51, RAD51B, RAD51C, RAD51D, WRN.

Results: A total of 13,312 tumors from 12,804 patients were included for analysis. At least one PGV in an HRD gene was found in 29.6% (3946/13,312) of all samples analyzed, with the highest frequency observed in endometrial tumors (2156/5087, 42.4%), uterine sarcomas (196/704, 27.8%), and epithelial ovarian tumors (1402/6052, 23.2%). There were also substantial rates of HRD PGVs in cervical and vulvar/vaginal tumors, and comparatively lower rates among germ cell and sex cord/stromal tumors (Table 1). Across all tumors, HRD genes with the highest frequencies of PGVs were ARID1A (19.6%), BRCA1 (3.9%), BRCA2 (3.7%), and ATM

(3.7%).

Table 1. Prevalence and distribution of PGVs in HRD genes among all gynecologic tumors analyzed.

Tumor Type	Frequency of tumors with ≥1 HRD PGV	HRD gene with highest PGV frequency
Epithelial ovarian	23.2% (1402/6052)	*ARID1A*, 8.4%
Sex-cord stromal	6.7% (16/239)	*FANCA*, 2.5%
Germ cell	6.3% (12/191)	*ARID1A*, 3.7%
Endometrial	42.4% (2156/5087)	*ARID1A*, 38.3%
Uterine sarcoma	27.8% (196/704)	*ATRX*, 16.9%
Cervical	16.4% (142/866)	*ARID1A*, 8.6%
Vulvar/vaginal	16.2% (28/173)	*ARID1A*, 4.3%; *BAP1*, 4.3%

Conclusion/Implications: NGS data demonstrate a substantial rate of somatic PGVs in HRD genes across most types of gynecologic tumors analyzed. These data suggest the need to expand routine functional HRD status assessment beyond epithelial ovarian tumors, and also suggest the need for clinical trials evaluating the efficacy of HRD targeting agents in these cancers.

PR002 / #853 / Poster Board #: 9

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

CATECHOLAMINES PROMOTE OVARIAN CANCER PROGRESSION THROUGH SECRETION OF CXC-CHEMOKINES

Ha Kyun Chang[1], Hyun Jung Kim[2], Sung Jong Lee[3], Kyun Heo[2]
[1]Korea University Ansan Hostpital, Department Of Obstetrics And Gynecology, Ansan, Korea, Republic of, [2]Kookmin University, Department Of Biopharmaceutical Chemistry, Seoul, Korea, Republic of, [3]Seoul St. Mary's Hospital, Obstetrics And Gynecology, Seoul, Korea, Republic of

Introduction: Catecholamines such as adrenaline (epinephrine) and noradrenaline (norepinephrine) are hormones that play a critical role in the body's "fight or flight" response, which is the physiological response to stress. Considerable evidence has accumulated in the last decade to support the notion that chronic stress is closely related to the growth, metastasis, and angiogenesis of ovarian cancer. The purpose of this study was to identify factors that increase the progression of ovarian cancer and to determine the possibility of inhibiting ovarian cancer progression using novel therapeutics.

Methods: In this study, we analyzed the conditioned media in SKOV3 ovarian cancer cell line treated with catecholamine to identify secreted proteins responding to chronic stress.

Results: We observed that epinephrine and norepinephrine enhanced the secretion and mRNA expression of CXC-chemokines (CXCL1, 2, 3, and 8). Neutralizing antibody to CXCL8 and CXCL8 receptor (CXCR2) inhibitors significantly reduced catecholamine-mediated invasion of SKOV3 cells. Finally, we found that the concentration of CXCL1 and CXCL8 in the plasma of ovarian cancer patients increased with stage
progression.

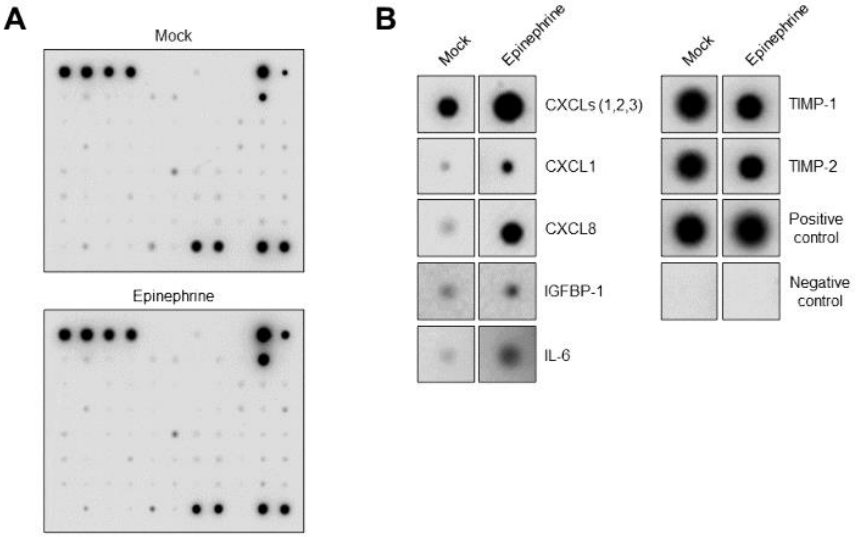

Fig. 2

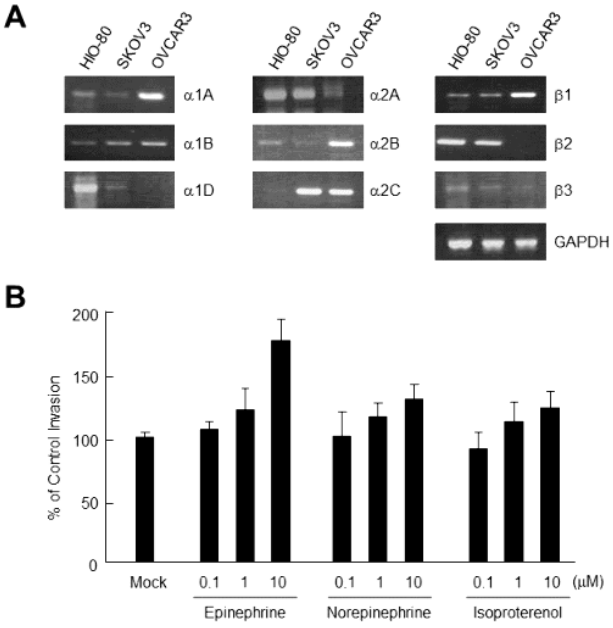

Fig. 1

Conclusion/Implications: Therefore, not only can CXCL1 and CXCL8 be used as diagnostic markers for ovarian cancer, but their inhibition also holds promise as a potential therapeutic option for suppressing ovarian cancer progression. Taken together, these findings suggest that stress-related catecholamines may influence ovarian cancer progression through the secretion of CXC-chemokines.

PR003 / #357 / Poster Board #: 1

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

PERIPHERAL PD-1+REGULATORY T CELLS FOR PREDICTING TREATMENT RESPONSE TO PARP INHIBITOR MAINTENANCE IN PATIENTS WITH EPITHELIAL OVARIAN CANCER

Junsik Park[1], Jung Chul Kim[1], Yoo-Na Kim[1], Yong Jae Lee[1], Sunghoon Kim[1], Sang Wun Kim[1], Su-Hyung Park[2], Jung-Yun Lee[1]
[1]Yonsei University College of Medicine, Obstetrics And Gynecology, Seoul, Korea, Republic of, [2]Korea Advanced Institute of Science and Technology, Graduate School Of Medical Science And Engineering, Daejeon, Korea, Republic of

Introduction: Poly (adenosine diphosphate [ADP]-ribose) polymerase inhibitors (PARPis) are becoming the standard of care for epithelial ovarian cancer (EOC). Recently, clinical trials of triple maintenance therapy (PARPi+anti-angiogenic agent+anti-PD-1/L1) are actively ongoing. Here, we investigated the immunological effects of PARPi or triple maintenance therapy on T cells and their impact on clinical responses.

Methods: We collected serial blood from EOC patients receiving PARPi therapy (cohort 1: PARPi, n=49; cohort 2: olaparib+bevacizumab+pembrolizumab, n=31). Peripheral T cells were analyzed using flow cytometry and compared according to the PARPi response. Progression-free survival (PFS) was assessed according to predictive biomarkers identified in a comparative analysis

Results: Regulatory T cells (Tregs) were suppressed by PARPi therapy, whereas PD-1 was not significantly changed. Short PFS group exhibited a higher percentage of baseline PD-1^{+}Tregs than long PFS group, and the patients with high percentage of PD-1^{+}Tregs before treatment showed poor PFS in cohort 1. However, the expression of PD-1on Tregs significantly decreased after receiving triple maintenance therapy, and the reduction in PD-1^{+}Tregs was associated with superior PFS in cohort 2 (P=0.0078).

Conclusion/Implications: PARPi suppresses Tregs, but does not affect PD-1 expression. Addition of PD-1 blockade to PARPi decreases PD-1^{+}Tregs, which have negative predictive value for PARPi monotherapy. Our data suggest that addition of PD-1 blockade to PARPi maintenance therapy is a promising option to improve survival outcomes for high-risk patients with ovarian cancer.

PR004 / #458 / Poster Board #: 12

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

CELL-FREE DNA FROM ASCITES IDENTIFIES CLINICALLY RELEVANT VARIANTS AND TUMOUR EVOLUTION IN A COHORT OF PATIENTS WITH ADVANCED OVARIAN CANCER

Bonnita Werner[1], Elyse Powell[1], Jennifer Duggan[2], Yeh Chen Lee[2,3], Ramanand Athavale[2,3], Michael Dean[4], Kristina Warton[1], Caroline Ford[1]
[1]Faculty of Medicine and Health, University of New South Wales, Gynaecological Cancer Research Group, School Of Clinical Medicine, Sydney, Australia, [2]Royal Hospital for Women, Gynaecologic Oncology Department, Sydney, Australia, [3]Faculty of Medicine and Health, University of New South Wales, School Of Clinical Medicine, Sydney, Australia, [4]National Cancer Institute, Laboratory Of Translational Genomics, Division Of Cancer Epidemiology And Genetics, Rockville, United States of America

Introduction: Somatic molecular profiling is more important than ever, as precision treatment for ovarian cancer advances. Tumour material for profiling can be accessed via malignant ascites, however cancer cells are often sparse in ascites and cell-free DNA (cfDNA) is not well studied.

Methods: Ascites-derived cfDNA from 14 patients (36-82 years), including 11 patients with sequential samples, was sequenced with the Illumina TSO-500 panel. Matched DNA from ascites-derived tumour cells (n=5) and archived FFPE-tissue from surgery (n=4) was sequenced using the same panel. cfDNA from one patient was additionally sequenced using an Oxford Nanopore Technology R9.4.1 MinION.

Results: Abundant cfDNA was identified in all ascites samples (up to 660 ng/mL), achieving similar read alignment and improved coverage compared to cell or FFPE-derived DNA. Somatic driver mutations were detected in 100% of cfDNA samples at mutation fractions of up to 79%. All clinically known variants were identified in ascites cfDNA (including 6 in BRCA1 or BRCA2), except for one case, where a TP53 mutation identified in FFPE-DNA was absent in ascites due to the clonal loss of chromosome 17 p-arm in tumour evolution; indicated by a decrease in Oxford Nanopore sequencing reads per kilobase over 17p relative to 17q (p=0.0015). Tumour evolution was also indicated by an increase in tumour mutational burden in samples collected subsequent to multiple cycles of chemotherapy (p=0.043).

Conclusion/Implications: We demonstrate the reliability of sequencing cfDNA from ascites for molecular profiling. This approach provides opportunistic access to tumour DNA, allowing a liquid biopsy of ovarian cancer in lieu of a traditional biopsy.

PR005 / #410 / Poster Board #: 71

Topic: ***AS03. Cervical Cancer***

OUTCOMES OF NEOADJUVANT CHEMOTHERAPY AND RADICAL HYSTERECTOMY FOR LOCALLY ADVANCED CERVICAL CANCER AT KIGALI UNIVERSITY TEACHING HOSPITAL, RWANDA

Eugene Ngabonziza[1], Rahel Ghebre[2], Rebecca J. Deboer[3], Diomede Ntasumbumuyange[1], Urania Magriples[4], Jessica Marie George[5], Surbhi Grover[6], Lisa Bazzett-Matabele[7]
[1]University of Rwanda, Obstetrics And Gynaecology, Kigali, Rwanda, [2]University of Minnesota, Obstetrics And Gynecology, Minneapolis, United States of America, [3]University of California San Francisco, Medical Oncology, San Francisco, United States of America, [4]Yale University, Obstetrics And Gynecology, New Haven, United States of America, [5]University of California Irvine, Information And Computer Science, Irvine, United States of America, [6]University of Pennsylvania, Radiation Oncology, Philadelphia, United States of America, [7]University of Botswana, Obstetrics And Gynaecology, Gaborone, Botswana

Introduction: To evaluate the clinical and surgical response of neoadjuvant(NACT) followed by radical hysterectomy, as well as recurrence rates and overall survival, in patients with locally advanced cervical cancer treated at Kigali University Teaching Hospital in Rwanda.

Methods: Retrospective descriptive study: data collected from eligible patients FIGO stage IB2-IIA2, some exceptional stage IIB. Patients treated with neoadjuvant carboplatin/paclitaxel chemotherapy every 3 weeks for 3-4 cycles before radical hysterectomy. Clinical response, recurrence and survival rates were determined.

Results: Between May 2016 and October 2018, 57 patients underwent NACT and 43(75.4%) were candidates for radical hysterectomy after clinical assessment. Median age was 56 years. 39(90.7%) patients received 3 cycles of NACT, 4(9.3%) received 4 cycles. Only 14% were HIV positive. FIGO stages were IB2 (32.6%), IIA1(27.9%), IIA2(30.2%) and IIB(9.3%). Mean tumor size before and after NACT was 5.9cm and 2.07cm, respectively. Thirty-eight(88.4%) patients underwent radical hysterectomy as planned. 5(11.6%) had surgery aborted due to metastatic disease, four(10.5%) had microscopic metastasis on final pathology. These nine(20.9%) patients were referred for adjuvant chemoradiation. Five(13.1%) patients showed no residual disease on final pathology. Mean time for follow up was 34.4 months. 32/41(78%) patients showed no evidence of recurrence, 8/41(19.5%) had documented recurrence and 2/43(4.7%) were lost to follow up. One and 2-year overall survival rates were 95.1% and 87%, respectively.

Conclusion/Implications: Neoadjuvant chemotherapy with radical hysterectomy is a feasible treatment option for locally advanced cervical cancer in limited resource settings. It can be an alternative treatment option in countries without radiation facilities if gynecologists skilled at radical surgery are available.

PR006 / #38 / Poster Board #: 69

Topic: ***AS03. Cervical Cancer***

TEN-YEAR OUTCOMES FOLLOWING LAPAROSCOPIC AND OPEN ABDOMINAL RADICAL HYSTERECTOMY FOR "LOW-RISK" EARLY-STAGE CERVICAL CANCER: A PROPENSITY-SCORE BASED ANALYSIS

Giorgio Bogani[1], Francesco Raspagliesi[1], Mario Malzoni[2], Mariangela Longo[1], Elisa Ervas[3], Jvan Casarin[4], Francesco Plotti[5], Roberto Angioli[5], Ilaria Cuccu[6], Camilla Turetta[6], Tullio Golia D'Auge[6], Violante Di Donato[7]
[1]Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Gynecologic Oncology, Milano, Italy, [2]Malzoni Medical Center, Gynecology, Avellino, Italy, [3]National Cancer Institute, Gynecologic Oncology, Milano, Italy, [4]University of Insubria, Gynecologic Oncology Unit, Varese, Italy, [5]Campus Biomedico, Gynecology, Roma, RM, Italy, [6]University La Sapienza, Gynecologic Oncology Unit, Roma, RM, Italy, [7]University La Sapienza, Gynecologic Oncology Unit, Rome, Italy

Introduction: Accumulating evidence suggested the detrimental effects of adopting minimally invasive surgery in the management of early-stage cervical cancer. However, long-term evidence on the role of minimally invasive radical hysterectomy in "low-risk" patients exists.

Methods: This multi-institutional retrospective study compared minimally invasive and open radical hysterectomies in low-risk early-stage cervical cancer patients. A propensity-score matching algorithm (1:2) was used to allocate patients into the study groups. Kaplan-Meir model was used to estimate 10-year progression-free and overall survival.

Results: Charts of 224 "low-risk" patients were retrieved. Overall, 50 patients undergoing radical hysterectomy were matched with 100 patients undergoing open radical hysterectomy. Minimally invasive radical hysterectomy was associated with a longer median operative time (224 (range, 100-310) vs. 184 (range, 150-240) minutes; p<0.001), lower estimated blood loss (10 (10-100) vs. 200 (100-1000) ml, p<0.001), and shorter length of hospital stay (3.8 (3-6) vs. 5.1 (4-12); p<0.001). The surgical approach did not influence the risk of having intra-operative (4% vs. 1%; p=0.257) and 90-day severe (grade 3+) postoperative complication rates (4% vs. 8%; p=0.497). Ten-year disease-free survival was similar between groups (94% vs. 95%; p=0.812; HR:1.195; 95%CI:0.275, 5.18). Ten-year overall survival was similar between groups (98% vs. 96%; p=0.995; HR:0.994; 95%CI:0.182, 5.424).

Conclusion/Implications: Our study appears to support emerging evidence suggesting that, for low-risk patients, laparoscopic radical hysterectomy does not result in worse 10-year outcomes compared to the open approach. However, further research is needed and open abdominal radical hysterectomy remains the standard treatment for cervical cancer patients.

PR007 / #569 / Poster Board #: 70

Topic: ***AS03. Cervical Cancer***

NEOADJUVANT CHEMOTHERAPY FOR LOCALLY ADVANCED CERVICAL CANCER. CAN CLINICAL-PATHOLOGIC FACTORS AND BIOMARKERS EXPRESSION COMBINED MODEL PREDICT THE CHEMORESPONSIVITY?

Antonino Ditto[1], Mariangela Longo[2], Umberto Leone Roberti Maggiore[1], Giulia Chiarello[3], Giorgio Bogani[1], Valentina Chiappa[1], Fabio Martinelli[1], Francesco Raspagliesi[1]
[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Gynecological Oncology Unit, Milan, Italy, [2]Filippo Del Ponte Hospital, University of Insubria, Department Of Obstetrics And Gynecology, Varese, Italy, [3]University of Bari, Department Of Biomedical Sciences And Human Oncology, Bari, Italy

Introduction: To evaluate the prognostic outcomes of NACT (neoadjuvant chemotherapy) in LACC (locally advanced cervical cancer) patients describing the predictive potential of biomarkers (p53, Bcl1 and Bcl2) and clinical-pathologic factors on chemoresponsivity.

Methods: Clinical-pathologic data of 88 consecutive patients with LACC who underwent NACT followed by nerve-sparing surgery with retroperitoneal lymphadenectomy at National Cancer Institute of Milan, between January 2000 and June 2013 were retrieved from the institutional database. Biomarkers were evaluated before and after NACT in the specimen. To investigate their role as predictors of response, we tried several statistical machine learning algorithms.

Results: Responders to NACT (55.7%) showed a 5 years survival between 100% (complete response) and 85.7% (partial response). Clinical factors (age, body mass index (BMI) and grade) were the most important predictors of response at random forest analysis. Area under the curve was 0.8676. Tree based boosting analysis revealed a significant trend towards worse response with p53 expression. Whereas Bcl-1 and Bcl-2, were not predictors for response to NACT. It confirmed that after adjusting for other prognostic factors, age, grade, BMI and tumor size were independent predictor of response to NACT, while p53 was moderately related to response to NACT. The final logistic regression reported that age and grade were significant factors unlike p53.

Conclusion/Implications: Combined model including clinical pathologic variables plus p53 did not predict NACT response. Although prognosticate chemoresponsitivity is still an ongoing problem in LACC patients, NACT followed by surgery remain a safe treatment in young patients with brilliant oncologic outcome without clinical sequalae related to radio-chemotherapy.

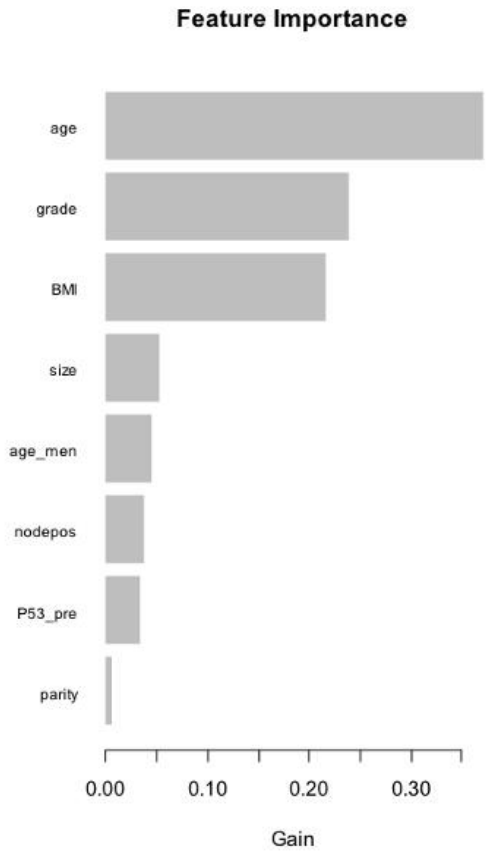

Figure A. Combined model. Importance of Clinical factors plus biomarkers pre-treatment as predictors of response to NACT at the tree based boosting analysis. Area under the curve (crude estimate): 0.8676

Model including important clinical variables (age, grade, BMI) and P53

Coefficients	Estimate	Std. Error	z value	Pr(>|z|)	
Intercept	-4.617930	1.477627	-3.125	0.00178 **	
(Age, 2)1	-2.389034	2.556175	-0.935	0.34999	
(Age, 2)2	4.584633	2.477788	1.850	0.06427 .	
Grade	1.650186	0.527809	3.126	0.00177 **	
(BMI, 2)1	-3.859540	2.503281	-1.542	0.12312	
(BMI, 2)2	4.275325	2.511159	1.703	0.08866	
P53	-0.007895	0.536679	-0.015	0.98826	
	Df	**Deviance Resid.**	**Df**	**Resid. Dev**	**Pr(>Chi)**
NULL			87	120.855	
(Age, 2)	2	8.1077	85	112.747	0.0173550
Grade	1	11.8158	84	100.931	0.0005873 ***
(BMI, 2)	2	5.0863	82	95.845	0.0786192
P53_pre	1	0.0002	81	95.845	0.9882643

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Table A. Variables of importance with logistic regression model

PR008 / #805 / Poster Board #: 62

Topic: ***AS03. Cervical Cancer***

EFFICACY AND SAFETY OF BVAC-C IN HPV TYPE 16 OR 18 POSITIVE CERVICAL CARCINOMA WHO FAILED 1ST PLATINUM BASED CHEMOTHERAPY: A PHASE I/IIA STUDY

Chel Hun Choi[1], Jeong-Won Lee[2], Eun-Suk Kang[2], Duck Cho[2], Yong-Man Kim[2], Kidong Kim[3], Jae-Weon Kim[4], Hee Seung Kim[5], Young Tae Kim[2], Jung-Yun Lee[3], Myong Cheol Lim[4], Chang Yuil Kang[6], Byoung Gie Kim[7]
[1]Samsung Medical Center, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of, [2]Research Institute for Future Medicine, Samsung Medical Center, Sungkyunkwan University School Of Medicine, Seoul, Korea, Republic of, [3]Seoul National University Bundang Hospital, Department Of Obstetrics And Gynecology, Seongnam, Korea, Republic of, [4]Seoul National University Hospital, Clinical Trial Center, Seoul, Korea, Republic of, [5]Konkuk University Hospital, Obstetrics And Gynecology, Seoul, Korea, Republic of, [6]Cellid, Phamacology, Seoul, Korea, Republic of, [7]Samsung Medical Center, Sungkyunkwan University School of Medicine, Obgyn, Seoul, Korea, Republic of

Introduction: BVAC-C, a B cell- and monocyte-based immunotherapeutic vaccine transfected with recombinant HPV E6/E7, has been shown to be well tolerated in HPV positive recurrent cervical carcinoma in a phase I study. This phase IIa study aimed to determine the antitumor activity of BVAC-C in patients with HPV 16 or 18 positive recurrent cervical cancer who had experienced recurrence after one prior platinum-based combination chemotherapy.

Methods: Primary endpoints were safety and objective response rate (ORR) assessed by independent radiologist per RECIST version 1.1. Secondary endpoint included Disease control rate (DCR), progression-free survival (PFS), and overall survival (OS).

Results: Of the 30 patients available for analysis, the objective response rate (ORR) was 19.2%, the disease control rate (DCR) was 53.8%, and the median progression-free survival (PFS) was 5.8 months. Median overall survival (OS) was 17.7 months. Immune responses of patients after vaccination were shown to be correlated with clinical responses of them.

Conclusion/Implications: BVAC-C represents a promising treatment option in the second-line setting for this patient population, with a manageable safety profile. Further studies are needed to identify potential biomarkers of response.

PR009 / #1507 / Poster Board #: 75

Topic: ***AS03. Cervical Cancer***

REAL-WORLD HEALTH ECONOMIC EVALUATION OF DNA METHYLATION MARKER FOR TRIAGE OF HRHPV-POSITIVE WOMEN IN CERVICAL CANCER SCREENING IN CHINA

Yu Ligh Liou[1], Hsiang Yu Chuang[2], Pei Liu[2], Xitong Jin[2], Huiyun Fan[2], Lei Li[3]
[1]The First Affiliated Hospital of Guangdong Pharmaceutical University, Clinical Precision Medicine Research Center, Guangzhou, China, [2]Beijing OriginPoly Bio-Tec Co., Ltd, Medical, Beijing, China, [3]Peking Union Medical College Hospital,, Department Of Obstetrics And Gynecology, National Clinical Research Center For Obstetric & Gynecologic Diseases, Beijing, China

Introduction: Cervical cancer is a leading cause of cancer death among women in China. High-risk human papillomavirus (hrHPV) testing is the gold standard for cervical cancer screening, but it has limited specificity, leading to over-referral of women to colposcopy. DNA methylation markers are emerging as promising biomarkers for the triage of hrHPV-positive women. This study aims to evaluate the health economic impact of using DNA methylation markers for the triage of hrHPV-positive women in cervical cancer screening, based on a large-scale real-world dataset in China. The study will also explore approaches to reduce the usage of colposcopy.

Methods: The study enrolled 15,470 women and collected cervical cells to test for HPV and DNA methylation. The results showed that DNA methylation markers can identify CIN2+ and the study estimated the economic benefits of using this method.

Results: The study enrolled 15,470 women aged 30-60. The DNA methylation markers had a high sensitivity and negative predictive value for identifying CIN2+ cases, meaning that they were good at identifying women who did and did not have CIN2+. The cost-effectiveness analysis showed that incorporating PAX1-JAM3 methylation testing into the screening program could significantly reduce unnecessary colposcopies and increase the detection rate of CIN2+ at an acceptable cost.

Conclusion/Implications: The study found that PAX1-JAM3 methylation testing could significantly reduce unnecessary colposcopies and increase the detection rate of CIN2+ at an acceptable cost. These findings suggest that PAX1-JAM3 methylation testing is a promising new biomarker for the triage of hrHPV-positive women in cervical cancer screening in China.

PR010 / #135 / Poster Board #: 65

Topic: ***AS03. Cervical Cancer***

CLINICOPATHOLOGICAL CHARACTERISTICS AND ONCOLOGICAL OUTCOMES OF THREE SUBTYPES OF NEUROENDOCRINE CARCINOMA OF THE CERVIX: A MULTICENTER RETROSPECTIVE STUDY OF 288 PATIENTS IN CHINA

Yu Gu, Yang Xiang
Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Department Of Obstetrics And Gynecology,, Beijing, China

Introduction: Neuroendocrine carcinoma of the cervix (NECC) is a rare pathological classification of cervical cancer, and is divided into small cell neuroendocrine carcinoma (SCNEC), large cell neuroendocrine carcinoma (LCNEC) and mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN).

Methods: This multicenter, retrospective study enrolled 288 patients. The primary outcomes were progression-free survival (PFS) and overall survival (OS). The Kaplan-Meier method and Cox proportional hazard analysis were performed to determine risk factors of PFS and OS.

Results: With a median follow up of 25 months, the 5-year PFS of NECC, SCNEC, LCNEC and MiNEN was 40.2%, 40.4%, 30.3%, and 41.6%, respectively; and the 5-year OS was 45.4%, 44.0%, 32.3%, and 50.3%, respectively. In the whole cohort, it showed that LVSI (HR=1.996, 95%CI:1.275~3.126, p=0.003), NACT (HR=1.691, 95%CI: 1.040~2.748, p=0.034), and >2/3 stromal invasion (HR=2.009, 95%CI:1.222~3.303, p=0.006) were independent risk factors of PFS; age>45 (HR=1.956, 95%CI: 1.170~3.272, p=0.011), LVSI (HR=1.722, 95%CI: 1.016~2.918, p=0.043) and >2/3 stromal invasion (HR=1.778, 95%CI: 1.024~3.087, p=0.041) were independent risk factors for OS and that adjuvant chemoradiotherapy was an independent protective factor of OS (HR=0.175, 95%CI: 0.079~0.388,

p<0.001).

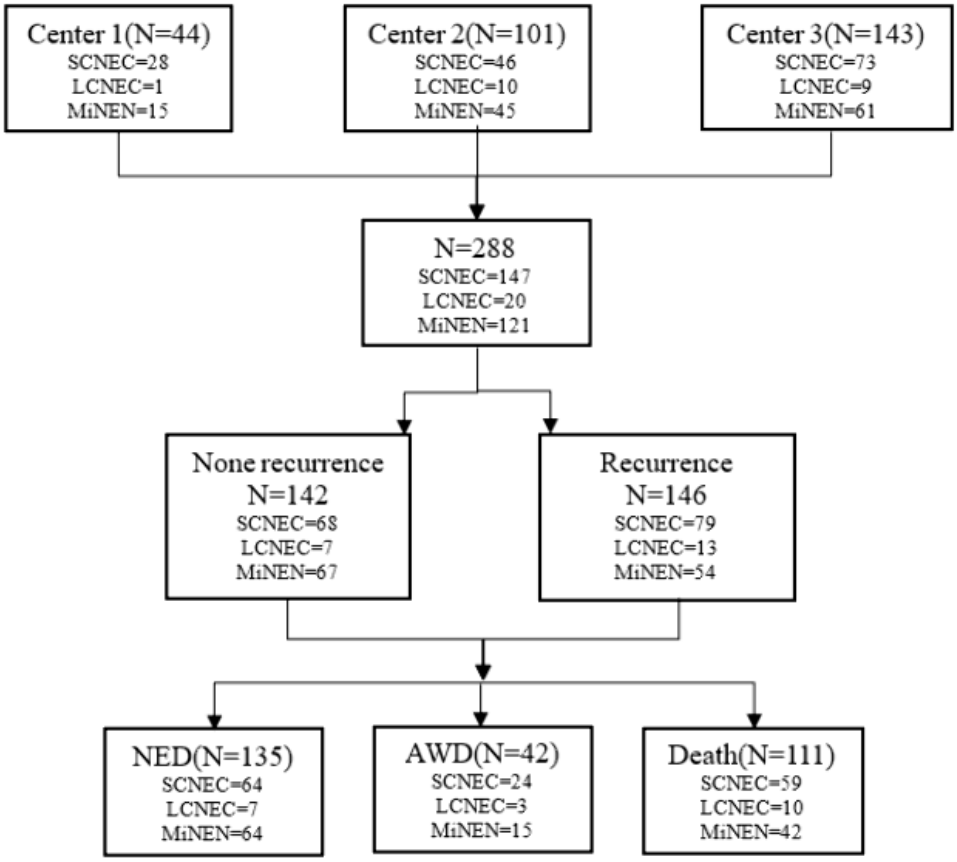


Figure1. The flow diagram of the study. Center1 : Shengjing hospital of China medical university; Center2: Sichuan province Cancer Hospital; Center3: Peking union medical college hospital; SCNEC: small cell neuroendocrine carcinoma; LCNEC: large cell neuroendocrine carcinoma; MiNEN: mixed neuroendocrine-non-neuroendocrine neoplasm; NED: no evidence of disease; AWD: alive with disease.

Conclusion/Implications: This multicenter retrospective study first focused on three pathological subtypes of NECC including SCNEC, LCNEC and MiNEN. SCNEC has a worse biological behavior than the other two types. Patients with MiNEN did not have better prognosis compared to patients with SCNEC and LCNEC at the same stage. LVSI and >2/3 stromal invasion and adjuvant chemoradiotherapy are prognostic factors for PFS; age, LVSI, and >2/3 stromal invasion and adjuvant chemoradiotherapy are prognostic factors for OS in patients with NECC.

PR011 / #162 / Poster Board #: 72

Topic: ***AS03. Cervical Cancer***

THE INCIDENCE OF PERIOPERATIVE LYMPHATIC COMPLICATIONS AFTER RADICAL HYSTERECTOMY AND PELVIC LYMPHADENECTOMY BETWEEN ROBOTIC AND LAPAROSCOPIC APPROACH: A SYSTEMIC REVIEW AND META-ANALYSIS

Jong Ha Hwang, Bo Wook Kim
International St. Mary's Hospital, Obstetrics And Gynecology, Incheon, Korea, Republic of

Introduction: Although many studies have reported perioperative complications after radical hysterectomy and pelvic lymph node dissection using robotic and laparoscopic approaches, the risk of perioperative lymphatic complications has not been well identified. The aim of this meta-analysis is to compare the risks of perioperative lymphatic complications after robotic radical hysterectomy and lymph node dissection (RRHND) with laparoscopic radical hysterectomy and lymph node dissection (LRHND) for early uterine cervical cancer.

Methods: We searched the PubMed, Cochrane Library, Web of Science, ScienceDirect, and Google Scholar databases for studies published up to July 2022 comparing perioperative lymphatic complications after RRHND and LRHND while treating early uterine cervical cancer. Related articles and bibliographies of relevant studies were also checked. Two reviewers independently performed the data extraction.

Results: of 19 eligible clinical trials (15 retrospective studies and 4 prospective studies) comprising 3,079 patients were included in this analysis. Only 107 patients (3.48%) had perioperative lymphatic complications, of which the most common was lymphedema (n = 57, 1.85%), followed by symptomatic lymphocele (n = 30, 0.97%), and lymphorrhea (n = 15, 0.49%). When all studies were pooled, the odds ratio (OR) for the risk of any lymphatic complication after RRHND compared with LRHND was 1.27 (95% confidence interval: 0.86-1.98; p = 0.527). In the subgroup analysis, study quality, country of research, and publication year were not associated with perioperative lymphatic complications.

Conclusion/Implications: A meta-analysis of the available current literature suggests that RRHND is not superior to LRHND in terms of perioperative lymphatic complications.

PR012 / #858 / Poster Board #: 63

Topic: ***AS03. Cervical Cancer***

COMPARISONS OF SURVIVAL OUTCOMES OF LAPAROSCOPIC VERSUS OPEN RADICAL HYSTERECTOMY IN EARLY CERVICAL CANCER WITH INCIDENTALLY IDENTIFIED PATHOLOGIC HIGH-RISK FACTORS

Seung Jun Lee, Se Ik Kim, Dong Hoon Suh, Hee Seung Kim, Kidong Kim, Hyun Hoon Chung, Jae Hong No, Yong Beom Kim, Jae-Weon Kim, Noh Hyun Park, Yong-Sang Song, Chel Hun Choi, Maria Lee
Seoul National University Hospital, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of

Introduction: Previously, we suggested that patients with cervical cancer with tumors ≤2 cm on preoperative magnetic resonance imaging (MRI) are safe candidates for laparoscopic radical hysterectomy (LRH). Here, we aimed to investigate whether LRH deteriorates the prognosis of patients with incidentally identified high-risk factors on pathologic examination.

Methods: We identified patients with 2009 FIGO stage IB1 cervical cancer who underwent Type C LRH or open radical hysterectomy (ORH) at three tertiary hospitals between 2007 and 2018. Those with a tumor ≤2 cm on preoperative MRI who adhered to the practice guidelines for adjuvant treatment were included. Survival outcomes were compared between the LRH and ORH groups. Subgroup analyses were conducted according to presence of lymph node metastasis (LNM) and/or parametrial invasion (PMI).

Results: In total, 498 patients were included: 299 in the LRH group and 199 in the ORH group. The ORH and LRH groups showed similar 5-year progression-free survival (PFS) (92.9% vs. 91.6%; P=0.615) and 5-year overall survival (OS) rates (96.8% vs. 97.2%; P=0.439). On pathologic examination, 49 (9.8%) and 16 (3.2%) patients had LNM and PMI, respectively, and 10 (2.0%) had both. In the LNM subgroup, 5-year PFS rate was not significantly different between the ORH and LRH groups (91.7% vs. 73.2%; P=0.169). In the PMI subgroup, no difference in PFS was observed between the two groups (P=0.893).

Conclusion/Implications: LRH might not deteriorate recurrence and mortality rates in CC patients with a tumor size ≤2 cm when adjuvant treatment is appropriately administered, even if pathologic LNM and PMI are incidentally identified.

PR013 / #1503 / Poster Board #: 68

Topic: ***AS03. Cervical Cancer***

TORIPALIMAB COMBINED WITH BEVACIZUMAB AND CHEMOTHERAPY AS FIRST-LINE TREATMENT FOR REFRACTORY, RECURRENT OR METASTATIC CERVICAL CANCER: A SINGLE-ARM, OPEN-LABEL, PHASE II TRIA

Chen Li[1], Peng Peng[1], Hairong Yao[2], Dantong Liu[2], Yonglan He[3], Shikai Liu[2], Ninghai Cheng[1], Dongyan Cao[1], Yang Xiang[1]
[1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Peking Union Medical College, Department Of Obstetrics And Gynecology, Beijing, China, [2]Cangzhou Central Hospital, Department Of Gynecology, Cangzhou, China, [3]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Peking Union Medical College, Department Of Radiology, Beijing, China

Introduction: Treatment options for refractory, recurrent, or metastatic cervical cancer (R/M CC) are limited. This study evaluated the efficacy and safety of toripalimab combined with bevacizumab and platinum-based chemotherapy as first-line treatment for refractory R/M CC.

Methods: Patients (≥18 years) who had no prior systemic treatment with histologically confirmed refractory R/M CC were eligible. Patients received toripalimab (240mg, D1, q3W) plus bevacizumab (7.5mg/kg, D1, q3W) and platinum-based chemotherapy (paclitaxel 175mg/m^2+ cisplatin 50mg/m^2 or carboplatin AUC=5, D1, q3W) for 6 cycles, followed by the maintenance of toripalimab plus bevacizumab (q3W) for 12 months or until disease progression or intolerable toxicity occurred. The primary endpoint was the objective response rate (ORR) per RECIST v1.1. The secondary endpoints were safety profiles, disease control rate (DCR), progression-free survival (PFS), and overall survival (OS).

Results: A total of 23 patients were in the final analysis. The median follow-up duration was 9.6 months (95% CI, 6.4 to 12.8). The ORR was 78.3% (95% CI, 56.3 to 92.5), 1 (4.3%) patient achieved CR and 17 (73.9%) attained PR. The DCR was 91.3% (95% CI, 72 to 98.9). The median PFS and OS were not reached. Any grade treatment-related adverse events (TRAEs) occurred in 91.7% of patients, and the most common were neutropenia (58.3%), ATCH increased (37.5%), and anemia (37.5%). The grade ≥ 3 TRAEs occurred in 58.3%. No grade ≥ 3 irAEs occurred.

Conclusion/Implications: Toripalimab combined with bevacizumab and platinum-based chemotherapy has demonstrated promising clinical efficacy as the first-line treatment for patients with refractory R/M CC while showing a tolerable safety profile.

PR016 / #541 / Poster Board #: 77

Topic: ***AS03. Cervical Cancer***

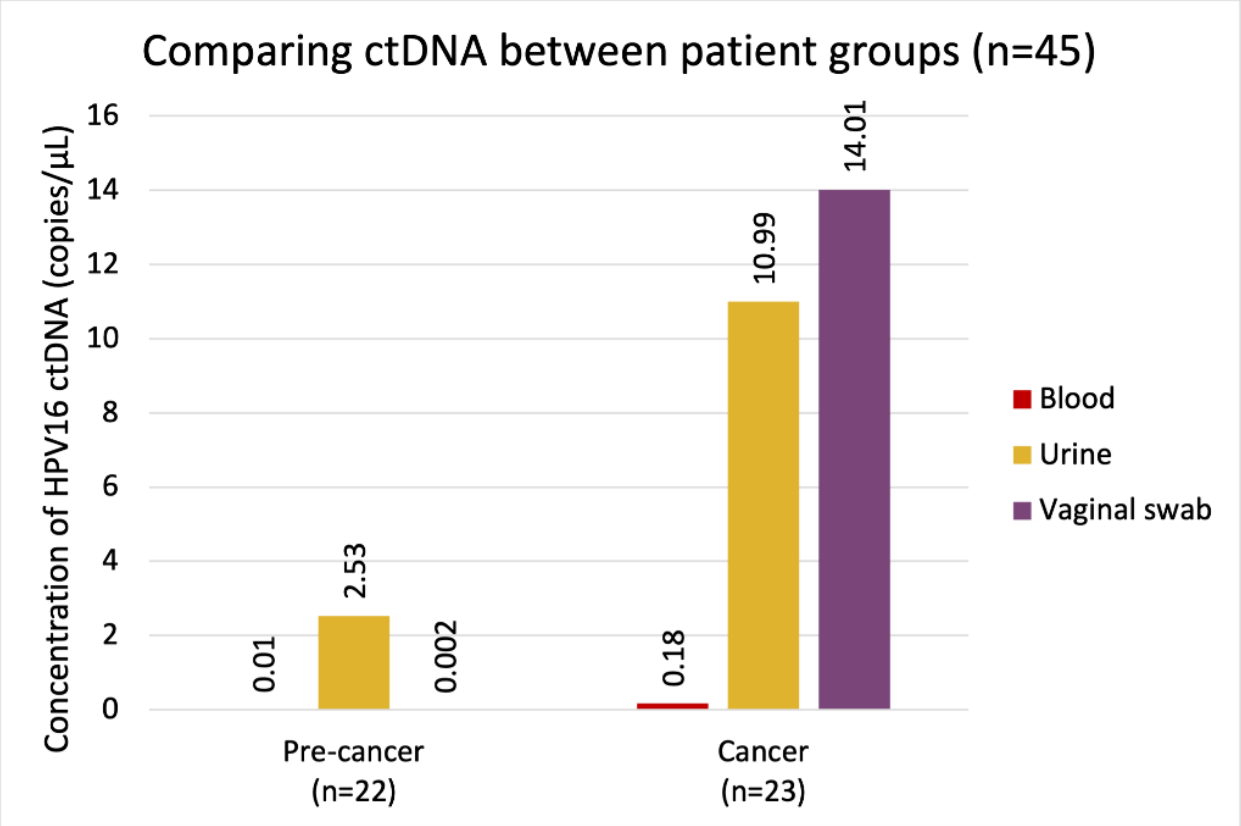
DETECTION OF HUMAN PAPILLOMVIRUS CIRCULATING TUMOR DNA (CTDNA) AS A NOVEL APPROACH TO CERVICAL CANCER SCREENING AND MONITORING

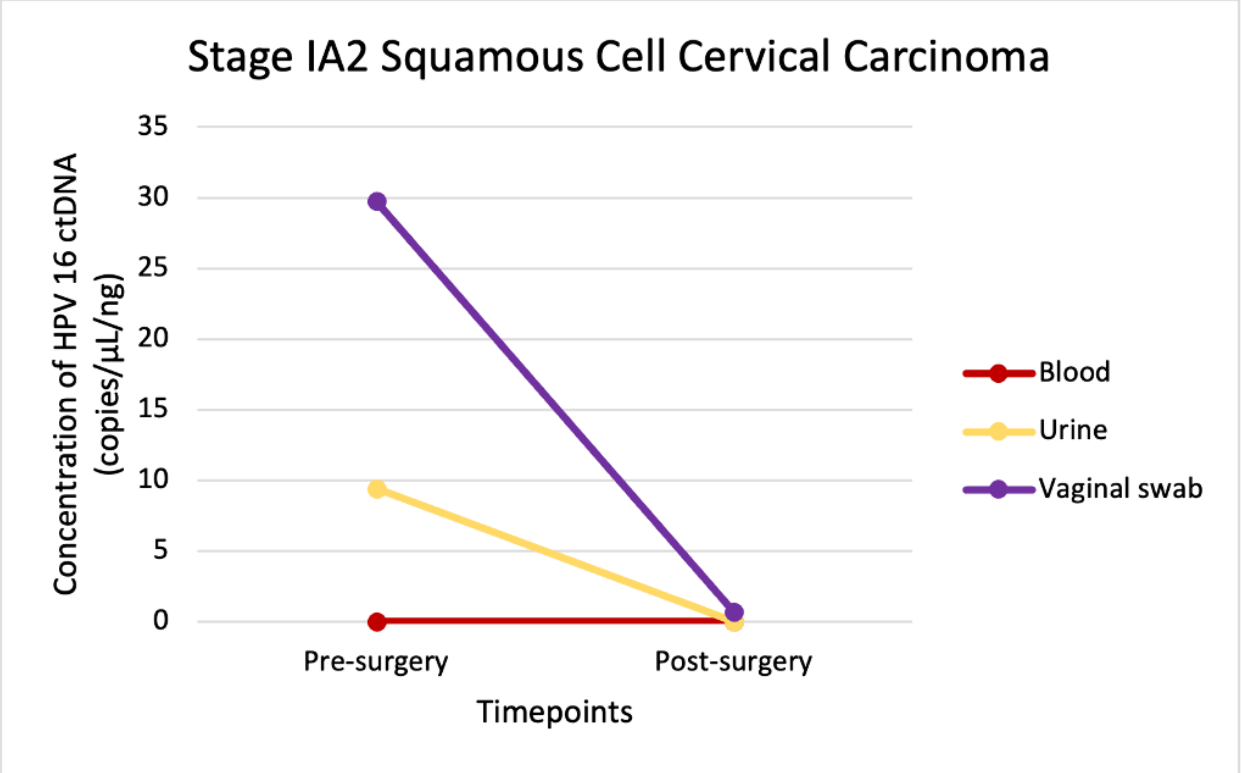
Erica Mandato[1], Tadhg Ferrier[1], Simane Warsame[1], Hila Tabrizian[1], Fady Mansour[2], Basile Tessier-Cloutier[3], Xing Zeng[4], Julia Burnier[5], Shuk On Annie Leung[6]
[1]Research Institute of the McGill University Health Centre (RI-MUHC), Pathology, Montreal, Canada, [2]MUHC, Gynecology, Minimally Invasive Gynecology And Obstetrics, Montreal, Canada, [3]Cancer Research Program RI-MUHC, Pathology, Montreal, Canada, [4]MUHC, Gynecologic Oncology, Montreal, Canada, [5]Cancer Research Program RI-MUHC, Oncology, Montreal, Canada, [6]Cancer Research Program RI-MUHC, Gynecologic Oncology, Montreal, Canada

Introduction: Cervical cancer is the 4th most common cancer in women worldwide. Majority of cases are caused by human papillomavirus (HPV) infection and early detection is possible with cytology and/or HPV-DNA. However, cytology has a low sensitivity, and the HPV-DNA test has a low specificity in distinguishing transient from clinically significant HPV infections. Furthermore, there are limited non-invasive options for surveillance post-treatment. Liquid biopsy is a non-invasive approach aimed at addressing these limitations. This study aimed to demonstrate that HPV circulating tumour (ct)DNA levels in blood, urine, and vaginal swabs correlate with extent of disease.

Methods: Using ddPCR, primers were designed to target the viral E7 oncogene sequence from high-risk HPV subtypes (hrHPV 16, 18 and 33). Samples were collected from patients with cervical dysplasia ranging from low to high grade (pre-cancer group, n=22) and patients with a new cervical cancer diagnosis (cancer group, n=23).

Results: HPV ctDNA was detected in more cancer patients (13/23, 56.5%) than pre-cancer patients (1/22, 4.5%). Among the ctDNA-positive patients, the concentration was higher in the urine and vaginal swabs compared to blood. Furthermore, samples collected from cancer patients at multiple timepoints (n=7) showed that ctDNA decreased post-
treatment.


Comparing ctDNA between patient groups (n=45)
Concentration of HPV16 ctDNA (copies/µL)
16
14
12
10
8
6
4
2
0
0.01
2.53
0.002
0.18
10.99
14.01
Pre-cancer
(n=22)
Cancer
(n=23)
Blood
Urine
Vaginal swab


Stage IA2 Squamous Cell Cervical Carcinoma
Concentration of HPV 16 ctDNA (copies/µL/ng)
35
30
25
20
15
10
5
0
Pre-surgery
Post-surgery
Timepoints
Blood
Urine
Vaginal swab

Conclusion/Implications: HPV ctDNA levels correlated to the extent of disease and was detectable in different liquid biopsy samples. Liquid biopsy has the potential to serve as a non-invasive complementary method to existing techniques both in screening and monitoring of cervical pre-cancer and cancer. Future work will explore other hrHPV subtypes and the performance of individual analytes.

PR017 / #434 / Poster Board #: 66

Topic: ***AS03. Cervical Cancer***

A PHASE II STUDY OF OXALIPLATIN WITH ORAL S-1 FOR PATIENTS WITH RECURRENT NON-SQUAMOUS CELL CARCINOMA OF UTERINE CERVIX (TOHOKU GYNECOLOGIC CANCER UNIT 206 STUDY)

Takayuki Nagasawa[1], Tadahiro Shoji[1], Shingo Hosomi[1], Yohei Chiba[1], Sho Sato[1], Eriko Takatori[1], Yositaka Kaido[1], Masahiro Kagabu[1], Tsukasa Baba[1], Yoshihito Yokoyama[2]
[1]Iwate Medical University School of Medicine, Obstetrics And Gynecology, Yahaba, Iwate,, Japan, [2]Hirosaki University, Department Of Obstetrics And Gynecology, Hirosaki, Japan

Introduction: Recurrent cervical non-squamous cell carcinoma (non-SCC) is resistant to treatment and has a poor prognosis. The efficacy and safety of S-1/oxaliplatin (SOX) therapy in patients with recurrent non-SCC of uterine cervix were examined in a phase II study.

Methods: Fourteen patients were enrolled from January 2013 to December 2022. S-1 was orally administered for 14 days at a dose of 80-120 mg/body/day with oxaliplatin being administered intravenously at a dose of 100 mg/m^2 on day 1. Each treatment cycle was 21 days, and repeated until disease progression or serious adverse events occurred. The antitumor effect, adverse events, progression-free survival (PFS), and overall survival (OS) were investigated.

Results: The median age of the patients was 54 (41-73) years. The PS was 0 in 10 and 1 in 4 patients. The median number of prior regimens was 2 (1-5). The histological type was usual type adenocarcinoma in 10 patients, endometrioid carcinoma, clear cell carcinoma, signet-ring cell carcinoma and unclassified in 1. The overall response rate was 35.7%, and the disease control rate was 64.2%. As for hematologic toxicities of grade 3 or more severe, leukopenia, neutropenia, anemia and thrombocytopenia occurred in 21.4%, 35.7%, 42.8 and 35.7%, respectively, as for non-hematologic toxicities, fatigue occurred in 7.1%, of the patients. The median PFS and OS were 5 (1-17) months, 14 (3-23) months respectively.

Conclusion/Implications: These results suggest that SOX therapy is useful for the treatment of recurrent non-SCC of uterine cervix, having a promising antitumor effect and minimal adverse effects.

PR018 / #841 / Poster Board #: 78

Topic: ***AS03. Cervical Cancer***

THE FEASIBILITY OF SENTINEL LYMPH NODE MAPPING USING INTRA-ABDOMINAL INDOCYANINE GREEN INJECTION IN OPEN SURGERY FOR PATIENTS WITH CERVICAL CANCER

So Hyun Nam[1], Ok-Ju Kang[1], Ju-Hyun Kim[1], Shin-Wha Lee[1], Jeong-Yeol Park[1], Dae-Yeon Kim[1], Jong-Hyeok Kim[1], Kyu-Rae Kim[2], Yong Man Kim[1]
[1]Asan Medical Center, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of, [2]Asan Medical Center, Department Of Pathology, Seoul, Korea, Republic of

Introduction: Recently, open radical hysterectomy in early-stage cervical cancer has been preferred after the LACC trial was published. Also, the role of sentinel lymph node (SLN) mapping is increasing in the surgical treatment of cervical cancer. We evaluated the feasibility of SLN mapping by intra-abdominal indocyanine green (ICG) injection during open surgery for cervical cancer.

Methods: This single-center, retrospective study included all patients who underwent intra-abdominal SLN mapping followed by radical surgery (including hysterectomy and trachelectomy) and systematic pelvic lymphadenectomy at Asan Medical Center. The novel intra-abdominal SLN technique was conducted with injection of 2 mL of 0.5 mg/mL ICG into either side between isthmus and cervix after dissection of bladder peritoneum. SLN was detected using the SPY Portable Handheld Imager (Stryker, Kalamazoo, Michigan, US).

Results: From June 2020 to April 2023, eighty-five patients, newly diagnosed FIGO 2018 stage IA1 to IIIC1p cervical cancer who underwent open radical hysterectomy or trachelectomy, were included in this study. Of these patients, 78 (91.8%) underwent radical hysterectomy and 7 (8.2%) underwent radical trachelectomy. The SLN detection rate was 98.8% (84/85), with 83.5% (71/85) bilateral detection. All the frozen pathology results were consistent with the final pathology, with 15 (17.6%) patients who had nodal metastasis. Intra-abdominal SLN mapping achieved the sensitivity of 100% and the negative predictive value (NPV) of 100%.

Conclusion/Implications: Intra-abdominal SLN mapping with ICG seems to be a feasible and reliable technique in patients with cervical cancer who are planned to undergo open radical surgery.

PR019 / #180 / Poster Board #: 80

Topic: ***AS03. Cervical Cancer***

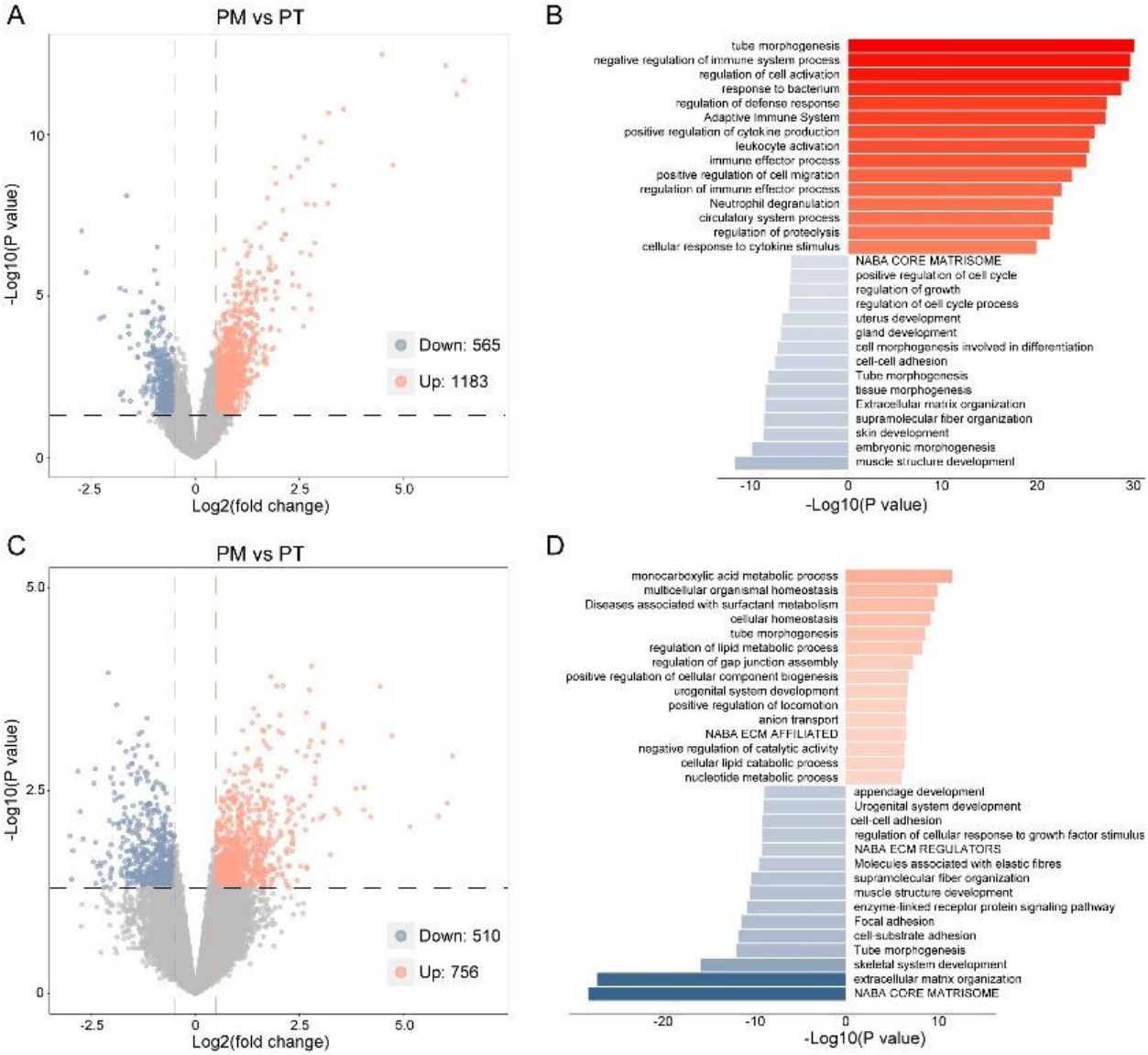
CLINICAL CHARACTERISTICS AND TRANSCRIPTOMIC ANALYSIS OF IMMUNE ACTIVE MICROENVIRONMENT IN PULMONARY METASTATIC CERVICAL CANCER

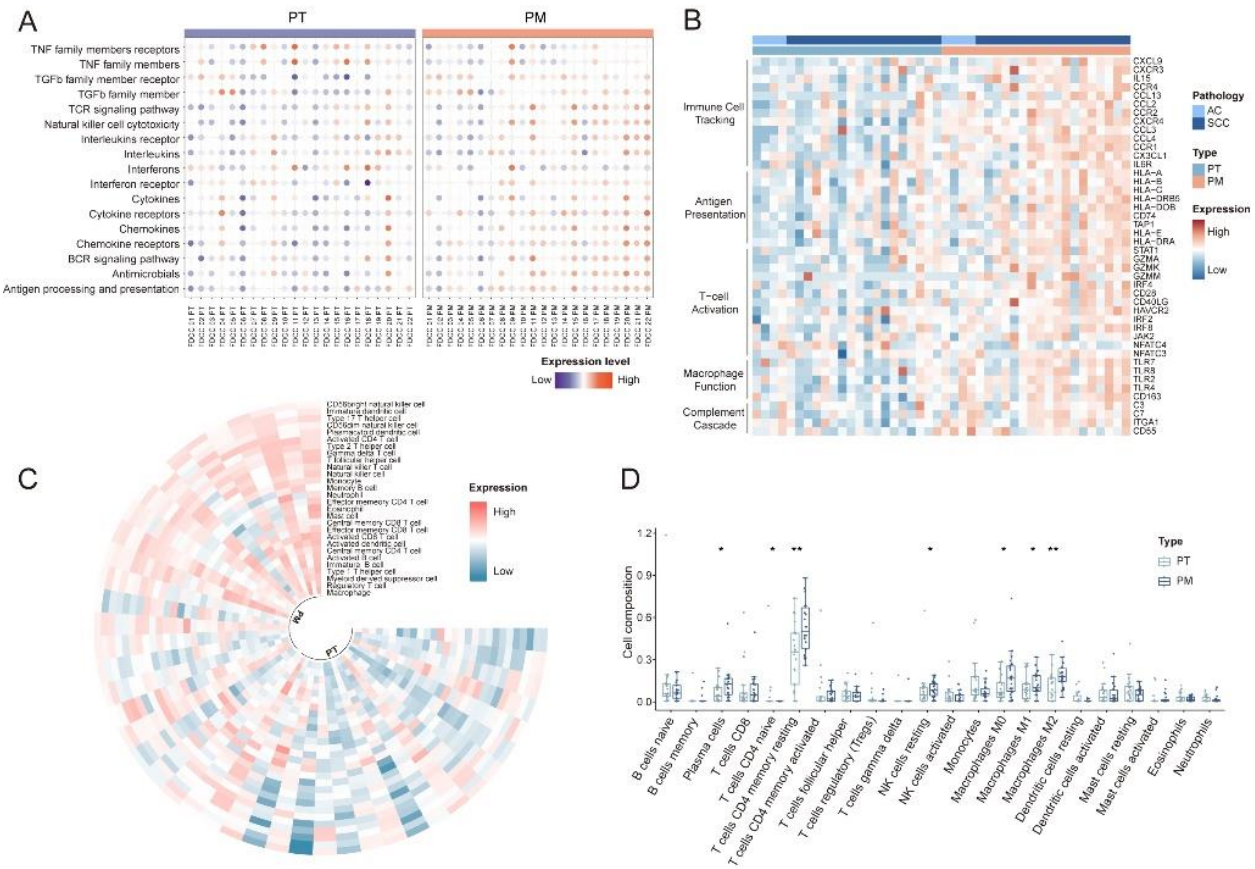
Wei Jiang[1], Hongyu Liu[2], Huijuan Yang[2], Xuan Pei[1]
[1]Fudan University Shanghai Cancer Center, Gynecologic Oncology, shanghai, China, [2]Fudan University Shanghai Cancer Center, Gynecologic Oncology, Shanghai, China

Introduction: Pulmonary metastasis, as the most common hematogenous site in cervical cancer, has limited therapeutic options and uncertain prognosis. We analyzed clinicopathological features of patients with postoperative lung metastasis from cervical cancer to explore the risk factors for lung metastasis. Through mapping pulmonary oligometastatic transcriptomic profiles, we analyzed their molecular characteristics to find potential therapeutic targets for pulmonary metastasis.

Methods: A total of 795 patients with early-stage cervical cancer who underwent radical surgery were retrospectively studied for lung metastasis, and transcriptomic analysis was performed on 22 paired primary cervical tumors and pulmonary oligometastasis.

Results: A total of 48 in 795 early-stage cervical cancer patients developed lung metastasis during a median follow-up of 57 months. Lung metastasis was more frequent in patients with advanced clinical stage and those with rare histological subtypes. Twenty-two patients with pulmonary oligometastasis were subjected to lung metastasectomy with a median relapse-free survival of 20.2 months and a overall survival of 71.1 months. Immune-related genes and pathways were enriched and highly expressed in pulmonary oligometastasis compared to primary tumor. Gene set enrichment analysis revealed that the PD-1 signaling pathway was positively enriched in pulmonary oligometastatic group. Immunohistochemistry staining analysis confirmed that PD-L1 expression was upregulated in pulmonary oligometastasis compared to the corresponding primary tumor. A clinical case of postoperative lung metastasis from cervical cancer was reported, in which the patient had a partial response after immunotherapy.


A
PM vs PT
-Log10(P value)
Log2(fold change)
Down: 565
Up: 1183
B
tube morphogenesis
negative regulation of immune system process
regulation of cell activation
response to bacterium
regulation of defense response
Adaptive Immune System
positive regulation of cytokine production
leukocyte activation
immune effector process
positive regulation of cell migration
regulation of immune effector process
Neutrophil degranulation
circulatory system process
regulation of proteolysis
cellular response to cytokine stimulus
NABA CORE MATRISOME
positive regulation of cell cycle
regulation of growth
regulation of cell cycle process
uterus development
gland development
cell morphogenesis involved in differentiation
cell-cell adhesion
Tube morphogenesis
tissue morphogenesis
Extracellular matrix organization
supramolecular fiber organization
skin development
embryonic morphogenesis
muscle structure development
-Log10(P value)
C
PM vs PT
-Log10(P value)
Log2(fold change)
Down: 510
Up: 756
D
monocarboxylic acid metabolic process
multicellular organismal homeostasis
Diseases associated with surfactant metabolism
cellular homeostasis
tube morphogenesis
regulation of lipid metabolic process
regulation of gap junction assembly
positive regulation of cellular component biogenesis
urogenital system development
positive regulation of locomotion
anion transport
NABA ECM AFFILIATED
negative regulation of catalytic activity
cellular lipid catabolic process
nucleotide metabolic process
appendage development
Urogenital system development
cell-cell adhesion
regulation of cellular response to growth factor stimulus
NABA ECM REGULATORS
Molecules associated with elastic fibres
supramolecular fiber organization
muscle structure development
enzyme-linked receptor protein signaling pathway
Focal adhesion
cell-substrate adhesion
Tube morphogenesis
skeletal system development
extracellular matrix organization
NABA CORE MATRISOME
-Log10(P value)



Conclusion/Implications: Metastasectomy is an effective strategy for cervical cancer patients with pulmonary oligometastasis. Immune checkpoint blockades may be promising for patients with lung metastases.

PR020 / #632 / Poster Board #: 79

Topic: ***AS03. Cervical Cancer***

IMPACT OF THE LACC TRIAL ON THE ONCOLOGIC OUTCOMES OF CERVICAL CANCER UNDERGOING SURGICAL TREATMENT

Gabriella Schivardi[1], Luigi De Vitis[1], Ludovica Nazzaro[1], Michela Gaiano[1], Maria Teresa Achilarre[1], Alessia Aloisi[1], Ilaria Betella[1], Simone Bruni[1], Annalisa Garbi[1], Giovanni Aletti[1,2], Vanna Zanagnolo[1], Angelo Maggioni[1], Nicoletta Colombo[1,3], Fancesco Multinu[1]
[1]IRCCS European Institute of Oncology, Gynaecological Surgery, Milan, Italy, [2]University of Milan, Oncology And Hemato-oncology, Milan, Italy, [3]University of Milan-Bicocca and Gynecologic Oncology Program, European Institute of Oncology IRCCS, Department Of Medicine And Surgery, Milan, Italy

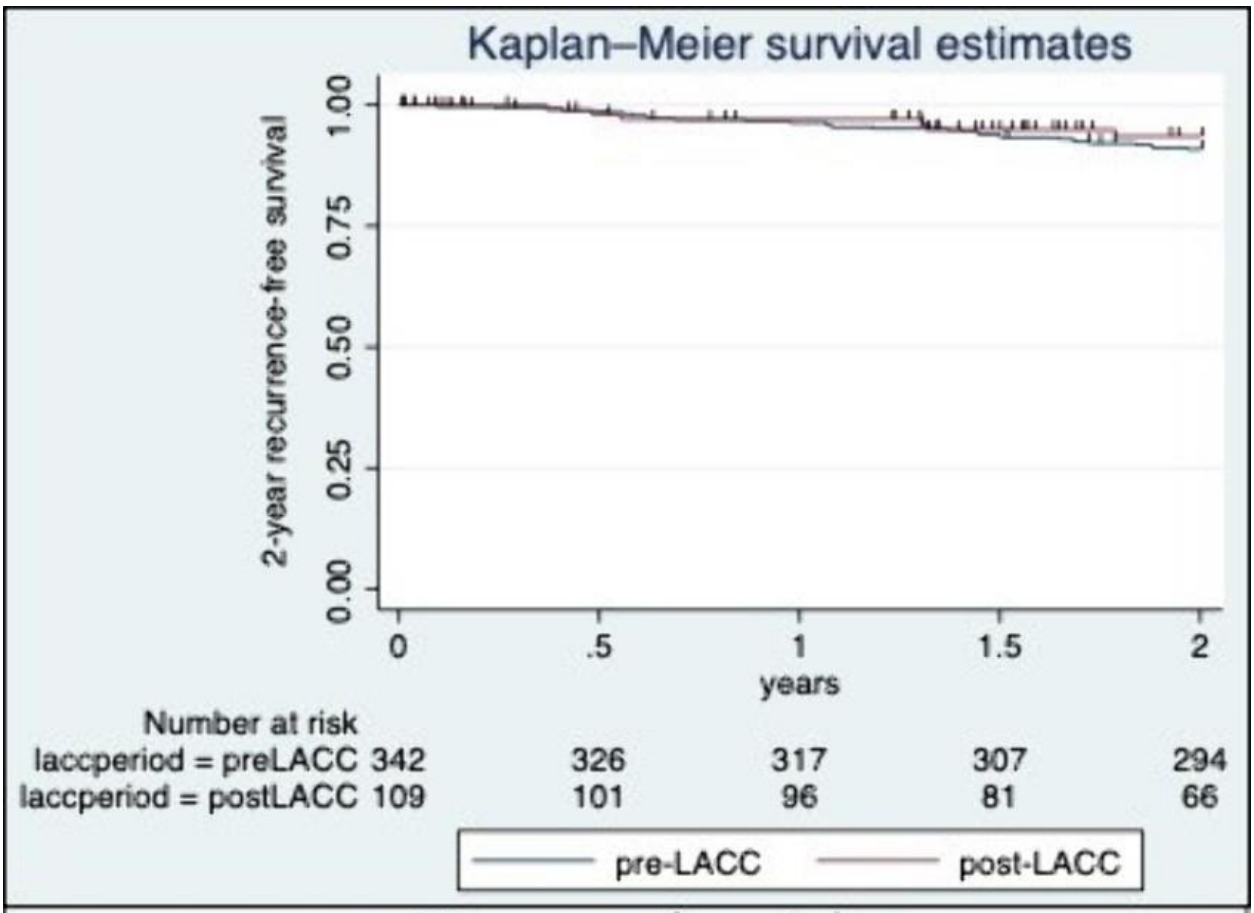
Introduction: The impact of the LACC trial's results on oncologic outcome has not been assessed. This study aimed to compare 2-year recurrence-free survival before and after the LACC trial for cervical cancer patients undergoing surgical treatment.

Methods: Cervical cancer patients who underwent radical hysterectomy and pelvic lymphadenectomy at the European Institute of Oncology, Milan from January 2010 to December 2021 were retrospectively identified. Following the LACC trial's results, robotic-assisted surgery was limited to patients with no residual disease after conization. We performed univariate analysis to compare clinicopathological characteristics between the pre-LACC period (January 2010-March 2018) and post-LACC period (April 2018-December 2021). Survival analysis was performed using a log-rank test to compare 2-years recurrence-free survival during the pre- and post-LACC period.

Results: Among 451 patients meeting inclusion criteria, 342 (75,8%) underwent surgery during the pre-LACC period and 109 (24,2%) during the post-LACC period. The rate of the robotic-assisted approach decreased from 60,8% to 23,8% from the pre- to the post-LACC period, while the open approach increased from 39,2% to 76,1% ($p < 0.001$). Recurrence was observed in 36 patients (8%) within the first 2 years following surgery. No recurrences were observed in patients treated with robotic-assisted surgery during the post-LACC period. No difference in 2-year recurrence-free survival was observed between the pre-and post-LACC period

	Total N= 451(%)	Pre-LACC N=342(%)	Post-LACC N=109(%)	P value
Age (mean, SD)	46,21 (10,99)	45,88 (10,77)	47,25 (11,65)	0,26
BMI (mean, SD)	23,33 (4,21)	23,32 (4,12)	23,37 (4,51)	0,90
Previous conization				
Yes	201 (44,6)	148 (43,3)	53 (48,6)	0,33
No	250 (55,4)	194 (56,7)	56 (51,4)	
Surgical approach				
Open	217 (48,1)	134 (39,2)	83 (76,1)	<0 001
Robotic	234 (51,9)	208 (60,8)	26 (23,9)	
Stage				
IA1 (LVSI +)	7(1,6)	6 (1,7)	1 (0,9)	
IA2	28 (6,2)	18 (5,3)	10 (9,2)	
IB1	180 (39,9)	127 (37,1)	53 (48,6)	
IB2	122 (27,1)	100 (29,2)	22 (20,2)	
IB3	15 (3,3)	13 (3,8)	2 (1,8)	0,14
IIA1	6 (1,3)	6 (1,8)	0	
IIA2	1 (0,2)	1 (0,3)	0	
IIB	14 (3,1)	11 (3,2)	3 (2,8)	
IIIC1	73 (16,2)	57 (16,7)	16 (14,7)	
IIIC2	2 (0,4)	2 (0,6)	0	
IVA	3 (0,7)	1 (0,3)	2 (1,8)	
Histology				
Adenocarcinoma	202 (44,8)	157 (45,9)	45 (41,3)	
Squamous carcinoma	216 (47,9)	156 (45,6)	60 (55)	0,031
Adenosquamous	32 (7,1)	29 (8,5)	3 (2,8)	
carcinoma	1 (0,2)	//	1 (0,9)	
Other				
Grade				
1	19 (4,2)	11 (3,2)	8 (7,3)	
2	181 (40,1)	136 (39,8)	45 (41,3)	0,19
3	194 (43,1)	148 (43,3)	46 (42,2)	
Missing	57 (12,6)	47 (13,7)	10 (9,2)	
Margin				
Negative	433 (96)	326 (95,3)	107 (98,2)	0,36
Positive	13 (2,9)	12 (3,5)	1 (0,9)	
Missing	5 (1,1)	4 (1,2)	1 (0,9)	
Close margin				
No	409 (90,7)	311 (90,9)	98 (89,9)	0,95
Yes	34 (7,5)	25 (7,3)	9 (8,3)	
Missing	8 (1,8)	6 (1,8)	2 (1,8)	
LVSI (N 407)				
No	225 (55,3)	163 (54,2)	62 (58,5)	0,44
Yes	182 (44,7)	138 (45,8)	44 (41,5)	
Stromal invasion				
1/3 superficial	72 (16)	49 (14,3)	23 (21,1)	
1/3 middle	87 (19,3)	62 (18,1)	25 (22,9)	0,12
1/3 deep	242 (53,6)	189 (55,3)	53 (48,6)	
Missing	50 (11,1)	42 (12,3)	8 (7,4)	
Tumor Size (mean- SD)	19,30 (11,4)	19,91 (11,5)	17,59 (10,9)	0,08
Treatment performed				
Observation	312 (69,2)	234 (68,4)	78 (71,5)	
RT +/-CHT	121 (26,8)	96 (28,1)	25 (22,9)	0,60
CHT	10 (2,2)	7 (2)	3 (2,8)	
Missing	8 (1,8)	5 (1,5)	3 (2,8)	

(p=0,45).



2-Year recurrence-free survival

	Total (N)	pre-LACC (N)	post-LACC(N)	Log-rank P value
Observed events	36	30	6	0,45
Expected events	36,00	28,13	7,87	

Conclusion/Implications: The LACC trial led to a significant change in the surgical approach to cervical cancer. The decreased use of robotic surgery did not have an impact on the 2-year recurrence-free survival in our population.

PR021 / #417 / Poster Board #: 64

Topic: ***AS03. Cervical Cancer***

A RETROSPECTIVE STUDY OF BEVACIZUMAB COMBINED WITH CHEMORADIOTHERAPY IN PRIMARY TREATMENT OF STAGE III-IVA CERVICAL CANCER

Mingzi Tan, Yuhua Gao
Liaoning Cancer Hospital & Institute, Gynecological Radiation, Shenyang, China

Introduction: While bevacizumab inhibits tumor angiogenesis, it can temporarily "normalize" tumor blood vessels, improve tumor blood flow and oxygen supply, thereby enhancing the effects of radiotherapy and chemotherapy. Therefore, bevacizumab as neoadjuvant therapy or radiosensitizer on the prognosis of patients with locally advanced cervical cancer (III-IVA stage) deserves further study.

Methods: This study retrospectively analyzed and compared the prognosis of patients with locally advanced (III-IVA stage) cervical cancer who were diagnosed and treated in our hospital from 2019 to 2022. The primary endpoint was progression-free survival, and the secondary endpoint was overall survival.

Results: There were 57 people in the bevacizumab combined with radiochemotherapy group, and 152 people in the radiochemotherapy group during the same period. There was no significant difference in OS between the two groups. At 12 months, 18 months, 24 months, and 36 PFS, the bevacizumab combined with chemoradiotherapy group was significantly higher than that of the radiochemotherapy group, and the comparison between the two groups was statistically significant.

Conclusion/Implications: The recurrence rate within 3 years of patients with locally advanced (III-IVA stage) cervical cancer treated with bevacizumab combined with radiochemotherapy was significantly lower than that of patients with radiochemotherapy. The primary treatment with bevacizumab combined with radiochemotherapy can significantly improve the prognosis of locally advanced (III-IVA stage) cervical cancer patients.

PR022 / #469 / Poster Board #: 67

Topic: ***AS03. Cervical Cancer***

CLINICAL AND DOSIMETRIC STUDY OF OCCULT UTERINE TANDEM IMPERFECT IMPLANTATION IN HDR-BRACHYTHERAPY FOR CERVICAL CANCER

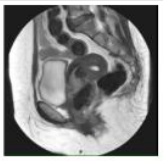
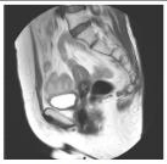
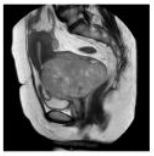
Xiujuan Zhao[1], Haiyan Wu[1], Ying Tang[1], Dongling Zou[2], Qi Zhou[1]
[1]Cancer Hospital Affiliated to Chongqing University, Gynaecological Cancer, Chongqing, China, [2]Cancer Hospital Affiliated to Chongqing University, Gynaecological Cancer, chongqing, China

Introduction: To analyzed the clinical outcomes and dose changes imperfect uterine tandem implantation in HDR-brachytherapy for cervical cancer.

Methods: We reviewed the imperfect intrauterine insertion images during November 2020 and July 2021. The physicist designed 2D and 3D plans on prescription (6Gy) for perfect and imperfect images. Evaluates the clinical outcome and predicts NTCP of perfect and imperfect placement. The CTV_{ref}, V_{ref}, COIN, EQD2 of OARs and NTCP were extracted using corresponding formulas. The differences two plans were compared using paired t-test.

Results: 41 of 1742 brachytherapy images showed 24 of 319 patients(7.52%). According to imperfect position of uterine tandem, we divided it into four types: inadequate implantation, anterior, posterior wall and fundus perforation. CTV_{ref} and V_{ref} in PER-3D group is superior to PER-2D. COIN only met the requirements in the PER-3D group (>0.64). EQD2 of OARs and NTCP were the lowest in PER-3D group. In inadequate implantation, IM-group improves EQD2 and NTCP of rectum,sigmoid colon and small intestine($P<0.05$) in 3D; NTCP of bladder is added to IM-group($P<0.05$) in 2D. In anterior wall perforation, IM-group increases EQD2 of OARs and NTCP of rectum and small intestine in 3D, and IM-group increases EQD2 and NTCP of OARs (sigmoid and small intestine) ($P<0.05$) in 2D. In posterior wall perforation,IM-group increased EQD2 and NTCP of rectum and sigmoid in both plans. In fundus perforation, IM-group increased EQD2 of
sigmoid.

Fig 1. Diverse anatomical situations during brachytherapy of cervix (sagittal view) .A)Normal sized and anteverted, B)retroverted uterus, C)acutely anteflexed uterus, D)short uterus, E)presence of obstructing cervical mass.

				
Normal sized and anteverted uterus	Retroverted uterus	Acutely anteflexed uterus	Small uterus	Presence of bosturcting cervical mass
A	B	C	D	E

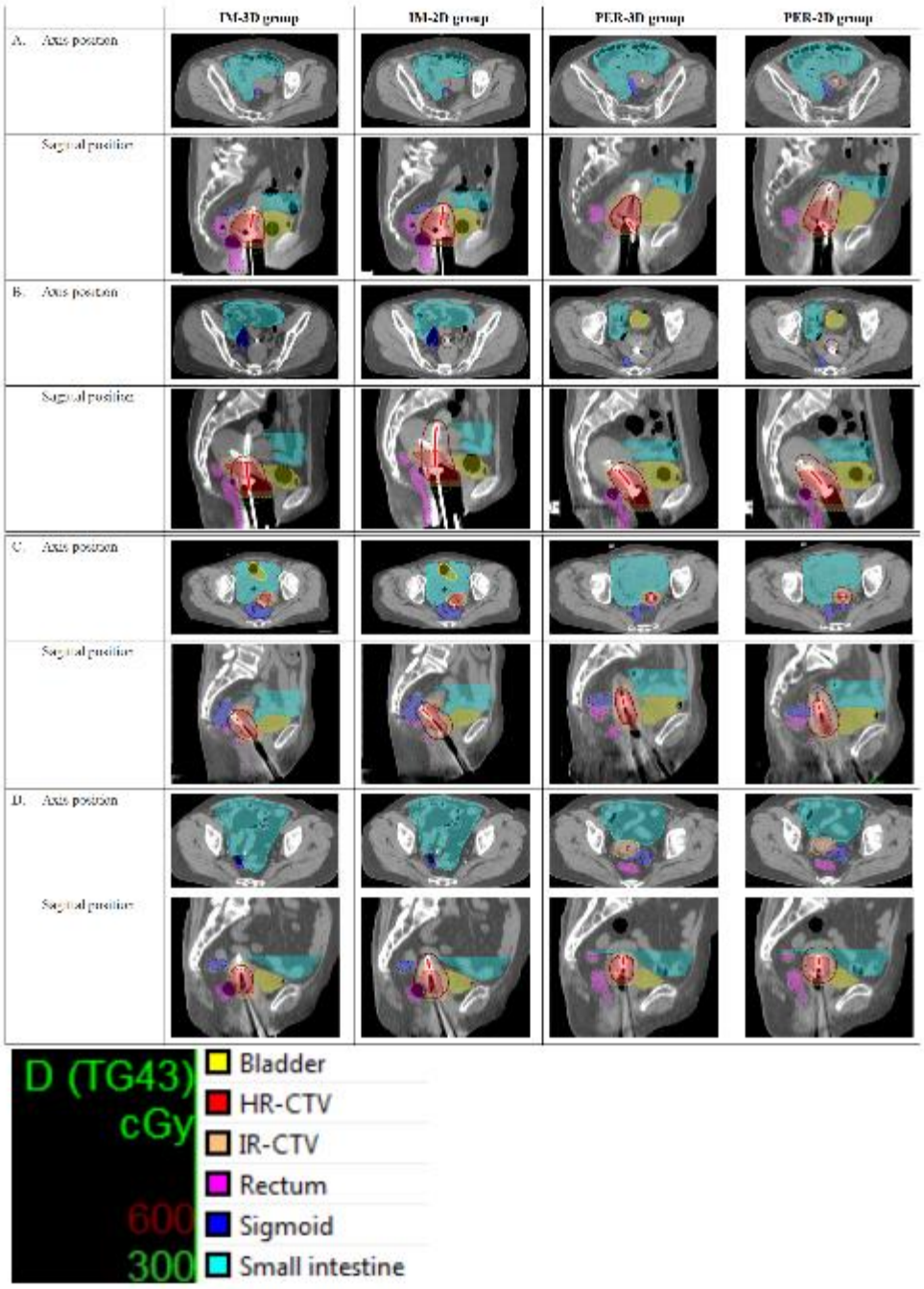


Fig 2. Comparison of dose distribution between patients with and without satisfaction with intrauterine tube placement brachytherapy plan

Conclusion/Implications: PER-3D is the optimal planning to meet the brachytherapy of cervical cancer. It is recommended to correct the imperfect insertion of the uterine canal before clinical treatment.

PR023 / #503 / Poster Board #: 40

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

EVALUATION OF THE COMBINATION LENVATINIB AND PEMBROLIZUMAB IN ENDOMETRIAL CANCER; A REAL WORLD MULTI-INSTITUTIONAL REVIEW OF PRACTICE PATTERNS, EFFICACY AND TOLERABILITY

Bradley Corr[1], Samantha Thomas[2], Paulina Haight[3], Elizabeth Stock[4], Jessica Floyd[1], Lindsay Borden[5], Irina Tunnage[6], Angeles Alvarez Secord[7], Rebecca Arend[8], Amanda Jackson[9], Jason Wright[10], Gottfried Konecny[11], Tara Castellano[12], Emily Ko[13], Sarah Podwika[14], Floor Backes[3], Daniel Spinosa[1], Margaret Mullen[4], Christina Washington[5], Bhavana Pothuri[6], Carsen Smitherman[2], Alfonsus Harsono[8], Hanaa Khadraoui[9], Yukio Suzuki[10], Ritu Salani[15], Kristina Powell[13], Shalini Subbarao[14], Stephanie Gaillard[16]
[1]University of Colorado, Obstetrics And Gynecology, Aurora, United States of America, [2]Duke University, Biostatistics, Durham, United States of America, [3]The Ohio State University, Obstetrics And Gynecology, Columbus, United States of America, [4]Washington University, Obstetrics And Gynecology, St. Louis, United States of America, [5]The University of Oklahoma, Obstetrics And Gynecology, Oklahoma city, United States of America, [6]New York University, Obstetrics And Gynecology, New York City, United States of America, [7]Duke University, Gynecologic Oncology, Durham, United States of America, [8]University of Alabama, Obstetrics And Gynecology, Birmingham, United States of America, [9]University of Cincinnati, Obstetrics And Gynecology, Cincinnati, United States of America, [10]Columbia University, Obstetrics And Gynecology, New York City, United States of America, [11]UCLA, Obstetrics And Gynecology, Los Angeles, United States of America, [12]LSU, Obstetrics And Gynecology, New Orleans, United States of America, [13]University of Pennsylvania, Obstetrics And Gynecology, Philaldelphia, United States of America, [14]University of Virginia, Obstetrics And Gynecology, Charlottesville, United States of America, [15]UCLA, Ob/gyn, Los Angeles, United States of America, [16]Johns Hopkins University, Obstetrics And Gynecology, Baltimore, United States of America

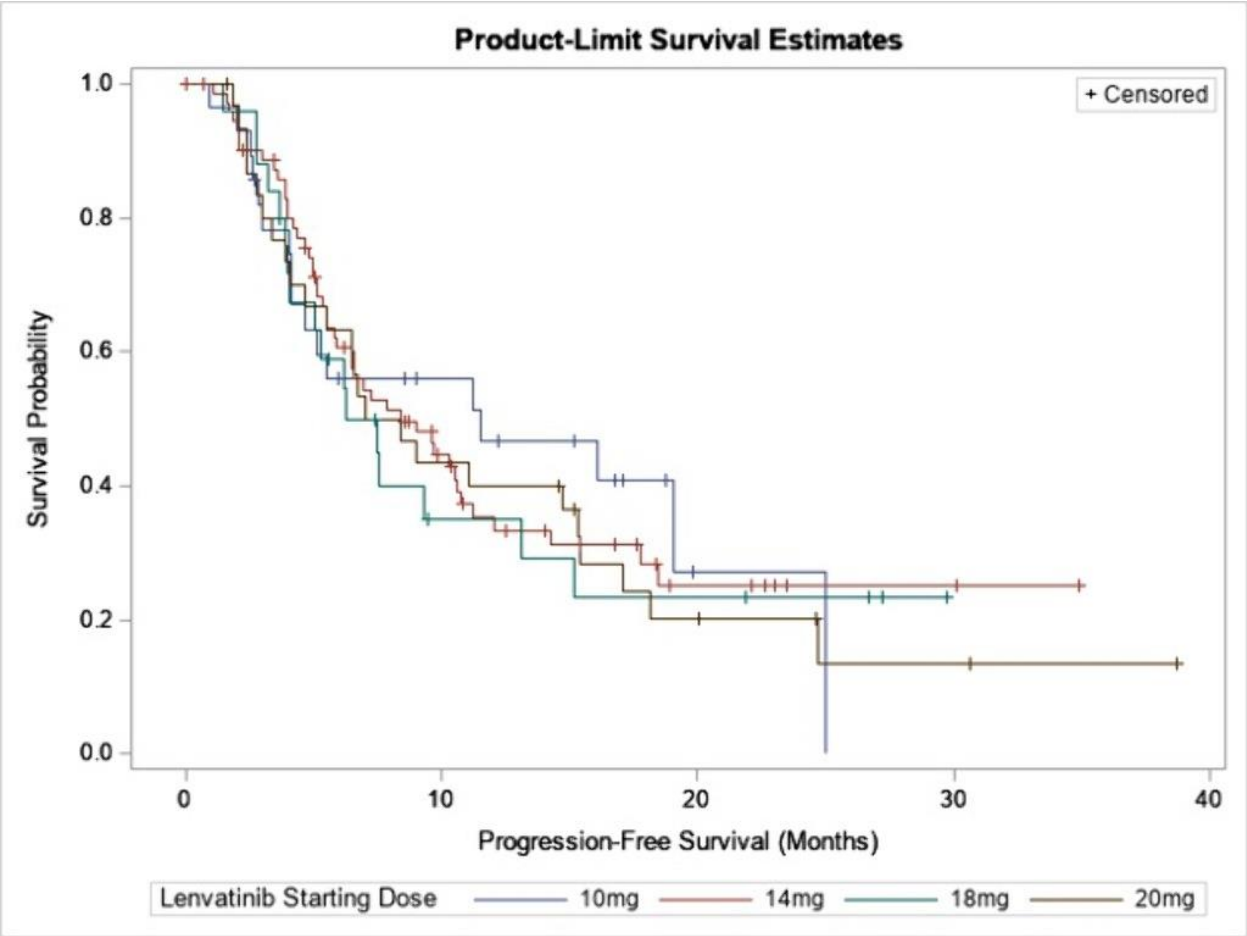
Introduction: Keynote-775 defined the SOC for MMRp recurrent EC. AEs with recommended dosing of lenvatinib/pembrolizumab led to dose reductions in 66.5% of patients. Real world prescription patterns vary significantly from clinical trial. We describe prescribing patterns and outcomes across a multi-institutional consortium.

Methods: A national multidisciplinary consortium was utilized to study patients with advanced/recurrent EC treated with lenvatinib/pembrolizumab. Treatment decisions were based on the physician's recommendation.

Results: 217 patients across 14 institutions were identified. Histologic subtypes were 34.1% endometrioid, 39.6% serous, 9.7% carcinosarcoma, 10.1% mixed, and 2.8% clear cell. 82.9% were MMRp and 4.6% were MMRd. Median dose intensity of lenvatinib was 14mg. Lenvatinib starting dose was 20mg in 17.1%, 18mg in 12.9%, 14mg in 41%, 10mg in 15.7%. Rates of any grade >=3 AE related to lenvatinib were 20mg (13.5%), 18mg (17.9%), 14mg (7.9%), 10mg (17.6%) (p=0.31). Pembrolizumab dosing was 200mg Q3W in 85.6% and 400mg Q6W in 6.5%. ORR (p=0.38), PFS (p=0.97) & OS (p=0.31) were similar in White vs. Black patients. ORR in relation to Lenvatinib starting dose 20mg, 18mg, 14mg, 10mg was 27%, 35.7%, 39.3%, 44.1% (p=0.08). In relation to Lenvatinib starting dose, 12-month PFS rates were 40%, 35%, 35%, 47% respectively (p=0.92), 12-month OS were 59%, 66%, 56%, 51% respectively (p=0.79), and median duration of therapy was 5.1, 4.1, 4.8, 4.6 months respectively (p=0.52).

Conclusion/Implications: In a real-world analysis, the predominant starting dose is 14mg lenvatinib and 200mg pembrolizumab. Grade >=3 AE's, 12-month PFS/OS, ORR & duration of therapy related to lenvatinib starting dose were not statistically

different.


Product-Limit Survival Estimates
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Survival Probability
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Progression-Free Survival (Months)
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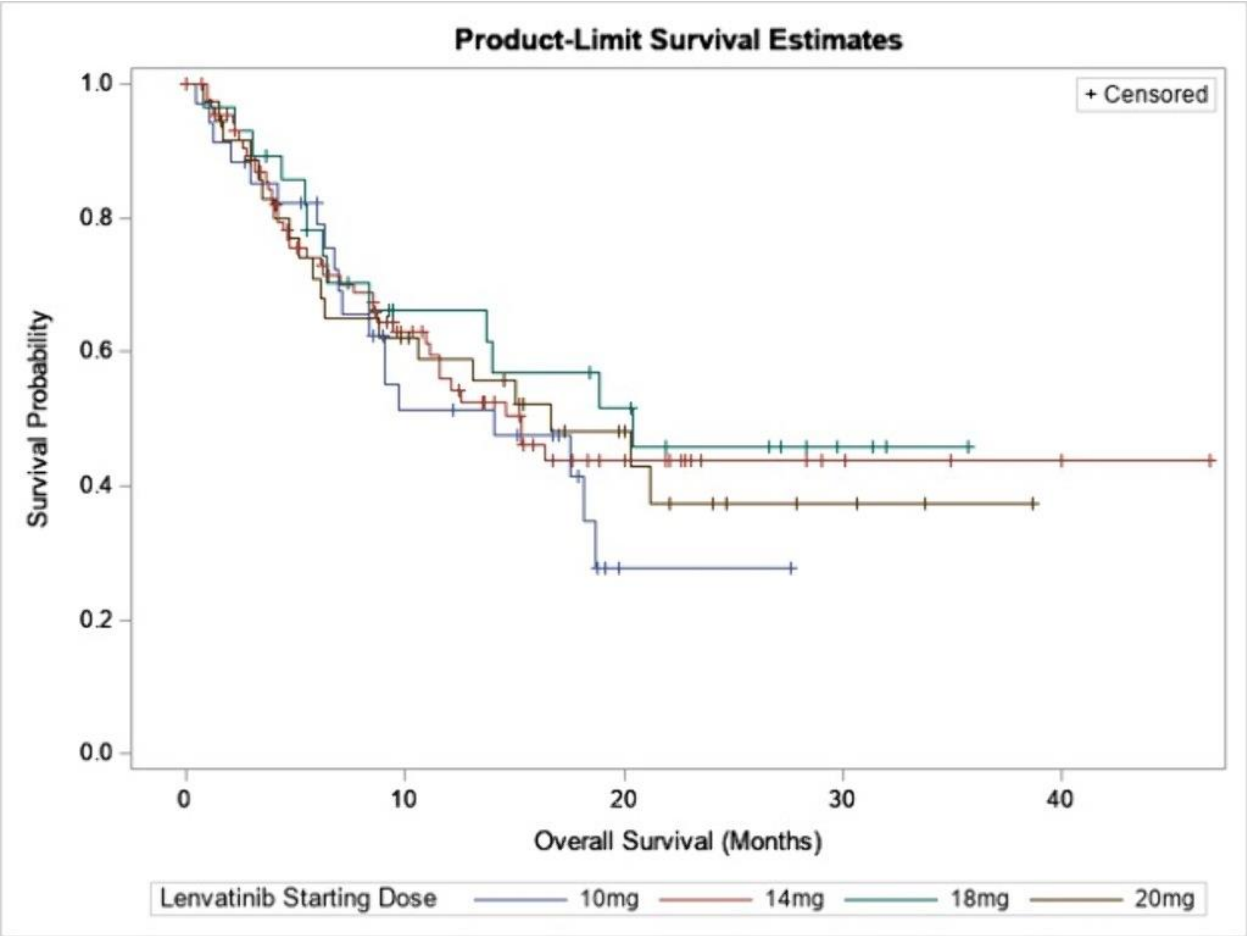
Product-Limit Survival Estimates
+ Censored
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Overall Survival (Months)
Lenvatinib Starting Dose
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14mg
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20mg

PR024 / #394 / Poster Board #: 50

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

MOLECULAR PROFILING OF P53 MUTANT ENDOMETRIAL CANCER REVEALS DISTINCT SUBGROUPS WITH OPPORTUNITIES FOR PERSONALIZED THERAPEUTIC APPROACHES

Felix Blanc-Durand[1], Claire J.H. Kramer[2], Etienne Rouleau[3], Antoine Vasseur[3], Tjalling Bosse[4], Stephanie De Boer[5], Richard Edmondson[6], Melanie Powell[7], Emma Crosbie[6], Naveena Singh[8], Jessica Mcalpine[8], Helen Mackay[9], Pamela Pollock[10], Linda Mileshkin[11], Clare Scott[12], Yi Wan Lim[13], Siew Eng Lim[14], Natalie Yan Li Ngoi[13], David Tan[14], Alexandra Leary[1]
[1]Institut Gustave Roussy, Medical Oncology, Villejuif, France, [2]Leiden University Medical Center and DGOG, Department Of Pathology, Leiden, Netherlands, [3]Institut Gustave Roussy, Cancer Biology, Villejuif, France, [4]Leids Universitair Medisch Centrum (LUMC), Department Of Pathology, Leiden, Netherlands, [5]Leiden University Medical Center, Radiation Oncology, Leiden, Netherlands, [6]Manchester Academic Health Science Centre, Medical Oncology, Manchester, United Kingdom, [7]St Bartholomew's Hospital, Medical Oncology, London, United Kingdom, [8]Vancouver General Hospital, Pathology, Vancouver, Canada, [9]Odette Cancer Centre Sunnybrook Health Sciences Centre, Medical Oncology, Toronto, Canada, [10]Queenslans University of Technology, Institute Of Health And Biomedical Innovation, Brisbane, Canada, [11]Peter MacCallum Cancer Centre, Medical Oncology, Melbourne, Australia, [12]Walter and Eliza Hall Medical Research Institute, Clinical Translation Centre, Melbourne, Australia, [13]National University Cancer Institute, Medical Oncology, Singapore, Singapore, [14]National University Cancer Institute Singapore, Department Of Haematology-oncology, Singapore, Singapore

Introduction: Endometrial cancer (EC) can be classified into four molecular subgroups: POLE mutant, MSI/dMMR, non-specific profiles and P53 mutant (P53mut). P53mut EC comprise ~20% of cases and have the worst prognosis. There is an urgent medical need to better understand P53mut EC in order to propose effective new therapeutic strategies.

Methods: We conducted a retrospective analysis of P53abn EC patients from PORTEC3 (NCT00411138) with available DNA for a large-scale panel sequencing (Discovery Cohort). Results were confirmed on an independent cohort of EC patients (Gustave Roussy, France and National University Cancer Institute, Singapore) identified by their molecular profile using FoundationOneCDX or FoundationOne Liquid CDX panel (Validation Cohort). Molecular findings were correlated with clinicopathologic features from medical record review.

Results: 39 P53abn cases were included in the discovery cohort. Molecular profiling was able to distinguish 4 mutually exclusive subgroups: CCNE1 amplified (15%), ERBB2 amplified (21%), PTEN alteration (21%) and a non-specific group. In the Validation Cohort, 71 P53mut EC patients were included. Median age was 66 years, 40% were serous, 30% endometrioid and 20% carcinosarcoma. 38% presented with primary metastatic diseases. We detected the same four molecular subgroups defined by CCNE1amp (13%), ERBB2amp (16%), and PTEN mutation or loss (34%). Only two patients (3%) harbored co-alterations. We did not observe any overall survival difference between these subgroups.

Conclusion/Implications: Among P53mut EC, we detected 3 nearly mutually-exclusive molecular subgroups: CCNE1 amplified, ERBB2 amplified and PTEN loss, accounting together for 60% of cases. Whether these subgroups might benefit from personalized therapeutic strategies is currently being explored.

PR025 / #182 / Poster Board #: 35

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

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

Gang Chen, Zhe Hu
Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, National Clinical Research Center For Gynecology And Obstetrics, Wuhan, China

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 endometroid 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: EEEC was featured by exclusive germline muataions,a higher BMI and downstream dysregualted lipid metabolism signaling. Our integrated multi-omics analysis unexpectedly revealed an exposome-related mutational signature to be associated with EEEC leading to EEEC specific CTNNB1 and SIGLEC10 hotspot mutations and downstream protein pathway disturbance. Interestingly, in EEECs SIGLEC10^{Q144K} mutation resulted in aberrant Siglec-10 protein expression and promoted progestin resistance by interacting with ERα. 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, encompass-ing obesity, genetic susceptibility, and environmental exposure, that are concomitant with pathogenesis and progestin resistance. Furthermore, we identified biomarkers for progestin response in EEEC fertility-sparing treatment. These attributes can be utilized to promote primary prevention and early detection of EEECs.

PR026 / #185 / Poster Board #: 36

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

PROTEOGENOMICS DECIPHER DISTINCT METASTASIS PATTERNS AND BIOMARKERS OF ENDOMETRIAL CARCINOMA

Gang Chen, Zhe Hu, Zimeng Wu, Chaoyang Sun
Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, National Clinical Research Center For Gynecology And Obstetrics, Wuhan, China

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 diffrerent 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.

PR027 / #815 / Poster Board #: 42

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

CLINICAL IMPACT OF ULTRASTAGING OF SENTINEL LYMPH NODE MAPPING WITH INDOCYANINE GREEN INJECTION IN PATIENTS WITH ENDOMETRIAL CANCER

Sang Hyun Cho[1,2], Hye Min Kim[3], Sang Wun Kim[4]
[1]St. Vincent's Hospital, The Catholic University of Korea, Obstetrics And Gynecology, Suwon, Korea, Republic of, [2]Graduate School, Yonsei University College of Medicine, Obstetrics And Gynecology, Seoul, Korea, Republic of, [3]Yongin Severance Hospital, Yonsei University College of Medicine, Pathology, Yongin, Korea, Republic of, [4]Institute of Women`s Life Medical Science, Yonsei University College of Medicine, Obstetrics And Gynecology, Seoul, Korea, Republic of

Introduction: This retrospective study aimed to confirm the clinical impact of ultrastaging of sentinel lymph node (SLN) mapping with Indocyanine green (ICG) injection in patients with endometrial cancer (EC).

Methods: This retrospective study obtained data from the electronic medical records of Severance Hospital. The subjects included patients with EC who have undergone surgical staging with SLN mapping using ICG injection between June 2014 to December 2017 at Severance Hospital. The SLN paraffin blocks were sliced into two or three layers at an interval of 200 μm between the layers by 3 μm thickness. The immunohistochemistry was performed with anti-cytokeratin antibodies AE1/AE3.

Results: A total of 138 patients included (no metastasis (NM), n=124, 89.9%; macro-metastasis (MAC), n=2, 1.4%; micro-metastasis (MM), n=11, 8.0%; isolated tumor cells (ITC), n=1, 0.7%). A total of 1006 paraffin blocks were examined (NM, n=984, 97.8%; MAC, n=2, 0.2%; MM, n=13, 1.3%; ITC, n=7, 0.7%). The 5-year disease-free survival significantly differed according to the results of ultrastaging (NM, 94.9%; MAC and MM, 69.2%; $p<0.001$). The 5-year overall survival was no significant difference in the status of ultrastaging (NM, 97.4%; MAC and MM, 100%; $p=0.579$). Analyzing the Cox proportional hazards model, the prognostic factor of recurrence was ultrastaging (Hazard Ratio 5.70, [95% Confidence Interval 1.50-21.68], $p=0.011$). The ultrastaging had no prognostic impact on the overall survival.

Conclusion/Implications: The ultrastaging detected more MAC, MM, and ITC of SLN and was a prognostic factor of recurrence in patients with EC. Further study is needed for the clinical impact of ultrastaging for adjuvant therapy of EC.

PR028 / #496 / Poster Board #: 29

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

THE EFFICACY OF METFORMIN IN MEGESTROL ACETATE-BASED FERTILITY-SPARING TREATMENT FOR PATIENTS WITH ENDOMETRIAL ATYPICAL HYPERPLASIA AND ENDOMETRIAL CANCER: LONG-TERM OUTCOMES OF A RANDOMISED CONTROLLED TRIAL

Youting Dong
Shanghai Medical college, Fudan University, Shanghai, Shanghai Medical College, Shanghai, China

Introduction: To assess the long-term efficacy of metformin in megestrol acetate(MA)-based fertility-sparing treatment for patients with endometrial atypical hyperplasia (EAH) and endometrioid endometrial cancer (EEC).

Methods: Patients with EAH or EEC were firstly stratified, then randomised to receive MA (160 mg orally, daily) or MA (160 mg orally, daily) plus metformin (500 mg orally, three times a day).

Results: The complete remission rate, disease-free survival (DFS) rate and pregnancy rate had no significant difference between two treatment groups. However, the DFS rate was higher in the metformin plus MA group than in the MA-only group in non-obese (body mass index＜28 kg/m^2) patients with EAH (hazard ratio [HR] = 2.677, 95% confidence interval [CI] = 1.066-6.727; Log Rank P = 0.029), while had a lower tendency in obese patients with EAH (HR = 0.224, 95% CI = 0.045-1.223; Log Rank P = 0.062). According to cox proportional hazards regression analysis, undergoing assisted reproductive treatment (HR = 2.358, 95% CI = 1.069-5.204; Log Rank P = 0.034) was identified as an independent risk factor for recurrence, whereas younger patients were found to have a higher probability to achieve pregnancy (HR = 0.568, 95% CI = 0.332-0.973; Log Rank P = 0.039).

Conclusion/Implications: Currently, there is no sufficient evidence to support that the utilization of metformin plus MA can significantly improve the prognosis of patients with EAH or EEC compared to MA monotherapy. However, obese patients with endometrial lesions may benefit from the addition of metformin.

PR029 / #227 / Poster Board #: 44

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

ROBOT-ASSISTED VERSUS CONVENTIONAL LAPAROSCOPIC SURGERY FOR ENDOMETRIAL CANCER: LONG-TERM COMPARISON OF OUTCOMES

Kyung Jin Eoh[1], Tae-Joong Kim[2], Jeong-Yeol Park[3], Hee Seung Kim[4], Jiheum Paek[5], Young Tae Kim[6]
[1]Yongin Severance Hospital, Obstetrics And Gynecology, Yongin, Korea, Republic of, [2]Samsung Medical Center, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of, [3]Asan Medical Center, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of, [4]Seoul National University Hospital, Obstetrics And Gynecology, Seoul, Korea, Republic of, [5]Ajou University School of Medicine, Departments Of Obstetrics And Gynecology, Suwon, Korea, Republic of, [6]Yonsei Cancer Center, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of

Introduction: There is a lack of multi-institutional large-volume and long-term follow-up data on comparisons between robot-assisted surgery and conventional laparoscopic surgery. This study compared the surgical and long-term survival outcomes between patients who underwent robot-assisted or conventional laparoscopic surgery for endometrial cancer.

Methods: We retrospectively reviewed the data of patients from five large academic institutions who underwent either robot-assisted or conventional laparoscopic surgery for the treatment of endometrial cancer between 2012 and 2017, ensuring at least 5 years of potential follow-up. Intra- and postoperative outcomes, long-term disease-free survival, and overall survival were compared.

Results: The study cohort included 1,003 unselected patients: 551 and 452 patients received conventional laparoscopic and robot-assisted surgery, respectively. The median follow-up duration was 57 months. Postoperative complications were significantly less likely to occur in the robot-assisted surgery group than in the laparoscopic surgery group (7.74% vs. 13.79%, P = 0.002). There were no significant differences in survival: 5-year disease-free survival was 91.2% versus 90.0% (P = 0.628) and overall survival was 97.9% versus 96.8% (P = 0.285) in the robot-assisted and laparoscopic surgery cohorts, respectively. Cox proportional hazard regression models demonstrated that the mode of surgery was not associated with disease-free survival (hazard ratio, 0.897; confidence interval, 0.563–1.429) or overall survival (hazard ratio, 0.791; confidence interval, 0.330–1.895) after adjusting for confounding factors.

Conclusion/Implications: Robot-assisted surgery for endometrial cancer is associated with similar long-term survival outcomes but fewer postoperative complications as compared to conventional laparoscopic surgery.

PR030 / #559 / Poster Board #: 41

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

PAX2 IS REGULATED BY ESTROGEN/PROGESTERONE THROUGH PROMOTER METHYLATION IN ENDOMETRIOID ADENOCARCINOMA AND TAKE THE IMPORTANT ROLE IN CARCINOGENESIS VIA THE AKT/MTOR SIGNALING PATHWAY

Qingping Jiang, Hui Chen
Third Affiliated Hospital, Guangzhou Medical University, Pathological Department, Guangzhou, China

Introduction: PAX2 (Paired box 2) and PTEN inactivation were reportedly as important biomarkers for endometrioid intraepithelial neoplasia (EIN) and Endometrioid endometrial carcinoma (EEC). However, though PTEN was extensively studied, the role of PAX2 in EEC carcinogenesis still remains unclear.

Methods: Public databases and clinical paired paraffin-embedded tissues were used to analyze PAX2 expression in EEC. Cell function tests and mouse xenograft models were utilized to study the biological functions of PAX2. Pyrosequencing and demethylating drug 5-Aza-dc were used to verify promoter methylation in clinical tissues and cell lines, respectively. The mechanism underlying the regulatory effect of estrogen (E2) and progesterone (P4) on PAX2 expression was investigated by receptor block assay and double luciferase reporter assay.

Results: PAX2 expression was significantly down-regulated in EIN and EEC tissues, its overexpression inhibited EEC cell malignant behaviors in vivo and in vitro and inhibited the AKT/mTOR signaling pathway. PAX2 inactivation in EEC was related to promoter methylation, and its expression was regulated by E2 and P4 through their receptors via promoter methylation.

Conclusion/Implications: Our findings elucidated the expression and function of PAX2 in EEC and firstly provided hitherto undocumented evidence of the underlying molecular mechanisms. PAX2 expression is suppressed by estrogen prompting its methylation through estrogen receptor. Furthermore, PAX2 regulates the AKT/mTOR signaling pathway to influence EEC progression.

PR031 / #378 / Poster Board #: 33

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

A PREDICTIVE MODEL FOR LYMPH NODE METASTASIS USING A TUMOR LOCATION IN PRESUMED EARLY-STAGE ENDOMETRIOID ENDOMETRIAL CANCER PATIENTS

Tae-Wook Kong, Jimin Lee, Jeeyeon Kim, Joo-Hyuk Son, Suk-Joon Chang
Ajou University Medical Center, Obstetrics And Gynecology, Suwon, Korea, Republic of

Introduction: This study aimed to preoperatively identify high- and low-risk subgroups of patients with lymph node (LN) metastasis in presumed early-stage endometrioid endometrial cancer patients treated with systematic pelvic and para-aortic lymphadenectomy.

Methods: Clinicopathologic data of presumed early-stage endometrioid EC patients (N = 361) treated with total hysterectomy with systematic lymphadenectomy between March 2000 and July 2022 were analyzed. None of the patients had definite evidence of LN metastasis in a preoperative magnetic resonance imaging (MRI). Preoperative risk factors including tumor location on MRI for LN metastasis were used to identify variables associated with LN metastasis. Multivariate models were estimated using the backward logistic regression method.

Results: LN metastasis was confirmed in 19 patients (5.3%). Cervical stroma invasion on MRI (odds ratio, 4.386; 95% confidence interval, 1.020 – 18.852; P = 0.047), Cornual location on MRI (odds ratio, 36.208; 95% confidence interval, 7.902 – 165.913; P < 0.001), and lower uterine segment/isthmic location on MRI (odds ratio, 8.454; 95% confidence interval, 1.567 – 45.610; P = 0.013) were independent variables for LN metastasis. Patients were categorized into low- and high-risk groups according to risk criteria. Significant differences in the rates of LN metastasis were observed between the groups (0.4% vs. 22.2%, P < 0.001).

Conclusion/Implications: A model using tumor location including uterine cornua and lower uterine segment/isthmus was significantly correlated with the risk of LN metastasis. Even in presumed early-stage endometrioid endometrial cancer patients, therefore, tumor location including cornua and isthmus should be investigated to determine whether to perform sentinel LN biopsy or lymphadenectomy.

PR032 / #594 / Poster Board #: 43

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

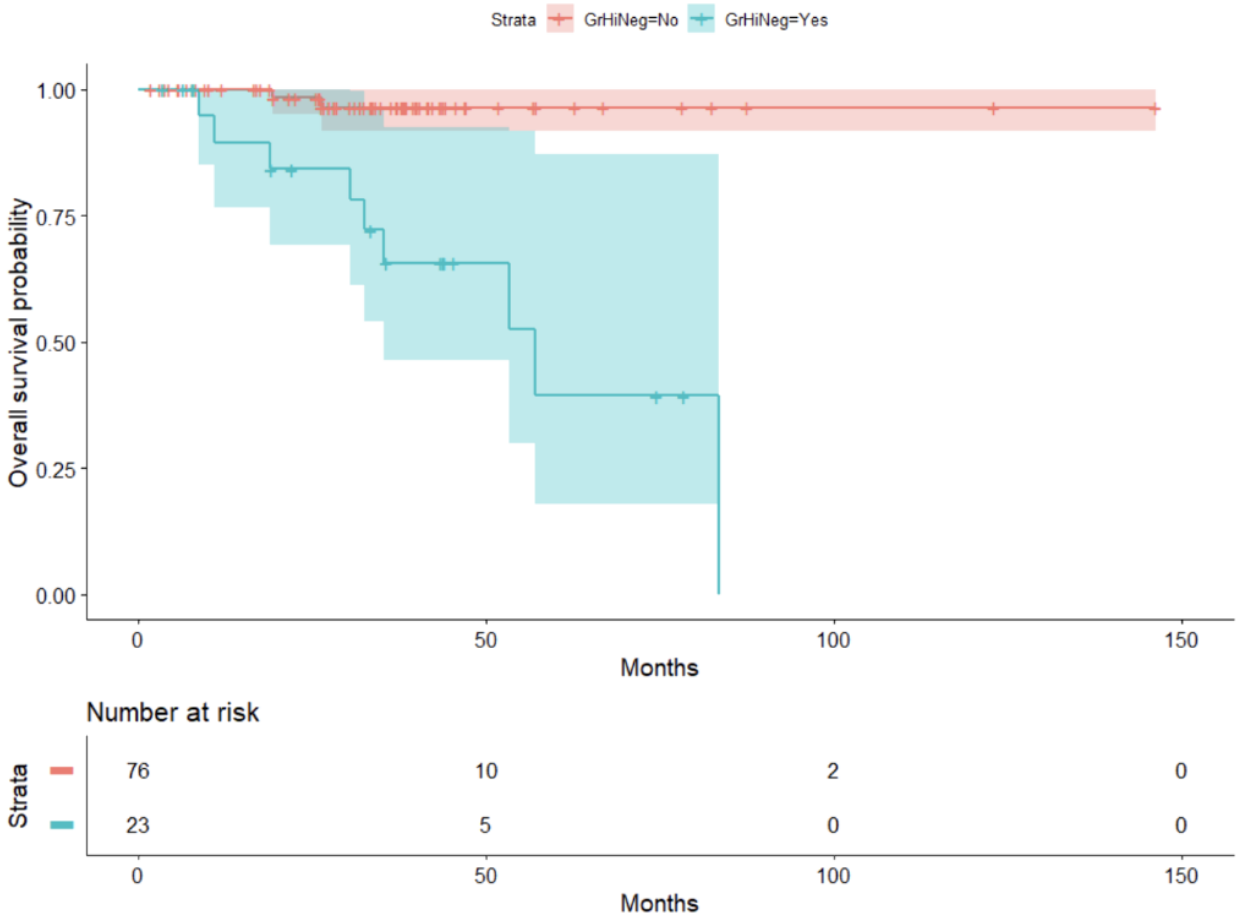
REFINING COPY NUMBER-LOW ENDOMETRIAL CARCINOMA BY ESTROGEN RECEPTOR IMMUNOHISTOCHEMISTRY

Clarissa Lam[1], Lora Ellenson[2], Britta Weigelt[2], Nadeem Abu-Rustum[1], Amir Momeni-Boroujeni[2]
[1]Memorial Sloan Kettering Cancer Center, Gynecologic Surgery, New York, United States of America, [2]Memorial Sloan Kettering Cancer Center, Department Of Pathology, New York, United States of America

Introduction: To further subclassify copy number-low endometrial carcinomas (CNL-EC) based on immunohistochemistry (IHC) with prognostic implications.

Methods: We compiled EC patients who received their primary treatment at our institution from 2014 to 2022, and who had CNL-EC based on a surrogate of The Cancer Genome Atlas (TCGA) prognostic EC molecular subtype. Estrogen receptor (ER) and PTEN IHC was performed.

Results: A total of 104 patients with CNL-EC were included. Eighty eight of 104 (84.6%) were ER positive by IHC, with 86 of 88 (97.7%) with endometrioid morphology. ER-positivity was found in conjunction with PTEN mutation, identified by genomic profiling, in 81.8[EL1] %. After combining histology and grade into a single variable (low-grade vs high-grade endometrioid or non-endometrioid (NE)) multivariate analysis demonstrated that only ER IHC status and the combined histology/grade variable are significant contributors to overall survival (HR=8.6 and 9.8, respectively, P=0.02 and P=0.002, respectively). Of the 14 deaths documented in this cohort, all but three had either high-grade and/or NE, or ER-negative
tumors.


Strata
GrHiNeg=No
GrHiNeg=Yes
1.00
0.75
0.50
0.25
0.00
Overall survival probability
0
50
100
150
Months
Number at risk
Strata
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10
2
0
23
5
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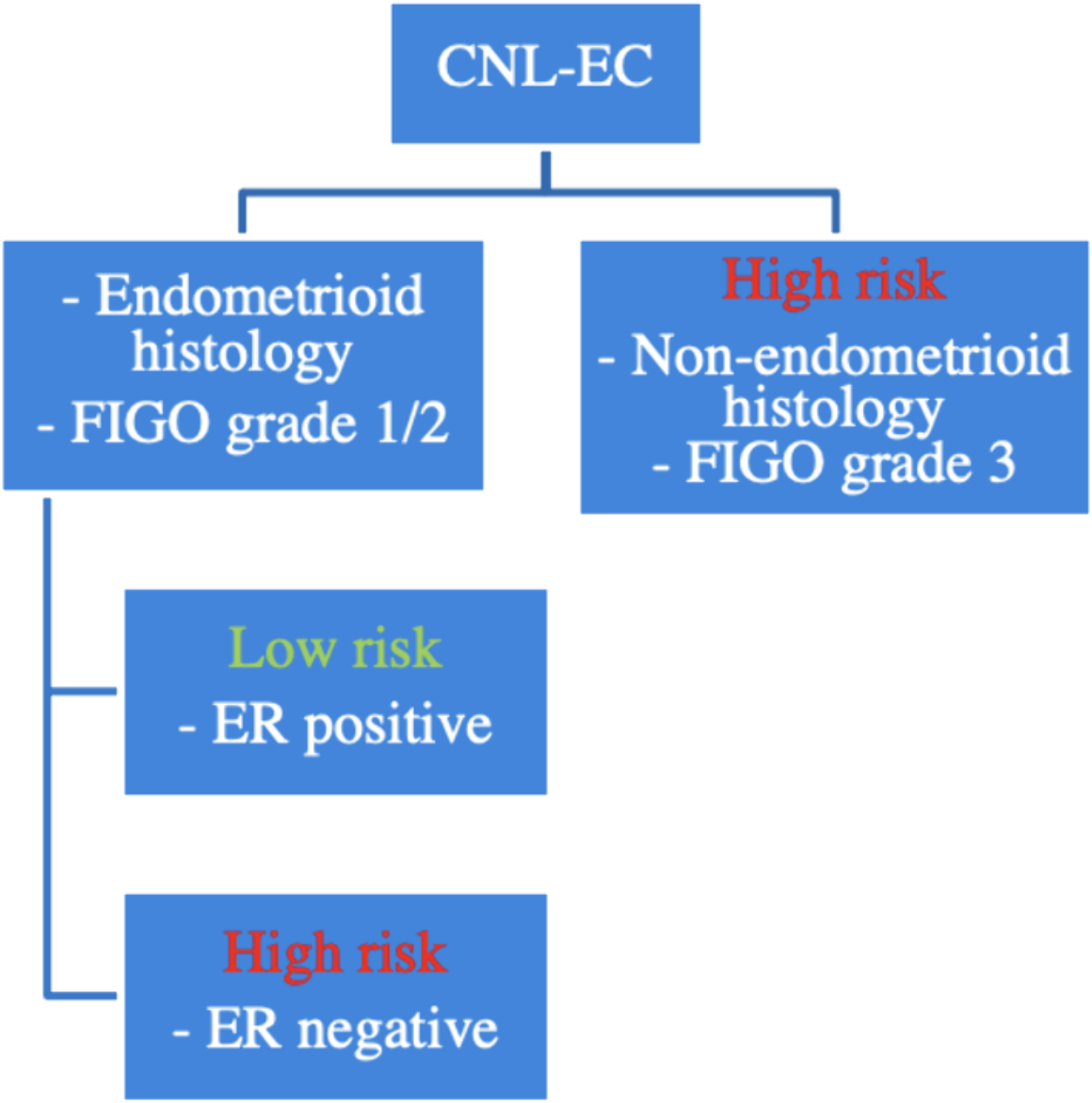
Months



Conclusion/Implications: These data highlight the importance of ER-IHC testing in CNL-EC and supports subclassify CNL tumors into 2 prognostic groups: a higher-risk group including FIGO grade 3, ER-negative endometrioid tumors and/or non-endometrioid features, and a more favorable group (FIGO grade 1/2 endometrioid ER positive carcinomas). Utilizing ER-IHC with histology and FIGO grade allows for better risk-stratification of patients with CNL-EC.

PR033 / #878 / Poster Board #: 47

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

DIAGNOSTIC AND PROGNOSTIC ROLE OF CIRCULATING NEUTROPHIL EXTRACELLULAR TRAP MARKERS AND PREKALLIKREIN IN PATIENTS WITH ENDOMETRIAL CANCER

Seung Jun Lee[1], Se Ik Kim[2], Jae-Weon Kim[3], Maria Lee[2]
[1]Seoul National University Hospital, Obstetrics And Gynecology, Seoul, Korea, Republic of, [2]Seoul National University Hospital, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of, [3]Seoul National University, Obstetrics And Gynecology, Seoul, Korea, Republic of

Introduction: Tumor-promoting inflammation is among the hallmarks of cancer. Prekallikrein is among the acute-phase reactants in the inflammatory response; moreover, neutrophils release nuclear contents into the extracellular space to create neutrophil extracellular traps (NET). We aimed to investigate the diagnostic and prognostic utilities of circulating plasma NET markers and prekallikrein for endometrial cancer.

Methods: Circulating levels of three NET markers (histone-DNA complex, cell-free DNA, and neutrophil elastase) and prekallikrein were measured in 100 patients with endometrial cancer and 30 healthy controls. We used an area under the receiver operating characteristic curve (AUC) analysis to investigate their diagnostic and prognostic utilities for HGSOC.

Results: Compared with healthy controls, patients with endometrial cancer showed significantly higher levels of the three NET markers and prekallikrein. Patients with advanced-stage endometrial cancer showed significantly higher levels of the cell-free DNA ($P<0.001$), compared with those with early-stage endometrial cancer. Further, the levels of histone-DNA complex, neutrophil elastase, and prekallikrein did not significantly differ according to the cancer stage. All markers showed significant diagnostic utility. Notably, a logistic regression-based model that comprised all four markers showed the strongest diagnostic power (AUC, 0.901). In multivariate analyses, neutrophil elastase was identified as an independent poor prognostic factor for overall survival and progression-free survival in patients with endometrial cancer.

Conclusion/Implications: The levels of the three NET markers and prekallikrein might be novel diagnostic and prognostic markers for endometrial cancer.

PR034 / #973 / Poster Board #: 34

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

ONCOLOGIC OUTCOMES OF ROBOT-ASSISTED LAPAROSCOPY VERSUS LAPAROSCOPY FOR THE TREATMENT OF APPARENT EARLY STAGE ENDOMETRIOID ADENOCARCINOMA OF THE UTERUS

Yu Hui Lim[1], Christian Dagher[1], Nadeem Abu-Rustum[1,2], Jennifer Mueller[1], Yukio Sonoda[1], Oliver Zivanovic[1], Vance Broach[1], Mario Leitao[1]
[1]Memorial Sloan Kettering Cancer Center, Gynecology Service, Department Of Surgery, New York, United States of America, [2]Memorial Sloan Kettering Cancer Center, Gynecologic Oncology, New York, United States of America

Introduction: To compare long-term oncologic outcomes in women with apparent uterine confined (or early-stage) endometrioid endometrial cancer undergoing minimally invasive surgical (MIS) staging with or without robotic assistance (RA).

Methods: We performed a retrospective chart review of all patients with apparent early-stage endometrioid endometrial cancer diagnosed at Memorial Sloan Kettering Cancer Center between January 2008 and January 2018. Clinicopathologic, surgical, and survival data were collected. Appropriate statistical methods were applied.

Results: Of 1728 patients, 1389 (80.4%) underwent RA-laparoscopy, and 339 (19.6%) laparoscopy. Median age at diagnosis was 60 years, range (24-92), median body mass index (BMI) at diagnosis was 30.2 kg/m2, range (15.1-71.2). Patient demographics and tumor characteristics were similar in the two groups. Perioperative complications were similar in both groups (9.9% vs 7.7%, p=0.2). A higher proportion of patients in the RA group were discharged on day 0 (19.2% v 5.3%, p<0.001). Median follow-up was similar in the RA vs. laparoscopy group (55.7 months vs 52.9 months, p=0.37). Comparing the RA and laparoscopic groups, the recurrence rate (9.5% vs. 7.4%, p=0.22), 5-year progression-free survival (88.5% vs. 90%, p=0.38), and 5-year overall survival (89% v 89%, p=0.74) were not significantly different.

Conclusion/Implications: In apparent early-stage endometrioid endometrial cancers, surgical staging using RA-laparoscopy was not associated with any significant increase in adverse survival outcomes compared to laparoscopy.

PR035 / #95 / Poster Board #: 45

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

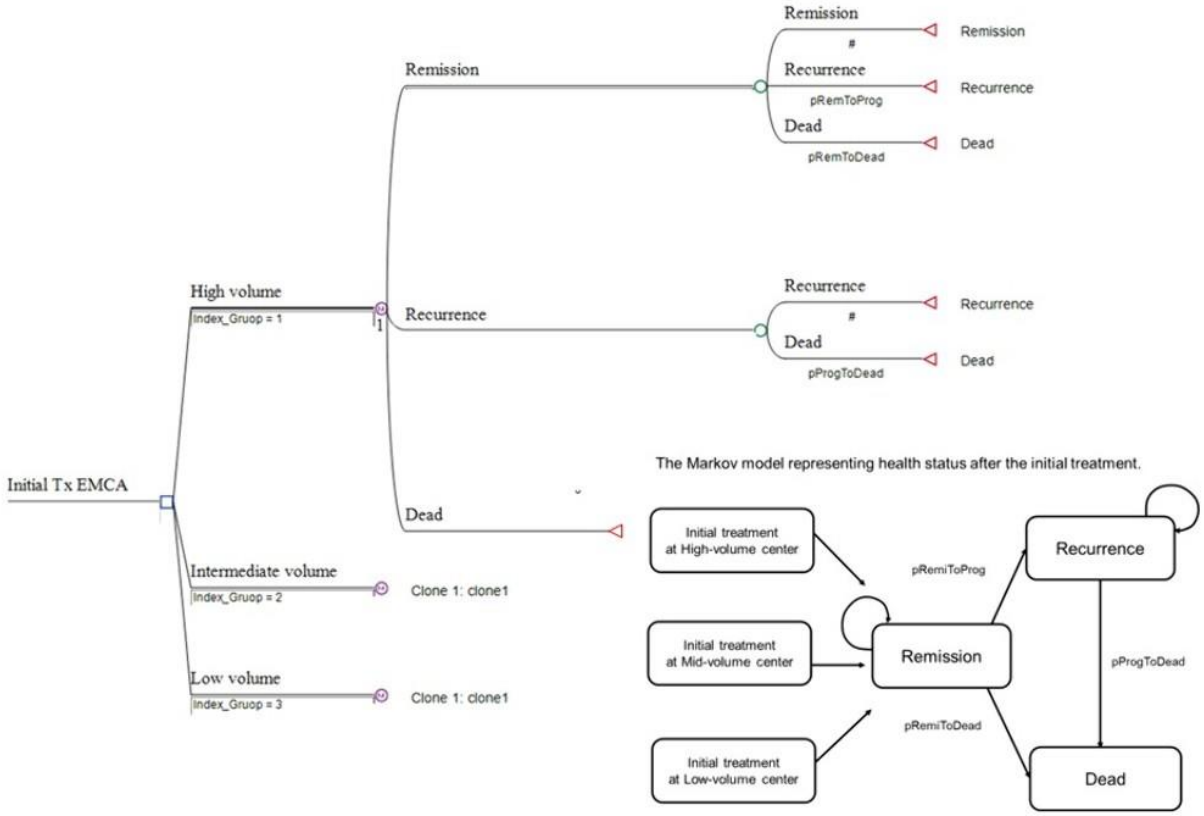
A COST-EFFECTIVENESS ANALYSIS OF HOSPITAL TREATMENT VOLUME AND SURVIVAL OUTCOMES IN PATIENTS WITH ENDOMETRIAL CANCER IN JAPAN

Hiroko Machida[1], Mikio Mikami[2], Koji Matsuo[3], Daisuke Aoki[4], Takayuki Enomoto[5], Aikou Okamoto[6], Hidetaka Katabuchi[7], Satoru Nagase[8], Masaki Mandai[9], Nobuo Yaegashi[10], Wataru Yamagami[4]
[1]Tokai University School of Medicine, Obstetrics And Gynecology, Isehara, Japan, [2]Tokai University School of Medicine, Obstetrics And Gynecology, Isahara, Japan, [3]University of Southern California,, Gynecologic Oncology, Los angeles, United States of America, [4]Keio University School of Medicine, Gynecologic Oncology, Tokyo, Japan, [5]Niigata University School of Medicine, Gynecologic Oncology, Niigata, Japan, [6]Jikei University School of Medicine, Gynecologic Oncology, Minatoku, Japan, [7]Faculty of Life Sciences, Kumamoto University, Gynecology, Kumamoto, Japan, [8]Yamagata University Faculty of Medicine, Gynecologic Oncology, yamagata, Japan, [9]Graduate School of Medicine, Kyoto University, Gynecologic Oncology, Kyoto, Japan, [10]Tohoku University, Gynecologic Oncology, Sendai, Japan

Introduction: The hospital treatment volume affects survival outcomes for endometrial cancer; notably, the initial treatment at high-volume centers improved survival outcomes. We assessed the cost-effectiveness of hospital treatment volume and survival outcomes in patients with endometrial cancer.

Methods:

Fig1. Decision tree representing the initial treatment pathway of EMCA.



A decision-analytic model was evaluated following assessment strategies regarding the costs and effects: 1) hospital treatment volume (low-, moderate-, and high-volume centers) and 2) post-operative recurrent risk factors based on pathological findings (adjuvant therapy in high- and intermediate-risk or without adjuvant therapy in low risk). Input data were derived from the Japan Society of Obstetrics and Gynecology database, systematic literature searches, and the Diagnosis Procedure Combination database in Japan. Quality-adjusted life years (QALYs) were used as a measure of effectiveness. The model was built from a public healthcare perspective, and the impact of uncertainty was assessed with sensitivity analyses.

Results:

Table1. Incremental analysis.

Strategy	Cost	Incr Cost	Eff	Incr Eff	Dominance
High volume	¥3,777,830		4.28		Reference
Intermediate volume	¥3,836,413	¥58,582	4.25	-0.04	Dominated
Low volume	¥3,892,959	¥115,129	4.21	-0.07	Dominated

2

A base-case analysis showed that treatment at high-volume centers was the most effective strategy for patients with endometrial cancer, and the incremental cost-effectiveness ratio was below a willingness-to-pay threshold of ¥5,000,000 with a maximum of ¥3,777,830 / 4.28 QALY. Treatment at the high-volume centers was dominant compared to intermediate- or low-volume centers with the efficiency and cost-effectiveness. Sensitivity analyses showed that the model outcome was robust to input value changes. With a willingness-to-pay threshold of ¥5,000,000, treatment at the high-volume center remained cost-effective in at least 73.6% of iterations.

Conclusion/Implications: Treatment at high-volume centers is the most cost-effective strategy to guide the need for treatment centralization in patients with endometrial cancer.

PR036 / #142 / Poster Board #: 39

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

A NOVEL IMMUNE SUBTYPE CLASSIFICATION OF THE COPY-NUMBER HIGH ENDOMETRIAL CANCER

Mingyi Mao, Fang Jiang, Yang Xiang
Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Department Of Obstetrics And Gynecology, Beijing, China

Introduction: The TCGA molecular subtype of endometrial cancer has played a crucial role in predicting prognosis and guiding treatment. Specifically, the copy-number high (CNH) subtype has been associated with poor prognosis and marked heterogeneity. The tumour immune subtype provides a new perspective, and its combination with the molecular subtype facilitates precise diagnosis and treatment for patients.

Methods: We collected 60 cases of CNH endometrial carcinoma in the TCGA database. Based on the enrichment scores of immune-related gene signatures, we used unsupervised cluster analysis to identify heterogeneous immune subtypes, and described their immune characteristics and prognosis. We also identified the prognostic marker through differential gene analysis and lasso regression analysis. Finally, we observed the distribution of the marker in tissues using immunohistochemical staining, and validated its prognostic value in independent samples.

Results: We defined two immune subtypes, immune-hot (IH) and immune-cold (IC), which differed in immune cell infiltration, cytokine and chemokine expression and prognosis. The IH subtype has significantly stronger immune activation than the IC subtype, showing a significant infiltration of immune effector cells and high expression of relevant chemokines, with a better prognosis. By analyzing differentially expressed genes, we identified GZMM as a prognostic biomarker, confirming its unique prognostic value in CNH endometrial cancer. Additionally, we observed the correlation between GZMM and prognosis in immunohistochemical staining.

Conclusion/Implications: This study revealed heterogeneous immune subtypes in CNH endometrial cancer and identified the prognostic biomarker GZMM. The stratified classification strategy combined with molecular and immune subtypes provides a reference for future clinical practice.

PR037 / #494 / Poster Board #: 48

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

PRE-TREATMENT SYSTEMIC INFLAMMATORY MARKERS PREDICT SURVIVAL IN ENDOMETRIAL CANCER: A JAPANESE GYNAECOLOGIC ONCOLOGY GROUP (JGOG) 2043 EXPLORATORY DATA ANALYSIS

Shin Nishio[1], Kenta Murotani[2], Wataru Yamagami[3], Shiro Suzuki[4], Hidekatsu Nakai[5], Kazuyoshi Kato[6], Hideki Tokunaga[7], Hiroyuki Nomura[8], Yoshihito Yokoyama[9], Kazuhiro Takehara[10]
[1]Kurume University School of Medicine, Obstetrics And Gynecology, Kurume, Japan, [2]Kurume University School of Medicine, Biostatistics Center, Kurume, Japan, [3]Keio University School of Medicine, Department Of Gynecologic Oncology, Tokyo, Japan, [4]Aichi Cancer Center, Gynecology, Nagoya, Japan, [5]Kindai University, Department Of Obstetrics And Gynecology, Osakasayama, Japan, [6]Kitasato University School of Medicine, Obstetrics And Gynecology, Sagamihara, Japan, [7]Tohoku University Graduate School of Medicine, Obstetrics And Gynecology, Sendai, Japan, [8]Fujita Health University, Department Of Obstetrics And Gynecology, Toyoake, Japan, [9]Hirosaki University, Department Of Obstetrics And Gynecology, Hirosaki, Japan, [10]National Hospital Organization Shikoku Cancer Center, Department Of Gynecologic Oncology,, Matsuyama, Japan

Introduction: Inflammation predisposes patients to tumorigenesis by damaging DNA, stimulating angiogenesis, and potentiating pro-proliferative and anti-apoptotic processes. This study investigated whether pre-treatment systemic inflammatory markers (PTSIMs) are associated with survival outcomes in endometrial cancer (EC) patients.

Methods: Women with EC were recruited to the JGOG 2043 study. PTSIMs including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and hemoglobin, albumin, lymphocyte, and platelet (HALP) score were analysed in terms of clinicopathological factors, progression-free survival (PFS), and overall survival (OS). Optimal cut-off values for NLR, PLR, and HALP score were determined using the web application Cutoff Finder for PFS and OS. Survival estimates were calculated using the Kaplan–Meier method.

Results: In total, 712 patients were enrolled with a median age of 59 years and median body mass index (BMI) of 22.4 kg/m^2. The optimal cut-off values for PFS were 1.478 for NLR, 0.01695 for PLR, and 35.52 for HALP score. Similarly, the optimal cut-off values for OS were 1.88 for NLR, 0.02623 for PLR, and 19.87 for HALP score. Regarding the optimal cut-off values for PFS, NLR was associated with BMI; PLR with age, BMI, and stage; and HALP score with BMI, stage, and lymph node metastasis. For the optimal cut-offs for OS, NLR was associated with BMI, PLR, and BMI; and HALP score was associated with age and BMI. In PFS, HALP score was the prognostic factor. In OS, PLR and HALP score were prognostic factors.

Conclusion/Implications: PTSIMs are associated with survival outcomes in EC. In particular, HALP score was a prognostic factor for both PFS and OS.

PR038 / #248 / Poster Board #: 51

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

MANAGEMENT OF IMMUNE-RELATED ADVERSE EVENTS IN PATIENTS WITH PRIMARY ADVANCED OR RECURRENT ENDOMETRIAL CANCER: DOSTARLIMAB PLUS CHEMOTHERAPY COMPARED WITH CHEMOTHERAPY ALONE IN THE ENGOT-EN6-NSGO/GOG-3031/RUBY TRIAL

Zoltan Novák[1], Michael Gold[2], Jørn Herrstedt[3], Sarah Gill[4], Antonella Savarese[5], John Diaz[6], Stefan Kommoss[7], Guilherme Cantuaria[8], Ingrid Boere[9], Evelyn Fleming[10], Lucy Gilbert[11], Kathryn Pennington[12], Robert Holloway[13], Eirwen Miller[14], Rachel Miller[15], Matthew Powell[16], Christine Dabrowski[17], Shadi Stevens[18], Mansoor Raza Mirza[19], Carolyn Mccourt[20]
[1]Hungarian National Institute of Oncology, Department Of Gynecology, Budapest, Hungary, [2]Oklahoma Cancer Specialists and Research Institute, Department Of Gynecologic Oncology, Tulsa, United States of America, [3]Zealand University Hospital Roskilde and University of Copenhagen, Department Of Clinical Oncology And Palliative Care, Copenhagen, Denmark, [4]Nancy N and JC Lewis Cancer and Research Pavilion, Division Of Gynecologic Oncology, Savannah, United States of America, [5]IRCCS Istituti Fisioterapici Ospitalieri, Istituto Nazionale Tumori Regina Elena, Department Of Medical Oncology, Rome, Italy, [6]Miami Cancer Institute at Baptist Health South Florida, Chief Of Gynecologic Oncology, Miami, United States of America, [7]AGO Study Group, University Hospital Tübingen, Department Of Women's Health, Tübingen, Germany, [8]Georgia NCORP, Department Of Gynecologic Oncology, Atlanta, United States of America, [9]Erasmus MC Cancer Centre, Department Of Medical Oncology, Rotterdam, Netherlands, [10]Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Division Of Gynecologic Oncology, Lebanon, United States of America, [11]McGill University Health Centre, Division Of Gynecologic Oncology, Montreal, Canada, [12]University of Washington, Division Of Gynecologic Oncology, Department Of Obstetrics And Gynecology, Seattle, United States of America, [13]Advent Health Cancer Institute, Gynecologic Oncology Program, Orlando, United States of America, [14]Western Pennsylvania Hospital, Allegheny Health Network, Division Of Gynecologic Oncology, Pittsburgh, United States of America, [15]University of Kentucky Markey Cancer Center, Division Of Gynecologic Oncology, Department Of Obstetrics And Gynecology, Lexington, United States of America, [16]Washington University School of Medicine, National Cancer Institute Sponsored Nrg Oncology, St Louis, United States of America, [17]GSK, Clinical Safety, Waltham, United States of America, [18]GSK, Oncology Clinical Development, London, United Kingdom, [19]Rigshospitalet, Copenhagen University Hospital, Copenhagen, and Nordic Society of Gynaecological Oncology-Clinical Trial Unit, Department Of Oncology, Copenhagen, Denmark, [20]Washington University School of Medicine, Washington University in St. Louis, Division Of Gynecologic Oncology, St. Louis, United States of America

Introduction: Dostarlimab+carboplatin-paclitaxel demonstrated PFS and OS benefits vs carboplatin-paclitaxel in patients with primary advanced or recurrent endometrial cancer (pA/rEC). Here, we report on the management of immune-related adverse events (irAEs) in the RUBY (NCT03981796) trial.

Methods: Patients with pA/rEC were randomized 1:1 to dostarlimab 500 mg, or placebo, plus carboplatin AUC 5 and paclitaxel 175 mg/m^2 Q3W for 6 cycles, followed by dostarlimab 1000 mg, or placebo, Q6W for up to 3 years. AEs were assessed according to CTCAE v4.03. irAEs were defined as CTCAE grade ≥2 from a predefined list.

Results: The safety population included 487 patients who received ≥1 dose of treatment (241 dostarlimab+carboplatin-paclitaxel; 246 placebo+carboplatin-paclitaxel). irAEs related to dostarlimab or placebo were reported by 38.2% in the dostarlimab+carboplatin-paclitaxel arm and 15.4% in the placebo+carboplatin-paclitaxel arm; grade ≥3 irAEs related to dostarlimab or placebo were reported by 12.4% and 3.3%, respectively (Table). Only 7.9% and 3.7% of patients discontinued dostarlimab or

placebo because of an irAE, respectively; there were no irAE-related deaths. Of those experiencing irAEs in the dostarlimab+carboplatin-paclitaxel arm, 63.5% were treated with steroids, immunosuppressants, and/or thyroid therapy; 73.6% resolved (median resolution 10.0 days). Of the 36.5% patients not receiving steroids, immunosuppressants, and/or thyroid therapy, 80.0% resolved (median resolution 8.0 days). Management and resolution frequency were similar in the placebo+carboplatin-paclitaxel arm (Table).

Conclusion/Implications: In the RUBY trial, most irAEs were mild and resolved. Few patients discontinued dostarlimab because of irAEs. The irAE profile observed in the dostarlimab+carboplatin-paclitaxel arm showed similar trends as that observed with dostarlimab

monotherapy.

Event, n (%)	Dostarlimab+ carboplatin-paclitaxel (N=241)	Placebo+ carboplatin-paclitaxel (N=246)
Any irAE[a]	137 (56.8)	88 (35.8)
Related to dostarlimab/placebo	92 (38.2)	38 (15.4)
Any irAE grade ≥3	40 (16.6)	15 (6.1)
Related to dostarlimab/placebo	30 (12.4)	8 (3.3)
Any irAE leading to dostarlimab/placebo discontinuation	19 (7.9)	9 (3.7)
Any irAE leading to death	0	0
Treatment related irAEs in ≥5% of patients in either arm		
Hypothyroidism	27 (11.2)	7 (2.8)
Arthralgia	14 (5.8)	16 (6.5)
Rash	16 (6.6)	5 (2.0)
Alanine aminotransferase increased	14 (5.8)	2 (0.8)
Treatment related irAEs grade ≥3 in ≥1% of patients in either arm		
Rash	9 (3.7)	3 (1.2)
Aspartate aminotransferase increased	5 (2.1)	1 (0.4)
Alanine aminotransferase increased	5 (2.1)	0
Rash maculopapular	5 (2.1)	0
Treatment-related irAEs leading to treatment discontinuation in ≥1% of patients		
Infusion-related reaction	3 (1.2)	1 (0.4)
Rash maculopapular	3 (1.2)	0
Any irAE treated with steroid, immunosuppressant, and/or thyroid therapy	87 (63.5)	52 (59.1)
Resolved with steroid, immunosuppressant, and/or thyroid therapy	64 (73.6)	43 (82.7)
Time to resolution, median, days	10.0	1.0
Any irAE not treated with steroid, immunosuppressant, and/or thyroid therapy	50 (36.5)	36 (40.9)
Resolved without steroid, immunosuppressant, and/or thyroid therapy	40 (80.0)	26 (72.2)
Time to resolution, median, days	8.0	11.0

[a]irAEs are defined as grade 2 and above from a predefined list

PR039 / #272 / Poster Board #: 49

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

VALUE OF THE NEW ENDOMETRIAL CANCER RISK MOLECULAR CATEGORIZATION SYSTEM 2020 ESGO/ESTRO/ESP IN PREDICTING SURVIVAL AND RECURRENCE

Yung-Taek Ouh[1], Hyun Woong Cho[2], Jae Kwan Lee[2], Yikyeong Chun[3], Jin Hwa Hong[2]
[1]Korea University Ansan hospital, Obstetrics And Gynecology, Gyeonggi, Korea, Republic of, [2]Korea University Guro Hospital, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of, [3]Korea University Guro Hospital, Pathology, Seoul, Korea, Republic of

Introduction: A joint ESGO/ESTRO/ESP committee updated their evidence-based endometrial cancer guidelines in 2020 and suggested a new risk category including both clinicopathologic and molecular factors. We applied the new risk grouping and compared the ESMO 2013 and ESMO 2016 risk classification system.

Methods: The histological subtype, myometrial invasion, grade, and presence of lympho-vascular space invasion were confirmed. Prior to POLE sequencing, immunohistochemistry was used to analyze the MLH1, MSH2, MSH6, PMS2 and p53. We investigated prognosis and the adjuvant therapy according to the different classifications of the 2013 ESMO, 2016 ESMO, and 2020 ESGO.

Results: A total of 137 endometrial cancer patients were identified. Molecular subtyping showed 6.6% POLEmut, 18.2% MMRd, 16.8% p53abd, and 58.4% NSMP, with a statistically significant difference in overall survival ($p < 0.001$). According to molecular classification, the survival rate for p53abd was the lowest at 34.8%, but all 9 patients with POLEmut survived. Ten patients were reclassified downward, and five patients were reclassified upward. According to the 2020 ESGO classification, the high risk group received no adjuvant therapy in 22.8% and only brachytherapy in 3.2% whereas 16.7% of the low risk group underwent EBRT.

Conclusion/Implications: In comparison to the 2016 ESMO classification, 15 of the 137 (10.9 %) patients were reclassified by the 2020 ESGO new molecular classification. The use of molecular risk categories in 2020 is practical and exhibits a considerable difference in survival. IHC for TP53 and MMR and POLE sequencing can result in a considerable proportion of patients having their risk groups upgraded or downgraded.

PR040 / #109 / Poster Board #: 57

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

METFORMIN AS AN ADJUNCT TO PROGESTIN THERAPY IN ENDOMETRIAL HYPERPLASIA AND EARLY-STAGE ENDOMETRIAL CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Patricia Ann Factor, Koleen Pasamba
University of the Philippines - Philippine General Hospital, Department Of Obstetrics And Gynecology, Manila, Philippines

Introduction: Metformin has been studied for its anti-proliferative effects in endometrial cells, and it is hypothesized to have a synergistic effect with progestin therapy in suppressing endometrial cell proliferation. This systematic review and meta-analysis aimed to determine the efficacy of adjunctive metformin in the clinical regression of endometrial hyperplasia and early-stage endometrial carcinoma.

Methods: This meta-analysis followed the Cochrane methodology and adhered to the PRISMA 2020 guidelines. Randomized controlled trials (RCTs) were included if they enrolled reproductive-aged women with endometrial hyperplasia (with and without atypia) and endometrial carcinoma who were treated with progestin and metformin. The primary outcome was the complete response rate at 12-16 weeks, and secondary outcomes included relapse rate, clinical pregnancy rate, and live birth rate. Odds ratios (ORs) and 95% confidence intervals (CIs) were used for dichotomous data.

Results: Six RCTs were included. The addition of metformin to progestin therapy may increase the complete response rate of endometrial hyperplasia without atypia (OR 5.12, 95% CI 1.17 to 22.41; n=102) and live birth rates (OR 2.51, 95% CI 1.34 to 4.69; n=188) compared to progestin therapy alone, but the certainty of the evidence is low. Metformin did not have a significant effect on the clinical response of endometrial hyperplasia with atypia and endometrial carcinoma, relapse rates, and clinical pregnancy rates.

Conclusion/Implications: Current evidence is uncertain on the potential benefit of metformin with progestin in endometrial hyperplasia and carcinoma. Future high-quality randomized controlled trials with larger sample sizes and longer follow-up periods are needed to support practice recommendations.

PR041 / #821 / Poster Board #: 37

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

LOW ACCURACY OF PREOPERATIVE SAMPLING FOR DIAGNOSING UTERINE CARCINOSARCOMA

Eveline Pham[1], Caroline Van Den Berg[1], Rachel Van Es[1], Floris Groenendijk[2], Helena C. Doorn[1], Heleen Van Beekhuizen[1]
[1]Erasmus MC Cancer institute, University Medical Center Rotterdam, Gynaecology Oncology, Rotterdam, Netherlands, [2]Erasmus MC Cancer institute, University Medical Center Rotterdam, Pathology, Rotterdam, Netherlands

Introduction: Uterine carcinosarcoma (UCS) is a histological subtype of endometrial cancer, with a biphasic morphology. This challenges diagnosing UCS accurately pre-operatively via aspiration biopsy, hysteroscopic biopsies, or dilatation and curettage. This is important as preoperative diagnosis of UCS could impact treatment choices. The aim of this study is to determine the accuracy of each method in diagnosing UCS.

Methods: Pathology reports were acquired from the Dutch Nationwide Pathology Databank of patients diagnosed with UCS in pre- and/or postoperative histology between 2001 to 2021. Patients without available pre- or postoperative pathology reports were excluded. The postoperative histology was set as reference. A 2x2 table was plotted to compute the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for each sampling method.

Results: 1273 patients were included. Overall sensitivity and specificity of preoperative diagnostic sampling was 35.5% and 73.9% respectively. None of the methods were superior. The sensitivity for aspiration biopsy (n=714) was 30%, with a specificity of 82%, a PPV of 85%, and a NPV of 26%. Hysteroscopic biopsy (n=56) had a sensitivity of 30% and a specificity of 79%, while the sensitivity of dilatation and curettage (n=111) was 38% and specificity 67%. The PPV of hysteroscopic biopsy and dilatation and curettage were 73% and 78%, and the NPV of these sampling methods were 37% and 26%

respectively.

Table 1. Results of diagnostic values in endometrial sampling methods

Preoperative diagnostic test [N](%)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Aspiration biopsy 714 (40.5)	30	82	85	26
Hysteroscopic guided biopsy 56 (3.2)	30	78.9	73	37
Dilatation and curettage 111 (6.3)	38	67	78	26
Second aspiration biopsy 45 (2.6)	29	91	91	29
Overall preoperative diagnostic tests 1266 (71.8)	35	74	81	27

Conclusion/Implications: Preoperative sampling methods have a low accuracy in diagnosing UCS, irrespective of the sampling technique. This highlights the need for novel preoperative diagnostic or pathologic assessment, i.e. via p53 immunohistochemistry or hypermethylation profiles.

PR042 / #442 / Poster Board #: 38

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

SURVIVAL BENEFIT OF CYTOREDUCTIVE SURGERY IN PATIENTS WITH PRIMARY STAGE IV ENDOMETRIAL CANCER: A SYSTEMATIC REVIEW & META-ANALYSIS.

Eveline Pham[1], Nanda Horeweg[2], Jacolien Van Der Marel[3], Linda Nooij[1]
[1]Leiden University Medical Center, Gynaecology, Leiden, Netherlands, [2]Leiden University Medical Center, Radiation Oncology, Leiden, Netherlands, [3]Rooseveltkliniek, Gynaecology, Leiden, Netherlands

Introduction: The role of cytoreductive surgery (CRS) in primary stage IV endometrial cancer (EC) remains debatable due to lack of evidence from large studies and heterogeneity of stage IV EC. To address this, we conducted a systematic review and meta-analysis to investigate the survival benefit of CRS in patients with primary stage IV EC.

Methods: Five medical literature databases were systematically searched for original studies reporting survival data on primary stage IV EC by outcome of CRS (complete, optimal, or incomplete resection). Pooled hazard ratio's (HR) were calculated using a random-effects model.

Results: Twelve studies, including 733 patients, were analysed. Of them, 187 (26%) had complete CRS and 146 patients (20%) optimal CRS. In five studies, including 79 patients (11%), complete and optimal CRS were combined. Ten studies reported a significant overall survival (OS) benefit after complete (18-48 months), and optimal CRS (13-34 months) compared to incomplete CRS (7-19 months). In patients with serous EC or extra-abdominal metastasis, a benefit of complete/optimal CRS was also observed. The pooled data showed improved OS from complete/optimal vs. incomplete CRS (HR=0.38, 95% CI 0.21-0.69, p=0.0016) (figure 1). Heterogeneity between studies was substantial.

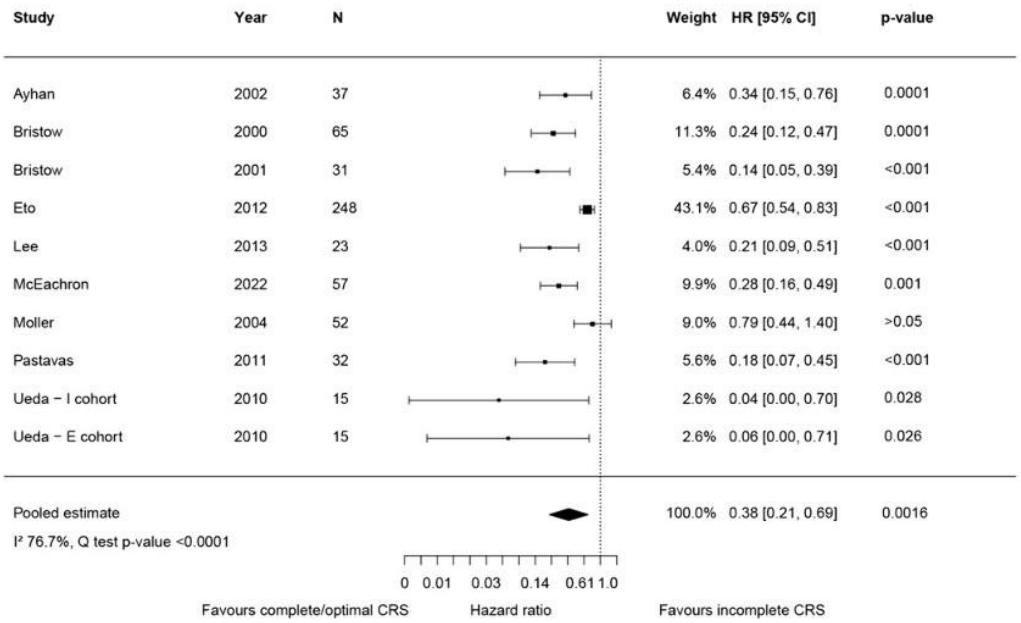


Figure 1. Forest plot of the meta-analysis comparing complete and optimal CRS vs incomplete CRS. The p-value are the values mentioned by the authors.

Conclusion/Implications: This study indicates an OS benefit of complete/optimal CRS for patients with primary stage IV EC, including patients with serous EC or extra-abdominal metastasis. A superior survival benefit was seen after complete CRS compared to optimal CRS. Despite the considerable heterogeneity between studies, our findings suggest that CRS should be considered in the treatment of patients with primary stage IV EC.

PR043 / #416 / Poster Board #: 46

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

RESTAGING UTERINE CANCER PATIENTS WITH THE 2023 FIGO GUIDELINES: CLINICAL CHARACTERISTICS AND SURVIVAL DIFFERENCES.

Rosemary Senguttuvan[1], Nicole Lugo Santiago[1], Adrian Kohut[1], Nora Ruel[2], Jeff Lin[1], Edward Wang[3], Mihae Song[1], Ernest Han[1], Joshua Cohen[1]
[1]City of Hope, Department Of Surgery, Durate, United States of America, [2]City of Hope, Biostatistical Core, Durate, United States of America, [3]City of Hope, Medical Oncology, Duarte, United States of America

Introduction: The landscape of endometrial cancer (EC) classification is undergoing a dramatic transformation as the disease moves towards molecularly driven categorization. Four molecular subtypes have been shown to portend different prognostic outcomes: POLE-hypermutated, p53 mutation, mismatch repair deficient (MMRd), and no specific molecular profile (NSMP). The recently released 2023 FIGO guidelines take into consideration histologic grade/subtype, lymphovascular invasion, and molecular categorization into staging.

Methods: A retrospective review was conducted of EC patients treated between January 2018 and April 2023 at a comprehensive cancer center. Demographic information was collected, and patients were restaged according to the new guidelines. Molecular data was collected. Kaplan-Meyer progression free survival (PFS) 3-year estimates were conducted for subgroups.

Results: 441 patients were included in analysis. 121 (27.4%) patients' stages changed with the new guidelines; 118 patients were upstaged and 3 were downstaged. Upstaged patients originally stage IA had a significantly lower PFS compared to patients with no stage change (74.4% v 93.4%). A trend towards increased PFS was noted in early-stage patients when 2018 staging was compared to 2023 staging (stage I: 83.9% v 88.5%, p=0.2); stage II: 76.5% v 77.1%, p=0.6). Of the molecular data available, MMRd was the most common subtype (58/441, 13.2%) followed by p53 (57/441, 12.9%) and NSMP (51/441, 11.6%). p53 mutation negatively impacted PFS regardless of stage (stage I 28.9%, II 19.0%, III 39.4%, IV
11.7%).

Table 1. Demographics and restaging information

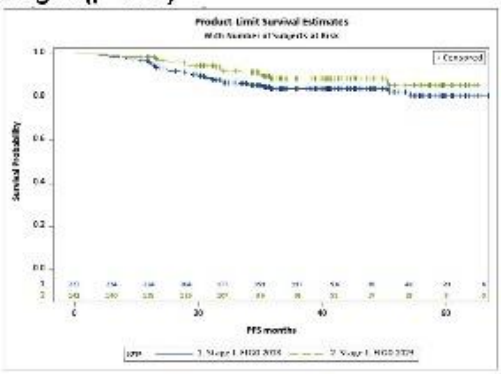
	All Patients (n=441)	2018 FIGO Stage								
		IA (n=151)	IB (n=86)	II (n=41)	IIIA (n=25)	IIIB (n=15)	IIIC1 (n=40)	IIIC2 (n=22)	IVA (n=3)	IVB (n=58)
Age at diagnosis	63.5 (56.9 - 70.0)	62.3 (54.3 - 69.9)	66.1 (60.6 - 72.1)	66.4 (59.2 - 70.4)	56.4 (52.5 - 62.3)	62.0 (59.5 - 75.4)	65.2 (56.7 - 70.7)	67.3 (60.7 - 74.1)	58.5 (44.9 - 78.9)	61.2 (56.5 - 69.2)
Race										
American Indian or Alaska native	4 (0.9%)	1 (0.7%)	3 (3.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Asian	49 (11.1%)	15 (9.9%)	7 (8.1%)	6 (14.6%)	7 (28.0%)	0 (0.0%)	3 (7.5%)	4 (18.2%)	1 (33.3%)	6 (10.3%)
Hawaiian or PI	2 (0.5%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Black	32 (7.3%)	11 (7.3%)	5 (5.8%)	2 (4.9%)	2 (8.0%)	1 (6.7%)	4 (10.0%)	2 (9.1%)	0 (0.0%)	5 (8.6%)
White	323 (73.2%)	116 (76.8%)	66 (76.7%)	29 (70.7%)	13 (52.0%)	12 (80.0%)	29 (72.5%)	14 (63.6%)	2 (66.7%)	43 (74.1%)
Unknown/Declined	31 (7.0%)	7 (4.6%)	5 (5.8%)	4 (9.8%)	2 (8.0%)	2 (13.3%)	4 (10.0%)	2 (9.1%)	0 (0.0%)	4 (6.9%)
Ethnicity										
Hispanic or Latino	149 (33.8%)	50 (33.1%)	29 (33.7%)	9 (22.0%)	6 (24.0%)	6 (40.0%)	13 (32.5%)	9 (40.9%)	2 (66.7%)	26 (44.8%)
Non-Hispanic or Latino	268 (60.8%)	96 (63.6%)	52 (60.5%)	29 (70.7%)	17 (68.0%)	7 (46.7%)	24 (60.0%)	13 (59.1%)	1 (33.3%)	29 (50.0%)
Other or Unk	24 (5.4%)	5 (3.3%)	5 (5.8%)	3 (7.3%)	2 (8.0%)	2 (13.3%)	3 (7.5%)	0 (0.0%)	0 (0.0%)	3 (5.2%)
FIGO grade postoperatively										
1	137 (31.1%)	70 (46.4%)	22 (25.6%)	16 (39.0%)	8 (32.0%)	3 (20.0%)	11 (27.5%)	4 (18.2%)	1 (33.3%)	3 (5.2%)
2	103 (23.4%)	33 (21.9%)	33 (38.4%)	6 (14.6%)	5 (20.0%)	5 (33.3%)	10 (25.0%)	5 (22.7%)	0 (0.0%)	6 (10.3%)
3	198 (44.9%)	46 (30.5%)	31 (36.0%)	18 (43.9%)	12 (48.0%)	7 (46.7%)	19 (47.5%)	13 (59.1%)	2 (66.7%)	49 (84.5%)
FIGO 2023 stage semi-collapsed										
IA1 or IA2	103 (23.3%)	103 (68.2%)								
IA3	3 (0.7%)				3 (12.0%)					
IB	38 (8.6%)		38 (44.2%)							
IIA	16 (3.6%)			16 (39.0%)						
IIB	35 (7.9%)	15 (10.6%)	15 (17.4%)	4 (9.8%)						
IIC	86 (19.5%)	32 (21.2%)	33 (38.4%)	21 (51.2%)						
IIIA1 or IIIA2	21 (4.8%)				21 (84.0%)					
IIIB	1 (0.2%)					1 (6.7%)				
IIIB1 or IIIB2	15 (3.4%)				1 (4.0%)	14 (93.3%)				
IIIC1	40 (9.1%)						40 (100%)			
IIIC2	21 (4.7%)							22 (100%)		
IVA	3 (0.7%)								3 (100%)	
IVB	37 (8.4%)									37 (63.8%)
IVC	21 (4.8%)									21 (36.2%)
Not staged	1 (0.2%)									
Stage was changed 2018 to 2023										
Yes	125 (28.3%)	48 (31.8%)	48 (55.8%)	2 (4.9%)	6 (24.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	21 (36.2%)
No	315 (71.5%)	103 (68.2%)	38 (44.2%)	39 (95.1%)	19 (76.0%)	15 (100%)	40 (100%)	22 (100%)	3 (100%)	39 (67.2%)
Unstaged	1 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Final Histology										
Endometrioid	285 (64.6%)	110 (72.8%)	70 (81.4%)	21 (51.2%)	18 (72.0%)	9 (60.0%)	26 (65.0%)	10 (45.5%)	2 (66.7%)	18 (31.0%)
Endometrioid + high-risk histology	32 (7.3%)	8 (5.3%)	6 (7.0%)	2 (4.9%)	2 (8.0%)	3 (20.0%)	4 (10.0%)	1 (4.5%)	0 (0.0%)	6 (10.3%)
Papillary serous	88 (20.2%)	21 (13.9%)	7 (8.1%)	13 (31.7%)	5 (20.0%)	3 (20.0%)	7 (17.5%)	7 (31.8%)	1 (33.3%)	25 (43.1%)
Other high-risk histology	25 (5.7%)	8 (5.3%)	2 (2.3%)	4 (9.8%)	0 (0.0%)	0 (0.0%)	2 (5.0%)	3 (13.6%)	0 (0.0%)	6 (10.3%)
Mixed high-grade histologies	7 (1.6%)	1 (0.7%)	1 (1.2%)	1 (2.4%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)	3 (5.2%)
Hyperplasia with atypia	2 (0.5%)	2 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
No residual cancer	1 (0.2%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Molecular analysis performed										
Yes	174 (39.5%)	47 (31.1%)	30 (34.9%)	17 (41.5%)	12 (48.0%)	6 (40.0%)	15 (37.5%)	10 (45.5%)	1 (33.3%)	36 (62.1%)
No	267 (60.5%)	104 (68.9%)	56 (65.1%)	24 (58.5%)	13 (52.0%)	9 (60.0%)	25 (62.5%)	12 (54.5%)	2 (66.7%)	22 (37.9%)
Molecular categorization										
MMRd	58 (13.2%)	19 (12.6%)	14 (16.3%)	7 (17.1%)	3 (12.0%)	2 (13.3%)	3 (7.5%)	6 (27.3%)	1 (33.3%)	3 (5.2%)
MMRd+POLE	1 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)
NSMP	51 (11.6%)	16 (10.6%)	9 (10.5%)	3 (7.3%)	6 (24.0%)	1 (6.7%)	5 (12.5%)	0 (0.0%)	0 (0.0%)	11 (19.0%)
POLE	5 (1.1%)	1 (0.7%)	2 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (1.7%)
p53	57 (12.9%)	10 (6.6%)	5 (5.8%)	7 (17.1%)	3 (12.0%)	3 (20.0%)	5 (12.5%)	4 (18.2%)	0 (0.0%)	20 (34.5%)
p53-MMRd-POLE	1 (0.2%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

* One patient was included in analysis that was unstaged

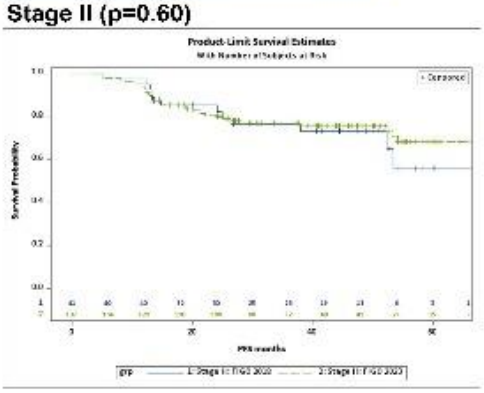
Figure 1. Progression free survival differences in early-stage patients with 2018 to 2023 staging comparison.

	FIGO Stage [2018]	3y PFS estimates	95% CI
I	Stage change (upstaged)	83.9%	(78.3, 88.2)
	No stage change	88.5%	(81.2, 93.0)
II	Stage change (upstaged)	76.5%	(59.6, 87.1)
	No stage change	77.1%	(68.8, 83.4)

Stage I (p=0.20)



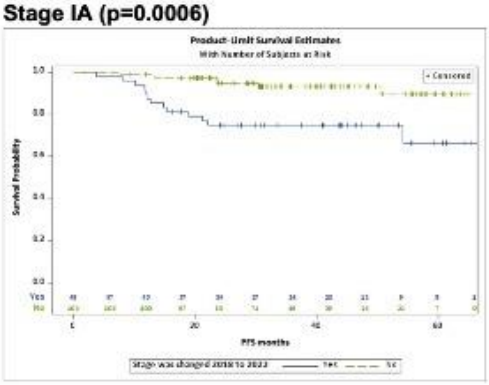
Stage II (p=0.60)



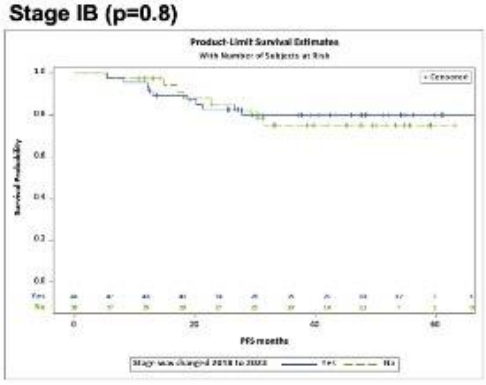
PFS for Stage IA and IB patients, stratified by changed stage status by 2023

	FIGO Stage [2018]	3y PFS estimates	95% CI
IA	Stage change (upstaged)	74.7%	(59.7, 84.8)
	No stage change	93.4%	(85.8, 97.0)
IB	Stage change (upstaged)	80.0%	(64.9, 89.1)
	No stage change	75.2%	(56.2, 86.8)

Stage IA (p=0.0006)



Stage IB (p=0.8)



Conclusion/Implications: Restaging EC patients with the 2023 guidelines resulted in upstaging of a significant proportion of patients with resulting survival differences. p53 mutation impacted survival negatively regardless of stage.

PR045 / #233 / Poster Board #: 58

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

RUCAPARIB PLUS SN38 IN SEROUS ENDOMETRIAL CANCER

Conway Xu[1], Xiaonan Hou[2], Erik Jessen[3], Chen Wang[3], S. John Weroha[2]
[1]Mayo Clinic, Obstetrics And Gynecology, Rochester, United States of America, [2]Mayo Clinic, Medical Oncology, Rochester, United States of America, [3]Mayo Clinic, Quantitative Health Sciences, Rochester, United States of America

Introduction: Serous endometrial cancer (EC) is the deadliest subtype because of high recurrence rates and few proven targeted therapies in this setting. Leveraging a tendency to have homologous recombination deficiency (HRD) and the development of novel topoisomerase inhibitor-based antibody drug conjugates, this study aimed to test synergy between poly (ADP-ribose) polymerase inhibitor, rucaparib, and SN38, an active metabolite of DNA topoisomerase I inhibitor, irinotecan.

Methods: A genomic instability score (GIS) was derived from low-pass whole genome sequencing-based bioinformatics analysis and calculated for 34 patient derived xenograft (PDX) tumors, of which eight had serous histology. EC PDX tumors were treated with rucaparib and SN38 in ex vivo 3D cell culture experiments using RealTime Glo to assess viability after 4-5 days. Synergy was assessed by calculating the combination index (CI) using Chou-Talalay method. Clinical information was extracted for correlation.

Results: 62.5% (5/8) of serous EC PDX tumors had GIS≥42 while only 19.2% (5/26) of non-serous ones did. Synergy (CI<1.0) between rucaparib and SN38 was demonstrated in 85.7% (6/7) of serous EC PDX ex vivo 3D cell culture experiments, but only 62.5% (10/16) of non-serous ones. 66.7% (6/9) of serous EC primary patient 3D cell culture experiments also showed synergy.

Conclusion/Implications: Most serous EC PDX tumors had high GIS, consistent with HRD, compared to a minority of non-serous histologies. Combination therapy demonstrated synergy in almost all serous and most non-serous EC PDX models. Additional studies including more tumors and in vivo correlation are needed to assess the predictive value of GIS on synergy between rucaparib and SN38.

PR046 / #280 / Poster Board #: 54

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

THE GENOMIC LANDSCAPE OF DISTANT METASTATIC ENDOMETRIAL CANCER

Bill Zammarrelli[1], Subhiksha Nandakumar[2], Elizabeth Kertowidjojo[3], Bastien Nguygen[2], Arrnaud Da Cruz Paula[3], Eric Rios-Doria[4], Shaleigh Smith[2], Amir Momeni-Boroujeni[3], Carol Aghajanian[5], Jennifer Mueller[1], Nadeem Abu-Rustum[1], Nikolaus Schulz[2], Lora Ellenson[3], Britta Weigelt[3]
[1]Memorial Sloan Kettering Cancer Center, Gynecology Service, Department Of Surgery, New York, United States of America, [2]Memorial Sloan Kettering Cancer Center, Department Of Epidemiology And Biostatistics, New York, United States of America, [3]Memorial Sloan Kettering Cancer Center, Department Of Pathology, New York, United States of America, [4]University of Washington Medical Center, Division Of Gynecologic Oncology, Department Of Obstetrics And Gynecology, Seattle, United States of America, [5]Memorial Sloan Kettering Cancer Center, Department Of Medicine, New York, United States of America

Introduction: While the genomic landscape of untreated primary endometrial carcinoma (EC) is well characterized, the molecular underpinnings of distant metastatic EC are poorly understood. We sought to define genomic alterations associated with distant metastatic EC.

Methods: We obtained sequencing data from distant metastatic ECs from a total of 1888 ECs subjected to a clinical tumor-normal sequencing panel between 8/2013 and 6/2020; these metastatic ECs were compared against 711 primary ECs using appropriate statistical analyses.

Results: One hundred thirty-seven ECs met the study inclusion criteria, with distant metastases in the lung (n=66, 48%), liver (n=21, 15%), soft tissue (n=15, 11%), distant lymph nodes (n=15, 11%), gastrointestinal tract (n=10, 7%), central nervous system (n=5, 4%), bone (n=4, 3%), and renal system (n=1, 1%). The majority of distant metastases were of copy number (CN)-high (42%) or CN-low (39%) molecular subtype; 18% were microsatellite instability (MSI)-high and 1% were of POLE molecular subtype. Distant EC metastases were significantly more chromosomally unstable compared with primary ECs ($p<0.0001$) and were enriched in AKT1, CTNNB1, ANKRD11, and ZFHX3 mutations. Clinically actionable alterations, particularly tumor mutational burden (TMB) ≥10 mut/Mb and MSI-high status, were significantly less common in metastatic compared with primary ECs (4% vs 29%; $p=0.017$). Epigenetic, PI3K, and TP53 pathways were the most commonly altered pathways among all anatomic sites.

Conclusion/Implications: Compared with primary tumors, distant metastatic ECs exhibited increased chromosomal instability but decreased hypermutator phenotypes. Exploitation of genetic differences to understand the pathogenesis of metastatic EC is necessary to develop biomarkers for targeted therapy.

PR047 / #570 / Poster Board #: 30

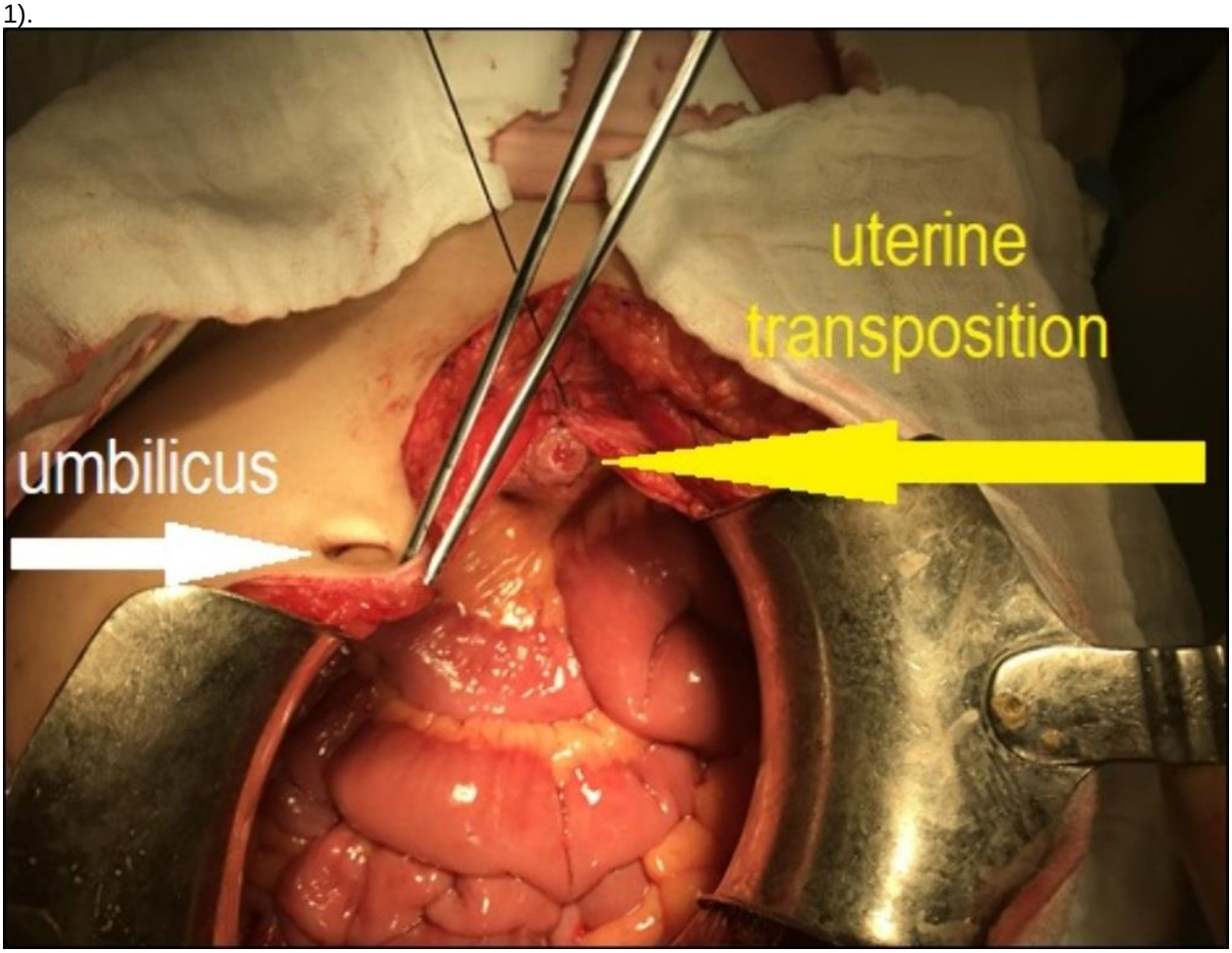
Topic: ***AS05. Fertility/Pregnancy***

UTERINE TRANSPOSITION IN THE TREATMENT OF INVASIVE CERVICAL CANCER FOR PRESERVE FERTILITY

Vitaly Antipov[1], Evgeniya Moskovskaya[1], Alena Chernyashova[2], Sergei Krasilnikov[3]
[1]LTD Vita clinic, Gynecologyc Oncology, Moscow, Russian Federation, [2]Oncology Research Institute Tomsk, Gynecologic Oncology, Tomsk, Russian Federation, [3]E.N. Meshalkin National Medical Research Center, Ministry of Health of Russia, Novosibirsk, Gynecologic Oncology, Novosibirsk, Russian Federation

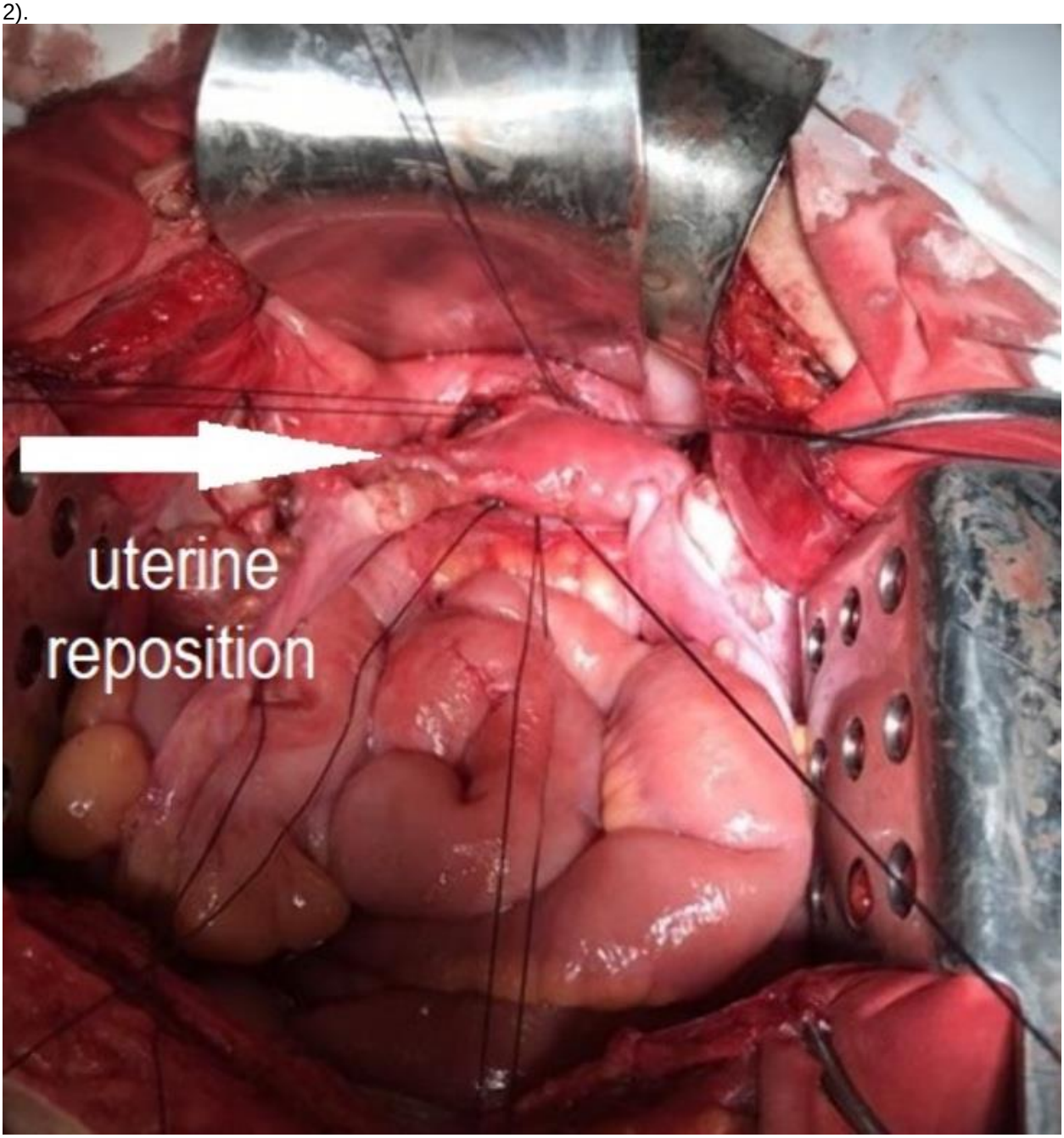
Introduction: Indications for a radical trachelectomy can be significantly expanded if an adjuvant concurrent chemoradiotherapy can be provided. These conditions can be achieved by the uterine transposition which must be done during the period of radiotherapy. When the radiation treatment is completed, the uterus can be repositioned back to the pelvic.

Methods: Our research has included 11 patients with stage Ib1-IIb cervical cancer. Median of their age is 29 year old. At the first step of treatment, 2-3 courses of chemotherapy were carried out. At the second step radical trachelectomy (Piver type III) with uterine and ovarian transposition were done (photo 1).



The oncological stages of operation corresponded to a routine radical trachelectomy. Paraumbilically uterine transposition created conditions for performing the radiotherapy. The third step included a

concurrent chemoradiotherapy. On the next step of treatment uterine reposition with utero-vaginal anastomosis was conducted (photo
2).



Today all the patients has no sign of recurrence and may start to realize the pregnancy.

Results: The median observation is 23,4 months so far. All our patient's menses have been recovered. No one has any signs of recurrence. Three of them are preparing to the in vitro fertilization.

Conclusion/Implications: The uterine transposition enhanced limits of treatment for patients with stage Ib1-IIb cervical cancer and makes feasible to provide a radiotherapy according to the prescribed standards and, haven't negative effect for ovarian function and menses. It is very important to continue and carrying out research which make possible to preserve fertility for patients with cancer.

PR048 / #466 / Poster Board #: 73

Topic: ***AS07. Global Health/Economic Challenges***

COST-EFFECTIVENESS ANALYSIS OF SINGLE-DOSE OR 2-DOSE OF BIVALENT, QUADRIVALENT, OR NONAVALENT HPV VACCINE IN A LOW/MIDDLE INCOME COUNTRY SETTING.

Wichai Termrungruanglert[1], Apichai Vasuratna[1], Nipon Khemapech[1], Piyalamporn Havanond Havanond[1], Tanitra Tantitamit[2]
[1]Chulalongkorn University, Department Of Obstetrics And Gynecology, Bangkok, Thailand, [2]Srinakharinwirot University, Obstetrics And Gynecology, Nakhonnayok, Thailand

Introduction: To evaluate the health impact and economic benefits of one dose or two doses of 2-valent (2vHPV), 4-valent (4vHPV), or 9-valent (9vHPV) HPV vaccine compared to no vaccination along with primary HPV testing in a low/middle income country setting, specifically in Thailand.

Methods: A Markov model was used to simulate HPV infection and cervical cancer in a cohort of 100,000 12-year-old HPV-naive girls. The study compared nine strategies: one dose and two doses of 2vHPV (Cervarix®), 2vHPV (Cecolin®), 4vHPV (Gardasil®), 9vHPV vaccine (Gardasil9®), and no vaccination. Main outcome measure was quality-adjusted life year (QALY) of each strategy. Incremental cost-effectiveness ratios (ICER) were estimated over a lifetime horizon, univariate and probabilistic sensitivity analyses were conducted for uncertain variables in different scenarios.

Results: In the base case scenario, all vaccination programs resulted in 41,298-71,057 QALYs gained with a cost saving of 14,914,186-19,821,655 USD compared to no vaccination. Based on the incremental analysis, two doses of 9vHPV vaccine was the most cost-effective strategy with an ICER of 406 USD/QALY. Sensitivity analysis showed that the probability of being cost-effective for two doses of 9vHPV vaccine was 80%, and uncertainty around the costs of vaccination and vaccine efficacy caused the largest variation in the cost-effectiveness findings.

Conclusion/Implications: Two doses of 9vHPV vaccine along with a primary HPV test for screening program represent the most cost-effective option for school-based HPV vaccination of 12-year-old girls in Thailand, with a lower willingness to pay of one time the per-capita GDP. This finding provides important evidence to policymakers for cervical cancer prevention.

PR049 / #741 / Poster Board #: 89

Topic: ***AS08. Gynecologic Pathology/Cytology and Disease Pathogenesis***

IMPROVED RISK PREDICTION IN HPV-ASSOCIATED ENDOCERVICAL ADENOCARCINOMA THROUGH ASSESSMENT OF BINARY SILVA PATTERN-BASED CLASSIFICATION: INTERNATIONAL MULTICENTER RETROSPECTIVE STUDY OF THE INTERNATIONAL SOCIETY OF GYNECOLOGICAL PATHOLOGISTS

Aime Powell[1], Anjelica Hodgson[2], Paul A. Cohen[3], Joseph Rabban[4], Kay Park[5], W. Glenn Mccluggage[6], C. Blake Gilks[7], Contributors From The International Society Of Gynecological Pathologists (Isgyp)[8], Naveena Singh[7], Esther Oliva[9]
[1]University of Notre Dame Australia, Institute For Health Research, Fremantle, Australia, [2]Toronto General Hospital, Laboratory Medicine Program, Toronto, Canada, [3]St John of God Subiaco Hospital and The University of Western Australia, Division Of Obstetrics And Gynaecology, Crawley, Perth, Australia, [4]University of California San Francisco, Department Of Pathology, San Francisico, United States of America, [5]Memorial Sloan Kettering Cancer Center, Department Of Pathology, New York, United States of America, [6]Belfast Health and Social Care Trust,, Department Of Histopathology, Belfast, United Kingdom, [7]Vancouver General Hospital, Department Of Anatomic Pathology, Vancouver, Canada, [8]International Society of Gynecological Pathologists, Isgyp, New York, United States of America, [9]Massachusetts General Hospital, Department Of Pathology, Boston, United States of America

Introduction: Endocervical adenocarcinomas (EACs) are neoplasms associated with diverse pathogenesis, morphology, and clinical behavior. The Silva pattern-based classification categorizes HPV-associated EACs based on the morphology of the invasion and predicts lymph node metastasis and recurrence. Traditionally the Silva classification was a three-tier system (pattern A, B, and C). A two-tier/binary system has recently been proposed whereby tumors are classified into low risk (pattern A/pattern B without lymphovascular invasion (LVSI)) and high risk (pattern B with LVSI/pattern C). Our aim was to develop a prognostic model for surgically treated FIGO stage IA2-IB3 EACs that incorporates patient age, LVSI, FIGO stage and three- and two-tier Silva systems.

Methods: The International Society of Gynecological Pathologists (ISGyP) established a multicenter consortium to pool de-identified individual patient data for patients with HPV-associated EACs. All participating pathologists completed mandatory online training.

Results:

Table 1. Characteristics of the study cohort (n = 792), stratified by pattern of invasion/Silva pattern

Characteristic	Pattern of invasion/Silva Pattern								p-value
	Pattern A		Pattern B *(no LVSI)*		Pattern B *(+ LVSI)*		Pattern C		
	n = 198	%	n = 195	%	n = 65	%	n = 334	%	
Age (years)									
< 50	149	75.3	151	77.4	56	86.2	226	67.7	0.005
≥ 50	49	24.7	44	22.6	9	13.8	108	32.3	
FIGO stage									
IA2	49	24.8	34	17.4	7	10.8	22	6.6	0.000
IB1	107	54.0	106	54.4	32	49.2	153	45.8	
IB2	36	18.2	48	24.6	22	33.9	127	38.0	
IB3	6	3.0	7	3.6	4	6.1	32	9.6	
IECC tumor type									
HPV adenocarcinoma, usual type	189	95.4	188	96.4	58	89.2	307	91.2	0.053
HPV adenocarcinoma, mucinous intestinal type	9	4.6	5	2.6	5	7.7	21	6.3	
HPV adenocarcinoma, mucinous NOS type	-	-	2	1.0	2	3.1	2	0.6	
HPV adenocarcinoma, mucinous signet-ring cell type	-	-	-	-	-	-	4	1.2	
Tumor grade									
G1	153	77.3	87	44.6	19	29.2	68	20.4	0.000
G2	43	21.7	94	48.2	41	63.1	222	66.5	
G3	1	0.5	4	2.1	3	4.6	37	11.0	
Not reported	1	0.5	10	5.1	2	3.1	7	2.1	
Lymphovascular invasion status									
Absent	198	100	195	100	-	-	215	64.4	0.000
Present	-	-	-	-	65	100	119	35.6	
Most extensive surgical procedure performed									
Excisional biopsy (CKC or LEEP)	2	1.0	2	1.0	-	-	2	0.6	0.016
Trachelectomy	15	7.6	20	10.3	8	12.3	20	6.0	
Extrafascial hysterectomy (+/- BSO)	20	10.1	15	7.7	-	-	14	4.2	
Radical hysterectomy (+/- BSO)	161	81.3	158	81.0	57	87.7	298	89.2	
Recurrence									
Yes	7	3.5	12	6.2	6	9.2	48	14.4	0.000
No	191	96.5	183	93.8	59	90.8	286	85.6	
Survival outcome									
Alive	194	98.0	192	98.5	62	95.4	321	96.1	0.041
Died of disease	1	0.5	2	1.0	3	4.6	12	3.6	
Died of unrelated causes*	3	1.5	1	0.5	-	-	1	0.3	

Abbreviations: BSO, bilateral salpingo-oophorectomy; CKC, cold knife cone; FIGO stage, International Federation of Gynecology and Obstetrics stage; LEEP, loop electrosurgical excision procedure; LVSI, lymphovascular space invasion; NOS, not otherwise specified.
*Died of unrelated causes data was excluded from the Fischer's exact test.

Table 2. Multivariate (adjusted) competing risk model investigating factors (including the pattern of invasion/Silva pattern as a binary classification system) associated with disease recurrence and disease specific survival for the cohort (n = 792).

Characteristic	Adjusted model					
	Disease recurrence			Disease specific survival		
	sHR	95% CI	p-value	sHR	95% CI	p-value
Age (years)						
<50	0.70	0.52 – 0.94	0.017	0.82	0.35 – 1.94	0.657
≥50	1.0	-	-	1.0	-	-
FIGO stage						
Stage IA2	0.33	0.10 – 1.02	0.055	0.58	0.11 – 3.01	0.513
Stage IB1	1.0	-	-	1.0	-	-
Stage IB2	1.17	0.79 – 1.73	0.423	1.43	0.70 – 2.92	0.332
Stage IB3	0.84	0.25 – 2.80	0.780	1.31	0.16 – 10.95	0.801
Pattern of invasion/Silva pattern (binary classification)						
Pattern A & Pattern B (-LVSI)	0.40	0.24 – 0.65	0.000	0.25	0.08 – 0.77	0.016
Pattern B (+LVSI) & Pattern C	1.0	-	-	1.0	-	-

Abbreviations: FIGO stage, International Federation of Gynecology and Obstetrics stage; LVSI, lymphovascular space invasion.

Our cohort comprised 792 HPV-associated EACs (Table 1). On multivariate analysis a binary Silva system was associated with recurrence-free and disease specific survival ($p<0.05$) while FIGO 2018 stage I substages were not. In the current three-tiered system, disease specific survival for patients with pattern B tumors did not significantly differ from those with pattern C tumors while those with pattern A tumors did (Table 2).

Conclusion/Implications: These findings highlight the need for future prospective studies to further investigate the prognostic significance of stage I HPV-associated EAC substaging and the inclusion of the binary Silva pattern of invasion classification, which includes LVSI status, as a component of treatment recommendations.

PR050 / #373 / Poster Board #: 59

Topic: ***AS08. Gynecologic Pathology/Cytology and Disease Pathogenesis***

CLINICOPATHOLOGIC AND GENOMIC ANALYSIS OF UTERINE SEROUS CARCINOMAS ARISING FROM ENDOMETRIAL HYPERPLASIA

Tiffany Sia[1], Douglas Allison[2], Arrnaud Da Cruz Paula[3], Edaise Da Silva[2], Qiqi Ye[2], Pier Selenica[2], Fresia Pareja Zea[2], Hunter Green[2], Nadeem Abu-Rustum[1], Britta Weigelt[2], Lora Ellenson[2]
[1]Memorial Sloan Kettering Cancer Center, Gynecology Service, Department Of Surgery, New York, United States of America, [2]Memorial Sloan Kettering Cancer Center, Pathology, New York, United States of America, [3]i3S Instituto de Investigação e Inovação em Saúde, Pathology, Porto, Portugal

Introduction: Uterine serous carcinoma (USC) typically arises from atrophic endometrium but may be associated with hyperplasia in 5-10% of cases. We sought to identify USC with concurrent hyperplasia and define if i) they are molecularly related, and ii) USC associated with hyperplasia are genetically distinct from those without.

Methods: Patients diagnosed with USC and hyperplasia on hysterectomy specimen between 1/2014 – 2/2021 were identified. Slides were reviewed by two gynecologic pathologists. Hyperplasia and carcinoma were microdissected separately and subjected to tumor-normal panel sequencing. Results were compared to atrophy-associated USC.

Results: Of 291 USCs with clinical sequencing and slides available for review, 10 cases were identified (3%), and eight cases with sufficient tissue were included. Recurrently mutated genes included TP53 (100%), PIK3CA (50%), PPP2R1A (50%), ARID1A (38%), and PTEN (25%). In seven patients (87.5%), USC and hyperplasia were clonally related and shared multiple mutations, including TP53 in 4 (57%) cases. In one clonally related case, USC and TP53 wild-type hyperplasia shared 1 of 11 mutations (PIK3CA hotspot mutation) while being distinct at the copy number level. In the last case, USC and hyperplasia were unrelated at the genetic level, and the hyperplasia was TP53 wild-type. The prevalence of ARID1A mutations was higher in hyperplasia-associated USC compared to atrophy-associated USC (43% vs. 0%, p=0.02).

Conclusion/Implications: Hyperplasia and USC were clonally related in most cases, commonly harboring TP53 hotspot mutations in both components. ARID1A mutations were more prevalent in hyperplasia- compared to atrophy-associated USC. These results suggest a novel origin of tumorigenesis in this rare subset of endometrial cancers.

PR051 / #484 / Poster Board #: 25

Topic: ***AS08. Gynecologic Pathology/Cytology and Disease Pathogenesis***

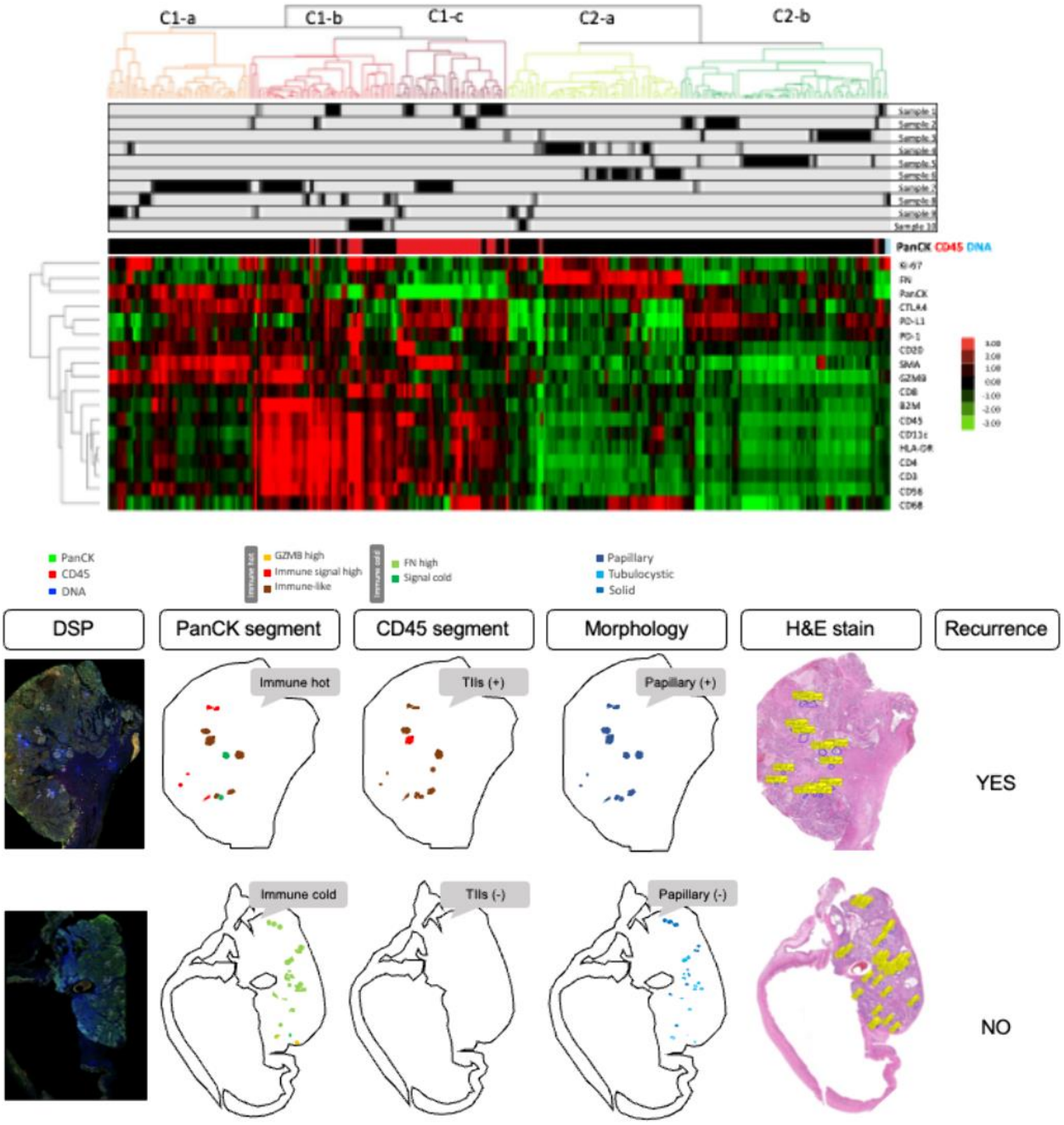
SPATIAL PROFILING OF OVARIAN CLEAR CELL CARCINOMA (OCCC) REVEALS IMMUNE-HOT FEATURES

Ya-Ting Tai[1], Wei-Chou Lin[2], Duncan Yi-Te Wang[3], Jieru Ye[2], Tuan Zea Tan[4], Lin-Hung Wei[5], Ruby Yun-Ju Huang[3]
[1]ational Taiwan University, Obstetrics & Gynecology, Taipei, Taiwan, [2]National Taiwan University Hospital, Pathology, Taipei, Taiwan, [3]National Taiwan University, School Of Medicine, Taipei, Taiwan, [4]Cancer Science Institute of Singapore, Genomics And Data Analytics Core, Singapore, Singapore, [5]National Taiwan University Hospital, Obstetrics And Gynecology, Taipei, Taiwan

Introduction: OCCC has high incidence in Asia with frequent occurrence at early stage but without sufficient data on molecular stratification for high-risk patients. Recently, immune-hot features have been proposed as an indicator for poor prognosis for early-stage OCCC. Specific patterns of intra-tumoral heterogeneity (ITH) associated with immune-hot features need to be defined.

Methods: Formalin-fixed paraffine embedded (FFPE) tumor sections from 10 early-stage OCCC patients were included. Digital Spatial Profiling (DSP) of 18 protein targets was conducted by using the nanoString GeoMx system to profile selected regions of interest (ROIs) based on the reference H&E staining morphology. Areas of illumination (AOIs) were defined according to ROI segmentation by the fluorescence signals of visualization markers pan-cytokeratin (PanCK), CD45, or DNA.

Results: Unsupervised hierarchical clustering of 252 AOIs showed 5 distinct clusters. PanCK+ AOIs with ‘immune-like (C1-c)’ (100%) and ‘fibronectin-high (C2-a)’ (45.3%, Chi-square p=2.8E-04) features were associated with OCCC recurrence. Tumor infiltrating immune cells (TIIs) have higher frequencies in PanCK segments with ‘immune signal high (C1-b)’ (45%, Chi-square: p=0.046) and ‘immune-like’ (25%, Chi-square p=0.046) features. Correlating with morphology, tumor samples with recurrence showed higher frequency (54.7%, Chi-Square p =1.01E-04) of papillary pattern. Plus, ROIs with papillary pattern have extremely high frequency (100%) of PanCK segments of ‘immune-like’ feature, higher frequency (65.2%, Chi-Square p=4.99E-04) of TIIs, and macrophage lineage immune mimicry with high intensity of CD68.



Conclusion/Implications: Spatial profiling of early-stage OCCC tumors revealed that immune mimicry of tumor cells, the presence of TIIs, and papillary pattern in morphology were associated with recurrence.

PR052 / #439 / Poster Board #: 26

Topic: ***AS11. Ovarian Cancer***

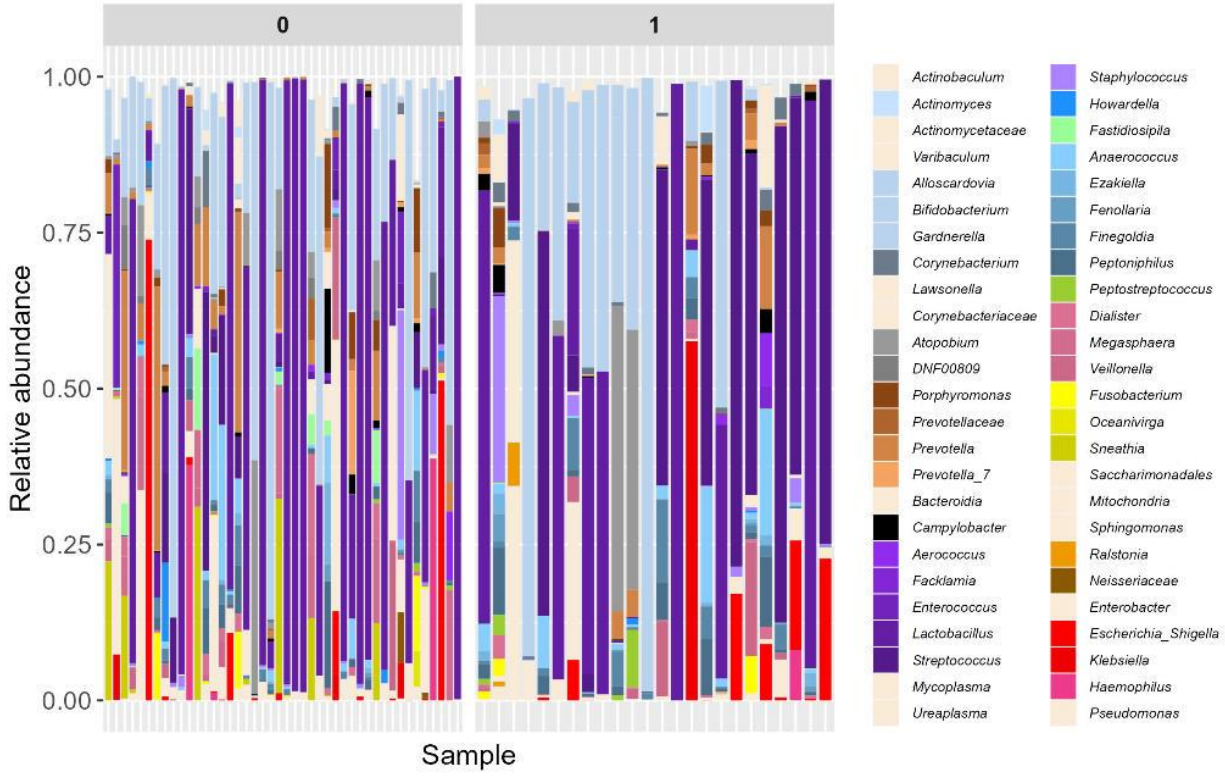
DISTINCT VAGINAL MICROBIOME OVARIAN CANCER PATIENTS – A POSSIBLE SCREENING AND PROGNOSTIC BIOMARKER?

Ronli Hershkovitch Neiterman[1], Lina Salman[1], Shilhav Meisel-Sharon[1,2], Tomer Bar Noy[1], Renat Reens Carmel[1], Shay Hantisteanu[1], Raphy Zarecki[1], Lea Reshaf[1], Mordechai Hallak[1], Haim Werner[1], Ilan Bruchim[1]
[1]Hillel Yaffe medical center, Obstetrics And Gynecology, Hadera, Israel, [2]Hillel yaffe medical center, Obstetrics And Gynecology, Hadera, Israel

Introduction: Microbiome plays an important role in development of cancer and response to chemotherapy. We aim to examine the significance of vaginal microbiome in epithelial ovarian cancer.

Methods: A prospective cohort study was conducted for evaluating the vaginal microbiome in newly diagnosed epithelial ovarian cancer (NEOC) patients, post-chemotherapy (PC) patients and healthy women. Samples were collected using a swab. DNA was extracted and amplified by PCR using universal primers of the prokaryotic 16S ribosome. Next-generation sequencing and taxonomical classification was then performed.

Results: Vaginal swab samples were collected from 21 NEOC patients, 27 PC and 22 controls. The microbiome analysis revealed statistically significant findings. Clostridiales bacterium S5 A14a and Anaerovoracaceae family were found to be abundant in patient who had previous malignancies ($p<0.01$) Clostridiales bacterium S5 A14a was also abundant in patient who had no pregnancies in the past ($p<0.001$). Clostridia UCG 014 family was found prominent in patient who died of disease ($p<0.01$).



Conclusion/Implications: We demonstrated a significant difference in vaginal microbiome in EOC patients who had a history of other malignancies. Interestingly, the Clostridiales species that are prominent are studied as a risk factor for developing tumors in PTEN carrier and Anaerovoracaceae was linked to esophageal cancer. We also demonstrated Clostridia UCG 014 abundance in patients that died of disease, a finding that was previously shown in mice studies and in patients with lung cancer. This may suggest a group of patients that can benefit from microbiome mapping as a screening tool and as a marker for poor prognosis.

PR053 / #1264 / Poster Board #: 3

Topic: ***AS11. Ovarian Cancer***

TREATMENT-FREE SURVIVAL ANALYSES FOR TRIALS OF PARP INHIBITORS MAINTENANCE THERAPY IN RELAPSED OVARIAN CANCER

Libing Xiang[1], Lina Shen[1], Yifei Tang[2], Yi Guo[3], Yulian Chen[1], Yixuan Liu[1], Rong Jiang[1], Zhenyu Wu[3], Rongyu Zang[1]
[1]Zhongshan Hospital, Fudan University, Ovarian Cancer Program, Department Of Gynecologic Oncology, Shanghai, China, [2]Fudan University, School Of Basic Medical Sciences, Shanghai, China, [3]School of Public Health, Fudan University, Department Of Biostatistics, Shanghai, China

Introduction: Improved overall survival (OS) with PARP inhibitors maintenance therapy in platinum-sensitive relapsed ovarian cancer (PSROC) was not determined. We performed treatment-free survival (TFS) with quality-adjusted OS analyses to measure their effects.

Methods: We pooled available data for TFS analysis from three trials (Study 19, SOLO2, and ARIEL3). OS was divided into time on protocol treatment exposure (T), time to subsequent treatment initiation or death (TFS), and time after the first subsequent therapy or death (REL). TFS with quality-adjusted OS analyses were calculated by multiplying mean time in each health state by its assigned utility (quality-adjusted OS = $u_t \times T + TFS + u_{rel} \times REL$) for two cohorts: all (BRCAm, BRCAwt, or unknown) or BRCAm patients, the area under each KM curve estimated using restricted mean time with threshold utility analyses.

Results: Restricted mean treatment duration was longer with PARP inhibitors than with placebo (all patients: 16.3 vs. 7.4 months, difference, 8.9 months, 95%CI 8.1-9.7; BRCAm: 17.1 vs. 8.1 months, 9.0, 8.1-9.9). Mean TFS was longer with PARP inhibitors (7.9 months) than with placebo (4.3 months; difference, 3.6, 2.0-5.1) among BRCAm patients. REL was longer with placebo (all patients: 11.7 vs. 20.5 months, -8.8, -10.1 to -7.6; BRCAm: 8.9 vs. 19.7 months, -10.8, -12.5 to -9.0). PARP inhibitors provided more quality-adjusted OS than placebo with a wider range of utility-weight values for BRCAm patients (-6.0 to +7.0 months) rather than all patients (-7.0 to +5.0 months).

Conclusion/Implications: BRCAm patients rather than all-patients population benefited from PARP inhibitors maintenance therapy in PSROC.

PR054 / #1517 / Poster Board #: 4

Topic: ***AS11. Ovarian Cancer***

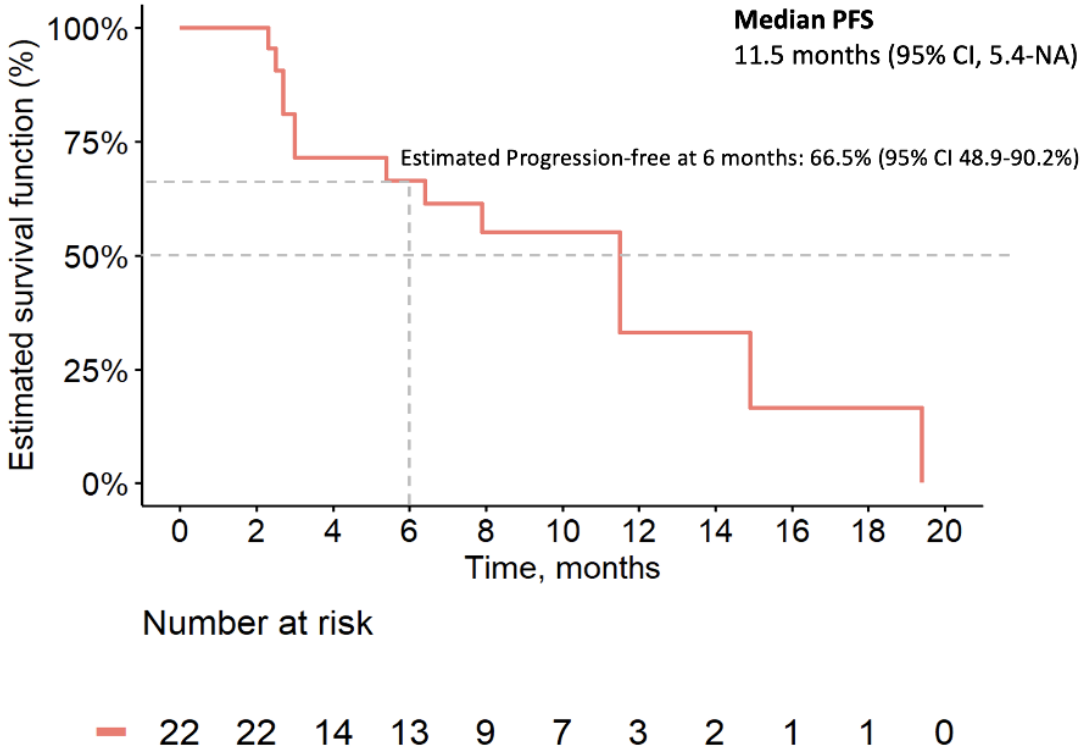
A SINGLE-ARM, PHASE II STUDY OF NIRAPARIB AND BEVACIZUMAB MAINTENANCE IN PATIENTS WITH PLATINUM-SENSITIVE, RECURRENT OVARIAN CANCER PREVIOUSLY TREATED WITH A PARP INHIBITOR (KGOG 3056/NIRVANA-R)

Hyun-Woong Cho[1], Jeong-Yeol Park[2], Byoung Gie Kim[3], Jae-Weon Kim[4], Myong Cheol Lim[5], Min Chul Choi[6], Dae Hoon Jeong[7], Jung-Yun Lee[8]
[1]Korea University Guro Hospital, Obstetrics & Gynecology, Seoul, Korea, Republic of, [2]Asan Medical Center, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of, [3]Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea, Republic of, [4]Seoul National University, Obstetrics And Gynecology, Seoul, Korea, Republic of, [5]Center for Gynecologic Cancer, National Cancer Center, Department Of Obstetrics And Gynecology, Goyang, Korea, Republic of, [6]CHA Bundang Medical Center, Comprehensive Gynecologic Cancer Center, Seongnam, Korea, Republic of, [7]Busan Paik Hospital, College of Medicine, Inje University, Department Of Obstetrics And Gynecology, Busan, Korea, Republic of, [8]Yonsei University Health System, Obstetrics And Gynecology, Seoul, Korea, Republic of

Introduction: The aim of NIRVANA-R trial is to investigate the efficacy of niraparib in combination with bevacizumab as a maintenance therapy in platinum-sensitive ovarian cancer patients who were previously treated with a PARP inhibitor(PARPi).

Methods: This study includes patients with platinum-sensitive recurrent ovarian cancer who had received at least two previous courses of platinum-containing therapy and had been treated with a PARPi. Patients who had responded to the last platinum regimen are eligible to participate in this study. Forty-four patients will be recruited. All enrolled patients are treated with niraparib and bevacizumab for maintenance therapy until disease progression. The primary endpoint of the study is 6-month progression-free survival (PFS) rate. A Simon 2-stage design is utilized. Target accrual is 22 patients in the first stage; 13 or more patients without progressive disease within 6 months is required to proceed to second stage.

Results:



We report the results from the first stage. Median age was 56 years old, high grade serous and motst of the patients (90.9%) had high-grade serous carcinoma. Of the 22 patients from the first stage, 9 had progressive disease within 6 months (6-month PFS rate 66.5%, 95% CI 48.9-90.2%). The efficacy boundary to proceed to the second stage was met. No grade 4 or 5 treatment-related adverse events (TREAs) were reported, and no TRAEs leading to treatment discontinuation.

Conclusion/Implications: Our findings indicate encouraging safety and activity of niraparib + bevacizumab as a maintenance therapy in platinum-sensitive ovarian cancer patients who were previously treated with a PARPi.

PR055 / #936 / Poster Board #: 14

Topic: ***AS11. Ovarian Cancer***

INFLUENCE OF SPATIAL TUMOUR HETEROGENEITY ON HOMOLOGOUS RECOMBINATION DEFICIENCY SCORES FOR HIGH GRADE SEROUS OVARIAN CANCER PATIENTS

Christina Fotopoulou[1], Elizabeth Christie[2], Marc Lorentzen[1], Maiqi Liu[1], Edward Curry[1], Chun Hei Kwok[1], Katherine Nixon[1], Jennifer Ploski[1], James Clark[1], Iain Mcneish[1], Jonathan Krell[1], Paula Cunnea[1]
[1]Imperial College London, Surgery And Cancer, London, United Kingdom, [2]Peter MacCallum Cancer Centre, Department Of Oncology, Melbourne, United Kingdom

Introduction: Extensive genomic instability and heterogeneity are characteristics of high-grade serous ovarian cancer (HGSOC), with deficiency in homologous recombination (HR) repair has been reported for approximately 50% of HGSOC patients. Testing tumours for HR-deficiency (HRD) status is now a clinically applicable test, with a HR score of >42 suggestive of HRD and thus, platinum or PARP-inhibitor sensitivity in HGSOC. We aimed to determine the influence of spatial heterogeneity on HR scores in disseminated HGSOC.

Methods: An algorithm detecting genomic scar HR scores was applied to genomic data from three cohorts of multi-site tumour samples – in-house Hammersmith hospital (HH) 45 patients n=5 tumours per patient; GSE38787 (n=24 patients) and GSE40546 (n=14 patients). A HR score is an unweighted sum of three independent measures of genomic instability: loss of heterozygosity (LOH), telomeric allelic imbalance (TAI), and large-scale state transition (LST). A cut-off >42 denotes HR-deficient.

Results: Heterogeneity in tumour HR scores were detected in each cohort with patients presenting with either all HRD tumours, all HRP tumours or mixed HR scores, showing both HRD and HR-Proficient (HRP) tumour scores: HH (22%); GSE38787 (17%); and GSE40546 (28%). Within the HH cohort, survival analysis revealed that patients with all HRP tumours and mixed HR status had worse survival (progression-free survival p=0.0052; overall-survival p=0.00092) than patients with all HRD tumours.

Conclusion/Implications: Our data demonstrating differences in HRD/HRP scores proposes that HR status may vary across disseminated HGSOC. Thus, implying that testing a single tumour biopsy may not accurately portray HGSOC tumour biology and could incorrectly guide clinical decision-making.

PR056 / #32 / Poster Board #: 17

Topic: ***AS11. Ovarian Cancer***

CLINICAL CHARACTERISTICS AND ONCOLOGICAL OUTCOMES OF RECURRENT ADULT GRANULOSA CELL TUMOR OF OVARY: A RETROSPECTIVE STUDY OF SEVENTY PATIENTS

Yu Gu[1], Yang Xiang[2]
[1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Department Of Obstetrics And Gynecology,, Beijing, China, [2]Peking Union Medical College Hospital, Department Of Obstetrics And Gynecology, Beijing, China

Introduction: To describe the clinicopathological characteristics of recurrent adult granulosa cell tumor (AGCT) and identify the risk factors for recurrence.

Methods: Seventy recurrent AGCT patients between 2000-2020 were retrospectively reviewed (Figure1). The primary outcomes were progression free survival after first recurrence (PFS-R), overall survival after first recurrence (OS-R) and recurrence frequency. The Kaplan-Meier (KM) analysis, Cox proportional hazard analysis, and the Prentice, Williams and Peterson counting process (PWP-CP) model were adopted.

Results: The 5-year PFS-R was 29.3%, and the 5-year OS-R was 94.9%. KM analysis demonstrated that patients with distant recurrence and PFS1 ≤60 months had worse PFS-R (P<0.05), and patients with PFS-R ≤ 33 months had worse OS-R (P=0.023). PFS1≤60 months (hazard ratio, HR 1.9, 95% confidence interval, CI, 1.1-3.4, P=0.028) was an independent risk factor for PFS-R, and local lesion at recurrence (HR 0.488, 95%CI 0.3-0.9, P=0.027) was an independent protective factor for PFS-R. PFS-R ≤33 months (HR 5.5, 95%CI 1.2-25.3, P=0.028) was an independent risk factor for OS-R (Table3). The PWP-CP analysis showed laparoscopic operation could significantly increase recurrence times (P=0.002, HR=3.4), and R0 at each recurrence operation could significantly decrease recurrence frequency (P < 0.001, HR < 0.001).

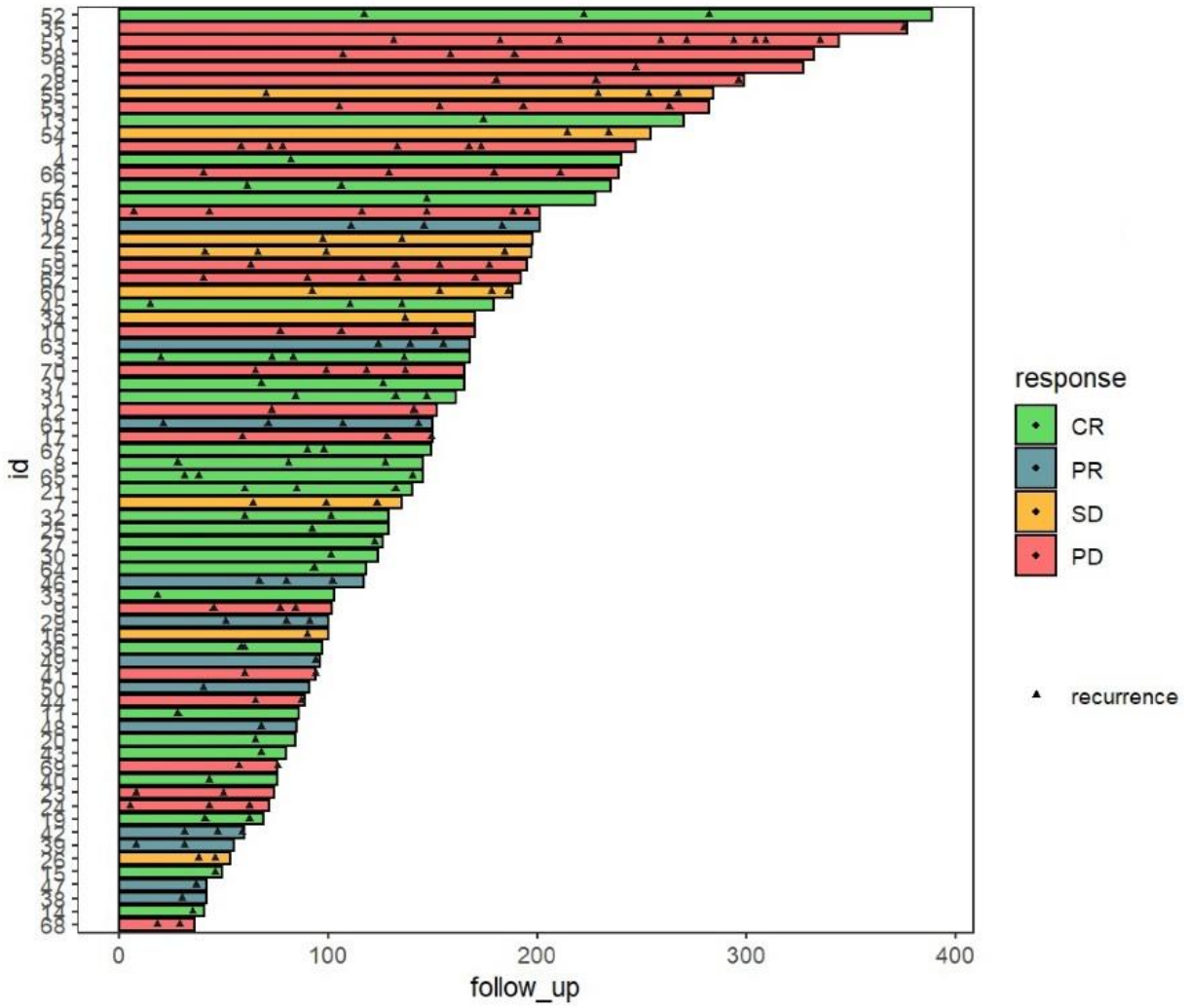


Table 3 Univariate and multivariate analysis of PFS-R and OS-R.

	PFS-R				OS-R			
	Univariate		Multivariate		Univariate		Multivariate	
	P	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)
Age≤46	0.113	1.618 (0.893, 2.931)			0.145	0.405(0.120, 1.366)		
Operation approach (TA)	0.966	0.982 (0.415, 2.322)			0.205	0.353(0.071, 1.769)		
Adjuvant chemotherapy	0.636	0.866 (0.477, 1.572)			0.787	0.846(0.252, 2.838)		
Tumor size(≤7.1cm)	0.339	0.740 (0.399, 1.371)			0.608	0.674(0.149, 3.045)		
Recurrence site(single)	0.079	0.551 (0.284, 1.071)			0.072	0.145(0.018, 1.186)	0.056	0.116 (0.013, 1.059)
Recurrence site(local)	0.018	0.466 (0.247, 0.876)	0.027	0.488(0.259, 0.922)	0.295	0.519(0.152, 1.773)		
R0 (first recurrence surgery)	0.179	0.642 (0.336, 1.226)			0.269	0.510(0.154, 1.684)		
PFS1≤60 months	0.017	2.007 (1.130, 3.565)	0.028	1.911(1.073, 3.402)	0.079	3.446(0.868, 13.683)	0.258	2.222 (0.557, 8.862)
PFS-R≤33months	-	-			0.023	5.156(1.249, 21.284)	0.028	5.505 (1.199, 25.259)

Conclusion/Implications: The present study is the largest report of patients with recurrent AGCT. It demonstrated that PFS1 ≤60 months and distant lesion at recurrence are independent risk factors for PFS-R, and PFS-R ≤33 months is an independent risk factor for OS-R. The PWP-CP model showed that the transabdominal approach and surgery reaching R0 could significantly decrease recurrence frequency.

PR058 / #188 / Poster Board #: 31

Topic: ***AS11. Ovarian Cancer***

MICRORNA-DEPENDENT INHIBITION OF WEE1 CONTROLS CANCER STEM-LIKE CHARACTERISTICS AND MALIGNANT BEHAVIOR IN OVARIAN CANCER

Woo Yeon Hwang, So Young Kim, Sun Woo Choi, Moon Yeon Hwang, Da Young Kang, Ji Eun Jung, Min Hyung Jung, Byung Su Kwon
Kyung Hee University Hospital, Obstetrics And Gynecology, Seoul, Korea, Republic of

Introduction: Cancer stem-like cells (CSCs) are recognized to be responsible for chemoresistance and tumor recurrence owing to their self-renewal capacity and differentiation potential. Although WEE1 is a promising target for anticancer therapies, its function in ovarian CSCs remains unknown. We present evidence that WEE1 regulates CSC properties and tumor resistance to carboplatin through a microRNA-dependent mechanism.

Methods: Plasmid DNA constructs were transfected into human ovarian cancer cell lines. RNA and protein were extracted from pathologically confirmed tumor tissues. The SKOV3 spheroid tumor model were developed. Immunofluorescence analyses were performed on the xenograft tumors. miR-424 and miR-503 were detected by quantitative real-time PCR and western blot analysis. Spheroid formation assay was performed to investigate the presence and self-renewal ability of CSCs.

Results: We found that WEE1 expression is upregulated in ovarian cancer spheroids because of the decreased expression of miR-424 and miR-503, which directly target WEE1. The overexpression of miR-424/503 suppressed CSC activity by inhibiting WEE1 expression, but restoring WEE1 expression reversed this effect. Furthermore, we demonstrated that NANOG modulates the miR-424/503-WEE1 axis that regulates the properties of CSCs. We also demonstrated the pharmacological restoration of the NANOG-miR-424/ 503-WEE1 axis and attenuation of ovarian CSC characteristics in response to atorvastatin treatment. Lastly, miR-424/503- mediated WEE1 inhibition re-sensitized chemoresistant ovarian cancer cells to carboplatin. Additionally, combined treatment with atorvastatin and carboplatin synergistically reduced tumor growth, chemoresistance, and peritoneal seeding in the intraperitoneal mouse models of ovarian cancer.

Conclusion/Implications: We identified a novel NANOG-miR-424/503-WEE1 pathway for regulating ovarian CSCs, which has potential therapeutic utility in ovarian cancer treatment.

PR059 / #861 / Poster Board #: 6

Topic: ***AS11. Ovarian Cancer***

FROM PHENOTYPE TO GENOTYPE: PEROPERATIVE PREDICTION OF HRD STATUS IN EPITHELIAL OVARIAN CANCERS (EOC) BASED ON SERUM CA-125, INTRAOPERATIVE TUMOUR CHARACTERISTICS AND SURGICAL RESECTABILITY

Aarthi Jayraj[1,2], Seyedemad Nejati[1], Talal Mansy[1], Asima Mukhopadhyay[1,3,4]
[1]James Cook University Hospital, Gynaecological Oncology, Middlesborough, United Kingdom, [2]Teesside University, Gynaecologic Oncology, Middlesbrough, United Kingdom, [3]Population Health Sciences Institute, Gynaecologic Oncology, Newcastle, United Kingdom, [4]Kolkata Gynecological Oncology Trials and Translational Research Group, Gynecological Oncology, Kolkata, India

Introduction: Our previous work showed that EOC patients who are homologous-recombination competent (HRC) have distinct per-operative characteristics including lower CA125 at presentation, infiltrative fibrotic tumour and lower optimal surgical cytoreduction rates (Mukhopadhyay et al, Cancer Res 2012). We hypothesized that HRC/BRCA-wild-type can be predicted based on tumour characteristics attributed to atypical tumour-stromal interaction leading to non-secretory phenotypes and higher desmoplasia resulting in poorer surgical outcomes.

Methods: A prospective study of stage III/IV high grade serous EOC patients operated over 2 years (01/2021-12/2022) were analysed to score phenotypical HRC/BRCA(pHRC) status based on CA-125 levels, pattern of tumour spread and completeness of surgical cytoreduction (Table). Pathological genomic HR status(gHRC) was determined from tumour tissue by Myriad MyChoice CDx Test assay. Reverse validation of pHRC score was performed against confirmed gHRC to assess predictability.

Scoring system for determining phenotypical HRC(pHRC) status

Scoring	0	1	2
Serum CA-125 at disease presentation	>500	≤ 500	
Pattern of tumour infiltration	Expansile	Indeterminate	Infiltrative
Surgical cytoreductive score	CC0	CC1/CC2	

Results: Of 40 patients enrolled, thirty were included for analysis. Reason for exclusion included insufficient tissue for HR profiling (n=4), inadequate assessment during surgery (n=4), unconfirmed primary site (n=2). Pattern of tumour spread was indeterminate in 12 patients and infiltrative in 13 patients. Pathologic HR analysis confirmed 19 patients were gHRC (genomic HRC). A pHRC score of ≥3 predicted gHRC with sensitivity of 73.6%, positive predictive value of 93.3% and specificity of 90.9%. All patients who scored 0 were proven to be HR deficient. Greatest discrepancy was noted in those with score of 2.

Conclusion/Implications: Intraoperative tumour phenotype allows for accurate prediction of HRC status. Phenotypic HRC status can be useful surrogate for genomic HRD assay with wider implication where HRD testing is unavailable.

PR060 / #838 / Poster Board #: 8

Topic: ***AS11. Ovarian Cancer***

IMPACT OF ASCITES AND PERITONEAL METASTATIC LESION VOLUMES, MEASURED BY NEWLY DEVELOPED DEEP LEARNING-BASED ALGORITHM, IN ADVANCED EPITHELIAL OVARIAN CANCER

Ui Suk Kim, Se Ik Kim, Maria Lee, Jae-Weon Kim, Hyun Hoon Chung
Seoul National University Hospital, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of

Introduction: We investigated the impact of ascites and peritoneal metastatic (PM) lesion volumes, measured by deep learning-based algorithm, on survival outcomes in advanced epithelial ovarian cancer.

Methods: Applying our newly developed deep learning-based auto-segmentation algorithm to pre-treatment computed tomography (CT) images obtained from 195 patients with advance-stage EOC, we measured volumes of ascites and PM lesions in the abdominal-pelvic cavity. Using the median values of ascites and PM lesion volumes as cut-off values, patients were divided into high- and low-volumetric ascites groups and high- and low-volumetric PM groups. Thereafter, survival outcomes were compared between the two groups.

Results: Of the study population, 34.9% had FIGO stage IV disease and 78.5% had high-grade serous carcinoma. Complete cytoreduction was achieved in 56.4%. The median volumes of ascites and PM lesions were 714.5 cm^3 and 341.1 cm^3, respectively. The high-volumetric ascites group showed significantly worse OS than the low-volumetric ascites group (5-year PFS rate, 68.7% vs. 46.1%, P=0.08), but similar PFS. In multivariate analyses adjusting for clinicopathologic factors, high-volumetric ascites was identified as an independent poor prognostic factor for OS (aHR, 1.801; 95% CI, 1.147-2.828; P=0.011). Limited to a subgroup of patients who achieved complete cytoreduction (n=110), high-volumetric PM was associated with significantly worse OS (aHR, 2.231; 95% CI, 1.066-4.669; P=0.033).

Conclusion/Implications: We successfully measured volume of ascites and PM lesions in the abdominal-pelvic cavity using the newly developed deep learning-based auto-segmentation algorithm. Our study results indicate that volumetric measurement of ascites and PM lesions might be novel prognostic factors for survival outcomes in patients with advanced-stage epithelial ovarian cancer.

PR061 / #869 / Poster Board #: 22

Topic: ***AS11. Ovarian Cancer***

A RETROSPECTIVE STUDY ON THE COMPARISON OF RESPONSIVENESS OF EACH CHEMOTHERAPY FOR RECURRENT OVARIAN CANCER AFTER MAINTENANCE TREATMENT WITH PARP INHIBITORS

Jung Chul Kim[1], Junsik Park[1], Yong Jae Lee[2], Eunji Nam[3], Sang Wun Kim[1], Sunghoon Kim[2], Young Tae Kim[4], Jung-Yun Lee[1]
[1]Yonsei University College of Medicine, Obstetrics And Gynecology, Seoul, Korea, Republic of, [2]Institute of Women's Life Medical Science, Yonsei University College of Medicine, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of, [3]Yonsei University College of Medicine, Department Of Obstetrics And Gynecology, Women's Cancer Center, Yonsei Cancer Center, Institute Of Women's Life Medical Science, Seoul, Korea, Republic of, [4]Yonsei Cancer Center, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of

Introduction: In the SOLO2 trial, olaparib demonstrated a significant benefit in disease-free survival in platinum sensitive recurrent ovarian cancer patients with BRCA1/2 mutations, so importance and utility of poly (adenosine diphosphate-ribose) polymerase inhibitors (PARPi) in therapy is gradually increasing. However, there is no medical agreement for treatment after recurrence in ovarian cancer patients who have been administered PARPi, so they are generally treated with platinum-based chemotherapy that have been used previously, or undergo surgery and radiation therapy. Therefore, this study was conducted to confirm the efficacy of each chemotherapy for recurrent ovarian cancer after using PARPi.

Methods: This retrospective study collected the data on recurrent ovarian cancer patients who have used PARPi after platinum-based chemotherapy in front-line to forth-line and using next chemotherapy of Liposomal doxorubicin (PLD)+Carboplatin, Belotecan+Cisplatin and Gemcitabin+Carboplatin from January 01, 2012 to April 30, 2023. The primary endpoint was progression free survival(PFS) from the date of disease progression after using PARPi to the date of next disease progression after using those chemotherapy

methods.

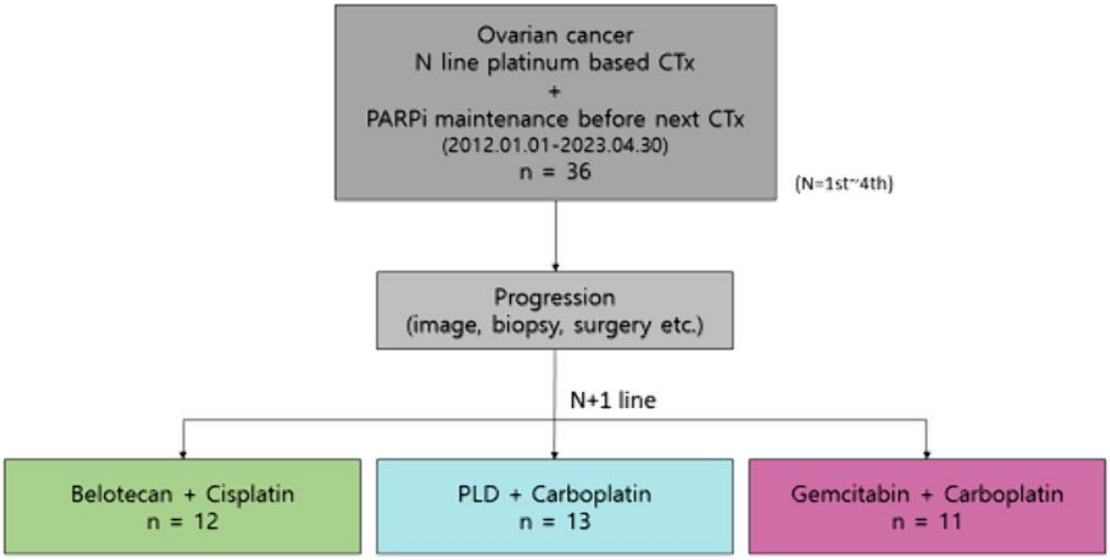


Figure 1) Schema

Results: There was a significant different PFS (p value = 0.0367) in the three groups. And overall, the Gemcitabin+Carboplatin group showed better results than the other two groups, in particular, a significant difference with the PLD+carboplatin group (p value = 0.0060, Hazard ratio : 2.964, 95% CI 1.128-7.791).

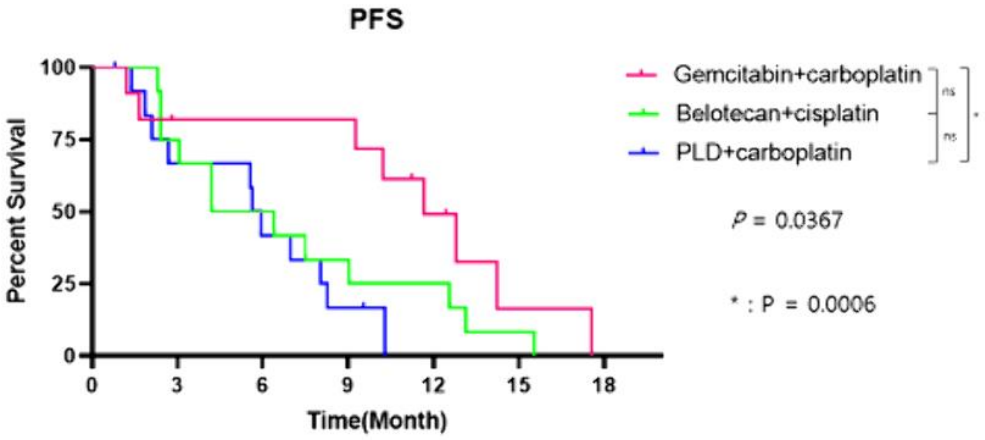


Figure 2) Progression free survival(PFS) in among three chemotherapies

Conclusion/Implications: In the treatment of recurrent ovarian cancer using platinum-based chemotherapy and PARPi, Gemcitabin + Carboplatin chemotherapy may show slightly better results than other chemotherapies, so additional research on this seems necessary.

PR062 / #686 / Poster Board #: 15

Topic: ***AS11. Ovarian Cancer***

FIRST-IN-HUMAN PHASE 1 STUDY OF TORL-1-23, A NOVEL CLAUDIN 6 (CLDN6) TARGETED ANTIBODY DRUG CONJUGATE (ADC) IN PATIENTS WITH OVARIAN CANCER

Gottfried Konecny[1], Andrea Wahner Hendrickson[2], Boris Winterhoff[3], Cinthiya Chander[1], Sanela Bilic[4], Simon Davenport[5], Adrine Chung[6], Lei-Lani Miller[6], Michael Press[5], Stephen Letrent[7], Dennis Slamon[8]
[1]UCLA, Obstetrics And Gynecology, Los Angeles, United States of America, [2]Mayo Clinic, 200 First St Sw, Rochester, United States of America, [3]University of Minnesota, Division Of Gynecologic Oncology, Minneapolis, United States of America, [4]Vanadro, Pharmacology, Urbandale, United States of America, [5]University of Southern California, Department Of Pathology, Los Angeles, United States of America, [6]Translational Research in Oncology-US, Clinical Operations, Los Angeles, United States of America, [7]TORL Biotherapeutics, Clinical Development, Culver City, United States of America, [8]University of California Los Angeles, Department Of Medicine, Los Angeles, United States of America

Introduction: CLDN6 is highly expressed in multiple cancers with little to no expression in normal tissues, thus is an ideal target to explore a novel therapeutic. TORL-1-23 is first-in-class ADC targeting the tumor-specific antigen CLDN6.

Methods: A first in human, 2-part study (TORL123-001 [NCT05103683]) is characterizing the safety, tolerability, pharmacokinetics (PK), maximum tolerated dose (MTD), and antitumor activity of TORL-1-23 monotherapy in participants with ovarian and other advanced solid tumors. Dose escalation (Part 1) implemented an accelerated titration design with up to 6 participants per dose level cohort. Dose expansion (Part 2) will assess participant cohorts with CLDN6-expressing tumors including gynecologic cancers using a CLDN6 IHC companion diagnostic.

Results: 19 patients with platinum-resistant/refractory ovarian cancer were evaluated across 8 dose levels (0.2 to 2.4 mg/kg IV every 3 weeks, 21 day cycles) (data cutoff 01APR2023). Most pts had ≥ 3 prior treatment lines in the metastatic setting. The most common treatment-related adverse events were Gr1 peripheral neuropathy (n=3), Gr1/2 fatigue (n=2), and Gr1 nausea (n=2). Dose-limiting toxicities have not been observed. PK data show sustained exposure over the dosing interval. Partial responses (PR) were reported in 6/18 efficacy evaluable participants with CLDN6+ ovarian cancer across all dose levels. 3 of 4 participants with ovarian cancer responded at the 2.4 mg/kg dose level.

Conclusion/Implications: In participants with heavily-pretreated CLDN6-expressing ovarian cancer, the novel TORL-1-23 ADC shows a favorable safety/tolerability profile and encouraging antitumor activity. Dose finding is ongoing to identify optimal doses for subsequent development.

PR063 / #79 / Poster Board #: 81

Topic: ***AS11. Ovarian Cancer***

SEROUS TUBAL INTRAEPITHELIAL CARCINOMA (STIC) OUTCOMES IN AN AVERAGE RISK POPULATION

Kimberly Stewart[1], Lien Hoang[2], Janice Kwon[1]
[1]University of British Columbia, Division Of Gynecologic Oncology, Vancouver, Canada, [2]Vancouver General Hospital, Department Of Pathology, Vancouver, Canada

Introduction: Serous tubal intraepithelial carcinoma (STIC) are precursors for high grade serous carcinomas (HGSC) of tubo-ovarian origin. It is most commonly encountered during risk-reducing surgery for patients with a BRCA germline pathogenic variant (PV). An isolated STIC at risk-reducing surgery is associated with a 27.5% risk of primary peritoneal HGSC at 10 years. There is little known about the risk of subsequent HGSC in an average risk patient found to have an isolated STIC. The objective of this study is to explore the outcomes of STIC diagnosed in a population of patients without a known hereditary mutation at the time of surgery.

Methods: Retrospective population based cohort study from British Columbia, Canada. Chart review of patients with an isolated STIC from January 2012 to May 2022. The estimated population prevalence of STIC, and outcomes including subsequent HGSC and BRCA mutations are described.

Results: Twenty nine patients were identified, including 20 patients with no known BRCA PV (“average risk”) undergoing primary surgery for non-risk reducing indications. The estimated prevalence of STIC in this population was 0.1%. Patients were followed for a median of 63 (9-127) months. Five of these 20 average risk patients (25%) developed HGSC at 18, 29, 70, 80, 106 months, and only 1 (5%) of these was subsequently found to have a BRCA PV.

Conclusion/Implications: STIC identified in average risk population patients with negative genetic testing are still at risk of subsequent HGSC. Recommendations for STIC management should be applied to all patients regardless of BRCA status.

PR064 / #206 / Poster Board #: 2

Topic: ***AS11. Ovarian Cancer***

MULTICENTER REAL-WORLD EXPERIENCES OF PARPI RECHALLENGE IN PATIENTS WITH OVARIAN CANCER IN CHINA

Jin Li[1], Feng Shao[2], Lingjun Zhao[3], Fei Zheng[4], Hua Zhu[5], Enchun Li[6], Wei Zhou[7], Guorong Yao[8], Jie Liu[9], Jianxiao Zheng[10], Shan Pan[11], Yue Zhang[12], Xiaohua Wu[1]
[1]Fudan University Shanghai Cancer Center, Department Of Gynecologic Oncology, Shanghai, China, [2]Cancer Hospital of the University of Chinese Academy of Sciences (Zhejiang Cancer Hospital), Gynecologic Surgical Department, Hangzhou, China, [3]Ningbo Women & Children's Hospital, Department Of Gynecology, Ningbo, China, [4]Ningbo No.2 Hospital, Department Of Gynecology, Ningbo, China, [5]The First Affiliated Hospital of Wenzhou Medical University, Department Of Gynecology, WenZhou, China, [6]Women's Hospital School of Medicine Zhejiang University, Department Of Gynecology, Hangzhou, China, [7]Taizhou Hospital of Zhejiang Province, Department Of Gynecology, Taizhou, China, [8]Huzhou Central Hospital, Department Of Integrated Chinese And Western Medicine, Huzhou, China, [9]Jinhua People's Hospital, Department Of Gynecology, Jinhua, China, [10]Yueqing People's Hospital, Department Of Integrated Chinese And Western Medicine, Wenzhou, China, [11]Jiaxing University Affiliated Women and Children Hospital, Department Of Gynecology, Jiaxing, China, [12]The First Affiliated Hospital, Zhejiang University School of Medicine, Department Of Gynecology, Hangzhou, China

Introduction: The OReO/ENGOT Ov-38 trial showed maintenance olaparib rechallenge improved progression-free survival (PFS) compared with placebo. However, subpopulation benefit more from Poly (ADP-ribose) polymerase inhibitors (PARPi) rechallenge was unclear. The objective of this real-world study is to evaluate the effectiveness, safety and explore benefit population of PARPi rechallenge in China.

Methods: This multi-center, non-interventional study included patients with PARPi-treated recurrent ovarian cancer who rechallenged PARPi as maintenance therapy or salvage treatment at 12 institutions between June 2019 and March 2023. Patients' demographics and outcomes were analyzed.

Results: Seventy patients were included, and the median follow-up time was 13.0 months. Fifty-six (80%, 56/70) patients received PARPi as maintenance after maintenance therapy (Table). The median PFS (mPFS) was 10.6 months (95% confidence interval [CI], 7.1-12.0) with first PARPi (PARPi1) and 8.6 months (95% CI, 5.3-13.0) with PARPi retreatment (PARPi2) (Figure). 32.1%(18/56) patients were BRCA1/2 mutated, the PFS were not significantly different from BRCA wild-type or unknown patients (BRCAm vs. BRCAwt or unknown, HR=0.997 [95%CI: 0.480-2.072], P=0.9935). 87.5% (39/56) of patients switched to other PARPi when rechallenging. Patients switched to other PARPi rechallenging had numerically longer mPFS compared with those didn't switch (mPFS: 8.6 vs. 7.7 months; HR=0.820 [95%CI: 0.394-1.707], P=0.5958). Overall, 4.3% (3/70) discontinued PARPi2 due to adverse events, most commonly due to hematologic adverse

Patients' Characteristic	Total (N = 70) N (%)
Age, years	
Median (Q1-Q3)	58 (53-63.75)
***BRCA* mutation status, *n* (%)**	
Wild-type or unknown	43 (61.4)
BRCA1/2 mutated	27 (38.6)
Histology, *n* (%)	
High-grade serous carcinoma	68 (97.1)
Endometrioid	1 (1.4)
Others	1 (1.4)
Name of PARPi1	
Olaparib	50 (71.4)
Niraparib	20 (28.6)
Treatment phase of PARPi1	
Neoadjuvant	1 (1.4)
Maintenance therapy	67 (95.7)
Salvage treatment	2 (2.9)
PARPi1 treatment outcomes	
Disease progression	61 (87.2)
Adverse events	5 (7.1)
Others	4 (5.7)
Switch to other PARPi or not after PARPi1	
Switch	48 (68.6)
No switch	22 (31.4)
Treatment phase of PARPi2	
Maintenance therapy	57 (81.4)
Salvage treatment	13 (18.6)
Lines of PARPi2	
1	1 (1.4)
2	18 (25.7)
3	30 (42.9)
≥4	21 (30.0)
Treatment pattern of PARPi rechallenge	
Maintenance after maintenance	56 (80.0)
Treatment after maintenance	11 (15.7)
Treatment after treatment	2 (2.9)
Maintenance after neoadjuvant	1 (1.4)
Name of PARPi2	
Olaparib	23 (32.8)
Niraparib	42 (60.0)
Fuzoloparib	3 (4.3)
Pamiparib	2 (2.9)
PARPi2 treatment outcomes	
Still on treatment	24 (34.3)
Disease progression	43 (61.4)
Adverse events	3 (4.3)

events.

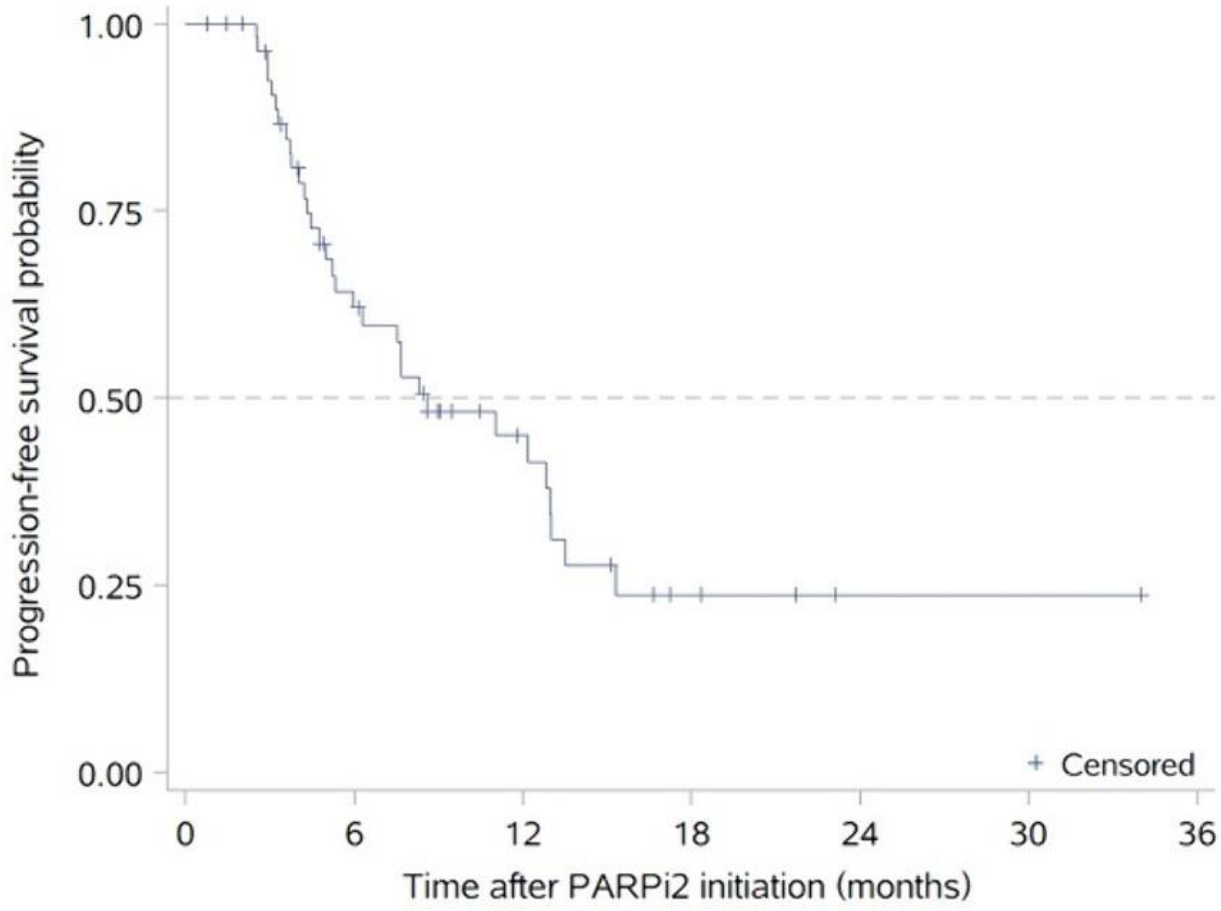


Fig. Kaplan-Meier plot of progression-free survival of patients receiving PARPi2 as maintenance therapy after PARPi1 maintenance therapy (N=56)

Conclusion/Implications: Our study is the first multicenter real-world study to evaluate the rechallenge of PARPi in ovarian cancer patients in China. There is a pressing need to identify the biomarkers except BRCA to select appropriate patients for PARPi rechallenge.

PR065 / #611 / Poster Board #: 7

Topic: ***AS11. Ovarian Cancer***

METASTATIC PATTERN OF OVARIAN CANCER DELINEATED BY TRACING THE EVOLUTION OF MITOCHONDRIAL DNA MUTATIONS

Zhiyang Xu, Xingguo Wang, Shujuan Liu
Fourth Military Medical University, Department Of Obstetrics And Gynecology, Xijing Hospital,, Xi'an, China

Introduction: Ovarian cancer (OC) is the most lethal gynecologic tumor and is characterized by a high rate of metastasis. Challenges in accurately delineating the metastatic pattern have greatly restricted the improvement of treatment in OC patients.

Methods: We applied multiregional sampling and high-depth mitochondrial DNA (mtDNA) sequencing to determine the metastatic patterns in advanced-stage OC patients. Somatic mtDNA mutations were profiled from a total of 195 primary and 200 metastatic tumor tissue samples from 35 OC patients.

Results: Our results revealed remarkable sample-level and patient-level heterogeneity. In addition, distinct mtDNA mutational patterns were observed between primary and metastatic OC tissues. Further analysis identified the different mutational spectra between shared and private mutations among primary and metastatic OC tissues. Analysis of the clonality index calculated based on mtDNA mutations supported a monoclonal tumor origin in 14 of 16 patients with bilateral ovarian cancers. Notably, mtDNA-based spatial phylogenetic analysis revealed distinct patterns of OC metastasis, in which a linear metastatic pattern exhibited a low degree of mtDNA mutation heterogeneity and a short evolutionary distance, whereas a parallel metastatic pattern showed the opposite trend. Moreover, a mtDNA-based tumor evolutionary score (MTEs) related to different metastatic patterns was defined. Our data showed that patients with different MTESs responded differently to combined debulking surgery and chemotherapy. Finally, we observed that tumor-derived mtDNA mutations were more likely to be detected in ascitic fluid than in plasma samples.

Conclusion/Implications: Our study presents an explicit view of the OC metastatic pattern.

PR066 / #652 / Poster Board #: 18

Topic: ***AS11. Ovarian Cancer***

ASSESSING CANCER-RELATED FINANCIAL TOXICITY AND ASSOCIATION WITH PATIENT-REPORTED OUTCOMES AMONG PATIENTS WITH RECURRENT OVARIAN CANCER

Naomi Adjei, Charlotte Sun, Gladys Estrada, Sol Basabe, Amy Schneider, Larissa Meyer
MD Anderson Cancer Center, Gynecologic Oncology And Reproductive Medicine, Houston, United States of America

Introduction: Ongoing effects of cancer-related financial distress (CRFD) are not well described. We explored the correlation between CRFD and patient-reported outcomes (PROs) in a longitudinal study of individuals with recurrent ovarian cancer (ROC).

Methods: Participants with ROC completed validated PRO instruments at enrollment and every 3 months thereafter for ≤4 years. Instruments included FACIT-COST (financial distress among people with cancer), MDASI-O (symptom burden), FACT-O (quality of life), CESD-20 (depression), GAD-7 (anxiety), EQ-5D-5L (well-being), and Mini-IPIP (personality). Correlation between FACIT-COST and other PRO was assessed using Spearman correlation (rho).

Results: Table 1 highlights demographics (N=268; 1974 observations). Table 2 shows correlation between FACIT-COST and other PROs. There were weak positive correlations between the FACIT-COST and the FACT-O subscales and EQ-5D-5L VAS ($0.17<rho\leq0.33$, $p<0.001$), and weak negative correlation with GAD-7, CESD-20, Mini-IPIP Neuroticism, MDASI Symptom Severity, MDASI Symptom Distress, and MDASI-OC ($-0.34\leq rho\leq-0.27$, $p<0.001$). FACIT-COST had the strongest correlation with anxiety and depression (rho=-0.34, p<.001), neuroticism (rho=-0.34, p<.001), and symptom severity (rho=-0.32, p<.001). Patients with annual household income > $75K had a stronger positive correlation than those with ≤ $75K for social well-being (rho=0.33 and 0.20, <0.001). Lower financial distress was associated with lower anxiety and depression, lower symptom burden, and better overall well-being (p<.01 for

Table 1: Patient Demographic Characteristics (n=268)

Characteristic	N (%)
Median age at diagnosis (range)	62.4 years (30.5, 83.7)
Median time since diagnosis at study enrollment (range)	36.5 months (10.0, 260.7)
Race	
White	231 (86.2)
Black	22 (8.2)
Other	15 (5.6)
Marital Status	
Married/partnered	191 (71.3)
Divorced	33 (12.3)
Widowed	21 (7.8)
Single/never married or partnered	23 (8.6)
Number of people in immediate household	
1-2	198 (73.9)
3-4	59 (22.0)
5+	11 (4.1)
Number of patients with children < 18 yrs old in household	
None	233 (86.9)
1-2	26 (9.7)
3+	9 (3.4)
Highest education (n=267; 1 pt with missing data)	
Less than grade 12	8 (3.0)
High school diploma or equivalent	35 (13.1)
Some college	62 (23.2)
College degree or higher	162 (60.7)
Primary healthcare coverage	
Medicare	114(42.5)
Private	149 (55.6)
Other	5 (1.8)
Employment (n=267; 1 pt with missing data)	
Currently employed, full-time	70 (26.2)
Currently employed, part-time	28 (10.5)
Homemaker	27 (10.1)
Retired	112 (41.9)
Disabled	22 (8.2)
Unemployed	8 (3.0)
Annual household income	
≤ $25K	24 (9.0)
> $25K but ≤ $35K	12 (4.5)
> $35K but ≤ $50K	33(12.3)
> $50K but ≤ $75K	30 (11.2)
> $75K	169 (63.1)

all).

Table 2. Correlation coefficients (rho) between overall financial toxicity scores (FACIT-COST) and patient-reported outcomes (PROs) among patients with recurrent ovarian cancer stratified by annual household income, (p-value).

PRO instrument*,¤	≤$75K (n=99)**	>$75K (n=168)**	p-value for income groups
GAD-7 (Anxiety)	-0.327 (p<.001)	-0.362 (p<.001)	0.410
VAS from EQ-5D-5L for the question "My health today is"	0.151 (p<.001)	0.139 (p<.001)	0.800
Physical Wellbeing (PWB)	0.290 (p<.001)	0.262 (p<.001)	0.530
Social Wellbeing (SWB)	0.204 (p<.001)	0.326 (p<.001)	0.007
Emotional Wellbeing (EWB)	0.348 (p<.001)	0.302 (p<.001)	0.290
Functional Wellbeing (FWB)	0.328 (p<.001)	0.291 (p<.001)	0.400
FACT-O subscale (ovarian cancer QOL)	0.307 (p<.001)	0.252 (p<.001)	0.220
CESD-20 (Depression)	-0.334 (p<.001)	-0.361 (p<.001)	0.530
Mini-IPIP Neuroticism	-0.487 (p<.001)	-0.219 (p<.001)	0.100
MDASI Symptom Severity	-0.326 (p<.001)	-0.283 (p<.001)	0.330
MDASI Symptom Distress (Interference)	-0.254 (p<.001)	-0.287 (p<.001)	0.470
MDASI Ovarian Symptoms	-0.323 (p<.001)	-0.215 (p<.001)	0.020

* The total number of PROs completed across all time points exceeded 1970 surveys, except the Mini-IPIP completed at one time point only (n=133).

** Patients who did not report household income were excluded from subgroup analysis.

¤*PRO instruments:*

*Functional Assessment of Chronic Illness Therapy-Comprehensive Score for Financial Toxicity (**FACIT-COST**), score range 0-44, higher score = better financial well-being.*

*General Anxiety Disorder-7 (**GAD-7**), score 5=mild, 10=moderate, 15=severe levels of anxiety.*

*Visual Analog Scale (**VAS**) of the EuorQol-5 Dimensions-5 Levels (**EQ-5D-5L**), score range 0-100, 100 = best health status.*

*Functional Assessment of Cancer Therapy – General (**FACT-G**) domains:*

- *Physical Well-being (**PWB**), score range 0-28, higher score = better PWB.*
- *Social Well-being (**SWB**), score range 0-28, higher score = better SWB.*
- *Emotional Well-being (**EWB**), score range 0-24, higher score = better EWB.*
- *Functional Well-being (**FWB**), score range 0-28, higher score = better FWB.*

*FACT-Ovarian Cancer Subscale (**FACT-O**), score range 0-44, higher score = better QOL (quality of life).*

*Center for Epidemiologic Studies Depression Scale (**CESD-20**), score range 0-60, higher score=higher likelihood of depression.*

*Mini International Personality Item Pool (**Mini-IPIP**), Five-Factor personality model:*

- *Extraversion, lower score = introversion*
- *Agreeableness, lower score = more assertive*
- *Conscientiousness, lower score = more impulsive*
- *Neuroticism, lower score = more equipped to cope with cancer-related stress*
- *Openness, lower score = conventional*

*MD Anderson Symptom Inventory-Ovarian Cancer (**MDASI-OC**), score range 0-10, higher score = worse symptom burden.*

- *MDASI Symptom Severity, assess core symptoms*
- *MDASI Symptom Distress/Interference, score range 0-10, higher score = more interference with functioning.*
- *MDASI Ovarian Symptoms (ovarian cancer specific subscale)*

Conclusion/Implications: Patients with lower CRFD were more likely to report lower levels of anxiety, depression, and symptom burden, and higher levels of physical, social, emotional, and functional well-being. Efforts to ameliorate financial toxicity may yield a high return on investment with more sweeping implications on mental, emotional and physical wellbeing.

PR067 / #586 / Poster Board #: 21

Topic: ***AS11. Ovarian Cancer***

CHEMOTHERAPY COMPLETION IN THE OLDER ADULTS WITH EPITHELIAL OVARIAN, FALLOPIAN TUBE, AND PRIMARY PERITONEAL CANCER AT A UNIVERSITY HOSPITAL IN THAILAND

Nicha Assavapokee, Natacha Phoolcharoen, Somsook Santibenchakul, Ruangsak Lertkhachonsuk
Faculty of Medicine, Chulalongkorn University, Obstetrics And Gynecology, Bangkok, Thailand

Introduction: Older patients with epithelial ovarian, fallopian tube, and primary peritoneal cancer (EOC) are often not offered potentially curative treatments, which can result in worse oncologic outcomes. We explored the difference in chemotherapy completion rate and reasons for discontinuation between older (≥70 years) and younger (< 70 years) patients with EOC.

Methods: This retrospective cohort study was conducted in patients with EOC at King Chulalongkorn Memorial Hospital, Thailand, from January 2009 to June 2021. The association between younger/older patients with chemotherapy early discontinuationwas examined with Multivariable logistic regression analysis. The reasons for chemotherapy discontinuation were collected.

Results: Among 757 EOC patients, 108 were older, and 649 were younger. The chemotherapy completion rate was lower in older than younger patients, with a statistically significant (84.3% vs. 92.6%, p=0.007). Regardless of discontinuation due to disease progression, the completion rate was comparable in both groups (93.5 vs. 95.7%, p=0.456). Dose reduction and grade 3-4 hematotoxicity were more often in the elderly group. The univariable logistic regression model showed that older age (≥70 years) was significantly associated with early chemotherapydiscontinuation (OR 2.39; 95%CI 1.29, 4.24). However, after adjusting for potential confounders, age did not significantly associate with the early discontinuation (aOR 1.20; 95%CI 0.54,2.66). Multiple comorbidities and types of surgery were identified as independent factors of the chemotherapy discontinuation.

Conclusion/Implications: It is feasible for chemotherapy completion in older adults with EOC. Age only is not the determinant of chemotherapy completion. Comorbidity and disease status are crucial in determining chemotherapy discontinuation.

PR068 / #140 / Poster Board #: 23

Topic: ***AS11. Ovarian Cancer***

PREVALENCE AND EFFECT OF MALNUTRITION ON SURGICAL AND ONCOLOGICAL OUTCOMES IN ADVANCED OVARIAN CANCER PATIENTS

Kittithach Pischart, Khemanat Khemworapong, Pattama Chaopotong, Vuthinun Achariyapota
Faculty of Medicine Siriraj Hospital, Mahidol University, Division Of Gynecologic Oncology, Department Of Obstetrics And Gynecology, Bangkok, Thailand

Introduction: In patients with advanced ovarian cancer, malnutrition is a significant concern. It might be associated with poor treatment outcomes. This study aims to determine the prevalence of malnutrition in advanced ovarian cancer patients and investigate the effect of malnutrition on surgical and oncological outcomes for the disease.

Methods: 290 advanced ovarian cancer patients (FIGO stage 3-4) who were never diagnosed as “malnutrition” for another reason were enrolled in the study. We determined malnutrition status using the geriatric nutritional risk index (GNRI). Information derived from medical records was gathered, including BMI, treatment complications, and length of hospital stay.

Results: This study showed 137 of 290 patients (47.2%) have malnutrition. Anemia and CKD were presented concomitant with malnutrition. Malnutrition impacts both surgical and oncological outcomes, including the percentage of optimal surgeries (35.8% in the malnutrition group and 62.7% in the well-nourished group) and the length of hospital stays (malnourished patients stayed longer than the average by three days). It was also found that well-nourished patients had a higher overall survival rate of more than 12.97 months than those with malnutrition patients.

Conclusion/Implications: Advanced ovarian cancer patients frequently had malnutrition. Malnutrition reduces optimal surgery rate, may lengthen hospital stays, and may reduce overall survival rates.

PR069 / #709 / Poster Board #: 24

Topic: ***AS11. Ovarian Cancer***

PROGNOSTIC IMPACT OF ERYTHROPOIETIN-STIMULATING AGENTS DURING FRONT–LINE CHEMOTHERAPY IN PATIENTS WITH OVARIAN CANCER: A KOREAN MULTICENTER COHORT STUDY

Seung-Hyuk Shim[1], Eunbi Jang[2], Eun Jung Yang[2], Hee Seung Kim[3], Shin Wha Lee[4], Sung Jong Lee[5], Suk-Joon Chang[6], Myong Cheol Lim[7], Chel Hun Choi[8]
[1]Konkuk University Hospital, Obstetrics And Gynecology, Seoul, Korea, Republic of, [2]Konkuk University School of Medicine, Obstetrics And Gynecology, Seoul, Korea, Republic of, [3]Seoul National University College of Medicine, Obstetrics And Gynecology, Seoul, Korea, Republic of, [4]Asan Medical Center, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of, [5]Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Obstetrics And Gynecology, Seoul, Korea, Republic of, [6]Ajou University Medical Center, Obstetrics And Gynecology, Suwon, Korea, Republic of, [7]Center for Gynecologic Cancer, National Cancer Center, Department Of Obstetrics And Gynecology, Goyang, Korea, Republic of, [8]Samsung Medical Center, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of

Introduction: To evaluate whether erythropoiesis-stimulating agents (ESAs) treatment for chemotherapy-induced anemia (CIA) affect progression-free survival (PFS) in patients who received front–line chemotherapy following surgery for ovarian cancer.

Methods: We retrospectively reviewed all consecutive patients who received front-line chemotherapy after surgery during 2013–2019 from seven institutions. Patients were divided according to the use of ESA during front-line chemotherapy. Primary endpoint was PFS. The secondary endpoint included occurrence of thromboembolism. A propensity score matching (PSM) analysis was used to compare survival in matched cohorts.

Results: Overall, 2,147 patients (433 for ESA and 1,714 for No-ESA) were identified with median follow–up of 44.0 months. ESA group showed significantly higher proportion of stage III/IV disease (81.8% vs 61.1%; P<0.001) and postoperative gross residual (32.3% vs 21.2%; P<0.001) compared to No-ESA group. In multivariable Cox regression, use of ESA did not affect PFS (adjusted hazard ratio, 1.034; 95% confidence interval [CI], 0.891–1.201; P=0.661). The incidence of thromboembolism was 10.2% in the ESA group and 4.6% in the No-ESA group (adjusted odds ratio, 6.581; 95% CI, 3.261–13.281; P<0.001). When comparing the well-matched cohorts after PSM, PFS did not differ between the ESA (median PFS 38 months, range 0.1–77.2 months) and No-ESA group (median PFS 35 months, range 2.2–81.2 months)(P = 0.13, log rank test).

Conclusion/Implications: Use of ESA during front-line chemotherapy did not negatively affect PFS in patients with ovarian cancer after surgery but increased risk of thromboembolism.

PR070 / #391 / Poster Board #: 13

Topic: ***AS11. Ovarian Cancer***

PHASE I TRIAL OF TILVESTAMAB, A FUNCTION-BLOCKING ANTIBODY INHIBITING AXL, IN PLATINUM-RESISTANT/REFRACTORY HIGH GRADE SEROUS OVARIAN CANCER (PROC).

David Tan[1,2], Tuan Zea Tan[3], Jae-Weon Kim[4], Jung-Yun Lee[5], Byoung Gie Kim[6], David Micklem[7], Akil Jackson[8], Thomas Talbot[9], David Pinato[9,10], Charlie Gourley[11], Rebecca Kristeleit[12], Sarah Blagden[13,14], Line Bjorge[15,16]
[1]National University Hospital, Singapore, National University Cancer Institute, Singapore, Singapore, [2]National University of Singapore, National University Centre For Cancer Research (n2cr), Singapore, Singapore, [3]Cancer Science Institute of Singapore, Genomics And Data Analytics Core, Singapore, Singapore, [4]Seoul National University, Obstetrics And Gynecology, Seoul, Korea, Republic of, [5]Yonsei University College of Medicine, Department Of Obstetrics And Gynecology, Women's Cancer Center, Yonsei Cancer Center, Institute Of Women's Life Medical Science, Seoul, Korea, Republic of, [6]Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea, Republic of, [7]BerGenBio ASA, Research, Bergen, Norway, [8]BerGenBio Ltd, Clinical Development, Oxford, United Kingdom, [9]Imperial College London, Hammersmith Hospital, London, United Kingdom, [10]University of Piemonte Orientale, Division Of Oncology, Department Of Translational Medicine (dimet), Novara, Italy, [11]Western General Hospital, Edinburgh Cancer Centre, Edinburgh, United Kingdom, [12]Guys and St Thomas' NHS Foundation Trust, Oncology Clinical Trials, London, United Kingdom, [13]University of Oxford, Department Of Oncology, Churchill Hospital, Oxford, United Kingdom, [14]Oxford University NHS Foundation Trust, Early Phase Clinical Trials Unit, Oxford, United Kingdom, [15]University of Bergen, Haukeland University Hospital, Bergen, Norway, [16]University of Bergen,, Department Of Clinical Science, Center For Cancer Biomarkers Ccbio, Bergen, Norway

Introduction: AXL expression in PROC is associated with a poor prognosis, a mesenchymal (Mes) gene expression molecular subtype (GEMS) and resistance to platinum chemotherapy. Pre-clinically, the function-blocking antibody tilvestamab binds and inhibits AXL tyrosine kinase, reducing AXL expression and downstream signalling.

Methods: Patients (pts) with PROC and ≥2 previous lines of therapy were enrolled at 8 sites in Singapore, South Korea, UK and Norway in a multiple ascending-dose phase 1 study of safety, tolerability and pharmacokinetics, receiving 2-weekly intravenous tilvestamab at 1, 3 or 5mg/kg, as monotherapy. RECIST responses were evaluated by CT scan and serum CA-125 by GCIG criteria. Exploratory tissue-based pharmacodynamics were evaluated on 2 sequential biopsies (pre-treatment and 28 days on treatment).

Results: Of sixteen pts enrolled, 10 had tumors of Mesenchymal subtype pre-treatment.

Baseline characteristics	N=16	
Age (years)	Mean (SD)	60.6 (±9.7)
Height (cm)		159.7 (±10.3)
Weight (kg)		62.5 (±11.1)
Prior lines of therapy	Median (range)	3 (2 – 6)
Pre-treatment GEMS Sci Signal. 2016 Oct 4;9(448):ra97. doi: 10.1126/scisignal.aaf8175.	Mesenchymal (Mes) Epithelial-B (Epi-B) Stemlike-A (Stem-A)	10 4 1

Mean (SD) duration on therapy was 10.5 (±6.3) weeks. No adverse clinical or laboratory signals were noted; tilvestamab exhibited dose-proportional PK. Best RECIST response was stable disease (median 35 days duration), in 5 evaluable patients; no CA-125 responses were observed but 1 patient with Mes PROC experienced a 44% reduction in CA125 from baseline (at 5mg/kg). Reverse phase protein array revealed a significant reduction in AXL expression on treatment (log2Fc=-0.4, p=0.01, n=8 pairs). A tissue GEMS switch from Mesenchymal (pre-treatment) to Epithelial-B (on-treatment) was observed in 2 cases.

Conclusion/Implications: Tilvestamab was well-tolerated with some evidence of on-target pharmacodynamic changes as well as phenotypic change - from mesenchymal to epithelial - in 2/16 PROC tumours. Further studies are warranted, including drug combinations, in biomarker selected cohorts of OC.

PR071 / #502 / Poster Board #: 20

Topic: ***AS11. Ovarian Cancer***

A PHASE 2, SINGLE ARM, PROSPECTIVE CLINICAL STUDY OF ANTITINIB HYDROCHLORIDE COMBINED WITH LETROZOLE IN THE TREATMENT OF PLATINUM RESISTANT RECURRENT OVARIAN CANCER

Xipeng Wang, Jiarui Li, Lingxi Xing, Huihui Chen, Yizhi Wang
XinHua Hospital Affiliated to Shanghai JiaoTong University School of Medicine, Department Of Gynecology And Obstetrics, Shanghai, China

Introduction: We evaluated the feasibility of combining arotinib with letrozole in the treatment of platinum resistant recurrent ovarian cancer; expecting to delay or inhibit the progress of this troublesome clinical problem, avoid hospitalization, and extend survival.

Methods: This is a phase 2, single-arm, prospective study, we recruited patients with platinum resistant recurrent ovarian cancer at Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (China). Treatment lasted for one year or stoped when disease progression/death/intolerable side effects occurred. The imaging evaluation of related lesions were conducted every three cycles, the size changes of measurable lesions were determined according to the RECIST 1.1 standard. The adverse reactions were classified into I-IV levels according to NCI-CTCAE 4.0 standards. This study was registered with ClinicalTrials.gov, number NCT04720807.

Results: 28 patients were recruited and finally 24 patients were enrolled between Dec 16, 2020, and Mar 31, 2023. At the data cutoff date (Mar 31, 2023), 17 (70.83%) patients had completed the study, 7 (29.2%) patients was undergoing treatment. The ORR was 35% (95% CI 15.4–59.2) and DCR was 80% (95% CI 56.3-94.3) in the per population. The mPFS was 6.0 months (95% CI 3.79-8.21). There was no grade 4 adverse event, and the most common grade 3 adverse event was hypertension (6 [25%]), the main grade 1-2 adverse event included mucositis(6 [25%]), laryngitis (10 [41.7%]), et al. No treatment-related deaths were recorded.

Conclusion/Implications: The combination of oral arotinib and letrozole was promising candidate for platinum resistant ovarian cancer, with apparent therapeutic effect and slight toxicities.

PR072 / #1519 / Poster Board #: 52

Topic: ***AS11. Ovarian Cancer***

EFFORT: CLINICAL AND MOLECULAR FEATURES ASSOCIATED WITH CLINICAL BENEFIT FROM ADAVOSERTIB WITH OR WITHOUT OLAPARIB IN RECURRENT OVARIAN CANCER FOLLOWING PROGRESSION ON PARP INHIBITION (NCT03579316)

Naomi Adjei[1], Robert Coleman[2], Bryan Fellman[3], Sarah Tran[1], Ying Yuan[3], Tugba Yildiran Ozmen[4], Furkan Ozmen[4], Anil Sood[1], Pamela Soliman[1], Alexi A. Wright[5], Neil Horowitz[6], Susana Campos[7], Panagiotis Konstantinopoulos[6], David Gershenson[1], Karen Lu[1], Ami Patel[1], Charnelle Ruben[1], Alexis Rabbitt[6], Lone Ottesen[8], Dana Ghiorghiu[9], Robert Godin[10], Joyce Liu[6], Gordon Mills[4], Shannon Westin[1]
[1]The University of Texas MD Anderson Cancer Center, Gynecologic Oncology, Houston, United States of America, [2]US Oncology, Texas Oncology, Houston, United States of America, [3]The University of Texas MD Anderson Cancer Center, Department Of Biostatistics, Houston, United States of America, [4]Oregon Health and Sciences University, Precision Oncology, Portland, United States of America, [5]Dana-Farber Cancer Institute, Medical Oncology, Boston, United States of America, [6]Dana-Farber Cancer Institute, Division Of Gynecologic Oncology, Boston, United States of America, [7]Dana Farber Cancer Institute, Medicine, Boston, United States of America, [8]Adcendo Aps, Adcendo Aps, Copenhagen, Denmark, [9]AstraZeneca, Late Oncology R&d, Cambridge, United Kingdom, [10]AstraZeneca, Oncology External R&d, Waltham, United States of America

Introduction: EFFORT, a randomized noncomparative phase II study of adavosertib (WEE1 inhibitor) +/- olaparib [poly (ADP-ribose) polymerase inhibitor (PARPi)] in patients with PARPi-resistant ovarian cancer (OC), demonstrated efficacy and moderate toxicity. We report updated progression-free survival (PFS) and clinical/molecular features associated with clinical benefit from adavosertib (A) +/- olaparib (O).

Methods: Eligible patients had recurrent OC after progression on PARPi, measurable disease, and adequate end-organ function. Primary endpoint was objective response rate (ORR) per RECIST v1.1. Secondary endpoints included PFS and clinical benefit (ORR/stable disease > 4 months) based on BRCA status, homologous recombination deficiency (HRD), platinum sensitivity, and intervening alternate therapy after prior PARPi before trial enrollment. Replication stress and HRD are being assessed using novel pRPA32 and Rad51 foci.

Results: There were 35 evaluable patients on each arm. Patients received a median of 4 prior therapies (range 1-11), including olaparib (41%). Median PFS was 5.5 months (95% CI, 3.9-6.9) from A and 6.8 months (95% CI, 4.3-8.3) from A/O. Table 1 demonstrates clinical benefit based on clinical/molecular features. Clinical benefit was observed on both arms regardless of BRCA status, platinum sensitivity, or use of intervening therapy after PARPi. Figure 1 demonstrates clinical benefit based on platinum sensitivity, with intriguing activity in platinum-resistant disease.

Table 1: The efficacy of adavosertib with or without olaparib in the treatment of PARPi-resistant recurrent ovarian cancer based on various clinical and molecular features.

	Overall		*BRCA* Mutant		*BRCA* Wildtype		Platinum-sensitive		Platinum-resistant		Intervening Therapy After PARPi	
Response Category	A	A/O	A	A/O	A	A/O	A	A/O	A	A/O	A	A/O
Sample size	n=35	n=35	n=15	n=16	n=16	n=18	n=11	n=14	n=24	n=21	n=19	n=16
Best Overall Response, n(%)												
PR	8 (23)	10 (29)	3 (20)	3 (19)	5 (31)	7 (39)	2 (18)	3 (21)	6 (25)	7 (33)	5 (26)	5 (31)
SD	23 (66)	23 (66)	10 (67)	12 (75)	10 (63)	10 (56)	8 (73)	11 (79)	15 (63)	12 (57)	12 (63)	10 (63)
PD	4 (11)	2 (6)	2 (13)	1 (6)	1 (6)	1 (6)	1 (9)	0 (0)	3 (13)	2 (10)	2 (11)	1 (6)
ORR (95% CI)	22.9% (10.4-40.1)	28.6% (14.7-46.3)	20% (4 – 48)	19% (4 – 46)	31% (11-59)	39% (17-64)	18% (2-52)	21% (5-64)	25% (10-47)	33% (15-57)	26% (9-51)	31% (11-59)
DOR, months (95% CI)	5.5 (2.76-NE)	6.4 (2.8-14.6)	5.6 (5.5-NR)	6.4 (5.6-NR)	4.1 (2.8-NR)	8.7 (2.8-NR)	4.1 (2.8-NR)	8.7 (2.8-51)	5.5 (2.8-NR)	6.4 (4.1-NR)	4.1 (2.8-NR)	6.4 (4.1-NR)
SD > 4 months	14 (40%)	21 (60%)	7 (47%)	10 (62%)	6 (38%)	10 (56%)	5 (45%)	11 (79%)	11 (46%)	10 (47%)	7 (37%)	8 (50%)
CBR (95% CI)	62.9% (44.9-78.5)	88.6% (73.3-96.8)	67% (33-88)	81% (54-96)	69% (41-89)	94% (73-100)	63% (31-89)	100% (77-100)	63% (41-81)	81% (58-95)	63% (38-83)	81% (5-96)
Duration of Clinical Benefit, months (95% CI)	4.8 (3.9-7.3)	6.9 (4.3-10.1)	5.6 (4.6-8.1)	5.6 (3.7-NR)	4.1 (2.8-7.4)	8.4 (3.1-10.1)	5.8 (3.9-NR)	6.9 (2-9)	4.2 (3.0-7.3)	10.1 (4.1-NR)	4.1 (2.8-5.5)	6.4 (2.8-NE)
Median PFS, months (95% CI)*	5.5 (3.9-6.9)	6.8 (4.3-8.3)	6.2 (2.7-8.6)	5.3 (2.7-6.9)	5.1 (3.9-5.5)	8.4 (4.3-11.5)	5.1 (1.8-NR)	6.8 (4.2-8.5)	5.5 (3.9-6.9)	5.9 (3.9-11.5)	6.2 (3.8-8.7)	8.0 (5.3-10.6)

	No Intervening Therapy After PARPi		PARPi as Maintenance		PARPi as Treatment		Clinical Benefit (CR/PR/SD > 2 months) from prior PARPi		SD > 2 months on prior PARPi	
Response Category	A	A/O	A	A/O	A	A/O	A	A/O	A	A/O
Sample size	n=16	n=19	n=14	n=15	n=21	n=20	n=19	n=16	n=17	n=16
Best Overall Response, n(%)										
PR	3 (19)	5 (26)	4 (29)	5 (33)	4 (19)	5 (25)	4 (21)	4 (25)	2 (24)	2 (25)
SD	11 (69)	13 (68)	7 (50)	10 (67)	16 (76)	13 (65)	15 (79)	11 (69)	13 (76)	11 (69)
PD	2 (13)	1 (5)	3 (21)	0 (0)	1 (5)	2 (10)	0 (0)	1 (6)	0 (0)	1 (6)
ORR (95% CI)	19% (4-46)	26% (9-51)	29% (8-58)	33% (12-62)	19% (5-42)	25% (9-49)	21% (6-46)	25% (7-52)	24% (7-50)	25% (7-52)
DOR, months (95% CI)	7.4 (5.7-NR)	8.7 (2.8-NR)	4.1 (3.9-NR)	6.4 (4.1-NR)	4.5 (2.8-NR)	10.1 (2.8-NR)	5.5 (2.8-NR)	10.1 (2.8-NR)	5.5 (2.8-NR)	10.1 (2.8-NR)
SD > 4 months	7 (44%)	13 (68%)	4 (29%)	9 (60%)	10 (48%)	12 (60%)	9 (47%)	10 (63%)	8 (47%)	10 (63%)
CBR (95% CI)	63%	95%	57%	94%	67%	85%	68%	88%	71%	88%
	(35-85)	(74-100)	(29-82)	(68-100)	(43-86)	(62-97)	(43-87)	(62-98)	(44-90)	(62-98)
Duration of Clinical Benefit, months (95% CI)	5.8 (3.8-NR)	6.9 (3.7-10.1)	5.7 (2.6-NR)	6.4 (4.1-NR)	4.8 (3.0-8.1)	6.9 (2.8-NR)	4.6 (3.0-8.1)	10.1 (2.8-NR)	4.6 (3.0-8.1)	10.1 (2.8-NR)
Median PFS, months (95% CI)*	5.5 (2.7-6.0)	5.3 (2.7-8.5)	5.1 (1.5-7.1)	6.9 (3.9-10.3)	5.6 (4.2-6.9)	5.9 (3.9-11.5)	5.6 (4.2-8.6)	8.4 (2.7-11.5)	5.6 (3.9-6.9)	8.4 (2.7-11.5)

*Sample size for evaluable PFS varied and are as follows:
A arm (BRCA mutant, n=16; BRCA wildtype, n=16; Platinum-sensitive, n=13; Platinum-resistant, n=25; Intervening therapy after PARPi, n=17; No intervening therapy after PARPi, n=21; PARPi as maintenance, n=17; PARPi as treatment, n=21; CR/PR/SD > 2 months from prior PARPi, n=19; SD>2 months on prior PARPi, n=17);
A/O arm (BRCA mutant, n=21; BRCA wildtype, n=19; Platinum-sensitive, n=16; Platinum-resistant, n=24; Intervening therapy after PARPi, n=20; No intervening therapy after PARPi, n=21; PARPi as maintenance, n=19; PARPi as treatment, n=22; CR/PR/SD > 2 months from prior PARPi, n=18; SD>2 months on prior PARPi, n=18);
Abbreviations: Partial Response (PR), Stable Disease (SD), Progressive Disease (PD), Objective Response Rate (ORR), Duration of Response (DOR), Clinical Benefit Rate (CBR), progression-free survival (PFS), Adavosertib alone (A), Adavosertib and Olaparib (A/O), poly (ADP-ribose) polymerase inhibitor (PARPi), Complete response (CR), Homologous recombination deficiency (HRD), Not Reached (NR).

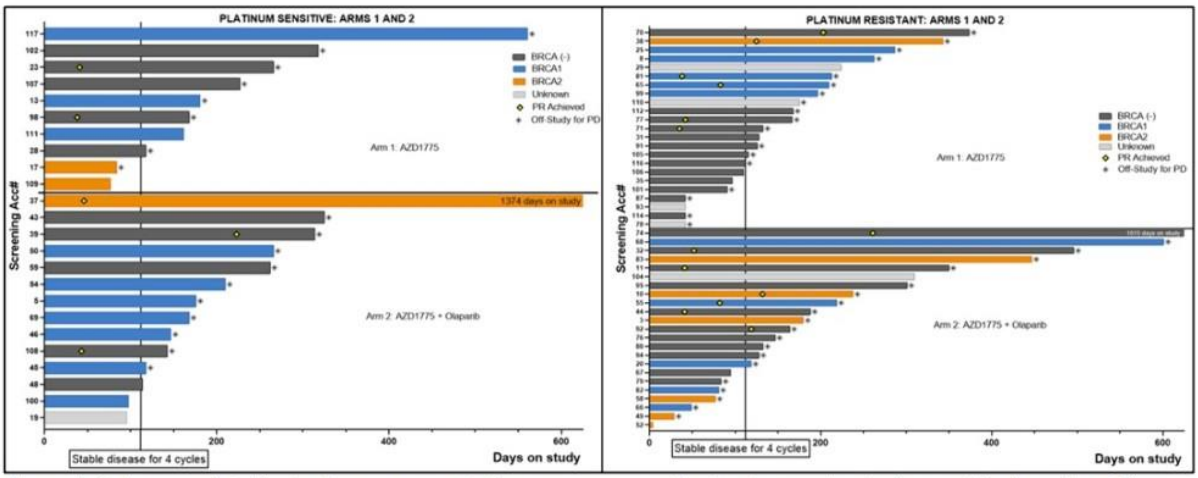


Figure 1: Swimmer plots illustrating response to therapy among patients who received adavosertib alone (Arm 1) vs adavosertib in combination with olaparib (Arm 2) by platinum sensitivity and *BRCA* mutation status. *Abbreviations: PD (progression of disease), PR (partial response), AZD1775 (adavosertib), BRCA- (BRCA wildtype), BRCA1 / BRCA2 (Breast Cancer gene 1 and 2)*

Conclusion/Implications: Efficacy of adavosertib +/- olaparib was retained across multiple clinical cohorts of PARPi-resistant OC, including BRCAwt and platinum-resistant disease. Ongoing analysis using a novel functional HRD assay consisting of concordant measurement of Rad51, gH2AX and geminin foci will elucidate the role of HRD in clinical benefit.

PR073 / #425 / Poster Board #: 19

Topic: ***AS11. Ovarian Cancer***

SENAPARIB, A PARP INHIBITOR, IN PATIENTS WITH BRCA1/2 MUTATED PLATINUM SENSITIVE RECURRENT OVARIAN CANCER: SUBGROUP ANALYSIS FROM SABRINA STUDY.

Xiaohua Wu[1], Jihong Liu[2], Li Wang[3], Zhongqiu Lin[4], Jing Wang[5], Chunyan Wang[6], Beihua Kong[7], Zhiqing Liang[8], Ying Cheng[9], Hongwu Wen[10], Ge Lou[11], Yi Huang[12], Ke Wang[13], Ruifang An[14], Xianqing Zhu[15], Huaijun Zhou[16], Ying Yue[17]
[1]Fudan University Shanghai Cancer Center, Department Of Gynecologic Oncology, Shanghai, China, [2]Sun Yat-sen University Cancer Center, Department Of Gynecologic Oncology, guangzhou, China, [3]Henan Cancer Hospital, Department Of Gynecologic Oncology, Zhengzhou, China, [4]Sun Yat-sen Memorial Hospital of Sun Yat-sen University, Department Of Gynecologic Oncology, Guangzhou, China, [5]Hu'nan Cancer Hospital, Department Of Gynecologic Oncology, Changsha, China, [6]Liaoning Cancer Hospital, Department Of Gynecologic Oncology, Shenyang, China, [7]Qilu hospital of Shandong University, Obstetrics & Gynecology, Jinan, Shandong province, China, [8]The Southwest Hospital of AMU, Department Of Gynecologic Oncology, Chongqing, China, [9]Jilin Cancer Hospital, Department Of Oncology, Changchun, China, [10]Peking Universtiy First Hospital, Department Of Oncology,, Beijing, China, [11]Harbin Medical University Cancer Hospital, Gynecological Oncology, Harbin, China, [12]Hubei Cancer Hospital, Department Of Gynecologic Oncology,, Wuhan, China, [13]Tianjin Cancer Hospital, Department Of Gynecologic Oncology, Tianjin, China, [14]The First Affiliated Hospital of Xi'an Jiao Tong University, Department Of Gynecologic Oncology, Xi'an, China, [15]Zhejiang Cancer Hospital, Department Of Gynecologic Oncology, Hangzhou, China, [16]Nanjing Drum Tower Hospital, Department Of Oncology, Nanjing, China, [17]First Hospital of Jilin University, Department Of Gynecologic Oncology, Changchun, China

Introduction: Senaparib (IMP4297) showed promising antitumor activity for advanced ovarian cancer (OC). This study aimed to evaluate the efficacy and safety of senaparib in patients(pts) with BRCA1/2 mutated platinum sensitive recurrent OC. Here we assessed the efficacy by prior therapies and types of platinum sensitive.

Methods: This open label, multicenter, single arm, phase II study (NCT04089189) enrolled recurrent OC pts with germline and/or somatic BRCA mutation who had previously received ≥ 2 lines of platinum-based chemotherapy(CT). Senaparib (100 mg oral QD) was administered until disease progression or unacceptable toxicity. The primary endpoint was independent review committee (IRC)-assessed objective response rate (ORR) per RECIST v1.1.

Results: As of 30 Jan 2023, 93 pts were enrolled. 59%/41% pts were partially/fully platinum sensitive. Median lines of prior systemic chemotherapy(CT) was 2 (range 2-7), and 71%/29% received 2 / ≥ 3 lines of CT. After a median follow up of 15.7 months, efficacy was assessed in 91 pts who received treatment of senaparib and ≥ 1 tumor evaluated and met the criteria for the response evaluable set. IRC had not finished the assessment and the efficacy assessed by investigators was showed in

table.

	Fully platinum sensitive (n=38)	Partially platinum sensitive (n=53)	2L prior CT (n=64)	≥ 3L prior CT (n=27)	Overall (n=91)
ORR, % (95%CI)	65.8% (48.6-79.9)	54.7% (40.6-68.2)	64.1% (51.0-75.4)	48.1% (29.2-67.7)	59.3% (48.4-69.2)
DCR, % (95%CI)	97.4% (84.6-99.9)	90.6% (78.6-96.5)	93.8% (84.0-98.0)	92.6% (74.2-98.7)	93.4% (86.2-97.5)
DOR, mo (95%CI)	12.0 (10.2-NR)	8.2 (6.8-9.6)	11.1 (9.1-13.0)	9.1 (6.8-11.5)	10.3 (8.2-12.0)
PFS, mo (95%CI)	13.9 (10.6-17.1)	8.3 (7.1-9.5)	12.3 (9.2-15.3)	9.1 (7.8-10.4)	11.1 (8.3-13.8)

Conclusion/Implications: Senaparib demonstrated clinically meaningful antitumor activity in OC pts of fully or partially platinum sensitive who had previously received ≥ 2 lines of CT.

PR075 / #291 / Poster Board #: 5

Topic: ***AS11. Ovarian Cancer***

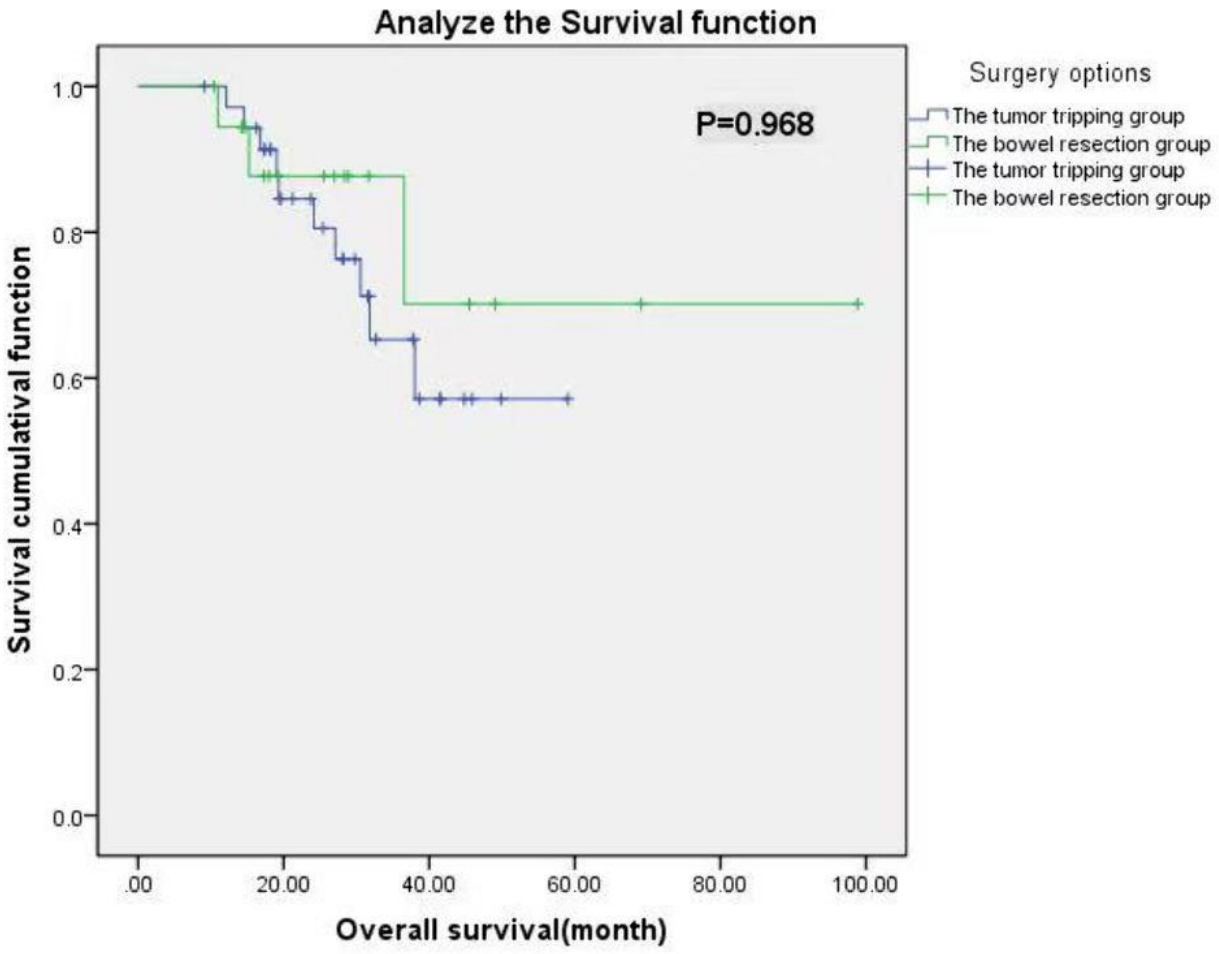
THE COMPARISON OF THE INFLUENCE OF BOWEL RESECTION OR BOWEL TUMOR STRIPPING ON THE PROGNOSIS IN PATIENTS WITH BOWEL METASTASES ORIGINATED FROM ADVANCED OVARIAN CANCER

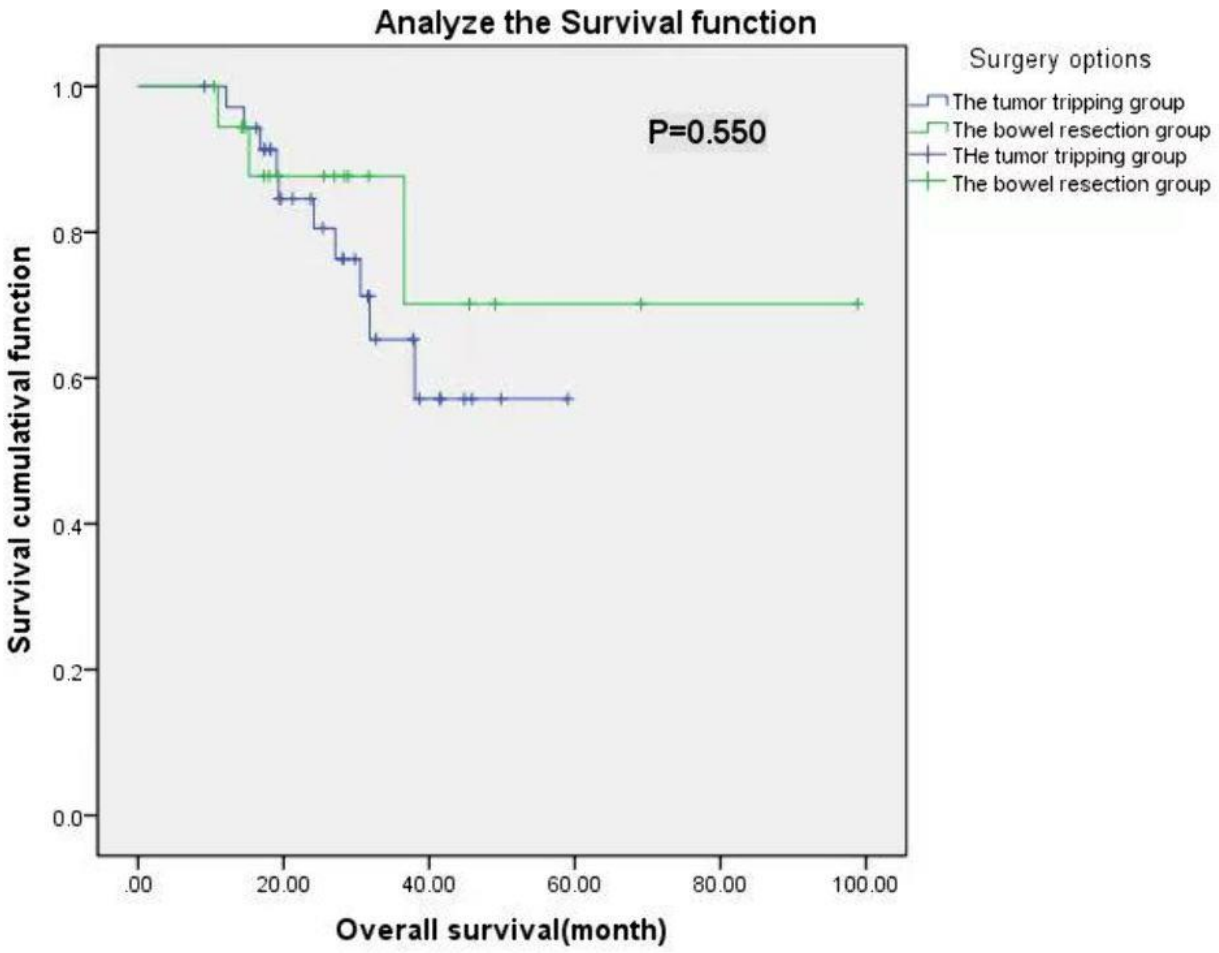
Zhengmao Zhang, Hongxia Wang, Jinxiu Wang
Fourth Hospital of Hebei Medical University, Gyn, Shijiazhuang, China

Introduction: To analyze the influence of bowel resection or bowel tumor stripping on the prognosis of patients with advanced epithelial ovarian cancer.

Methods: 255 Patients diagnosed as stage Ⅲ-Ⅳ epithelial ovarian cancer with bowel metastasis at single cancer center from Jan. 1st, 2015 to Dec. 31st 2020 were enrolled for retrospective analysis, and divided into two groups, one was bowel resection group (101 cases) the other was bowel tumor stripping group (154 cases).

Results:


Analyze the Survival function
P=0.968
Surgery options
The tumor tripping group
The bowel resection group
The tumor tripping group
The bowel resection group
Survival cumulativel function
1.0
0.8
0.6
0.4
0.2
0.0
.00
20.00
40.00
60.00
80.00
100.00
Overall survival(month)



In this cohort study R0 rate reached 75.4%. More stage Ⅳ and higher surgical complexity score patients were found in the bowel resection group than in tumor stripping group (P=0.021). The incidence of intraoperative blood infusion, pneumonia and pleural effusion in the bowel resection group was significantly higher than that in the bowel tumor stripping group. The incidence of anastomotic fistula was 1.98% in the bowel resection group vs 0% in the tumor striping group. 5-year overall survival (OS) and 5-year progression free survival (PFS) were similar between resection group and stripping group respectively, 65.8% vs 73.8%, 70.6% vs 80.3%. If the residual lesions were left only on intestinal wall, 5-year OS was not different from that in R0 bowel resection group, but 5-year PFS was much lower (P=0.032). If cytoreductive surgery reached R0, no matter PDS or IDS, 5-year OS and 5-year PFS were similar between two groups.

Conclusion/Implications: If R0 cytoreductive surgery was achieved, there was no negative effect of bowel tumor stripping for prognosis of advanced ovarian cancer. Excessive bowel resection did not increase overall survival.

PR076 / #172 / Poster Board #: 10

Topic: ***AS11. Ovarian Cancer***

COST-EFFECTIVENESS OF MAINTENANCE NIRAPARIB WITH AN INDIVIDUALIZED STARTING DOSAGE COMPARED TO ROUTINE SURVEILLANCE IN PATIENTS WITH PLATINUM-SENSITIVE RECURRENT OVARIAN CANCER IN CHINA

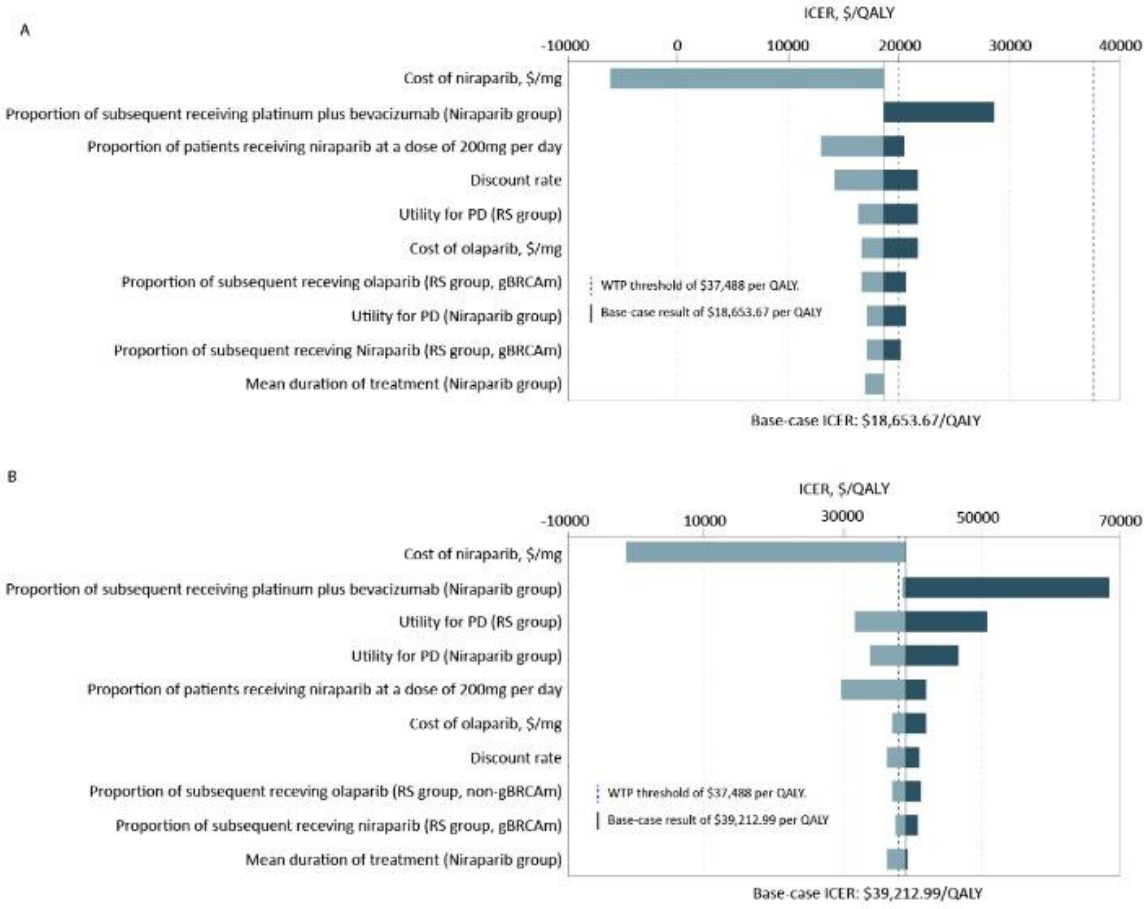
Yin Shi[1], Di Xiao[1], Shuishi Li[2], Shao Liu[1], Yu Zhang[3]
[1]Xiangya Hospital, Central South University, Department Of Pharmacy, Changsha, China, [2]Xiangya Hospital, Central South University, Department Of General Surgery, Changsha, China, [3]Xiangya Hospital, Central South University, Department Of Gynaecology, Changsha, China

Introduction: Niraparib maintenance treatment using individualized starting dosage (ISD) demonstrated improved survival outcomes for Chinese platinum-sensitive recurrent ovarian cancer (PSROC) patients versus routine surveillance in NORA trial. We elevated the cost-effectiveness of maintenance niraparib ISD vs routine surveillance in Chinese PSROC patients.

Methods: Clinical data from NORA trial was simulated using Markov model for costs and health outcomes. Quality-adjusted life years (QALYs), total costs and incremental cost-effectiveness ratios (ICERs) were measured. One-way and probabilistic sensitivity analysis were performed to estimate the model robustness. Scenario analyses were also conducted. Study period was from June 2022 to January 2023.

Results: Niraparib ISD increased QALYs by 0.59 and 0.30 in PSROC patients with and without germline BRCA (gBRCA) mutations, respectively vs routine surveillance; incremental costs were $10,860.79 and $12,098.54, respectively. The ICERs of niraparib ISD over routine surveillance were $18,653.67/QALY and $39,212.99/QALY, respectively. At the willingness-to-pay (WTP) threshold of $37,488/QALY, niraparib ISD enhanced the likelihood of cost-effectiveness from 9.35% to 30.73% in the gBRCA-mutated and from 0.77% to 11.74% in the non-gBRCA mutated patients. In China's highest per capita GDP region, 74.23% of gBRCA-mutated and 76.10% of non-gBRCA-mutated population considered niraparib to be cost-effective. The probability of maintaining niraparib being cost-effective for those covered by the National Basic Medical Insurance program was
100%.

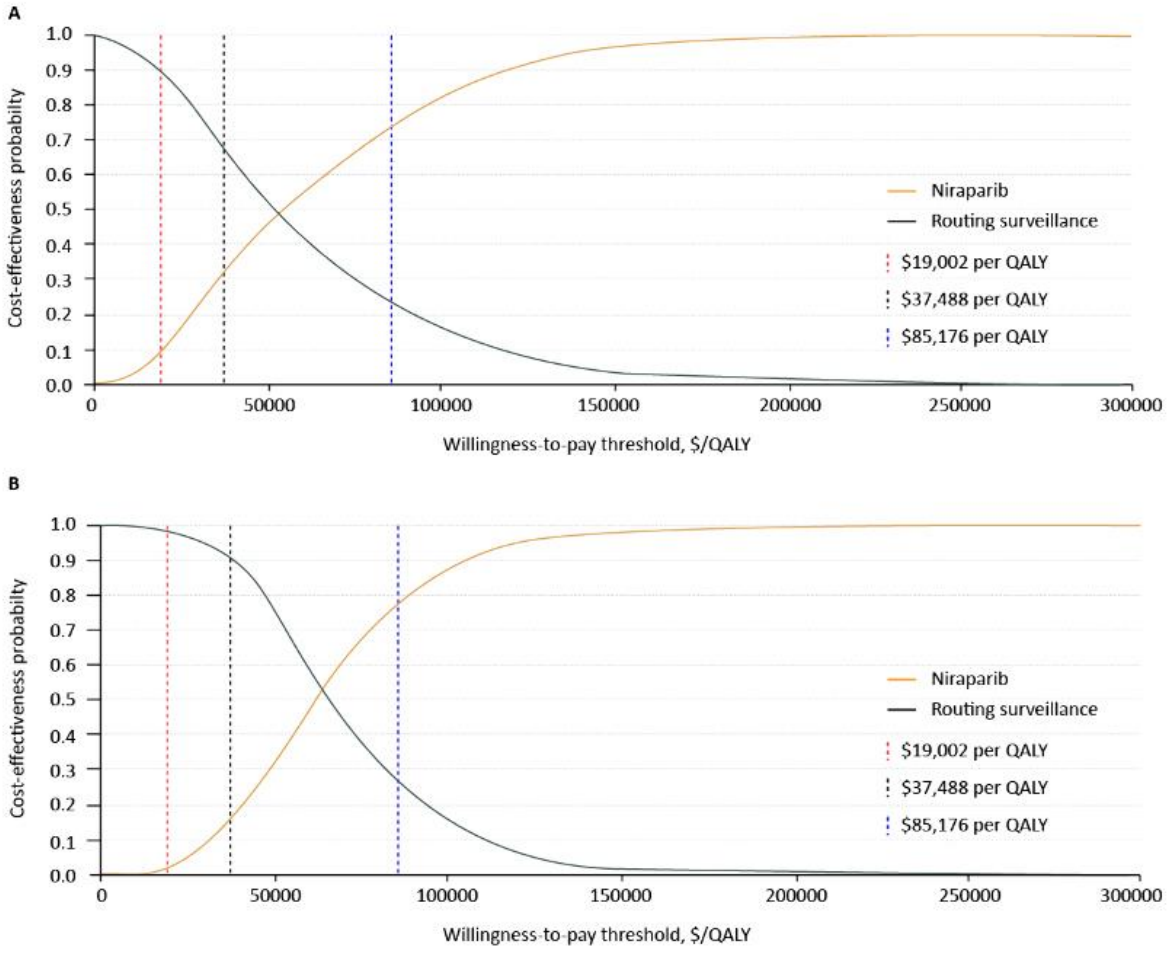
Figure 1. Tornado diagrams of one-way sensitivity analyses with greatest influence variables.



Association of variables with the ICER of niraparib versus routine surveillance for platinum-sensitive recurrent ovarian cancer (A) the *gBRCAm* cohort (B) the non-*gBRCAm* cohort.

PD, progressed disease

Figure 2. Cost-effectiveness acceptability curves generated from the probabilistic sensitivity analysis (10,000 iterations) for the niraparib and routine surveillance groups (A) g*BRCA*m cohort and (B) Non-g*BRCA*m cohort



Conclusion/Implications: Maintenance niraparib ISD is cost-effective in gBRCA-mutated PSROC patients vs routine surveillance in China. It is found to be expensive and more effective in non-gBRCA-mutated patients. The optimized niraparib price, economic status, and health insurance coverage may benefit the economic outcome.

PR077 / #690 / Poster Board #: 82

Topic: ***AS12. Palliative Care***

GYNECOLOGIC ONCOLOGISTS' PRACTICE PATTERNS AND ASSOCIATED BARRIERS TOWARD PALLIATIVE-HOSPICE CARE: A SURVEY OF THE KOREAN GYNECOLOGIC ONCOLOGY GROUP

Ga Won Yim[1], Soo Jin Park[2], Jae Man Bae[3], Shin Hye Yoo[4], Dong-Wook Shin[5], Won Moo Lee[6], Hee Seung Kim[2], Yoo Young Lee[7], Seung-Hyuk Shim[8]
[1]Dongguk University College of Medicine, Dongguk University Ilsan Hospital, Obstetrics And Gynecology, Goyang-si, Korea, Republic of, [2]Seoul National University Hospital, Obstetrics And Gynecology, Seoul, Korea, Republic of, [3]Hanyang University, 3department Of Obstetrics And Gynecology, Seoul, Korea, Republic of, [4]Seoul National University Hospital, Center For Palliative Care And Clinical Ethics, Seoul, Korea, Republic of, [5]Sungkyunkwan University School of Medicine, Department Of Family Medicine, Seoul, Korea, Republic of, [6]Hanyang University, Department Of Obstetrics And Gynecology, Seoul, Korea, Republic of, [7]Samsung Medical Center, Obstetrics And Gynecology, Seoul, Korea, Republic of, [8]Konkuk University Hospital, Obstetrics And Gynecology, Seoul, Korea, Republic of

Introduction: Gynecologic oncologists frequently care for patients with advanced cancer and at the end of life. A new legislation on Hospice, Palliative Care and Life-sustaining Treatment Decision (LSTD) has been enforced in Korea since 2018. However, there still exists barriers in integrating early and specialized palliative care (PC) into gynecologic cancer care. The objective of this study was to identify practice patterns, attitudes, and perceived barriers of PC among Korean gynecologic oncologists (GO).

Methods: Members were invited to participate in an anonymous online survey via the Google Forms. A Likert scale captured practice patterns, perceptions and barriers to timely PC implementation or referral.

Results: Ninety-three (55.4%) gynecologic oncologists completed the survey. The majority (82.8%) referred patients to specialty PC service, mainly for complex symptom management and subsequent referral to hospice. The timing of referral was most frequent when assumed prognosis was <1-2 months (34.8%). Almost half (49.5%) responded that early PC should be provided primarily by GOs and 40.9% felt the need for collaboration with PC specialists. The most frequently perceived PC barriers included patients' and families' unrealistic expectations (58.8%) and difficulty in prognostication (18.5%). The difficulties in discussing PC issues with patients were lack of knowledge in PC (28.3%), time constraints (26.5%), and physician distress. Most (94.6%) strongly agreed on the implementation of LSTD and felt the need for systematic training in palliative care (90.2%).

Conclusion/Implications: According to this cohort of KGOG members, patients' unrealistic expectations, difficulty in prognostication, and lack of physicians' knowledge were the most frequent barriers to providing PC.

PR078 / #804 / Poster Board #: 32

Topic: ***AS14. Pre-Invasive Disease***

A MULTICENTRE RANDOMISED CONTOLLED TRIAL ON THE OUTCOMES OF FERTILITY SPARING TREATMENT OF ATYPICAL ENDOMETRIAL HYPERPLASIA

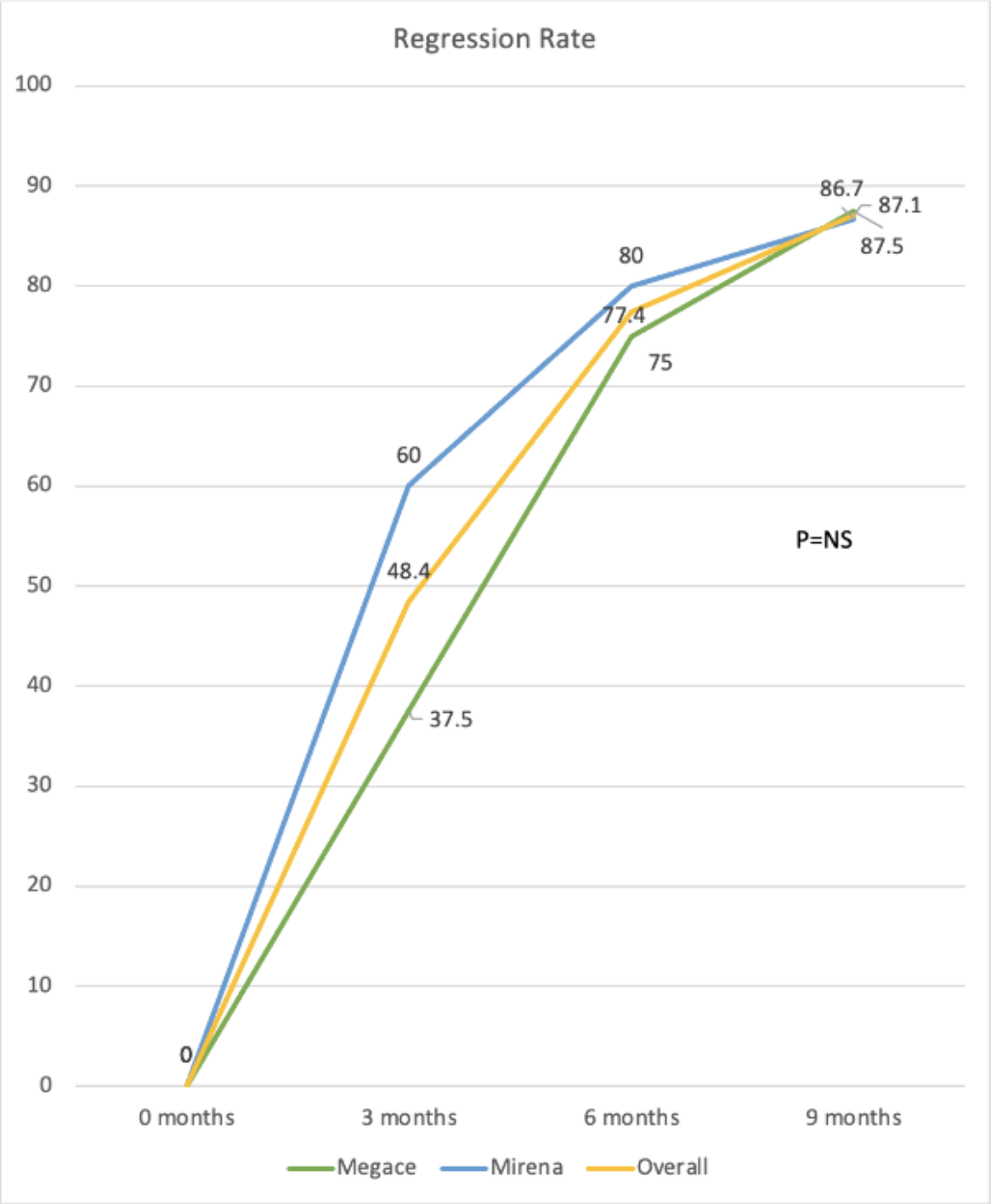
Charissa Goh[1], Joella Ang[2], Michelle Jia Min Loh[1], Whui Whui Lim[2], Pearl Tong[3], Ravichandran Nadarajah[2], Tze Tein Yong[2], Yen Ching Yeo[4], Jessie Phoon[1]
[1]KK Women's and Children's Hospital, Department Of Reproductive Medicine, Singapore, Singapore, [2]Singapore General Hospital, Department Of Obstetrics & Gynaecology, Singapore, Singapore, [3]National University Hospital, Division Of Gynaecologic Oncology, Department Of Obstetrics And Gynaecology, Singapore, Singapore, [4]KK Women's and Children's Hospital, Department Of Pathology And Laboratory Medicine, Singapore, Singapore

Introduction: Mirena and/or megestrol acetate (megace) are often used as medical treatment for atypical endometrial hyperplasia (AH) in women who are keen to preserved fertility. However, to-date, there has been no RCTs evaluating the performance of Mirena with megace in the treatment of AH.

Methods: The study team conducted a multi-centre randomised controlled trial (RCT) on the use of Mirena compared to megace in the treatment of AH from January 2020 to the January 2023. Women aged 40 years old and below were included and randomised to receive either Mirena or megace. The patients underwent an endometrial biopsy every 3 months for a maximum treatment duration of 9 months. The primary outcome assessed was the regression rate. The secondary outcomes assessed include side effects, patient acceptability and fertility outcomes.

Results: The RCT recruited 34 patients among 3 centres in Singapore. The mean age was 32.2 years and the mean BMI was 36.2 (range: 20 – 55.9). There were 31 patients who completed the study. The overall regression rate was 87.1% by 9 months with no significant difference between the two arms. There was no significant difference in side effects and weight change in both arms.

	Megace (N=16)
3-month regression N,(%)	6 (37.5)
6-month regression N,(%)	12 (75.0)
9-month regression N,(%)	14 (87.5)
Persistence N,(%)	1 (6.3)
Cancer N,(%)	1 (6.3)



Conclusion/Implications: Our study confirms a high regression rate of AH with medical treatment. Mirena is a non-inferior treatment compared to megestrol acetate.

PR080 / #375 / Poster Board #: 60

Topic: ***AS15. Rare Tumors***

GENOMIC EVOLUTION OF UTERINE LEIOMYOSARCOMA: A STUDY OF SERIAL RECURRENCES

Tiffany Sia[1], Kathryn Miller[1], David Brown[1], Pier Selenica[2], Arrnaud Da Cruz Paula[3], Nadeem Abu-Rustum[1], Mario Leitao[1], Sarah Chiang[2], Britta Weigelt[2], Martee Hensley[4]
[1]Memorial Sloan Kettering Cancer Center, Gynecology Service, Department Of Surgery, New York, United States of America, [2]Memorial Sloan Kettering Cancer Center, Pathology, New York, United States of America, [3]Memorial Sloan Kettering Cancer Center, Department Of Pathology, New York, United States of America, [4]Memorial Sloan Kettering Cancer Center, Gynecologic Medical Oncology, New York, United States of America

Introduction: Uterine leiomyosarcomas (uLMS) have high recurrence rates and frequently harbor structural aberrations in TP53 and RB1. We sought to compare molecular profiles of primary uLMS and matched serial recurrences to assess tumor evolution over time.

Methods: Patients diagnosed with uLMS between 1/1/2000 – 11/31/2020 who had primary tumor, ≥2 serial recurrences, and normal tissue available were identified. All slides were reviewed by an expert gynecologic pathologist. Samples were microdissected to enhance for tumor purity and subjected to tumor-normal targeted DNA next-generation sequencing (NGS).

Results: Tumor-normal NGS was performed on 42 tumor samples from 10 patients. The median age at diagnosis was 54 (range 30-69). The median number of recurrences was 3 (range 2–7); the median progression free survival was 45 months (range 4-163). At least one homozygous deletion affecting RB1 (50%), PTEN (30%), TP53 (30%), and/or BRCA2 (20%), as well as clonal mutations affecting TP53 (30%) and ATRX (10%), were early events and present across all samples of a given patient. Non-oncogene missense mutations were frequently shared across samples from a given case. As a group, chromosomal instability was found to be significantly higher across recurrences compared to primary tumors (mean fraction of genome altered 50% v 37.5%, p=0.035).

Conclusion/Implications: Primary uLMS and subsequent recurrences display genomic intra-individual concordance, with sustained driver mutations over time. Chromosomal instability was higher in recurrent tumors. The high BRCA2 homozygous deletion rate warrants exploration as a potential prognostic factor in uLMS.

PR081 / #468 / Poster Board #: 84

Topic: ***AS15. Rare Tumors***

EARLY STAGE OVARIAN IMMATURE TERATOMA: SURVEILLANCE OR CHEMOTHERAPY AFTER SURGERY? EXPERIENCE FROM CHINESE NATIONAL CENTER OF RARE DISEASE.

Xinyue Zhang, Jie Yang, Ying Zhang, Jinhui Wang, Jiaxin Yang
Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Obstetrics And Gynecology, Beijing, China

Introduction: To compare the survival outcomes between surveillance and adjuvant chemotherapy in patients with stage I ovarian immature teratomas (IMTs) who underwent fertility-sparing surgery.

Methods: In this retrospective cohort analysis, patients with stage IA Grade 2-3, stage IB and stage IC ovarian IMTs between 2011 to 2023 from PUMCH Rare Cancer Registry were identified. A shared decision about surveillance or chemotherapy was made by physician and patients or their guardians.

Results: A total of 103 patients were included. As the largest tertiary referral center of gynecologic germ cell tumor in China, 75 patients (72.8%) underwent surgery in local hospitals from 21 different provinces referred to us for further treatment. Forty patients chose surveillance after surgery. The median age at diagnosis was 19 years old (range 3-37). After a mean follow-up period of 29.9 months, only one patient with stage IA grade 2 IMT who underwent cystectomy had recurrence in the same ovary. The menstruation was not affected in all patients of reproductive age. Successful pregnancy was achieved in four patients without adverse events. In chemotherapy group, 63 patients received cisplatin-based adjuvant chemotherapy. Patient age, tumor stage and grade were similar in two groups. There was no statistical difference of 3-year disease free survival (DFS) and overall survival (OS) between two groups (Log Rank p=0.325 and
0.304).

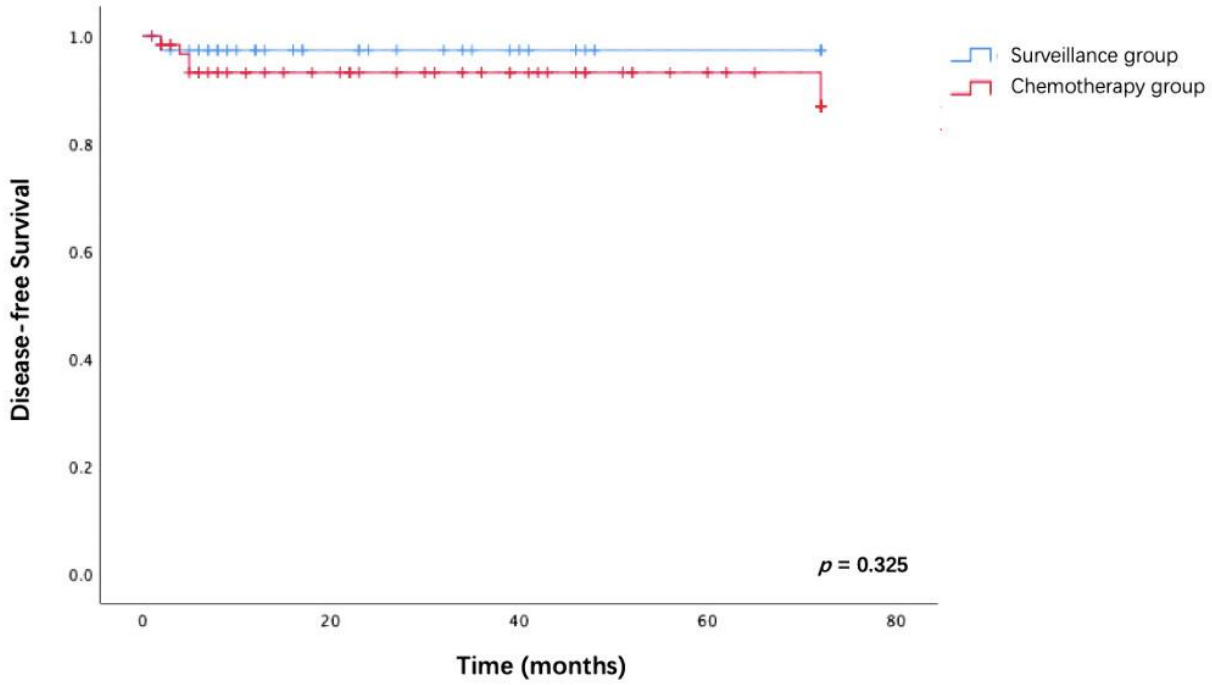


Figure 1. DFS of patients of surveillance vs chemotherapy group

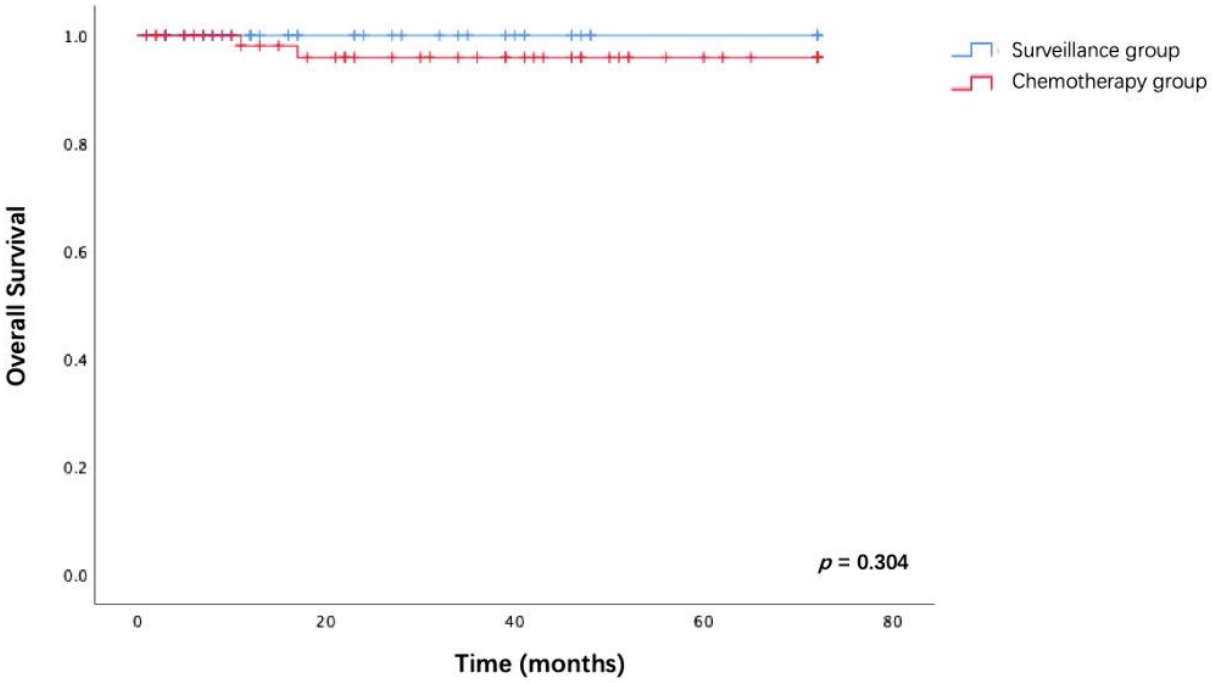


Figure 2. OS of patients of surveillance vs chemotherapy group

Conclusion/Implications: We did not observe survival differences in recurrence between patients with stage I ovarian IMTs who underwent adjuvant chemotherapy or not. Surveillance may be safe and preferable in early stage IMT patients who underwent complete resection of tumor.

PR084 / #64 / Poster Board #: 16

Topic: ***AS16. Screening/Early Detection***

COMPREHENSIVE SERUM GLYCOPEPTIDE SPECTRA ANALYSIS (CSGSA) TO IDENTIFY EARLY-STAGE OVARIAN CANCER

Masae Ikeda[1], Hiroko Machida[1], Hisamori Kato[2], Yoichi Kobayashi[3], Tomoyasu Kato[4], Nao Suzuki[5], Muneaki Shimada[6], Takuma Fujii[7], Mikio Mikami[8]
[1]Tokai University School of Medicine, Obstetrics And Gynecology, Isehara, Japan, [2]Kanagawa Cancer Center, Gynecology, Yokohama, Japan, [3]Kyorin University Faculty of Medicine, Obstetrics And Gynecology, Mitaka, Japan, [4]National Cancer Center, Gynecology, Tokyo, Japan, [5]St. Marianna University School of Medicine, Obstetrics And Gynecology, Kawasaki, Japan, [6]Tohoku University School of Medicine, Obstetrics And Gynecology, Sendai, Japan, [7]Fujita Health University School of Medicine, Obstetrics And Gynecology, Toyoake, Japan, [8]Tokai University School of Medicine, Obstetrics And Gynecology, Isahara, Japan

Introduction: Ovarian cancer is the most fatal of all female reproductive cancers, thus a new reliable and accurate screening test for ovarian cancer is urgently demanded. We established a think-outside-the-box screening method that combines cancer-related tumor markers and comprehensive glycan alterations in serum glycoproteins, which represent a physical state (CSGSA: comprehensive serum glycopeptide spectra analysis). We aimed to verify the diagnostic capability of CSGSA, a blood test to identify early-stage epithelial ovarian cancer (EOC) in this study.

Methods: We obtained sera of 564 EOC patients (55.8 ± 12.2 years) and 1,154 non-EOC controls (54.1 ± 12.0 years) from 13 facilities. Expression patterns of 1,712 glycopeptides detected by liquid chromatography mass spectrometry (LC-MS) and cancer-related tumor markers were analyzed by convolutional neural network (CNN) to discriminate an early-stage EOC.

Results: CSGSA CNN model discriminated early-stage EOC (Stage I) from non-EOC controls with ROC-AUC 0.929 (95% CI: 0.919-0.940), which exceeded those of current tumor markers, CA125 (0.840, 95% CI: 0.811-0.870) and HE4 (0.718, 95% CI: 0.675-0.760). Positive predictive value (PPV) correlated by the prevalence became 7.1% where EOC sensitivity was 51.7%.

Conclusion/Implications: We confirmed that the CSGSA discriminated early-stage EOC with high sensitivity and specificity. It is expected to identify early-stage EOC in asymptomatic women before EOC develops to advanced stage.

PR085 / #158 / Poster Board #: 90

Topic: ***AS16. Screening/Early Detection***

PREDICTORS OF LIFETIME CERVICAL CANCER SCREENING AND ASSOCIATION WITH SOCIAL DETERMINANTS OF HEALTH: CROSS-SECTIONAL EVIDENCE FROM THE CANADIAN LONGITUDINAL STUDY ON AGING

Melissa Lavecchia[1], Maura Marcucci[2], Amanda Selk[3], Parminder Raina[4], Waldo Jimenez[5], Andra Nica[5], Julie Nguyen[5]
[1]McMaster University, Division Of Gynecologic Oncology, Hamilton, Canada, [2]McMaster University, General Internal Medicine, Hamilton, Canada, [3]University of Toronto, Obgyn, Toronto, Canada, [4]McMaster University, Health Research Methods, Evidence, And Impact, Hamilton, Canada, [5]Juravinski Cancer Centre, McMaster University, Hamilton, Gynecologic Oncology, Hamilton, Canada

Introduction: Cervical cancer screening has resulted in a decrease in the occurrence of and death from cervical cancer. The Canadian Longitudinal Study on Aging (CLSA) prospectively collected health outcomes on >50,000 individuals. We sought to identify the prevalence of Canadian female participants having never undergone cervical cancer screening and the association with social determinants of health.

Methods: We performed a cross-sectional analysis from CLSA data. The main outcome was self-report of ever having undergone a pap test. Regression analyses, controlling for the complexity of the design and covariates, evaluated the association between self-reported lifetime cervical cancer screening and social determinants of health.

Results: The population-based sample comprised 22,910 participants aged 45-85, of whom 99.8% had available information on cervical cancer screening (n=22,720). The prevalence of never having undergone a pap was 14.1%; weighted prevalence, 11.8% (95%CI 11.0-12.6). Older age$_{(10\text{-year})}$ (OR 1.5, 95%CI 1.4-1.6), lower education$_{(\text{low vs. high})}$ (OR 1.5, 95%CI 1.2-1.9) and low household income$_{(\text{low vs. high})}$ (OR 1.7, 95%CI 1.3-2.3) were associated with absence of lifetime screening. Having a religious affiliation (OR 1.3, 95%CI 1.1-1.5) and never being married/lived in common-law (OR 1.5, 95%CI 1.2-1.9) were also associated with never having undergone screening. Notably, not having a family physician was an important contributing factor (OR 2.3, 95%CI 1.6-3.3). However, of participants who never underwent a pap test, 97% reported having a family physician.

Conclusion/Implications: Our analysis highlights inequities in access to cervical cancer screening in the Canadian context. This data can help inform targeted education and empowerment strategies to increase cancer screening uptake.

PR086 / #488 / Poster Board #: 91

Topic: ***AS16. Screening/Early Detection***

CAN HPV SELF SAMPLING BE USED FOR CERVICAL CANCER SCREENING IN INDIA?

Gauravi Mishra, Sharmila Pimple, Kavita Anand, Vasundhara Kulkarni, Sanjay Biswas, Anil Patil
Tata Memorial Hospital, Preventive Oncology, Mumbai, India

Introduction: Evidence from high income countries supports HPV-self sampling (HPV-SS) for improving cervical cancer screening coverage. Success of HPV-Self sampling (HPV-SS) in resource constrained countries like India with diverse population, will depend on developing impactful health education material, generating awareness towards cervical cancer and HPV-SS and on precision in performing test by beneficiaries. The current study was undertaken with objectives to determine knowledge, attitudes and practices (KAP), acceptability, barriers, agreement rates and prevalence of HPV in different population subgroups using varied methods of communication.

Methods: The current study enrolled 1600 women in age group of 30-55 yrs, from urban slums (500), urban non-slums (500) and rural (600) settings in Maharashtra, India. Information regarding cervical cancer and steps for collecting self sample was explained by two modalities; health education by trained health personnel in health education arm and through printed pictorial depiction in the pamphlet arm. One sample for HPV testing was collected by health personnel for each participant in both arms.

Results: Overall prevalence of HPV was 7.8% with no significant differences across the settings. Overall acceptance of HPV-SS was 98.4%. Awareness regarding cervical cancer and HPV-SS was similar across settings and modalities of education. The overall concordance rates between HPV-SS and health personnel collected sample was 94.8% (k=0.508, CI=0.458-0.559, p<0.001) and was similar across settings. Compliance for clinical assessment of screen positive women and for treatment was 76.8% and 80% respectively.

Conclusion/Implications: The study demonstrated that HPV-SS is acceptable, feasible and implementable in India and will assist in improving cervical cancer screening coverage.

PR087 / #201 / Poster Board #: 74

Topic: ***AS16. Screening/Early Detection***

PREVALENCE OF HIGH-RISK HPV DNA IN A SEMI-URBAN POPULATION OF UTTARAKHAND, INDIA USING A POINT-OF-CARE TEST

Shalini Rajaram[1], Shilpa Panta[2], Ayush Heda[1], Ajeet Singh Bhadoria[3], Latika Chawla[4], Himani Bhan[2], Varsha Kamath[4], Nevetha Ravichandran[4], Jaya Chaturvedi[4]
[1]AII India Institute of Medical Sciences, Rishikesh, Gynecologic Oncology (obstetrics & Gynecology), Rishikesh, India, [2]AIIMS Rishikesh, Obgyn, Rishikesh, India, [3]AIIMS Rishikesh, Community & Family Medicine, Rishikesh, India, [4]AII India Institute of Medical Sciences, Rishikesh, Obstetrics & Gynecology, Rishikesh, India

Introduction: WHO recommends a framework shift from screening with cytology and visual inspection methods, to detection of HPV DNA as the primary screening test and, endorses vaginal self-sampling as method of collection. This study was planned with the objective to determine the prevalence of HR-HPV 16/31 & 18/45 in vaginal samples using a real-time micro-PCR analyzer and to study the acceptability of self-sampling.

Methods: Micro-PCR test (Truenat®) was used on vaginal samples collected by self-sampling for detection of HR-HPV infections 16/31,18/45. A sample size of 975 women was calculated with 95% confidence, 20% relative precision and adjusting for 10% non-responder rate. Samples were collected in the community during Covid-19 pandemic. Prevalence of HR-HPV 16,18 was determined separately by RT-PCR using HPV-Q Real-time PCR kit (genes2me).

Results: Of 975 eligible women screened, prevalence was 4.6% with 45 women testing positive for HR-HPV (16/31,18/45). Of these 60% were confirmed positive for HR-HPV 16 & 18 by RT-PCR. Of the 45 positive women, 22(48.9%) underwent colposcopy and treated accordingly while the rest declined treatment. On studying acceptability of self-sampling, 943(96.72%) participants were ‘very satisfied’, 918(94.15%) found it to be ‘very comfortable’ and 863(88.51%) stated that they will strongly recommend it to other eligible women.

Conclusion/Implications: HR-HPV testing with limited genotyping showed a prevalence of 4.6%, 60% of these were HPV 16/18 positive. Point of care testing was feasible in the community and self-sampling was acceptable. Roughly 50% declined treatment, and reasons need to be looked into.

PR088 / #198 / Poster Board #: 27

Topic: ***AS16. Screening/Early Detection***

EZH2/EZH1 INHIBITOR TULMIMETOSTAT (CPI-0209): PRELIMINARY PHASE II RESULTS AND FIRST BIOMARKER FINDINGS IN PATIENTS WITH ARID1A-MUTANT OVARIAN CLEAR CELL OR ENDOMETRIAL CARCINOMAS (OCCC/EC)

Charles Drescher[1], Harriet Walter[2], Elvire Pons-Tostivint[3], Nehal Lakhani[4], Vincent Ribrag[5], Martin Gutierrez[6], Ryan Sullivan[7], Donald Harvey[8], Kalyan Banda[9], Michal Kwiatek[10], Alejandro Garcia-Sancho[11], Linda Duska[12], Pier Luigi Zinzani[13], Anjali Thakur[14], Lennart Kann[14], Rainer Boxhammer[14], Nicola Faulhaber[14], Julia Jauch-Lembach[14], Hedy Kindler[15]
[1]Swedish Cancer Institute, -, Seattle, United States of America, [2]University of Leicester and University Hospitals of Leicester NHS Trust, -, Leicester, United Kingdom, [3]Medical Oncology, University Hospital Nantes, Nantes, France, [4]START Midwest, -, Grand Rapids, United States of America, [5]Centre de Lutte Contre le Cancer (CLCC), Gustave Roussy (institut De Cancerologie Gustave-roussy), Villejuif, France, [6]Hackensack University Medical Center, -, Hackensack, United States of America, [7]Massachusetts General Hospital, -, Boston, United States of America, [8]Emory University School of Medicine and Winship Cancer Institute, -, Atlanta, United States of America, [9]Fred Hutchinson Cancer Center, -, Seattle, United States of America, [10]Centrum Medyczne Pratia Poznań, -, Skorzewo, Poland, [11]Hospital Universitario de Salamanca, Ibsal, Salamanca, Spain, [12]University of Virginia, -, Charlottesville, United States of America, [13]IRCCS Azienda Ospedaliero-Universitaria di Bologna Istituto di Ematologia “Seràgnoli” and Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale Università di Bologna, -, Bologna, Italy, [14]MorphoSys AG, -, Planegg, Germany, [15]University of Chicago, -, Chicago, United States of America

Introduction: ARID1A mutation (ARID1Amut) has a high incidence in OCCC (up to 60%) and EC (up to 40%), with evidence as a negative prognostic marker for treatment resistance and outcomes. EZH2 inhibition in ARID1Amut solid tumors results in tumor growth inhibition (Bitler et al. Nat Med 2015;21:231–238). Preliminary Phase II (NCT04104776) efficacy, safety, and biomarker findings from OCCC and EC cohorts receiving tulmimetostat are reported.

Methods: The Phase II study is evaluating tulmimetostat 350 mg once daily in 6 disease-based cohorts, including ARID1Amut OCCC/EC. Per Simon 2-stage design, expansion of enrolment (plus n=19 patients per cohort in Stage 2) requires objective response rate (ORR) ≥1/10 in Stage 1. Primary endpoint is ORR; secondary endpoints include safety. Evaluation of two additional dose levels was implemented for both cohorts, per FDA recommendation of Project Optimus, to inform on optimal tulmimetostat dose.

Results: 24 patients were enrolled (OCCC, n=14; EC, n=10); 50% of each cohort have received ≥3 prior treatment lines. Both cohorts are eligible for Stage 2 expansion, with 1 and 2 confirmed partial responses in patients with OCCC and EC, respectively (Table). The manageable safety profile across all 6 tumor cohorts (n=81) was consistent with known class effects; Grade ≥3 related adverse events (≥10% of patients) included thrombocytopenia, anemia, neutropenia, and diarrhea. Next generation sequencing did not reveal a specific hotspot for ARID1Amut locations impacting clinical outcome in patients with OCCC/EC.

Conclusion/Implications: These preliminary findings in heavily pre-treated patients with ARID1Amut OCCC/EC support continued investigation of tulmimetostat

monotherapy.

Table: Best responses*

		OCCC	EC
Efficacy evaluable, N		14	8
Best confirmed response,† n	CR	0	0
	PR	1	2
	SD	7	2
Best confirmed or unconfirmed response,† n	CR	0	0
	PR	4	3
	SD	4	1
No response, n	Progressive disease	6	2
	Not evaluable	0	1‡
	Discontinued without response assessment	0	1

CR, complete response; EC, endometrial carcinoma; OCCC, ovarian clear cell carcinoma; PR, partial response; SD, stable disease.

*data cut-off 14 February 2023; †Per RECIST 1.1; ‡Patient had a radiological assessment (stable disease) prior to the required protocol-specified window (at least 28 days).

PR089 / #862 / Poster Board #: 83

Topic: ***AS16. Screening/Early Detection***

ARTIFICIAL INTELLIGENCE-BASED DIAGNOSTIC SYSTEM FOR THE DETECTION OF ABNORMAL COLPOSCOPIC FINDINGS

Akihiko Ueda[1], Ken Yamaguchi[1], Sachiko Kitamura[1], Mana Taki[1], Koji Yamanoi[1], Ryusuke Murakami[1], Junzo Hamanishi[1], Masatsugu Ueda[2], Masaki Mandai[1]
[1]Kyoto University Graduated School of Medicine, Gynecology And Obstetrics, Kyoto, Japan, [2]Kio University, Faculty Of Health Sciences And Cytology Training Center, Nara, Japan

Introduction: Colposcopic examination requires sufficient training to detect cervical intraepithelial neoplasia (CIN) with (1) high diagnostic accuracy and (2) minimizing time and reducing tissue biopsies. This study aimed to develop an artificial intelligence (AI) based system which replicates expert colposcopic examination techniques, independent of examiner skill.

Methods: A retrospective analysis was performed using 8341 colposcopic videos from 2013 to 2019, consisting of seven cases of early-stage cervical cancer, 203 cases of CIN3, and 456 cases of CIN1. An AI-based lesion detection model was developed to identify major abnormal colposcopic findings. The model was first trained using annotated colposcopic findings with the highest acetic acid intensity in cervical cancer and CIN3 cases whose histological diagnoses were confirmed by biopsies. The developed AI model was then applied to CIN1 cases and the diagnostic accuracy of the lesions was evaluated.

Results: The AI-based model identified major abnormal colposcopic findings in cervical cancer and CIN3 cases with an area under the curve (AUC) of 0.89 for lesion area and 95% accuracy for number of lesions identified. The model also predicted minor abnormal colposcopic findings in CIN1 cases, with an AUC of 0.81 for detection of lesion area and 93% for identification of number of lesions. In addition, a heat map display based on the prediction results allowed visualization of the area of highest acetic acid intensity corresponding to the actual biopsy locations.

Conclusion/Implications: Newly developed AI-based diagnostic system for colposcopy could identify CIN lesions with high accuracy and suggest appropriate biopsy sites.

PR090 / #818 / Poster Board #: 92

Topic: ***AS17. Social Inequities and Impact on Cancer Outcomes***

PREVENTION AND MANAGEMENT OF CERVICAL CANCER: A GENDER-LENS REVIEW OF PROGRAMMATIC AND SOCIOCULTURAL DIMENSIONS IN BANGLADESH

Fariha Haseen[1], Jannatul Ferdous[2], Nurjahan Akter[1], Hridi Hedayet[1], Umme Haney[1], Syed Islam[1]
[1]Bangabandhu Sheikh Mujib Medical University, Epidemiology, Dhaka, Bangladesh, [2]Bangabandhu Sheikh Mujib Medical University, Gynecological Oncology, Dhaka, Bangladesh

Introduction: Due to the high prevalence of risk factors like early marriage, multiparity, low socioeconomic status, and limited screening, Bangladesh has a high burden of cervical cancer. Through a gender lens and an intersectional framework, this study seeks to understand the prevention and treatment of cervical cancer.

Methods: The study was held at four hospitals, namely Bangabandhu Sheikh Mujib Medical University, National Institute of Cancer Research and Hospital, Dhaka Medical College, and Mymensingh Medical College. Using a mixed methods approach, 174 clinically diagnosed patients were surveyed, and 22 qualitative interviews were conducted. Quantitative data were analyzed using inferential statistics, and qualitative data using thematic analysis.

Results: Poverty, along with other sociocultural practices like early marriage (92%) and high parity (36%), were identified to increase the vulnerability of women to cervical cancer. The study also identified multiple challenges patients with cervical cancer face during the diagnosis and treatment phases, such as financial and psychological. The risk was found in women in rural areas (OR=0.4; 95% CI: 0.168-0.799) compared to women in urban areas and those who faced financial constraints with beginning treatment compared to those who already began treatment (OR=1.0; 95% CI: 1.000 -1.018). The identified psychological difficulties included harmful social norms and fear of recurrence.

Conclusion/Implications: Economic and psychological vulnerability integrates with critical insights of intersectionality, which makes women more likely to develop cervical cancer and face difficulties after diagnosis.

PR091 / #367 / Poster Board #: 55

Topic: ***AS18. Surgical Techniques and Perioperative Management***

IMPROVING THE RATE OF SAME DAY DISCHARGE IN GYNECOLOGIC ONCOLOGY PATIENTS UNDERGOING MINIMALLY INVASIVE SURGERY – AN ENHANCED RECOVERY AFTER SURGERY QUALITY IMPROVEMENT INITIATIVE

Jennifer Mateshaytis[1], Pat Trudeau[1], Steven Bisch[1], Michael Chong[2], Sophia Pin[3], Gregg Nelson[1]
[1]University of Calgary, Obstetrics & Gynecology, Calgary, Canada, [2]University of Calgary, Anesthesiology, Calgary, Canada, [3]University of Alberta, Obstetrics & Gynecology, Edmonton, Canada

Introduction: Same-day discharge (SDD) in patients undergoing minimally invasive gynecologic oncology surgery (MIGOS) is a recent trend aligned with Enhanced Recovery After Surgery (ERAS) principles. SDD in MIGOS has been shown to be safe and feasible based on several recent studies. A baseline audit at our institution found the SDD rate in MIGOS to be 14%. To address this, we initiated an ERAS quality improvement (QI) project with the goal to increase the SDD rate in MIGOS >75%.

Methods: Four interventions were designed to address root causes identified for failed SDD following QI diagnostics: 1) SDD as the default discharge plan, 2) “Day Surgery” surgical booking, 3) development and implementation of an ERAS SDD order set, and 4) patient education SDD documents. A pre/post-intervention design was used (50 patients per group) and rate of SDD was measured together with patient demographics and surgical outcomes. Process and balancing measures were defined and tracked.

Results: SDD in MIGOS increased from 14% to 82% after the implementation of the above interventions (OR 28, p<0.0001, 95%CI 9.54-82.11). Improved SDD was achieved without negatively impacting postoperative rates of emergency department visits: 8% pre-, 4% post-intervention within 7 days (OR 0.48, p=0.678, 95%CI 0.09-2.74), 12% pre-, 10% post-intervention within 30 days (OR 0.8148, p=1.0, 95% CI 0.2317-2.86).

Conclusion/Implications: An ERAS QI initiative resulted in a substantial increase in SDD in MIGOS, without causing negative impacts on defined balancing measures.

PR092 / #646 / Poster Board #: 56

Topic: ***AS18. Surgical Techniques and Perioperative Management***

AVOIDING THE NEEDLE: APIXABAN FOR EXTENDED VENOUS THROMBOEMBOLISM PROPHYLAXIS AFTER MAJOR GYNECOLOGIC CANCER SURGERY.

Justin M. Mcginnis[1], Kimberly Stewart[1], Helia Jafari[2], Jennifer Santos[3], Jane Pattillo[3], Agnes Lee[4], Janice Kwon[1]
[1]University of British Columbia, Division Of Gynaecologic Oncology, Vancouver, Canada, [2]University of British Columbia, Faculty Of Science, Vancouver, Canada, [3]British Columbia Cancer Agency, Nursing, Vancouver, Canada, [4]University of British Columbia, Division Of Hematology, Vancouver, Canada

Introduction: Patients undergoing gynecologic cancer surgery at Vancouver General Hospital are recommended 28-days of low molecular weight heparin (LMWH) for post-operative thromboprophylaxis. Baseline survey (October 2021) revealed LMWH was associated with 91% adherence, but negatively impacted patient experience due to self-injection and cost. Our aim was to improve patient experience by reducing symptoms of pain and bruising by 50%, increasing adherence by 5%, and reducing financial toxicity over a 3-month period.

Methods: Patients were offered a choice between apixaban (2.5 mg PO BID) or LMWH (enoxaparin 40 mg SQ daily) at discharge. A multidisciplinary team informed project design, implementation, and evaluation. Process interventions included pre-printed orders and a multimodal patient and care team education program. Telephone survey and chart audit informed outcome, process and balancing measures. Data were analyzed using statistical process control charts, descriptive statistics, and Mann-Whitney (two-sided, significance <0.05).

Results: We included 127 consecutive patients from August to October 2022. Apixaban was chosen by 83.4% (n=106/127). Survey response rate was 73.2% (n=93/127). Patients who chose apixaban reported 72.8% reduction in pain, 52.9% reduction in bruising, 52.4% increase in comfort of administration, and 34.3% reduction in negative impact of the medication ($p<0.00001$ for all). Adherence was unchanged (92%). The proportion of patients paying less than $125 increased from 45% to 91%. There were no differences in balancing measures (bleeding, re-operation) and no VTE events.

Conclusion/Implications: Introduction of apixaban for extended post-operative thromboprophylaxis was associated with significant improvements in patient-reported quality measures and reduced financial toxicity. Apixaban has become standard of care at our centre.

PR093 / #279 / Poster Board #: 53

Topic: ***AS18. Surgical Techniques and Perioperative Management***

OUTCOMES ASSOCIATED WITH POSTOPERATIVE CHEMOTHERAPY FOLLOWING PELVIC EXENTERATION FOR RECURRENT OR PERSISTENT GYNECOLOGIC MALIGNANCIES

Bill Zammarrelli[1], Aashna Saini[2], Eric Rios-Doria[3], Effi Yeoshoua[1], Elizabeth Jewell[1], William Tew[4], Nadeem Abu-Rustum[1], Mario Leitao[1], Yukio Sonoda[1], Roisin O'Cearbhaill[4]
[1]Memorial Sloan Kettering Cancer Center, Gynecology Service, Department Of Surgery, New York, United States of America, [2]University of Massachusetts Memorial Medical Center, Department Of Obstetrics & Gynecology, Worcester, United States of America, [3]University of Washington Medical Center, Division Of Gynecologic Oncology, Department Of Obstetrics And Gynecology, Seattle, United States of America, [4]Memorial Sloan Kettering Cancer Center, Department Of Medicine, New York, United States of America

Introduction: Pelvic exenteration can be performed with curative or palliative intent for treatment of recurrent gynecologic malignancies. We evaluated progression-free survival (PFS) and overall survival (OS) in association with postoperative chemotherapy following pelvic exenteration for recurrent gynecologic malignancies.

Methods: We retrospectively reviewed patients with recurrent uterine, cervical, vulvar, or vaginal carcinoma who underwent pelvic exenteration from 5/01/2005-12/31/2019. Patients were excluded if surgery was performed for palliation without recurrence. Survival was assessed for allcomers and by uterine and cervical primary sites.

Results: Of 123 patients identified, 32% (39/123) were referred to medical oncology; 25 (64%) of 39 were offered and 19 (76%) of 25 received postoperative chemotherapy. Regimens included carboplatin/cisplatin and paclitaxel (n=12), another platinum doublet (n=4), or single-agent platinum (n=3). Patients who received postoperative chemotherapy, compared with those who did not, more often had positive surgical margins (21% vs. 7%, p=0.025), a uterine primary (58% vs. 18% p=0.003), and endometrioid histology (53% vs. 13% p=0.010). One patient in the no-chemotherapy group received postoperative pelvic radiation. Of the 19 patients who received postoperative chemotherapy, 7 (37%) recurred— 5 (26%) locally and 2 (11%) distantly (brain, bowel). There was no difference in 2-year PFS rate (68.4% SE ±1.1 vs. 68.9% SE ±0.05) or 2-year OS rate (78.9% SE ±1.0 vs. 74.5% SE ±0.05) between patients who did and did not undergo postoperative chemotherapy, respectively.

	Overall (N = 123)	Exenteration followed with postoperative chemotherapy (n = 19)	Exenteration followed with no postoperative chemotherapy (n = 104)	*P-value*
Median age at exenteration, years (range)	61 (28-86)	56 (28-79)	62 (30-86)	*0.319*
Median body mass index, kg/m² (range)	25.8 (17-60)	29.6 (24-37)	25.7 (17-60)	*0.968*
Race/Ethnicity, number (%)				*0.780*
Non-Hispanic White	97 (79%)	16 (84%)	81 (78%)	
Black	7 (6%)	1 (5%)	6 (6%)	
Asian	4 (3%)	0	4 (4%)	
Latino/Hispanic	10 (8%)	1 (5%)	9 (9%)	
Other/not defined	27 (22%)	1 (5%)	4 (4%)	
Type of exenteration, number (%)				*0.638*
Anterior	36 (29%)	6 (32%)	30 (29%)	
Posterior	8 (7%)	1 (5%)	7 (7%)	
Total	79 (64%)	12 (63%)	67 (64%)	
Median operative time, minutes (range)	538 (136-973)	541 (262-666)	537 (136-973)	*0.957*
Median estimated blood loss, mL (range)	718 (100-12000)	950 (300-12000)	700 (100-4150)	*0.305*
Margin status				***0.025***
Positive	11 (9%)	4 (21%)	7 (7%)	
Negative	112 (91%)	15 (79%)	97 (93%)	
Primary Site, number (%)				***0.003***
Cervical	41 (33%)	5 (26%)	36 (35%)	
Vulvar	30 (24%)	1 (5%)	28 (27%)	
Uterine	29 (24%)	11 (58%)	19 (18%)	
Vaginal	23 (19%)	2 (11%)	21 (20%)	
Primary Histology, number (%)				***0.010***
Squamous cell	68 (55%)	5 (26%)	63 (61%)	
Endometrioid	23 (19%)	10 (53%)	13 (13%)	
Adenocarcinoma	20 (16%)	3 (16%)	17 (16%)	
Other	12 (10%)	1 (5%)	11 (11%)	

Table 1. Clinicopathological demographics of patients who underwent pelvic exenteration compared with those who received postoperative chemotherapy and those who did not receive postoperative chemotherapy.

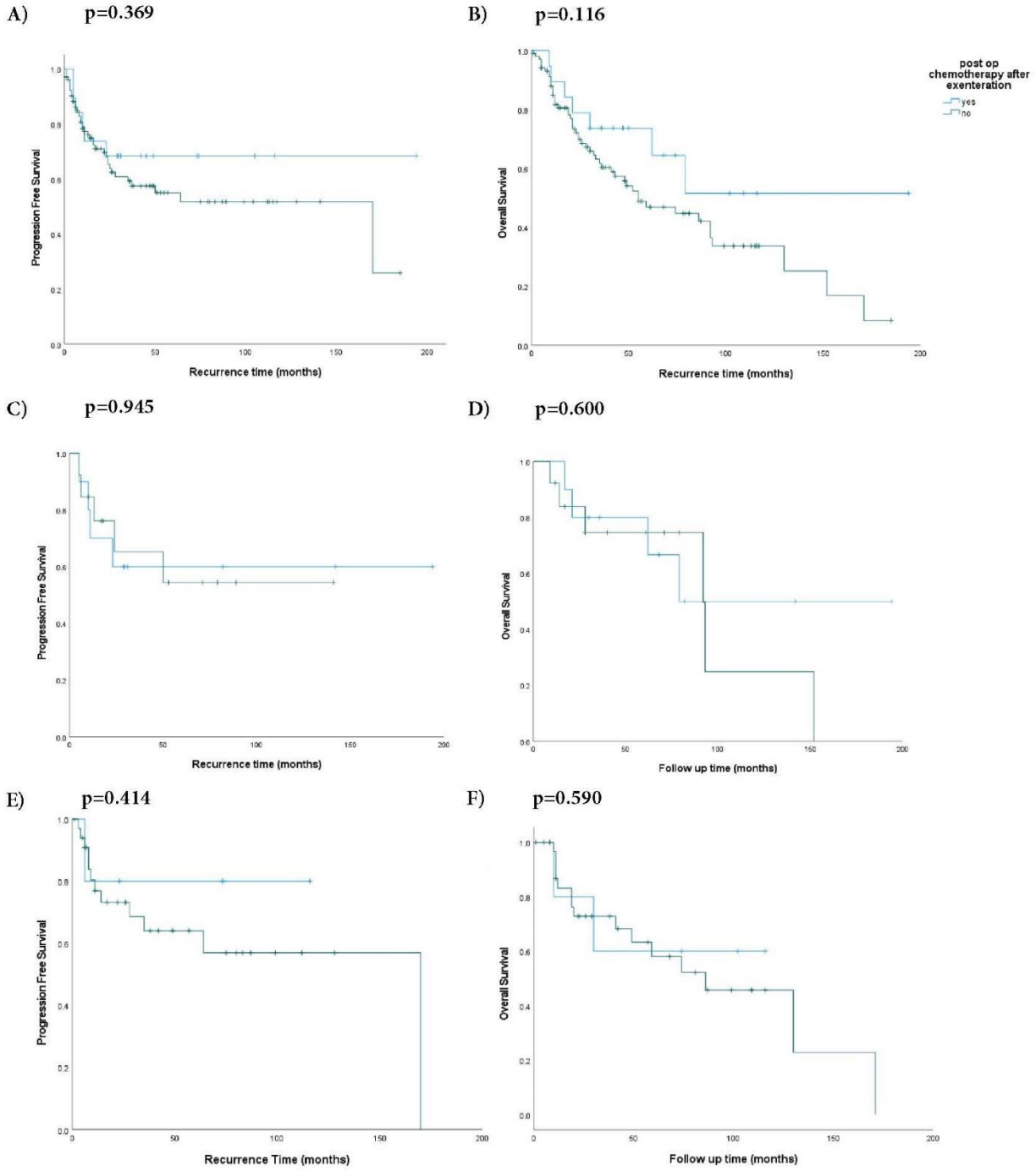


Figure 1. A) Progression-free survival for all patients compared by receipt of postoperative chemotherapy or not (n=123)
B) Overall survival for all patients compared by receipt of postoperative chemotherapy or not (n=123)
C) Progression-free survival for patients with uterine histology by receipt of postoperative chemotherapy or not (n=29)
D) Overall survival for patients with uterine histology by receipt of postoperative chemotherapy or not (n=29)
E) Progression-free survival for patients with cervical histology by receipt of postoperative chemotherapy or not (n=41)
F) Overall survival for patients with cervical histology by receipt of postoperative chemotherapy or not (n=41)

Conclusion/Implications: In this early assessment of postoperative chemotherapy following pelvic exenteration there was no association with outcome. Postoperative treatment decisions, especially in higher risk cases, require larger series and must be individualized.

PR095 / #215 / Poster Board #: 87

Topic: ***AS22. Vulvar and Vaginal Cancer***

HPV-ASSOCIATED AND HPV-INDEPENDENT VULVAR SQUAMOUS CELL CARCINOMA: IS THERE AN IMPACT OF RESECTION MARGINS ON LOCAL RECURRENCE?

Marilyn Boo[1], Lynn Sadler[2], Susan Bigby[3], Lois Eva[4]
[1]University of Auckland, Department Of Health Science And Department Of Medicine, Auckland, New Zealand, [2]Women's health Auckland City Hospital, Department Of Obstetrics And Gynecology, Auckland, New Zealand, [3]Middlemore Hospital, Department Of Histopathology, Auckland, New Zealand, [4]National Women's at Auckland City Hospital, Department Of Gynaecological Oncology, Auckland, New Zealand

Introduction: Vulvar Squamous Cell Carcinoma (VSCC) is classified as Human Papilloma Virus Associated (HPV-A) or HPV Independent (HPV-I), with HPV-I VSCC having greater risk of recurrence and poorer survival. Surgical guidelines do not distinguish between the aetiologies and all previous surgical margins publications report the aetiologies together, traditionally recommending a 8mm pathological margin. This study investigates the impact of resection margins on VSCC first local recurrence stratified by HPV-A and HPV-I subtypes.

Methods: A retrospective single centre clinico-pathological case note review of 314 patients treated with primary surgery for VSCC between January 1990 to December 2018. The impact of resection margins on first local recurrence was assessed for HPV-A and HPV-I tumours separately in both univariable and multivariable analyses.

Results: Local recurrences occurred in 9/143 HPV-A VSCC (6.3%) compared to 45/171 HPV-I VSCC (26.3%). In HPV-A VSCC, resection margins <8mm compared to >=8mm were not associated with local recurrence in univariable analysis (HR 0.63, 95% CI 0.17-2.39, p=0.50). Low case numbers prevented multivariable analysis. In HPV-I VSCC, resection margins <8mm were associated with increased local recurrence compared to >=8mm in univariable analysis (HR 1.90, 95% CI 1.05-3.44, p=0.03), but this finding was attenuated in the multivariable analysis (HR 1.55, 95% CI 0.79-3.05, p=0.20).

Conclusion/Implications: In HPV-I VSCC, there is some evidence that resection margins may impact local recurrence, but further prospective study is needed. Analysis for HPV-A VSCC was limited by the low recurrence rate. HPV testing may be utilised in VSCC management protocols to individualise treatment.

PR096 / #261 / Poster Board #: 85

Topic: ***AS22. Vulvar and Vaginal Cancer***

THE EFFECT OF KNOWN PATHOLOGICAL RISK FACTORS ON THE INCIDENCE OF METASTATIC LYMPH NODES AND SURVIVAL IN EARLY-STAGE VULVAR CANCER- SEER ANALYSIS.

Chen Nahshon[1], Mario Leitao[2], Ofer Lavie[1], Yakir Segev[1]
[1]Carmel Medical Center, Obstetrics & Gynecology, Haifa, Israel, [2]Memorial Sloan Kettering Cancer Center, Gynecology Service, Department Of Surgery, New York, United States of America

Introduction: We aimed to evaluate, in a large database of patients with vulvar cancer, the incidence of positive lymph nodes with relation to known pathological risk factors, and specifically among those with apparent low grade, small size tumors.

Methods: We used the Surveillance, Epidemiology and End Results (SEER) database to identify vulvar squamous cell cancer (SCC) patients, with known tumor size and regional lymph nodes examined. A comparison between patients who had positive and negative lymph nodes was conducted, with relation to survival. Subgroup analysis was conducted in patients diagnosed with grade 1 vulvar SCC and tumor size up to 2 cm according to the status of lymph nodes.

Results: Multivariate analysis found that both grade of disease and tumor size were significant factors in predicting lymph nodes status. Among those with tumors of low grade, small size tumors up to 2 cm, the odds ratio for positive lymph nodes was found to be 2.5 for those with tumor size more than 1 cm. In a multivariate survival analysis older age, larger tumor size and positive lymph nodes were independently associated with decreased survival.

Conclusion/Implications: Our study confirmed that among small size tumors, those above 1 cm size have a significantly increased risk for positive nodes compared to those under the size of than 1 cm, and among this specific group, patients with nodes positive have decreased survival. Future studies are needed to answer the question, if in the era of sentinel node procedure, it is safe to omit lymph node evaluation all together.

PR097 / #455 / Poster Board #: 86

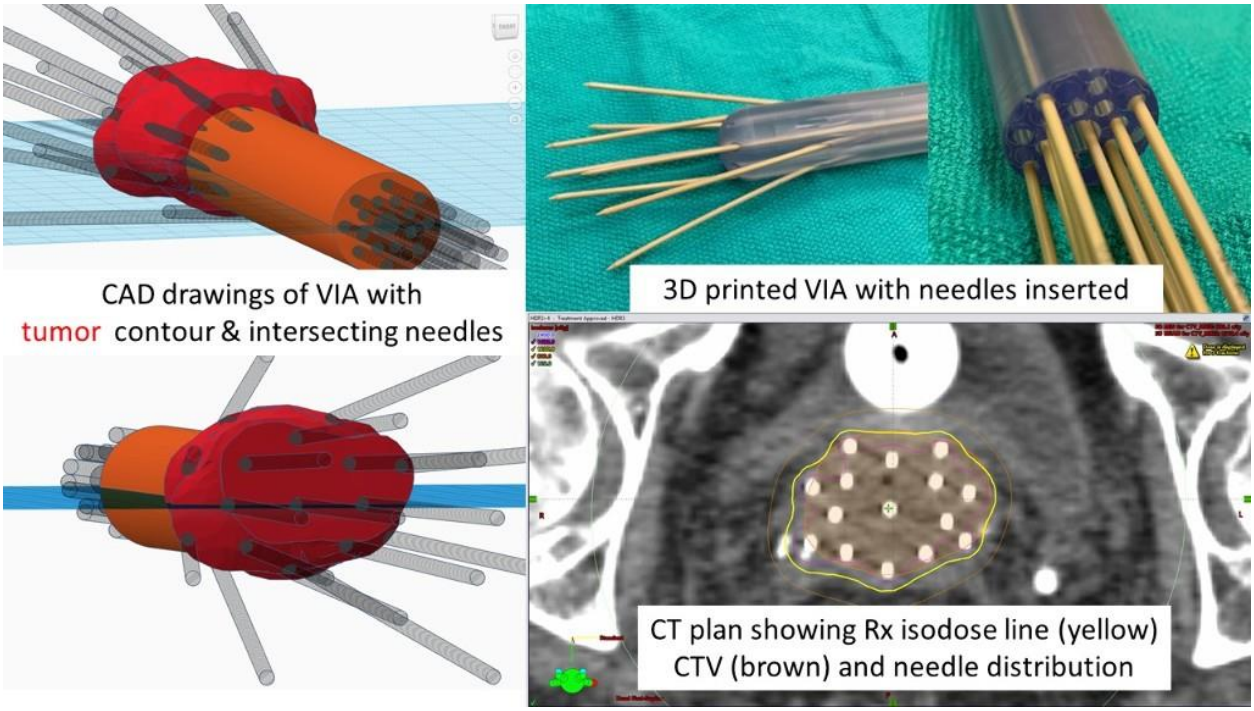
Topic: ***AS22. Vulvar and Vaginal Cancer***

3D-PRINTED VAGINAL INDIVIDUALIZED APPLICATOR (VIA) SIMPLIFIES PROCEDURE AND OPTIMIZES DOSIMETRY FOR GYNECOLOGIC INTERSTITIAL BRACHYTHERAPY

Thomas Niedermayr, Elizabeth Kidd
Stanford University, Radiation Oncology, Palo Alto, United States of America

Introduction: Optimally placing interstitial needles for interstitial only gynecologic brachytherapy requires time and expertise. Individualized vaginal templates to guide needles to dosimetrically beneficial positions could simplify interstitial procedures, decrease procedure time, improve needle distribution and optimize dosimetry.

Methods:



We developed a novel approach using 3D printed Vaginal Individualized Applicator (VIA) templates that contain internal channels that guide interstitial needles from the vaginal introitus to the desired locations within the tumor. A series of 9 patients underwent 2 interstitial procedures each separated by approximately 1 week with the first procedure involving standard freehand/template-based interstitial and the second procedure utilizing a customized VIA. All patients underwent a pre-brachytherapy MRI, and both CT and MRI were performed following interstitial placement.

Results: We have created and used clinically 3D printed VIA templates for interstitial gynecologic brachytherapy. In clinical use the novel VIA had an average procedure time of 44.8 minutes, approximately 43% shorter than the average of 79.1 minutes for the standard interstitial cases. The average CTV volume was 32.1 cc for the initial standard approach and 26.9 cc for VIA. The traditional and VIA cases averaged similar number of needles (14, 3) and maintained similar excellent dosimetry with an average CTV V100% of 94.4%, 94.5%, respectively.

Conclusion/Implications: Our team developed a novel 3D printed VIA template that significantly facilitates gynecologic interstitial brachytherapy by simplifying the placement of needles and significantly decreasing procedure time while maintaining excellent dosimetry.

PR098 / #798 / Poster Board #: 88

Topic: ***AS22. Vulvar and Vaginal Cancer***

HPV SCREENING IS EFFECTIVE AGAINST VAGINAL AND VULVAR CANCERS

Maija Vahteristo[1], Maarit Leinonen[2], Tytti Sarkeala[1], Ahti Anttila[1], Sirpa Heinävaara[1]
[1]Finnish Cancer Registry, Mass Screening Registry, Helsinki, Finland, [2]Finnish Institute for Health and Welfare, Department Of Knowledge Brokers, Helsinki, Finland

Introduction: Cervical cancer is not the only cancer attributable to human papillomavirus (HPV). Of vaginal cancers around 78% and of vulvar cancers around 25% are caused by HPV. The number of these cancers is estimated to grow among younger women as HPV prevalence rises. The world population growth and aging will also increase the burden of these cancers. Our aim was to examine if HPV screening for cervical cancer could have an additional beneficial effect and prevent also vaginal and vulvar cancers. To assess this, we used a long-term follow-up data of the Finnish randomized HPV screening trial.

Methods: Between 2003 and 2007, over 236 000 individuals were randomized (1:1) to HPV or to cytology screening in Southern Finland. The median follow-up time was 15 years. To compare the study arms, we calculated the incidence rate ratios for vaginal and vulvar cancers combined using Poisson regression. Analyses were performed with the intention to treat -principle.

Results: During 3,5 million person-years of follow-up, we detected a total of 51 vaginal or vulvar cancers and 12 cancer deaths in the HPV arm, and 78 cancers and 18 cancer deaths in the cytology arm. The incidence rate ratio for vaginal and vulvar cancers was 0.67 (95% CI 0.47–0.94) in the HPV arm compared to cytology arm.

Conclusion/Implications: Based on our results, HPV screening could prevent vaginal and vulvar cancers. The result is promising and suggests that the growing burden of vaginal and vulvar cancers could be reduced by HPV screening. Further research on the topic is needed.