Featured printed posters will be presented onsite following this schedule. The printed posters will be displayed on the 5th floor of the Meeting Venue in the Poster Area.

Featured poster presenters were requested to submit an E-Poster and a short audio file as well. Registered Delegates will have access to all posters in the E-Poster Gallery located within the Meeting Portal from September 28, 2022 (09:00 am EDT (New York)) until December 28, 2022.
MOLECULAR CLASSIFICATION OF ENDOMETRIAL CANCERS USING AN INTEGRATIVE DNA SEQUENCING PANEL

Soyoun Rachel Kim1, Leslie Oldfield2, Espin-Garcia Osvaldo3, Kathy Han4, Danielle Vicus5, Lua Eiriksson5, Alicia Tone1, Aaron Pollett7, Emily Van De Laar1, Stephanie Pederson2, Johanna Wellum2, Blaise Clarke7, Marcus Bernardini1, Sarah Ferguson1

1Princess Margaret Cancer Centre/University Health Network/Sinai Health Systems, Gynecology Oncology, Toronto, Canada, 2University of Toronto, Medical Biophysics, Toronto, Canada, 3Princess Margaret Cancer Centre/University Health Network, Biostatistics, Toronto, Canada, 4University of Toronto, Radiation Oncology, Toronto, Canada, 5Sunnybrook Health Science Center, Gynecologic Oncology, Toronto, Canada, 6Juravinski Cancer Centre, Gynecologic Oncology, Hamilton, Canada, 7University of Toronto, Laboratory Medicine And Pathobiology, Toronto, Canada

Objectives: Molecular classification of endometrial cancers (EC) is critical for prognostication, but adoption into clinical practice remains challenging due to complexity and costs of sequencing. We aimed to develop a simple molecular technique to classify EC using a high-depth targeted sequencing panel.

Methods: Leveraging on a prospective study of newly diagnosed EC from three cancer centers, 181 formalin-fixed paraffin-embedded (FFPE) samples were sequenced. Our panel identified somatic mutations, copy number variants, insertions/deletions, loss of heterozygosity, structural rearrangements and promoter methylation from a single aliquot of DNA. Variants were analyzed for pathogenicity and clinicopathologic information was collected.

Results: Of 181, 86 (48%) were classified as microsatellite instability-high (MSI-h/MMRd), of which 62 (72%) harbored MLH1 promoter methylation and 24 (27%) had pathogenic variants in MMR genes. Of cases with single classifier, three (1.6%) had POLE mutation (POLEmut), 15 (8%) had p53 variant (p53mut) and 61 (34%) had no specific molecular profile. Sixteen (9%) were multiple classifiers, with 8 (4%) MMRd-p53mut, 6 (3%) MMRd-POLEmut, 1 (0.5%) MMRd-POLEmut-p53mut, and 1 (0.5%) POLEmut-p53mut. Survival outcomes stratified similarly to TCGA, but when MMRd group was subclassified, MLH1 promoter methylated group did worse than those with somatic MMR pathogenic variants (OS 0.72 vs 1.00; p=0.013 and RFS 0.70 vs 0.92; p=0.032) whereas those with somatic MMR pathogenic variants had similar outcomes as the POLEmut subtype.
Conclusions: Our NGS panel can classify EC into 4 TCGA subgroups through a simplified process. The difference in survival between MLH1 methylated group within MMRd cohort suggests that further subclassification is required for accurate prognostication.
ARE MISMATCH REPAIR DEFICIENT ENDOMETRIAL CANCER RECURRENCES MORE SALVAGEABLE THAN INTACT COHORT?

Soyoun Rachel Kim¹, Ilias Ettayebi², Gabrielle Trepanier³, Lucy Zhao⁴, Emily Van De Laar¹, Espin-Garcia Osvaldo⁵, Aaron Pollett⁶, Lua Eiriksson³, Kathy Han⁷, Sarah Ferguson⁸
¹Princess Margaret Cancer Centre/University Health Network/Sinai Health Systems, Gynecology Oncology, Toronto, Canada, ²University of Toronto, Faculty Of Medicine, Toronto, Canada, ³Juravinski Cancer Centre, Gynecologic Oncology, Hamilton, Canada, ⁴McMaster University, Faculty Of Health Sciences, Hamilton, Canada, ⁵Princess Margaret Cancer Centre/University Health Network, Biostatistics, Toronto, Canada, ⁶University of Toronto, Laboratory Medicine And Pathobiology, Toronto, Canada, ⁷University of Toronto, Radiation Oncology, Toronto, Canada, ⁸University of Toronto, Gynecologic Oncology, Toronto, Canada

Objectives: Studies suggest increased radiosensitivity in mismatch repair deficient (MMRd) endometrial cancers (ECs) compared to MMR intact (MMRi) cohort. The aim of the study was to compare the recurrence patterns between MMRd and MMRi EC and assess whether the use of radiation leads to higher salvage in MMRd recurrences.

Methods: Newly diagnosed EC of all stages and histology were prospectively recruited from 3 cancer centers in Ontario, Canada between 2015-2018. Tumors were reflexively assessed for MMR by immunohistochemistry. Clinicopathological, survival and recurrence details were compared between the MMRd and MMRi cases.

Results: Of 666 cases, there were 83 (12%) recurrences, with 26 (31%) in MMRd and 57 (69%) in MMRi cohort after median follow-up of 26 months. There were no differences in their stage, grades, lymphovascular space invasion or type of adjuvant therapy. Local vaginal/pelvic recurrences were more common in the MMRd than MMRi cohort (65% vs. 30%) whereas distant recurrences were more common in MMRi cohort (70% vs. 35%). Post-recurrence survival was higher in MMRd cohort (43.8 vs 20 months; p=0.306). Of those with local recurrences, RT with curative intent was used in the majority (9/15 in MMRd and 7/8 in MMRi). All of those with local recurrences with MMRd tumors salvaged with curative intent RT are alive without disease (9 of 9), whereas only 2 with MMRi tumors are alive without disease (2 of 7).

Conclusions: MMRd ECs are more likely to recur locally with high rate of salvage with RT, possibly indicating the increased radiosensitivity in this cohort.
PROGNOSTIC RELEVANCE OF THE MOLECULAR BASED ESMO/ESTRO/ESP2020 RISK CLASSIFICATION IN ENDOMETRIAL CARCINOMA AFTER SURGICAL LYMPH NODE STAGING

Teresa Praetorius¹, Marcel Grube¹, Charlotte Meyer¹, Annika Rohner¹, Suzana Mittelstadt¹, Léa-Louise Volmer¹, Felix Neis¹, Sascha Hoffmann¹, Jürgen Andress¹, Christina Walter¹, Sara Brucker¹, Annette Staebler², Ernst Oberlechner¹, Bernhard Krämer¹, Stefan Kommoss¹
¹Tuebingen University Hospital, Department Of Women's Health, Tuebingen, Germany, ²Tuebingen University Hospital, Institute Of Pathology And Neuropathology, Tübingen, Germany

Objectives: The role of endometrial carcinoma (EC) molecular-based risk classification has not yet been fully explored in terms of surgical decision making. Our study aimed to investigate the prognostic relevance of the molecular-based ESMO/ESTRO/ESP2020 risk classification in EC patients after surgical lymph node staging.

Methods: Primary EC patients treated at the Tübingen University Women's Hospital between 2003 and 2016 were identified. Patients without surgical lymph-node staging and FIGO stage IV disease were excluded. Molecular-based risk classification was obtained after POLE sequencing and p53/MMR immunohistochemistry.

Results: Molecular, clinical and follow-up data was available in 424 patients. 370(87.3%) cases were endometrioid histotype, Grade distribution included 266(62.7%) G1, 73(17.2%) G2 and 85(20.0%) G3 tumors. 358(84.4%) patients were diagnosed with FIGO stage I, 23(5.4%) with stage II and 43(10.2%) with stage III disease. Molecular classification yielded 123(29.0%) MMRd, 208(49.1%) NSMP, 49(11.5%) p53 abnormal and 44(10.4%) POLE mutated tumors. Positive nodes were reported in 38(9%) patients. Low-risk was assigned in 229(54.0%), intermediate in 76(18.0%), high-intermediate in 46(10.8%) and high-risk in 73(17.2%) cases. In early stage (FIGO I), node negative tumors five year recurrence rates were 3.1% in low risk, 10.9% in intermediate risk, 22.2% in high-intermediate risk and 17.2% in high risk patients (p<0.001).

Conclusions: The adverse outcome of early stage high-intermediate and high-risk EC could not be explained by undetected lymphnode involvement in this series. Our findings may aid tailoring surgical EC treatment according to current molecular-based risk classification.
GENETIC TESTING FOLLOWING ABNORMAL IMMUNOHISTOCHEMISTRY RESULTS IN ENDOMETRIAL CANCER: A QUALITY IMPROVEMENT PROTOCOL

Hannah Karpel1, Maria Smith2, Allison Brodsky3, Bhavana Pothuri4

1New York University Grossman School of Medicine, Obstetrics And Gynecology, New York, United States of America, 2NYU Langone Health, Obstetrics And Gynecology, New York, United States of America, 3University of California San Diego, Obstetrics And Gynecology, La Jolla, United States of America, 4Gynecologic Oncology Group (GOG), Laura & Isaac Perlmutter Cancer Center, NYU Langone Health, Department Of Obstetrics/gynecology, New York City, United States of America

Objectives: Universal mismatch repair (MMR) immunohistochemistry (IHC) in endometrial cancer began at our institution in July 2015. In April 2017, genetic counselors (GC) obtained IHC data and contacted physicians to approve genetic counseling for Lynch Syndrome (LS) in eligible patients. We assessed if this protocol increased frequency of genetic counseling referrals (GCRs) and genetic testing (GT) in patients with abnormal MMR IHC.

Methods: We retrospectively (7/2015-6/2021) identified patients with abnormal MMR IHC at a large urban hospital. GCR and GT rates were compared between cases from 7/2015-4/2017 (pre-protocol) and 5/2017-6/2021 (post-protocol) with Fisher’s exact test.

Results: Of 717 patients with IHC testing, 156 (21.8%) had abnormal MMR results: MLH1/PMS2, 123; MSH2/MSH6, 10; MSH2/PMS2, 1; MSH6, 13; MLH1, 2; PMS2, 7. MLH1 hypermethylation was identified in 114 (73.1%) patients; 42 (26.9%) patients met criteria for LS screening with GT based on IHC results. Of 42 patients, 16 (38.1%) were identified before and 26 (61.9%) after protocol initiation. GCRs significantly increased from 11/16 (68.8%) to 25/26 (96.2%) in the pre-protocol versus post-protocol groups, p=0.02. There was no statistically significant difference in GT frequency between groups (10/16, 62.5% vs 23/26, 88.5%, p=0.06). Of 33 patients undergoing GT, 16 (48.5%) had LS: MSH6, 9; MSH2, 4; PMS2, 2; MLH1, 1.

Conclusions: Increased frequency of GCRs was observed following the protocol change, which is important as LS screening has clinical implications for patients and their families. Reflex protocols can maximize identification of patients for germline GT; alternatively universal GT can be considered in endometrial cancer (Levine et al. 2021).

<table>
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<tr>
<th>Table 1: Genetic Counseling and Genetic Testing Following Abnormal MMR IHC</th>
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<td>Outcome</td>
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<tr>
<td>Genetic Counseling Referral</td>
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<td>Germline Genetic Testing</td>
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Abbreviations: MMR, mismatch repair; IHC, immunohistochemistry
INTEGRATED PROFILING OF A PROSPECTIVE ENDOMETRIAL CANCER ORGANOID BIOBANK REVEALS HIGH HETEROGENEITY

Hege Berg1,2, Marta Hjelmeland1,2, Hilde Lien1,2, Heidi Espedal3,4, Sangita Pal5, Aashish Srivastava6, Tomasz Stokowy7, Ingunn Stefansson2,8, Line Bjørge1,2, Erling Hoivik1,2,4, Ingrid Haldorsen3,4, Rameen Beroukhim5,9, Camilla Krakstad1,2,5

1Haukeland University Hospital, Department Of Gynecology And Obstetrics, BERGEN, Norway, 2University of Bergen, Center For Cancer Biomarkers, Department Of Clinical Sciences, BERGEN, Norway, 3University of Bergen, Department Of Clinical Medicine, BERGEN, Norway, 4Haukeland University Hospital, Mohn Medical Imaging And Visualization Centre, Department Of Radiology, BERGEN, Norway, 5Harvard Medical School, Dana-farber Cancer Institute, Cancer Biology, MA, United States of America, 6Haukeland University Hospital, Department Of Bioinformatics, BERGEN, Norway, 7University of Bergen, Genomics Core Facility, Department Of Clinical Science, BERGEN, Norway, 8Haukeland University Hospital, Section Of Pathology, Department Of Clinical Medicine, BERGEN, Norway, 9Broad Institute of Harvard and MIT, Cancer Program, MA, United States of America

Objectives: Patient-derived cancer organoids have quickly developed as valuable tools for drug testing as they better represent the genetic background of the patient cohort. We recently published a protocol for establishing EC organoids from all types and grades of EC (Berg et al, Nat Comms Med 2021). We here present data from a prospectively collected biobank of organoids including all EC molecular subclasses. Models have been extensively profiled and evaluated for drug response, supporting high heterogeneity in EC.

Methods: Organoids were prospectively derived from resected EC tissue from consenting patients and cultured long-term in a chemically defined medium. Orthotopic xenograft mouse models, representing all subtypes of EC, were established by intra-uterine injection of organoids. All organoids were characterized by IHC, WES and RNA sequencing, and by single cell phenotyping. Organoids were treated with carboplatin, paclitaxel, and small molecule inhibitors against PARP, CHEK1/2, PIK3CA/mTOR, and CDK4/6.

Results: The organoids reflect the main molecular EC subtypes, including POLE, MSI, copy-number low and copy-number high models. We identified matched molecular alterations in patient tissue and corresponding organoids, even after long-term culturing and expansion in vivo. Model-specific chemotherapy responses were observed and reproduced in mouse models for selected organoids. Carboplatin-resistant organoids had more alterations in platinum-related genes, including BAX, DAB2IP, ATM and CASP2. However, type of genetic alteration differed between the resistant organoids. Treatment with small-molecule inhibitors identified heterogenous drug responses.

Conclusions: This state-of-the-art preclinical platform provides clinically relevant tools for use in preclinical drug trials.
A CURRENT PERSPECTIVE ON ENDOMETRIAL CARCINOMA (EC) RISK CLASSIFICATION:
RESULTS FROM AN EUROPEAN MULTICENTRE INITIATIVE.

Annika Rohner¹, Marcel Grube¹, Katharina Knoll², Amy Lum³, Christine Brambs⁴, Nina Pauly⁵, Felix Kommoss⁶, Sabine Heublein⁷, Marco Johannes Battista⁸, Suzana Mittelstadt¹, Teresa Praetorius¹, Annette Hasenburg⁶, Beyhan Ataseven⁵, Aline Talhouk⁹, Joachim Diebold⁴, Alain-Gustave Zeimet², Annette Staebler¹⁰, Jessica Mcalpine¹¹. Stefan Kommoss¹
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Objectives: EC management has been plagued by poor interobserver reproducibility of histomorphologic features for a long time. More recently integration of TCGA-inspired molecular classification into pathology reporting and treatment guidelines was recommended. It was the aim to investigate the impact of adding molecular classification to a patient cohort diagnosed in an era before molecular classification was introduced to routine practice.

Methods: Consecutive primary EC patients diagnosed in five major European gynonc centres in 2016 were identified and retrospectively submitted to molecular testing. Original risk classification (“RC16”, ESMO/ESTRO/ESGO 2016) was compared to current molecular-based risk assessment (“RC20”, ESGO/ESTRO/ESP 2020).

Results: 226 patients were identified, complete clinical and molecular data was available from 212 cases with a median follow-up time of 52.6 months. Median age was 65.0 years (30.9-90.9), 187 cases (88.2%) were endometrioid histotype. Grading included 92(43.4%) G1, 72(34.0%) G2, and 47(22.2%) G3 tumors. 107(50.5%) patients were diagnosed with FIGO stage IA, 55(25.9%) with IB, n=17(8.0%) with II, and 33(15.6%) with stage III/IV disease. Molecular classification yielded 46(21.7%) MMR-D, 18(9.0%) POLE, 47(22.2%) p53abn, and 100(47.2%) NSMP tumors. If RC16 was compared to RC20, an alteration of risk was observed in 20.2 % with a higher risk in 16(7.5%) and lower risk in 27(12.7%) respectively.

Conclusions: We were able to demonstrate significant alterations of endometrial carcinoma risk-assessment in a substantial number of patients after adding TCGA-derived molecular data to conventional risk classification. Molecular based management may help to avoid over- and undertreatment and will give rise to precision medicine strategies in endometrial carcinoma patient care.
FP007 / #877

POSTER ROUNDS WITH THE PROFESSORS: GROUP E3
29-09-2022 11:25 AM - 11:55 AM

HORMONAL BIOMARKERS REMAIN PROGNOSTIC RELEVANT WITHIN THE MOLECULAR CLASSIFICATION IN ENDOMETRIAL CANCER

Stephanie Vrede¹,², Willem Jan Weelden¹,², Hans Bulten³, Jutta Huvila⁴, Xavier Matias-Guiu⁵, Antonio Gil-Moreno⁶,⁷, Jasmin Asberger⁸, Sanne Sweegers⁹, Louis Putten², Heidi Küsters-Vandevelde⁹, Astrid Eijkelenboom³, Casper Reijnen¹⁰, Eva Colas¹¹, Vit Weinberger¹², Marc Snijders¹, Roy Kruitwagen²,¹³, Johanna Pijnenborg¹⁴

¹Canisius-Wilhelmina ziekenhuis, Obstetrics And Gynaecology, nijmegen, Netherlands, ²Radboud university medical center, Obstetrics And Gynaecology, Nijmegen, Netherlands, ³Radboud university medical center, Pathology, Nijmegen, Netherlands, ⁴University of Turku, Turku University Hospital, Department Of Pathology, Turku, Finland, ⁵Hospital Universitari Arnu de Vilanova, Pathology And Molecular Genetics And Research Laboratory, Lleida, Spain, ⁶Vall Hebron University Hospital, Gynaecology, Barcelona, Spain, ⁷Vall Hebron University Hospital, Pathology, Barcelona, Spain, ⁸Medical Center – University of Freiburg, Obstetrics And Gynaecology, Freiburg, Germany, ⁹Canisius-Wilhelmina ziekenhuis, Pathology, Nijmegen, Netherlands, ¹⁰Radboud university medical center, Radiation Oncology, Nijmegen, Netherlands, ¹¹Vall Hebron institute of research, Universitat Autònoma de Barcelona, Biomedical Research Group In Gynecology, Barcelona, Spain, ¹²University Hospital in Brno and Masaryk University, Obstetrics And Gynaecology, Brno, Czech Republic, ¹³Maastricht University Medical Center (MUMC), Department Of Obstetrics And Gynecology, Maastricht, Netherlands, ¹⁴Radboud university medical center, Department Of Obstetrics And Gynecology, Nijmegen, Netherlands

Objectives: The relevance of hormonal biomarkers in endometrial cancer (EC) has been well-established. A revised cut-off for estrogen receptor/progesterone receptor (ER/PR) expression into three subgroups was shown to improve prognostication, however, this has not been related to the four molecular subgroups. Therefore, we aimed to investigate the prognostic relevance of this three-tiered ER/PR model within the molecular subgroups in EC.

Methods: A retrospective multicenter study within the European Network for Individualized Treatment (ENITEC) network was performed. ER/PR expression was classified into: high-risk (0-10%), intermediate-risk (20-80%) and low-risk (90-100%). The molecular subgroups were conducted based on Next Generation Sequencing, allocating patients into polymerase epsilon (POLE)-mutant, microsatellite instable (MSI), tumor protein (TP53)-mutated and no-specific molecular profile (NSMP).

Results: A total of 387 patients were included with a median follow-up of 5.2-years. There were 8.3% (n=32) POLE-mutant, 22.5% (n=87) MSI, 13.7% (n=53) TP53-mutated and 55.6% (n=215) NSMP tumors. Among all molecular subgroups, patients with ER/PR 0-10% expression had significantly worse disease-specific survival (DSS) compared to ER/PR 20-80% or 90-100%. Interestingly within TP53-mutated, patients with ER/PR 90-100% expression showed an excellent DSS (100%) compared to ER/PR 20-80% and 0-10% (Figure 1). In multivariable analyses ER/PR 0-10%, TP53-mutated, lymphovascular space invasion and FIGO stage remained independent prognostic factors for reduced DSS (respectively, HR 2.59 (95%-CI 1.32-5.03) P=0.005, HR 2.71 (95%-CI 1.35-5.43) P=0.005, HR 2.27 (95%-CI 1.15-4.45) P=0.018, HR 4.42 (95%-CI 2.16-9.01)
P<0.001).

Figure 1: Disease-specific survival of the ER/PR subgroups within TP53-mutated.

Conclusions: ER/PR expression remains prognostic relevant in all molecular subgroups, strengthened by the three-tiered cut-off. We therefore recommend routine evaluation of ER/PR expression in clinical practice.
IMMUNOMETABOLIC CHANGES DURING WEIGHT LOSS INDUCE TUMOR IMMUNOGENICITY RESULTING IN TUMOR REGRESSION

Martin Brennan¹, Lydia Dyck¹, Hannah Prendeville¹, Donal Brennan², Lydia Lynch¹
¹Trinity College Dublin, School Of Biochemistry And Immunology, Dublin, Ireland, ²University College Dublin Gynaecological Oncology Group, Ucd School Of Medicine, Mater Hospital, Dublin, Ireland

Objectives: Endometrial cancer is the most common cancer of the female reproductive tract, and obesity is the greatest risk factor for endometrial cancer. We have recently found that in addition to enhancing tumor growth, obesity also impairs the anti-tumor immune response. Here, we investigated the effect of weight loss on the immune landscape of the tumor, during an interventional treatment for endometrial cancer in obesity patients.

Methods: Metabolic surgery was performed on 12 patients deemed suitable (>18 years, BMI of 40kg/m² and diagnosis of grade 1 or 2 endometrial adenocarcinoma). Bulk-RNA sequencing of tumor biopsies was performed before and after surgery/weight loss. Formalin-fixed, paraffin-embedded endometrial tumor biopsies were processed for immunohistochemical staining of PD-L1, CD8 and CD3.

Results: Of the 12 patients, all had significant weight loss 6 months post-surgery, with an average of 24% body fat loss. Complete pathological response was observed in 9 out of 12 patients, stable disease in 2 patients and progressive disease in one patient, at 6 months post-metabolic surgery. Tumor biopsy sequencing before and after weight loss shows a significant increase in HLA class I and class II genes. Immunostaining showed that weight loss increased CD8 T-cell infiltration and PD-L1 expression in endometrial tumors.

Conclusions: Our results demonstrate the important role of weight loss in directing anti-tumor immunity in obese endometrial cancer patients by creating a more immunogenic tumor environment through upregulation of HLA.
IMMUNE-RELATED ENDPOINTS IN PATIENTS WITH ADVANCED OR RECURRENT ENDOMETRIAL CANCER TREATED WITH DOSTARLIMAB IN THE GARNET STUDY

**Objectives:** Dostarlimab is a programmed death 1 (PD-1) inhibitor approved in the US as monotherapy in patients with mismatch repair deficient (dMMR) advanced/recurrent endometrial cancer (EC) that has progressed on or after platinum-based chemotherapy or dMMR solid tumors that have progressed on or after prior treatment, with no satisfactory alternative treatment options; and in the EU as monotherapy in patients with dMMR/MSI-H (microsatellite instability–high) advanced/recurrent EC that has progressed on or after platinum-based chemotherapy. We report efficacy endpoints by immune-related RECIST (irRECIST) per investigator assessment (IA) for the EC cohorts of the GARNET trial.

**Methods:** GARNET is a multicenter, open-label, single-arm phase 1 study. Assignment to cohort A1 (dMMR/MSI-H EC) or A2 (mismatch repair proficient [MMRp]/microsatellite stable [MSS] EC) was based on local assessment. Patients received 500 mg of dostarlimab intravenously Q3W for 4 cycles, then 1000 mg Q6W until disease progression, discontinuation, or withdrawal. Immune-related endpoints (irORR, irDOR, and irPFS) were prespecified secondary endpoints.

**Results:** The irRECIST efficacy-evaluable population included 152 dMMR/MSI-H and 160 MMRp/MSS patients with measurable disease at baseline and ≥6 months' follow-up per IA. irORR and irDOR were similar to the primary endpoints of ORR and DOR by BICR per RECIST v1.1 (Table). For dMMR/MSI-H, median irPFS was 11.2 mo versus median PFS of 6.0 mo, although the probability of remaining progression free at 6, 12, or 18 mo was similar. Safety was previously reported.
Conclusions: In line with the study primary endpoints, secondary efficacy endpoints by irRECIST demonstrate the benefit of dostarlimab in patients with EC.

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<td>Immune-related secondary endpoints (irRECIST by IA)</td>
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<td>Variable</td>
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<tr>
<td>Median follow-up, mo</td>
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<tr>
<td>iORR, n (%), 95% CI</td>
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<td>iPR, n (%)</td>
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<td>iDCR, n (%), 95% CI</td>
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<td>Response ongoing, n (%)</td>
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<td>Median iDOR (95% CI), mo</td>
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<td>Median iPFS, % (95% CI), mo</td>
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*IRRECIST includes 9 patients with dMMR/MSI-H EC and 4 patients with MMRP/MSS EC who were assessed as having measurable disease at baseline per IA.

**Includes CR, PR, and NR ≥12 weeks.

*Includes CR, PR, and SD ≥12 weeks.

BICR, blinded independent central review; CR, complete response; DCR, disease control rate; dMMR, mismatch repair deficient; DOR, duration of response; EC, endometrial cancer; IA, investigator assessment; ir, immune-related; MMRP, mismatch repair proficient; MSI-H, microsatellite instability-high; MSS, microsatellite stable; NR, not reached; ORR, objective response rate; PFS, progression-free survival; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.
MOLECULAR LANDSCAPE OF ERBB2/HER2 GENE AMPLIFICATION AMONG PATIENTS WITH ENDOMETRIAL CARCINOMA.

Dimitrios Nasioudis, Nawar Latif, Ashley Haggerty, Lori Cory, Sarah Kim, Mark Morgan, Fiona Simpkins, Emily Ko
University of Pennsylvania, Division Of Gynecologic Oncology, Philadelphia, United States of America

Objectives: Investigate the incidence of ERBB2/HER2 gene amplification among patients with endometrial cancer.

Methods: The AACR GENIE v12.0 database was accessed and patients with endometrioid (EEC), serous (USC), clear cell (UCC) and carcinosarcoma (UCS) and data on copy-number gene alterations were selected for further analysis. Incidence of ERBB2/HER2 gene amplification was investigated while the genomic profile of patients with ERBB2 amplification was further explored. Data from the OncoKB database was utilized to determine pathogenic gene alterations.

Results: A total of 2784 patients were identified; 1648 with EEC (1708 samples), 573 with UPSC (593 samples), 389 with UCC (389 samples) and 93 with UCS (94 samples). Overall incidence of ERBB2 amplification was 4.5% (n=124); 12% (n=71) for UPSC, 8.5% (n=8) for UCC, 7.2% (n=28) for UCS and 1% (n=17) for EEC. Among samples with ERRB2 amplification, the most prevalent alterations involved the TP53 (91%), PIK3CA (47%), CCNE1 (23%), FBXW7 (24%), MYC (13%), PIK3R1 (17%), KRAS (10%), ARID1A (8%), and ERBB3 (8%) genes. For patients with EEC and ERBB2 amplification, 64.7% (n=11) had a TP53 mutation. However, among patients with EEC and a TP53 mutation (n=304), the overall incidence of ERBB2 amplification was 3.6%.

Conclusions: While ERBB2 amplification is frequently encountered among patients with USC, a high incidence was also observed among those with UCC, and UCS. For patients with EEC, incidence of ERBB2 amplification is low, especially in the absence of TP53 mutations. Half of tumors with ERBB2 amplification harbored a PIK3CA mutation providing rationale of the combination of transtuzumab with mTOR/AKT inhibitors in future trials.
IS REFLEX MLH1 PROMOTER HYpermethylation TESTING FOLLOWING MLH1 LOSS BY IMMUNOHISTOCHEMISTRY IN ENDOMETRIAL CARCINOMA BEST PRACTICE?

Anna Plotkin, Ekaterina Olkhov-Mitsel, Sharon Nofech-Mozes
Sunnybrook Health Sciences Centre, Laboratory Medicine And Molecular Diagnostics, Toronto, Canada

Objectives: Reflex screening of newly diagnosed endometrial carcinomas (EC) was introduced in Ontario for women <70 in 2018 and regardless of age in 2020. MLH1 deficient (MLH1-d) cases by immunohistochemistry (IHC) are further analyzed to detect MLH1 promoter hypermethylation (MLH1PHM). Women with MLH1PHM tumors are considered at low risk for Lynch Syndrome and forgo referral to cancer genetic clinics. Regardless of MLH1PHM status, MLH1-d IHC helps to classify EC according to TCGA-based molecular classification and for consideration of immunotherapy. This study sought to examine the proportion of MLH1PHM in MLH1-d cases.

Methods: Retrospective audit of pathology reports (2018-2021) in a major community laboratory in Ontario, Canada (Life Labs) identified EC samplings that were evaluated by IHC for MMR proteins (MLH1, MSH2, MSH6, and PMS2) followed by MLH1PHM test, when appropriate.

Results: Among 1229 consecutive EC samples tested by MMR-IHC, 14 could not be classified due to insufficient tumor cells or ambiguous staining. The remaining 1215 ECs were classified into MMR-d (n=324, 26.7%) or proficient (n=891, 73.3%). Among MMR-d cases, 274 showed loss of MLH1 and 206 had available MLH1 methylation testing data. MLH1PHM was detected in 201/206 (97.6%), designated as most likely sporadic whereas 5/206 cases (2.4%) were not hypermethylated raising the possibility for Lynch syndrome.

Conclusions: Our audit confirms the feasibility of testing endometrial samplings for MMR-IHC and promoter hypermethylation testing. MLH1PHM accounts for vast majority of MLH1/PMS2-deficient cancers in a universally screened EC population. The very high proportion of MLH1PHM challenges the practice algorithm and raises the need to explore practice revision.
Objectives: Dostarlimab is an approved programmed death 1 (PD-1) inhibitor. PD-1 therapy can lead to immune-related adverse events (irAEs). Here we report on the management of irAEs across multiple tumor types evaluated in GARNET.

Methods: GARNET is a multicenter, open-label, single-arm phase 1 study with dose expansion in multiple tumor types: dMMR solid tumors, mismatch repair proficient EC, non–small cell lung cancer, and platinum-resistant ovarian cancer. Patients received 500 mg of dostarlimab intravenously Q3W for 4 cycles, then 1000 mg Q6W until disease progression, discontinuation, or withdrawal.

Results: At this third interim analysis of GARNET, the safety population included 605 patients. irAEs were experienced by 32.2%, with 10.1% of patients experiencing grade ≥3 irAEs (Table). Few, 5.5%, discontinued treatment because of an irAE. No irAEs led to death. Of patients experiencing irAEs, 64.6% were treated with immune modulatory medications (IMMs; referring to steroids, immune suppressant, and/or thyroid therapy); 58.7% of these patients experienced resolution. Average time to resolution was 69 days. For the 35.4% of patients not treated with IMMs, 56.5% experienced a resolution. Average time to resolution was 67 days. The most common irAEs were hypothyroidism (7.6%; 45 of 46 [97.8%] patients treated with thyroid therapy) and arthralgia (5.6%; 8 of 34 [23.5%] patients treated with steroids).

Conclusions: Across all tumor types evaluated in GARNET, 32.2% of patients experienced irAEs, 68.7% of whom experienced grade 2 events. 58.7% of patients experienced resolution of irAEs upon treatment.
with an IMM. Overall discontinuation due to irAEs was low.

<table>
<thead>
<tr>
<th>Event, n (%)</th>
<th>dMMR EC N=190</th>
<th>dMMR NEC N=191</th>
<th>MMRp EC N=145</th>
<th>NSCLC N=67</th>
<th>PROC N=14</th>
<th>Other* N=38</th>
<th>Overall monotherapy N=409</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any irAE</td>
<td>58 (31.9)</td>
<td>61 (31.9)</td>
<td>39 (26.9)</td>
<td>25 (37.3)</td>
<td>4 (28.6)</td>
<td>8 (21.1)</td>
<td>195 (32.2)</td>
</tr>
<tr>
<td>Grade 3 irAEs</td>
<td>20 (13.3)</td>
<td>19 (5.9)</td>
<td>13 (6.0)</td>
<td>8 (11.9)</td>
<td>0 (2.9)</td>
<td>1 (2.6)</td>
<td>61 (16.1)</td>
</tr>
<tr>
<td>Any irAEs leading to treatment discontinuation</td>
<td>14 (9.3)</td>
<td>8 (4.2)</td>
<td>8 (5.5)</td>
<td>3 (4.5)</td>
<td>0</td>
<td>0</td>
<td>33 (5.5)</td>
</tr>
<tr>
<td>irAEs in ≥1% of patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>13 (8.7)</td>
<td>10 (5.2)</td>
<td>12 (8.3)</td>
<td>7 (10.4)</td>
<td>1 (7.1)</td>
<td>3 (7.9)</td>
<td>46 (7.6)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>10 (6.7)</td>
<td>7 (3.7)</td>
<td>9 (6.2)</td>
<td>6 (9.0)</td>
<td>1 (7.1)</td>
<td>1 (2.6)</td>
<td>34 (5.6)</td>
</tr>
<tr>
<td>Grade 3 irAEs in ≥1% of patients</td>
<td>4 (2.7)</td>
<td>6 (3.1)</td>
<td>3 (2.1)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>13 (2.1)</td>
</tr>
<tr>
<td>Alanine aminotransferase increased</td>
<td>1 (0.7)</td>
<td>5 (2.6)</td>
<td>5 (3.4)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11 (1.8)</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>2 (1.3)</td>
<td>1 (0.5)</td>
<td>1 (0.7)</td>
<td>2 (3.0)</td>
<td>0</td>
<td>0</td>
<td>6 (1.6)</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>3 (2.0)</td>
<td>3 (1.6)</td>
<td>2 (1.4)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>8 (1.3)</td>
</tr>
<tr>
<td>irAEs leading to treatment discontinuation in ≥1% of patients</td>
<td>3 (2.0)</td>
<td>2 (1.0)</td>
<td>1 (0.7)</td>
<td>2 (3.0)</td>
<td>0</td>
<td>0</td>
<td>8 (1.3)</td>
</tr>
</tbody>
</table>

*Other includes 16 patients with MMR status unknown EC, 12 patients with MMR status unknown NEC, and 7 patients with MMRp NEC.

irAEs are identified as any grade 2 adverse event based on prespecified predefined terms.

dMMR, mismatch repair deficient; EC, endometrial cancer; IMM, immune modulatory medication; irAE, immune-related adverse event; MMRp, mismatch repair proficient; NEC, non-endometrial cancer; NSCLC, non–small cell lung cancer; PROC, platinum-resistant ovarian cancer.
SURVIVAL IMPACT OF ADJUVANT RADIOTHERAPY IN UTERINE CARCINOSARCOMA—A SEER BASED STUDY

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Objectives: While the role of adjuvant radiotherapy (aRT) has been well-established in the treatment of high-risk endometrial cancer, randomized trial data regarding aRT use in uterine carcinosarcoma (UCS), a rare subtype, is limited. Our objective is to compare the survival impact of aRT versus chemotherapy alone in the treatment of UCS using the Surveillance, Epidemiology, and End Results (SEER) database.

Methods: The SEER database was queried for all patients diagnosed with stage II-IV UCS. Patients were excluded who did not undergo surgery and chemotherapy. Survival was analyzed using the Kaplan-Meier method. Multivariate Cox regression analysis was used to evaluate the survival impact of aRT while controlling for patient age, diagnosis year, race/ethnicity, stage, grade, number of positive regional lymph nodes, and tumor size.

Results: A total of 2,362 patients were identified. A significant improvement in cause specific survival (CSS) was noted in patients who underwent combination therapy (vaginal brachytherapy [VB] plus external beam radiation therapy [EBRT]) versus chemotherapy alone (hazard ratio [HR] 0.805, 95% confidence interval [CI] 0.674-0.961, p<0.05). VB and EBRT each given exclusively versus chemotherapy alone resulted in improved overall survival (OS) ([VB HR 0.852, 95% CI 0.788-0.920, p<0.001], [EBRT HR 0.758, 95% CI 0.646-0.889, p=0.001]), but not cause specific survival (CSS). No difference in survival was found in VB or EBRT alone versus combination therapy, or in EBRT versus VB.

Cause specific survival by adjuvant radiotherapy group
**Conclusions**: Combination aRT with chemotherapy shows superior CSS compared to chemotherapy alone. This SEER database study validates aRT use in this rare subset of high-risk endometrial cancer.
PROCEDURAL INTERVENTIONS FOR OLIGOPROGRESSION DURING TREATMENT WITH IMMUNE CHECKPOINT BLOCKADE IN GYNECOLOGIC MALIGNANCIES

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Objectives: To evaluate feasibility and outcomes of procedural interventions for oligoprogressive disease among patients with gynecologic cancer treated with immune checkpoint blockade (ICB).

Methods: Patients with gynecologic cancers treated with ICB between 1/2013–10/2021 who underwent procedural interventions including surgical resection (OR), interventional radiology ablation (IR), or radiation therapy (RT) for oligoprogressive disease were identified. Procedures performed before ICB initiation, or ≥6 months (mos) after ICB completion were excluded. Long ICB duration prior to intervention was defined as ≥6 mos. PFS and OS were calculated from procedure date until disease progression or death, respectively.

Results: During the study period, 887 patients received ICB. Among patients with oligoprogressive disease, 41 underwent procedural intervention: 10 OR, 3 IR, and 28 RT. Primary tumor type included uterine (74%) and ovarian (23%). ICB regimen included PD-1/PD-L1 inhibitor (46%), PD-1/PD-L1 inhibitor + tyrosine kinase inhibitor (29%), PD-1/PD-L1 inhibitor + CTLA-4 inhibitor (12%), and PD-1/PD-L1 inhibitor + other (12%). Sites of oligoprogression included abdomen (32%), lung (17%), bone (17%), distant lymph node (17%), and vagina (10%). Subsequent treatment included continuation of same therapy (49%), other ICB (10%), or chemotherapy (29%). Short vs long ICB duration pre-procedure demonstrated median PFS of 9.2mos versus 5.6mos, and median OS of 36.1mos and 22.0mos, respectively.

Conclusions: Procedural interventions for patients with oligoprogression on ICB are feasible and demonstrate favorable outcomes. Early intervention appears to associate with prolonged PFS & OS. With expanding use of ICB, it is important to investigate combined modalities to maximize therapeutic benefit for patients with gynecologic cancers.
ONCOLYTIC ADENOVIRUS MEM-288 ENCODING MEMBRANE-STABLE CD40L AND IFN BETA INDUCES AN ANTI-TUMOR IMMUNE RESPONSE IN A HIGH GRADE SEROUS OVARIAN CANCER MOUSE MODEL

Pamela Peters¹, Regina Whitaker¹, Felicia Lim², Shonagh Russell³, Justin Pollara³, Elizabeth Bloom¹, Kyle Strickland⁴, Mark Cantwell⁵, Amer Beg⁶, Andrew Berchuck¹, Scott Antonia⁷, Rebecca Previs¹
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Objectives: This study investigates a novel approach for immune recruitment to the ovarian cancer microenvironment using an oncolytic adenovirus, MEM-288, encoding a modified membrane-stable CD40L (MEM40) and IFNβ.

Methods: Mouse ovarian cancer cells (STOSE-luc) were injected intraperitoneally into 7-week FVB mice and randomized to treatment with saline (n=8), GFP-expressing adenovirus (Adv-GFP, n=9) or MEM-288 (n=9) on days 12 and 15 with euthanasia on day 27. Tumors were dissociated and evaluated via flow cytometry. Splenocytes were dissociated and incubated with STOSE-luc target cells for IFN-γ enzyme-linked immunospot (ELISPOT) assay. Statistical tests of significance were calculated by one-way ANOVA.

Results: MEM-288-treated mice demonstrated improved tumor control compared to Adv-GFP and saline across multiple parameters (mean ± SD), including ascites volume (0.02 ± 0.04 mL vs. 1.1 ± 1.5 mL vs. 1.6 ± 0.95 mL; p=0.01); metastatic sites (3.1 ± 0.8 vs. 4.4 ± 2.2 vs. 5.4 ± 1.4; p=0.03); and tumor weight (0.41 ± 0.21 g vs. 0.91 ± 1.1 g vs. 1.1 ± 0.66 g; p=0.20). These anti-tumor effects directly correlated with T cell-associated immune responses in the tumor microenvironment through expansion of tumor-infiltrating CD8+ T-cells (p = 0.0005). MEM-288 induced a systemic immune response with increased number of tumor-reactive T-cells in splenocytes via IFN-γ ELISPOT assay (p=0.004) compared to other groups. CD8+ T-cell inhibitory markers CTLA4+/PD1- (p= 0.002) and CTLA4+/PD1+ (p=0.01) were decreased with MEM-288
**Conclusions:** MEM-288 has potent anti-tumor activity in an immune competent ovarian cancer mouse model, likely through recruitment of cytotoxic T-cells and promotion of a systemic anti-tumor T-cell response.
IMMUNE PROPERTIES OF TUMOR-INFILTRATING LYMPHOCYTES IN OVARIAN CLEAR CELL CARCINOMA RELATIVE TO OVARIAN HIGH-GRADE SEROUS CARCINOMA

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Objectives: A recent series of clinical trials have demonstrated the potential efficacy of immune checkpoint inhibitors (ICIs) for ovarian clear cell carcinoma (OCCC). However, little is known about the immune characteristics of OCCC. In this study, we investigated the immunologic properties of tumor-infiltrating lymphocytes (TILs) in patients with OCCC to elucidate therapeutic responses to ICIs.

Methods: We analyzed peripheral blood mononuclear cells (PBMCs) and TILs from patients with ovarian cancer. CD8 and regulatory T (Treg) cells of treatment-naïve OCCC (n=22) and high-grade serous carcinoma (HGSC) patients (n=35) were compared using flow cytometry.

Results: First, we explored the immune characteristics of OCCC-infiltrating T cells. The percentages of CD8 and FoxP3⁺CD4 T cells were higher in TILs than in PBMCs. Most CD8 TILs were CCR7⁻CD45RA⁻ effector memory lymphocytes. CD8 TILs exhibited higher expression of PD-1, CD39, CD103, granzyme B, Ki-67 and TCF-1, compared with peripheral CD8 T cells. Tumor-infiltrating Treg cells were enriched with CD45RA FoxP3high effector Treg cells and showed higher expression of PD-1, CTLA-4, 4-1BB, OX-40, CD39, and CCR8, compared with peripheral Treg cells. Second, we compared TILs from patients with OCCC and HGSC. The percentage of tumor-infiltrating Treg cells was significantly lower in OCCC than in HGSC. Furthermore, tumor-infiltrating Treg cells in OCCC showed lower TOX expression and less
proliferative ability than those in HGSC.

**Conclusions:** Overall, while the exhausted phenotypes of CD8 TILs in OCCC were similar to those in HGSC, OCCC showed less infiltration of highly suppressive Treg cells. Further research is warranted to investigate infiltrating Treg cell activity in OCCC.
ROLE OF GENOME-WIDE METHYLATION PROFILING OF CIRCULATING CELL-FREE DNA BY METHYLATED DNA SEQUENCING (MED-SEQ) IN ADVANCED-STAGE OVARIAN CANCER

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1Erasmus MC Cancer institute, University Medical Center Rotterdam, Gynecologic Oncology, Rotterdam, Netherlands, 2Albert Schweitzer Hospital, Gynecology And Obstetrics, Dordrecht, Netherlands, 3Erasmus MC Cancer institute, University Medical Center Rotterdam, Department Developmental Biology, Rotterdam, Netherlands, 4Erasmus MC Cancer institute, University Medical Center Rotterdam, Internal Oncology, Rotterdam, Netherlands

Objectives: Finding circulating DNA methylation markers in blood may help in the prediction of treatment response and prognosis of patients with advanced-stage ovarian cancer (ASOC). The aim of this study is to identify differentially methylated regions in cell-free DNA (cfDNA) of patients with ASOC at different time points and to correlate this to clinical parameters.

Methods: Liquid biopsies were collected pre- and post-surgery from patients with ASOC (FIGO-stage IIIB-IV). Plasma-derived cfDNA was isolated and analyzed by a new high-throughput genome wide DNA methylation sequencing technique: MeD-seq. A trainingset of pre-surgery samples were compared with healthy controls to define DNA methylation signatures (Chi-square test with Bonferroni correction for multiple testing).

Results: Nine pre-surgical samples of patients with ASOC showed a clear distinct DNA methylation signature from nine healthy controls (p-value <0.0001). 31 pre-operative samples significantly differed from 38 post-operative samples (p-value <0.0001). The day post-surgery and FIGO-stage influenced the methylation profile independently. When adjusted for these parameters complete CRS could be distinguished from incomplete CRS. Also, there was a trend towards less hypermethylation in women without a relapse within 12 months for patients with FIGO-stage IV and liquid biopsies taken on day 3 post-operatively.

Conclusions: The MeD-seq assay provides a promising new method for genome wide cfDNA methylation profiling. Patients with ASOC could clearly be distinguished from healthy controls. Moreover, cfDNA methylation differed pre- and postoperatively. A potential future application is to use this methylation profile by predicting response to treatment and to predict at baseline which women will relapse within 12 months.
DOSE-DENSE, WEEKLY PACLITAXEL AND CARBOPLATIN WITH OR WITHOUT BEVACIZUMAB, IN METASTATIC OR RECURRENT CERVICAL CARCINOMA (FINAL ANALYSIS OF JCOG1311)

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Objectives: To assess the efficacy of dose-dense weekly paclitaxel plus carboplatin (ddTC) with or without bevacizumab in metastatic or recurrent cervical carcinoma, we conducted a phase II/III randomized controlled study comparing with conventional TC (cTC) with or without bevacizumab (JCOG1311, jRCTs0311800007). We previously reported that this study had not met the primary endpoint of phase II in ASCO2020.

Methods: Patients were randomly assigned to either cTC or ddTC arm The cTC was paclitaxel 175 mg/m² and carboplatin (AUC 5) on day 1. The ddTC was paclitaxel 80 mg/m² on day 1, 8, 15 and carboplatin (AUC 5) on day 1. Patients on both arms received bevacizumab 15 mg/m² if not contraindicated. The primary endpoint of phase II was response rate (RR), and that of phase III was overall survival (OS).

Results: A total of 122 patients was enrolled. The RR in ddTC arm was 60.7% and not higher than cTC arm (67.9%). The study was terminated early before starting phase III part. After a further two years of follow-up, the final analysis was conducted. Median OS and progression-free survival (PFS) in cTC arm was 17.7 months and 7.9 months, and in ddTC arm 18.5 months and 7.2 months, respectively. The median follow-up of surviving patients was 2.9 years. There were no significant differences between the arms either for OS or PFS. Adverse events related to bevacizumab in 82 patients included fistula in 5 patients and gastrointestinal perforation in 3 patients.

Conclusions: Dose-dense paclitaxel plus carboplatin was not promising for metastatic or recurrent cervical carcinoma.
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COST-EFFECTIVENESS OF PEMBROLIZUMAB FOR FIRST-LINE TREATMENT IN PATIENTS WITH PERSISTENT, RECURRENT, OR METASTATIC CERVICAL CANCER IN THE UNITED STATES

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Objectives: The FDA recently approved pembrolizumab in combination with chemotherapy, with or without bevacizumab, to treat patients with persistent, recurrent, or metastatic cervical cancer (PRMCC) whose tumors express PD-L1 (Combined Positive Score (CPS) ≥ 1). This study assesses the cost-effectiveness of pembrolizumab plus previous standard of care (SoC) vs previous SoC alone in this population from a US payer perspective.

Methods: Distinct from other evaluations, we modeled health outcomes and costs using a state transition model comprising the health states ‘pre-progression’, ‘post-progression’, and ‘death’ informed by patient-level data from the Phase 3 KEYNOTE826 (KN-826) trial. Time to progression, progression-free survival, post-progression survival, and time on treatment were extrapolated using parametric models to encompass all effects and costs, both discounted at 3% per annum. Costs included drug acquisition/administration, resource use, adverse events, and end-of-life. Real-world data informed the proportion of patients receiving subsequent treatment, weighted to the distribution in KN826, to reflect US clinical practice. Several subsequent treatment scenarios were explored. Parameter and model uncertainty were explored via deterministic/probabilistic sensitivity analyses.

Results: Pembrolizumab + SoC offers substantial incremental health benefits compared to SoC. At an additional cost of $203,700 each patient gains 1.90 life years (LYs) and 1.42 quality-adjusted life years (QALYs). The estimated incremental cost-effectiveness ratio over a lifetime (50 years) was $107,328/LY and $142,996/QALY. Based on probabilistic analysis, pembrolizumab has a 58.5% chance of being cost-effective at a willingness-to-pay threshold of $150,000/QALY.

Conclusions: Modeling suggests pembrolizumab + SoC is cost-effective for first-line treatment of CPS ≥ 1 patients with PRMCC in the US.
THE PROGNOSTIC VALUE OF PRESENCE OF PELVIC AND/OR PARA-AORTIC LYMPH NODE METASTASES IN CERVICAL CANCER PATIENTS; INFLUENCE OF THE NEW FIGO CLASSIFICATION (STAGE IIIC)

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Objectives: One of the major changes in the revised 2018 FIGO-staging system is the addition of stage IIIC, which includes patients with pelvic and/or para-aortic lymph node metastases. Therefore, we evaluated the prognostic value of positive pelvic and/or para-aortic lymph nodes in patients with cervical cancer.

Methods: A nationwide retrospective cohort study was performed by identifying all patients diagnosed with stage IB-IVA between 2005-2018 from the Netherlands Cancer Registry. Data was converted to the FIGO 2018 stage based on the TNM-classification. 5-year and overall survival rates (OS) were estimated with the Kaplan-Meier method.

Results: Of the included 6,082 patients, 1,740 patients, had pelvic and/or para-aortic lymph node metastases. For patients with FIGO 2009 stage IB-IB1-IIA-IIA1 with pelvic and/or para-aortic lymph node metastases 5-year survival is 77% and OS is 70%, without lymph node metastases survival rates are 92% and 87% (p<0.001). For FIGO 2009 stage IB2-IIA2-IIB, with pelvic and/or para-aortic lymph node metastases 5-year survival is 67% and OS is 62%, without lymph node metastases survival rates are 74% and 65% (p=0.009). FIGO 2009 stage IIIA-IIIB and IVA survival rates are not significantly influenced by pelvic and/or para-aortic lymph node metastases (p=0.640, p=0.939). Patients with FIGO 2018 stage IIIC have a 5-year survival of 65% and OS of 59%.

Conclusions: Patients with FIGO 2009 stage IB-IB1-IIA-IIA1-IB2-IIA2-IIB cervical cancer with positive pelvic and/or para-aortic lymph node metastases have a significant impaired survival compared to patients without metastases. Survival rates of patients with FIGO 2009 stage IIIA-IIIB-IVA are not significant affected by lymph node metastases.
THE DIAGNOSTIC ACCURACY OF COLPOSCOPY FOR CERVICAL INTRAEPITHELIAL NEOPLASIA 2+ AMONG HIV POSITIVE AND NEGATIVE SOUTH AFRICAN WOMEN.

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Objectives: We evaluated performance of Reid's Colposcopic Index (RCI) versus colposcopic impression (CI) to diagnose histologically confirmed CIN2+ lesions.

Methods: RCI was calculated as negative(RCI 0-2), low-grade(RCI 3-4), high-grade(RCI 5+); CI was logged as negative, low-grade/uncertain or high-grade. Directed punch biopsy (suspicious lesions) or blind punch biopsies (negative lesions) were taken. Worst of biopsy or treatment result was regarded as final histological diagnosis.

Results: Included were 725 participants; mean age 40.7 years; 46.8%(339/725) were HIV positive and 53.2%(386/725) HIV negative. In HIV positive and -negative groups, RCI was high-grade in 35.1%(119/339) and 11.1%(43/386)(p<0.0001) respectively; CI was high-grade in 30.1%(102/339) and 9.1%(35/386)(p<0.0001) respectively. Histology confirmed CIN2+ in 49.9%(169/339) HIV positive and in 29.5%(114/386) HIV negative women (p<0.0001). CIN3+ diagnosed in 26.8%(91/339) HIV positive and 13.0%(50/386) HIV negative participants. For RCI to predict CIN2+ in the HIV positive cohort, sensitivity, specificity, PPV and NPV were 80.6%, 56.9%, 64.6% and 75.0%, and for CI 82.4%, 56.3%, 61.8% and 76.6% respectively. For RCI in the HIV negative cohort these figures were 63.0%, 72.4%, 49.0% and 82.3%, and for CI 63.9%, 70.2%, 47.5% and 82.2% respectively.

Conclusions: Colposcopy test performance differs significantly between HIV positive and -negative cohorts. Validity of colposcopy in HIV positive women to identify possible CIN2 for biopsy is confirmed. Among HIV negative women sensitivity of colposcopy is relatively low and blind biopsies are warranted. RCI and CI performed equally in both HIV positive and negative cohorts. In this study, using the RCI scoring system did not contribute significantly to the accuracy to predict pre-invasive lesions.
INTEGRATING CERVICAL CANCER SCREENING WITH VOLUNTARY FAMILY PLANNING IN MOZAMBIQUE: THE MULHER STUDY

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Objectives: Mozambique has one of the highest rates of cervical cancer globally. The objective of our study is to implement integrated cervical cancer screening and voluntary family planning to scale up both services.

Methods: Women ages 30-49 in Maputo City and Gaza Province, Mozambique were prospectively enrolled in the study and offered integrated cervical cancer screening and/or voluntary family planning services as appropriate. Cervical screening included primary human papillomavirus (HPV) testing by self-collected or provider collected cervicovaginal samples. HPV-positive women underwent visual inspection with acetic acid (VIA) to determine eligibility for ablation (thermal ablation or cryotherapy), and if ineligible were referred for excision with loop electrosurgical excision procedure (LEEP) or cold-knife conization (CKC).

Results: From January 2020 to April 2022, 7,829 women underwent cervical screening. Median age was 37 years and 46.3% were women living with HIV (WLWH). 97% of women chose self-collection. The HPV positivity rate was 32.3% overall and 39.6% among WLWH. Of the 2,436 HPV-positive women, 2,153 (88.3%) returned for follow-up and treatment, including ablation (n=1988, 92.3%), LEEP (n=139, 6.5%) and CKC (n=4, 0.2%). 22 women (1.0%) were diagnosed with invasive cancer and referred to gynecologic oncology.

Conclusions: Our results suggest that it is feasible to perform cervical cancer screening with primary HPV testing in low-resource settings such as Mozambique. Participants preferred self-collection and almost 90% of screen positive women completed diagnostic work-up and treatment. Further study is ongoing to determine best practices for the integration of cervical screening with voluntary family planning services in Mozambique.
TISSUE-SPECIFIC METHYLATED DNA MARKER DISCRIMINATE AMONG ENDOMETRIAL, OVARIAN, AND CERVICAL CANCERS

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Objectives: DNA methylation occurs early in carcinogenesis and differ among cancer subtypes, suggest that these biomarkers might be useful in early detection and in defining site of origin in liquid biopsies.

Methods: Endometrial (EC), ovarian (OC) and cervical (CC) cancer MDMs were identified through methylome sequencing of primary tumor and benign gynecologic tissue DNA and independently validated in DNA from formalin fixed paraffin embedded (FFPE) tissues representing the same cancers and benign histologies. Twenty-five MDMs representing each organ site were selected as previously reported; DNA extracted from independent primary tissues was assayed by quantitative methylation specific PCR. MDMs were normalized to β-actin. MDM distributions were displayed using boxplots and intensity maps.

Results: 82 EC (16 serous, 18 carcinosarcoma, 7 clear cell, 17 endometrioid grade 1/2, 24 endometrioid grade 3), 82 OC (36 serous, 21 clear cell, 4 mucinous, 21 endometrioid), and 64 CC (36 squamous cell, 28 adenocarcinoma) were compared to controls of benign epithelium (29 cervicovaginal, 29 fallopian tube, 14 benign endometrial tissues). While CDO1 discriminated any cancer type from benign control tissue, cancer specificity was evident for most MDMs (Figure 1). Overlap of MDMs, such as c18orf18 among EC and OC clear cell and endometrioid histologies, is compatible with the origin of these OCs from endometriosis (Figure
Figure 2.
Conclusions: MDMs discovered and independently validated in EC, OC, and CC tissues discriminate among GC site origin. MDM testing in vaginal fluid and/or blood is warranted to assess GC detection and site-specificity via non-invasive liquid biopsy.
Objectives: To evaluate the oncologic outcome of surgical and radiological staging in patients diagnosed with stage I ovarian dysgerminoma who underwent a fertility-sparing surgery in a tertiary-care center in Monza, Italy.

Methods: We performed a retrospective, observational study of women with a histologically confirmed diagnosis of ovarian dysgerminoma referred to our Institution from 1980 to 2020. We collected patients’ characteristics, surgical procedures, postoperative management, disease recurrence rate, disease-free survival, and overall survival rates. Descriptive statistics were performed for baseline characteristics, while Fisher’s exact test was used to investigate the association between staging methods and recurrent disease. P<0.05 was considered significant.

Results: Of 131 patients diagnosed with ovarian dysgerminoma, 79 were diagnosed with early-stage disease and treated with fertility-sparing surgery. Forty-seven patients received intraperitoneal only or intraperitoneal plus retroperitoneal staging, while 32 were staged with imaging only. In the first group, one patient relapsed (2%), while 7 in the second group (22%) (p<0.05). No difference in recurrence rate was found between patients managed with intraperitoneal staging only (1/24) and with intraperitoneal plus retroperitoneal staging (0/23). Overall survival was similar in the surgical and radiological staging subgroups, with a five-year survival rate of 100% (median follow-up of 9.5 years).

Conclusions: Fertility-sparing surgical treatment is safe and feasible for patients with early-stage ovarian dysgerminoma. Surgical staging may reduce disease recurrence compared to nonsurgical staging. However, overall survival is not affected by the staging method.
ONCOLOGIC OUTCOME OF PATIENTS WITH STAGE I IMMATURE TERATOMA TREATED WITH SURVEILLANCE OR ADJUVANT CHEMOTHERAPY

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Objectives: Immature teratomas (ITs) are a rare disease representing about one-third of all malignant ovarian germ cell tumors. They are frequently diagnosed in young women, and fertility-sparing surgery (FSS) is often the treatment of choice. While stage IA grade 1 ITs do not require adjuvant chemotherapy (CT), its role in other stage I ITs is still controversial. We investigate the impact of surveillance versus adjuvant CT on the recurrence rate in stage I any grade ITs. This is the largest monocentric case series reported to the best of our knowledge.

Methods: Clinicopathological data were retrospectively collected from a cohort of patients with stage I ITs treated with FSS in one center between 1980 and 2019.

Results: Among the 74 patients included, 9 patients received adjuvant CT while 65 underwent active surveillance. Median follow-up was 188 months. The relapse rate was higher in patients with stage IC (29% vs 10% in stage IA/B) and grade 3 (22% vs 14% and 7% in grade 2 and 1, respectively), while no difference was found between surveillance and adjuvant CT groups (13.9% vs 11.1%) [p = 0.65]. Both in univariate [OR = 0.78; CI 95% 0.09-6.98 (p = 0.82)] and multivariate [OR = 0.25; CI 95% 0.02-2.66 (p = 0.25)] analysis, the post-surgical approach did not influence the recurrence rate.

Conclusions: These data support the feasibility of surveillance in stage I immature teratomas. However, the clinician must be aware of the higher risk of recurrence in stage IC and grade 3 immature teratomas.
Objectives: To evaluate Covid-19 pandemic impact on treatment patterns of cervical cancer (CC) in Brazilian public health system.

Methods: This real-world retrospective study used DATASUS datasets. Female aged ≥18 years with claims of CC (ICD-10-C53.*) were identified from January/2014-December/2020. Non-advanced (naCC - stage 1 and 2) and advanced (aCC - stage 3 and 4) were evaluated and compared treatment patterns in 2014-2019 vs 2020.

Results: A total of 206,861 women were included, being 26,815 in 2020 (49% newly diagnosed). 25.8% of the patients in 2020 had only surgery, compared to 39.2% in the period 2014-2019. The treatment patterns were evaluated only in the staged patients that corresponded to 44% (90,073) in the full cohort, and 75.8% in 2020's cohort. The overall proportion of 40% naCC and 60% aCC didn't change much in 2020, but key differences were observed in treatment patterns. The use of radiation (with/without surgery or chemo) was reduced in about 25%, notably from 87% to 62% and 61% in stages 1 and 2, respectively. Similarly, surgery (with/without radiation or chemo) reduced in all stages, 18% in stage 1. Isolated chemo adoption, on the other hand, increased in 2020 for all stages by an average of 22.6%, including in naCC, where for stage 1 patients increased from 7.7% to 30.2%.

Conclusions: This study undercovers the CC treatment gaps caused by Covid-19, from which the long-term impact still to be determined. The curative approaches were reduced due to hospitals collapse and may impact patient’s outcomes.
POSTER ROUNDS WITH THE PROFESSORS: GROUP C4  
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THE ROLE OF POSTOPERATIVE RADIATION AFTER RADICAL HYSTERECTOMY FOR WOMEN WITH EARLY-STAGE NEUROENDOCRINE CARCINOMA OF THE CERVIX: A META-ANALYSIS

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Objectives: Neuroendocrine carcinoma of the cervix (NECC) is an aggressive disease with high rates of nodal disease spread even in seemingly cervix-confined disease. Therefore, many providers prescribe postoperative radiation therapy in an effort to reduce recurrences. However, large studies evaluating the utility of this approach are lacking. The objective of this study was to determine recurrence and mortality in patients with early-stage NECC who had pelvic radiation after radical hysterectomy compared to those who did not receive radiation.

Methods: We performed a meta-analysis of 13 unique studies that reported recurrence and/or mortality for patients with early-stage NECC who underwent radical hysterectomy with or without adjuvant radiation therapy.

Results: In 6 studies that reported overall recurrence rates, 65 (51.6%) of 126 patients who received postoperative radiation recurred compared to 71 (37.0%) of 192 patients who did not (RR 1.25, 95% CI: 0.93–1.66, p=0.14). In 6 studies that reported pelvic recurrence rates, there were 15 pelvic recurrences (11.9%) in the 126 patients who received postoperative radiation compared to 46 pelvic recurrences (24.0%) in the 192 patients who did not (RR 0.59, 95% CI: 0.33 – 1.05, p= 0.07). In 12 studies that reported mortality rate, there were 129 deaths (33.1%) in 390 patients who received postoperative radiation therapy compared to 207 (35.1%) in 589 patients who did not (RR 1.00, 95% CI: 0.74-1.36, p=0.99).

![Figure 1. Recurrence rates for patients who underwent adjuvant post-operative radiation therapy versus those who did not.](image)
Conclusions: The addition of postoperative radiation therapy after radical hysterectomy may reduce pelvic recurrences but does not appear to decrease overall recurrence or death in women with early-stage NECC.
PATTERNS OF PALLIATIVE CARE UTILIZATION BY WOMEN WITH GYNECOLOGIC MALIGNANCIES IN ONTARIO, CANADA: A 13-YEAR POPULATION-BASED RETROSPECTIVE ANALYSIS

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Objectives: Early palliative care (PC) (≥6-12mo from death) has been associated with improved patient quality-of-life, less aggressive end-of-life care, and prolonged survival, and is understudied in gynecology. We characterized patterns of PC utilization and predictive factors in gynecologic cancer patients.

Methods: We conducted a population-based, retrospective cohort study of gynecologic cancer decedents in Ontario from 2006-2018 using ICES-linked administrative healthcare data. Multivariable logistic regression was used to determine factors associated with PC utilization.

Results: In this cohort of 16,237 women, 93.4% of decedents accessed palliative care, initially in the outpatient setting for 68.8% and institutionally for 31.2%. Palliative care was initiated a median 127 days before death (IQR 38-361d), and PC users accessed a median 8 institutional days (IQR 0-21d) and 41 community days (IQR 3-174d). While use of community PC gradually increased toward the end of life, use of institutional palliative care exponentially increased from 12 weeks until death. On multivariable analyses, factors significantly associated with an increased likelihood of receiving palliative care were longer cancer-related survival and Deyo-Charlson comorbidity score ≥1. Factors significantly associated with decreased likelihood of palliative care were age ≥80 years, diagnosis of uterine or vulvar-vaginal cancers, initial diagnosis of stage I-III malignancy (vs. stage IV), living rurally or in the third income quintile, or death after 2007.

Conclusions: While >90% of gynecologic cancer decedents accessed palliative care, median initiation was within the last 4 months of life (late PC), which may result in suboptimal quality of disease and end-of-life care. Access to PC may be inequitable.
Objectives: Access-to-care disparities are growing as gynecologic oncologist (GON) demand increases amidst rising gynecologic cancer rates. We characterized the geospatial distribution of the U.S. GON workforce relative to at-risk women over 20 years.

Methods: We utilized two U.S. physician registries to identify the 2001-2020 GON workforce. Practice locations were aggregated to county levels. Rural/urban were noted based on census designations. Choropleth maps were used to visually assess the spatial variation of the GON workforce relative to the at-risk female population and correlated with patterns in rurality.

Results: Between 2001-2020, the GON workforce increased steadily, plateauing circa 2017 (Figure 1). By 2020, there were 1,178 active GONs; 51.5% were early-to-mid career and 98.3% practiced in urban areas (representing only 37.3% of all counties). A disparity in practice geography was identified, with 1.09 GONs per 100,000 women in urban areas compared to 0.1 GONs per 100,000 women in rural areas (p < 0.0001). In total, 2,867 counties (representing 57.5 million at-risk women) did not have a GON. Additionally, there was no increase in rural GONs observed over time with only 1.7% in 2016–2020 relative to 2.2% in 2001-2005. Of the rural providers, fewer were early-to-mid career (23.5%) compared to late-career (76.5%); this trend persisted throughout all periods (Figure 2).
Conclusions: Over two decades, the U.S. GON workforce increased substantially, but not equitably, as a widening disparity in rural cancer care was noted over time. Policies and pipeline programs are needed to address this widening disparity in rural gynecologic cancer care.
ENHANCED RECOVERY AFTER SURGERY IN OPEN ABDOMINAL HYSTERECTOMY FOR MALIGNANT AND BENIGN DISEASE: A RANDOMISED CONTROL TRIAL

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Objectives: Enhanced recovery after surgery (ERAS) is a multidisciplinary protocol that incorporates several perioperative components To compare perioperative outcomes and patient satisfaction in ERAS versus conventional management in a tertiary care setting.

Methods: Sixty women who underwent hysterectomy through the open abdominal route for benign and malignant indications were recruited and randomized to two groups; ERAS vs. conventional. Sample size was calculated after fixing Type I error at 5% and power of study at 95%, assuming a standard deviation of 20%. Postoperative recovery, pain, hospital stay, complications and readmissions and patient satisfaction scores were analysed. Compliance to individual components and overall compliance was calculated.(CTRI/2020/02/023431)

Results: Duration of hospital stay was shorter in ERAS group: 3.87±1.25 vs 5.60±1.18 days (p-value=0.001) in benign cases and 5.27±2.34 vs 6.33±1.29 days( p-value=0.01) in malignancy. Decreased time to ambulation (p <0.001), time to resumption of enteral feeding ( p=0.022 and 0.002), passage of flatus( p=0.002 and 0.028), stool(p< 0.001 and p=0.003)and lower pain scores (p-value<0.001) were seen in benign and malignant cases on ERAS protocol. Complications were comparable in ERAS vs. conventional protocols for Grade 1 (p-value=0.359), Grade 2(p-value=1.000) and Grade 3(p-value=0.125). Patient satisfaction scores and readmissions between the two groups were comparable.

Conclusions: This trial showed a significant decrease in hospital stay, early ambulation, resumption of oral feeds, bowel motility and lower pain scores with ERAS protocol. Patient satisfaction scores did not differ between ERAS and conventional protocols and adoption of ERAS did not increase postoperative complications and readmissions.
COST STUDY OF PLASMAJET SURGICAL DEVICE VERSUS CONVENTIONAL CYTOREDUCTIVE SURGERY IN ADVANCED-STAGE OVARIAN CANCER PATIENTS

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Objectives: Adjuvant use of Neutral Argon Plasma (PlasmaJet® Surgical Device) during cytoreductive surgery (CRS) for advanced-stage epithelial ovarian cancer (EOC) improves surgical outcome. The aim of this study is to examine the costs of adjuvant use of the PlasmaJet during surgery compared to conventional cytoreductive surgery in advanced-stage EOC.

Methods: The patients were randomly assigned to surgery with or without the PlasmaJet. Analysis of the intra – and extramural healthcare costs were performed. Costs were divided in three categories: Costs of the diagnostic phase (T1), inpatient care up to discharge, including costs of surgery (T2), and outpatient care including chemotherapy until six weeks after the last cycle of chemotherapy (T3).

Results: Overall, 327 patients underwent cytoreductive surgery (surgery with PlasmaJet: N=157; conventional surgery: N=170). The mean total health costs were significantly higher for CRS with adjuvant use of PlasmaJet compared to conventional CRS (€19,414 vs. €18,165, p=0.017). Costs are divided in costs of the diagnostic phase (€2,034 vs. €1,974, p=0.890), costs of inpatient care (€10,956 vs. €9,556, p=0.003) and costs of outpatient care (€6,417 vs. €6,628, p=0.147).

Conclusions: Mean total health care costs of the use of PlasmaJet in CRS were significantly higher than for conventional CRS. This difference is fully explained by the additional surgery costs of the use of PlasmaJet. However, surgery with the use of the PlasmaJet leads to a significant higher percentage of complete CRS and a halving of stomas. A cost-effectiveness analysis will be performed once survival data are available.
POSTER ROUNDS WITH THE PROFESSORS: GROUP O7
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PREDICTION MODEL FOR COMPLETE CYTOREDUCTION AT PRIMARY CYTOREDUCTIVE SURGERY FOR ADVANCED OVARIAN CANCER BY INTEGRATING OF 18F-FDG PET/CT PARAMETERS AND CA-125

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Objectives: We aimed to develop a model predicting complete cytoreduction in primary cytoreductive surgery (CRS) using clinicopathologic characteristics and 18F-FDG PET/CT (PET)-derived parameters in advanced OC.

Methods: We retrospectively identified patients with stage III-IV OC who underwent primary CRS between June 2013 and February 2020 at two tertiary centers for development of a prediction model and for its validation. We divided abdominal cavity into three sections in PET images. The number of lesions in each section was counted and visual grading was conducted. Then, standardized uptake value (SUV), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) were estimated. We constructed various prediction models for complete cytoreduction by combination of clinicopathologic characteristics and PET-derived parameters. The model showing highest area under the receiver operating characteristic curve (AUC) was selected and its performance was evaluated for validation.

Results: Prediction models were designed with the development cohort (n=159). In variable selection, MTV, TLG, and the number of lesions above the renal vein were selected among PET-derived parameters with other clinical variables including CA-125 by AUC. The highest predictive performance was achieved by combination of CA-125 (<750 or ≥750 IU/ml), the number of lesions above the renal vein (<2 or ≥2) and MTV above the renal vein with AUC of 0.768. The model predicted complete cytoreduction with AUC of 0.771 in validation (n=166).

Conclusions: We successfully developed and validated PET-based prediction model for complete cytoreduction. It may be helpful for gynecologic oncologists to choose primary CRS or NACT in patients with stage III-IV OC in real-world practice.
THE VALUE OF PET/CT FOR CYTOREDUCTIVE SURGERY SELECTION IN RECURRENT OVARIAN CARCINOMA

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Objectives: To evaluate the role of PET/CT in predicting no residual disease (NRD) after secondary cytoreductive surgery (SCS) compared to MSK criteria, iMODEL and AGO Score.

Methods: We analyzed 122 patients with platinum-sensitive ovarian carcinoma submitted to SCS between July 2008 and December 2021. We excluded patients that did not have PET/CT, without sufficient data and who received chemotherapy before SCS. We ultimately included 69 patients.

Results: The median first relapse interval was 23 months (range, 6.05-104.2). Variables that correlated with NRD were PCI [OR 0.91 (0.83-0.99) 95%CI; p=0.044], ECOG0 [OR 8.0 (1.34-47.5) 95%CI; p=0.022] and number of lesions in PET/CT of ≤2 [OR 6.0 (1.24-28.9); 95%CI; p=0.026]. Considering patients with ≤2 lesions on the PET/CT, 92.3% had NRD. We recorded a sensitivity, PPV, NPV and accuracy of 85.7%, 92.3%, 33.3% and 81.2%, respectively. NRD would be achieved after fulfilling MSK criteria, iMODEL and AGO Score in 89.1%, 88.1% and 85.9%, respectively. The accuracy in prediction NRD of MSK criteria, iMODEL and AGO Score was 87%, 83.3% and 77.3%, respectively. PET/CT had a good agreement with AGO Score and iMODEL. The addition of PET/CT to the models increased the NRD rates (MSK+PET/CT, iMODEL+PET/CT and AGO+PET/CT NRDs in 92.2%, 91.8%, and 89.4%, respectively), however impaired their accuracy performance.

Conclusions: We found NRD in 92.3% after the presence of ≤2 lesions in PET/CT with an accuracy of 81.2%. PET/CT did not increase the accuracy performance of MSK criteria, iMODEL and AGO Score models.
Objectives: Residual disease at surgery is the most important prognostic factor for women with metastatic ovarian carcinoma (OC). Appropriate patient selection is challenging. Preoperative CT-scores are developed for primary debulking surgery (PDS), however during COVID19 pandemic interval debulking surgery (IDS) has increased. The aim of this single-center pilot-study was to assess the ability to predict complete gross resection (CGR) <1cm during PDS or IDS based on preoperative CT-scores in women with FIGO st IIIC/IV OC.

Methods: All women undergoing PDS or IDS 01/2021-01/2022 were preoperatively scored by a modified MSKCC algorithm including 6 CT criteria. Resectability and residual disease was registered.

Results: CT-score was noted in 135 women. 100/135 (74%) underwent surgery: 54 PDS, 46 IDS (figure1). Patients were deemed inoperable if debulking to ≤1cm was not feasible, 18/54 (33%) PDS-cases were inoperable. Median CT-score for this group was 4 (range 0-10). Of the remaining 36 PDS-cases, 33/36 (92%) achieved CGR and 3/36 (8%) R>1cm. Resectability based on CT-score is noted in table 1. Of the 81 cases triaged to NACT, 38 (47%) never underwent surgery. 36/46 (78%) women undergoing IDS achieved CGR, 2/46 (4%) R>1cm and 8/46 (17%) were inoperable. Overall, 6 women with CT-scores 1-2 were deemed inoperable. The limiting factor was bowel carcinomatosis for all. Preoperative CT-score of ≤6 and ≤ 4 predicted ≥ 50% CGR at PDS and IDS respectively.
Figure 1: Patient triage based on preoperative CT score
Conclusions: When exclusively assessing preoperative imaging, women with initial CT-score >7 should receive NACT or laparoscopic resectability-assessment. Women with CT-score ≤4 after NACT can be offered IDS.
COST-EFFECTIVENESS OF HYSTERECTOMY AT THE TIME OF RISK-REDUCING BILATERAL SALPINGOOOOPHORECTOMY FOR PATIENTS WITH BRCA1 MUTATIONS

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Objectives: More recent data suggests that patients with BRCA1 are at an increased risk of developing uterine serous cancers. This raises the question of whether a hysterectomy should be done at time of rrBSO. We developed a decision model to compare the cost-effectiveness of rrBSO with or without hysterectomy for patients with BRCA1 mutations.

Methods: A Markov model was created to simulate the clinical trajectory of a hypothetical cohort of 10,000 women aged 40 years of age with BRCA1 mutations undergoing rrBSO. The initial decision point in the model was whether a hysterectomy was performed at the time of rrBSO. A time horizon of 60 years was used. Postoperative morbidity and mortality were included in the model as well as risk for subsequent hysterectomy and prolapse after hysterectomy. Model probabilities, cost and utility values were derived with assumptions drawn from published literature. The effectiveness was calculated in terms of average quality adjusted life years (QALYs). The primary outcome was incremental cost-effectiveness ratios (ICERs), expressed in 2018 US dollars/QALYs. One way sensitivity analyses were performed to vary the assumptions across a range of plausible values.

Results: RrBSO with hysterectomy was the least costly strategy at $13,628, followed by rrBSO alone ($14,630). Hysterectomy at time of rrBSO was cost-effective compared with rrBSO. rrBSO alone was subjected to absolute dominance because it was both more costly and less effective. Multiple one-way sensitivity analyses did not substantially impact the cost-effectiveness.

Conclusions: Hysterectomy at time of rrBSO for BRCA1 patients constitutes a cost-effective management strategy.
Objectives: To identify trends in incidences of germ cell tumors and subtypes in large population registries in the US and Republic of China.

Methods: Data was obtained from the United States Cancer Statistics (USCS) and the Taiwan Cancer Registry between 2001 and 2018. SEER*Stat and Joinpoint regression programs were used to calculate incidences and trends. Native Chinese were defined as individuals from Taiwan. The incidence was adjusted by WHO 2000 standard population.

Results: Of 11,941 patients with germ cell tumors, 651 (5.5%) were US Asians and 1249 (10.5%) were Native Chinese. Over the 17-year study period, the overall incidence of germ cell cancers in Native Chinese is nearly 2-fold higher compared to US Asians 0.66 vs. 0.36 per 100,000. In Native Chinese, the incidence is increasing with an average annual percent change (AAPC) at 1.4% (p=0.006) whereas in US Asians there is no change (AAPC=-0.10%, p=0.89). To further evaluate the trends in Native Chinese, we found that the incidence (in 2018) of immature teratomas was nearly 3-fold higher compared to dysgerminoma and yolk-sac tumors (0.32 vs. 0.11 vs. 0.10). Moreover, immature teratomas are increasing at 3.46% per year (p<0.001) whereas the dysgerminoma and yolk-sac tumors have remained stable. An intersectional analysis showed Native Chinese at age 10-14 with immature teratoma had the highest annual increase (7.56%, p=0.016).

Conclusions: Incidences of germ cell tumors have increased in Native Chinese but remained stable in US Asians. The higher incidence and increasing rates of the immature teratoma subtype warrants further studies on potential genetic and environmental factors.
TRENDS IN PHASE 3 CLINICAL TRIALS IN OVARIAN CANCER FROM 2001-2021

Katherine Cotangco¹, Arya Aliabadi², Caitlin Johnson³, Amandeep Mann⁴, Ritu Salani¹, Joshua Cohen¹, Daniel Kapp⁵, John K Chan⁴
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Objectives: To determine the trends and progress of clinical trials on ovarian cancer over the last 20 years.

Methods: From 2001 to 2021, all phase 3 clinical trials were identified from clinicaltrials.gov. Demographics and characteristics were analyzed for comparison and trends using chi square analysis.

Results: Of 43,641 ovarian cancer patients enrolled in 58 clinical trials, 19 were based in the US and 39 were based internationally. There were 35 (60%) government sponsored trials vs. 23 (40%) industry trials. 18 (31%) trials studied chemotherapies vs. 40 (69%) targeted therapies; 17 (30%) trials incorporated biomarkers. The median number of patients per trial was 581 (range 50-1952), and those using PFS vs. OS was 35 (60%) vs. 14 (24%). To evaluate trends, we studied two time periods, 2001-2010 and 2011-2021. There was an increase in industry sponsored trials (5% (2001-2010) vs. 49% (2011-2021); p-value<.05), targeted therapy trials (10% to 43%; p-value <.05), biomarker use (BRCA, HRD, PDL1) (67% to 89%; p-value<.05), and incorporation of PFS endpoint (57% to 70%; p-value=0.3). There was a decrease in the median number of patients enrolled per trial (n= 820 to 426) and in the proportion of patients with comorbidities (ECOG>2) (17% to 7%; p-value=0.2).

Conclusions: Over the past 20 years, targeted therapy trials incorporating biomarker use has increased, but the number of patients enrolled and those with comorbidities has decreased. These trends in trial design and enrollment are important in understanding the applicability of their results to our patients.
ASSESSING ROBUSTNESS OF AN ARTIFICIAL INTELLIGENCE DERIVED HISTOLOGICAL BIOMARKER ACROSS DIFFERENT SITES OF DISEASE AND IN SERIAL SECTIONS IN TUBO-OVARIAN HIGH-GRADE SEROUS CARCINOMA

Rayan Krishnan¹, Ekin Tiu¹, Vrishab Krishna¹, Vivek Nimgaonkar¹, Hriday Bhambhvani¹, Odhran O'Donoghue¹, Damir Vrabac¹, Anirudh Joshi¹, Brooke Liang², Xiaoming Zhang³, Lucy Han⁴, Aihui Wang⁵, Viswesh Krishna¹, Brooke Howitt⁶

¹Valar Labs Inc, Computational Oncology, Palo Alto, United States of America, ²Stanford Health Care, Pathology, Palo Alto, United States of America, ³Stanford Medicine, Department Of Pathology, Palo Alto, United States of America, ⁴Stanford, Pathology, Palo Alto, United States of America, ⁵Stanford School of Medicine, Pathology, Stanford, United States of America, ⁶Stanford University School of Medicine, Obstetrics And Gynecology, Gynecologic Oncology, Palo Alto, United States of America

Objectives: Histological biomarkers may produce different predictions for a single patient when using whole slide images of biopsies from different sites and even serial sections of the same tissue. Previous work had developed a signature of AI-derived morphologic features correlated with response to platinum-based chemotherapy in tubo-ovarian high-grade serous carcinoma (HGSC) specimens from The Cancer Genome Atlas (TCGA) (hazard ratio: 0.35). We aim to assess the robustness of this marker across different sites of disease and in serial sections.

Methods: 489 sections from 10 tissue microarrays (TMA) corresponding to 44 patients with HGSC from Stanford Hospital were included in this study. Using the digitally scanned histologic images, we computed geometric features of nuclei extracted from tissue regions using segmentation models. TMA sections were stratified into low and high responder groups by the histologic signature previously associated with platinum-based chemotherapy response. Concordance (c-index (C)) and mean pairwise percent difference (MPPD) across all cores for a given patient were calculated to assess the robustness of the signature.

Results: The prediction of the morphologic signature is consistent when computed across all cores/slides per patient (C:0.66, MPPD:30%). When stratified by site, the signature is similar across serial sections for samples from the ovary (C:0.71, MPPD:22%) and the omentum (C:0.70, MPPD:25%). The signature is also consistently robust irrespective of anatomic site (C:0.62, MPPD:26%).

Conclusions: The artificial intelligence derived histological biomarker associated with response to platinum-based chemotherapy is generalizable across both ovarian and omental sites and consistent between serial sections in patients with HGSC.
Objectives: Platinum-based chemotherapy is the standard of care first-line systemic treatment for patients diagnosed with advanced stages of tubo-ovarian high-grade serous carcinoma (HGSC). While the majority of patients respond, roughly 15% of patients are platinum-resistant. We aimed to develop an artificial intelligence-based platform leveraging routine pre-treatment histopathology specimens to predict platinum-based chemotherapy response.

Methods: 87 patients from The Cancer Genome Atlas (TCGA) and 19 patients from Stanford Hospital with HGSC who received platinum-based chemotherapy post resection were included in this study. Using scanned hematoxylin and eosin-stained (H&E) images, we extracted nuclei images from tissue regions using segmentation models and computed geometric features of these nuclei. In the TCGA cohort, quantitative features of the nuclear geometry were correlated with Progression Free Survival (PFS) using a multivariable Cox Proportional Hazards (CPH) model in order to construct a signature associated with platinum treatment benefit. The signature was assessed with a Kaplan Meier Estimator and log rank test by comparing the PFS between the high and low cohorts stratified by the signature in the internal TCGA and external Stanford cohorts.

Results: The artificial intelligence derived histological biomarker is able to stratify patients into high and low responders to platinum-based chemotherapy with statistical significance (logrank test - internal: p=0.000556, external: p=0.00571), achieving hazard ratios of 0.227 (95% CI: 0.092,0.559) on the internal TCGA test cohort and 0.132 (95% CI: 0.025,0.704) on the external Stanford Hospital validation cohort.

Conclusions: An artificial intelligence derived histological biomarker utilizing only routine whole-slide histopathology images can robustly predict responders and non-responders to platinum-based chemotherapy.
TCGA-OV Cohort Kaplan Meier

Time passed (months)

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Stanford Ovarian Cohort Kaplan Meier

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HOMOLOGOUS RECOMBINATION DEFICIENCY AND CYCLIN E1 AMPLIFICATION ARE CORRELATED WITH IMMUNE CELL INFILTRATION AND SURVIVAL IN HIGH-GRADE SEROUS OVARIAN CANCER

Lilian Van Wagensveld1, Julliete Van Baal2, Maite Timmermans3, Duco Gaillard4, Lauri Borghuis4, Seth Coffelt5, Effraim Rosenberg6, Christianne Lok2, Hans Nijman6, Loes Kooreman7, Annegien Broeks8, Joyce Sanders4, Marco De Bruijn9, Rianne Van Der Wiel4, Roy Kruitwagen9, Maaike Van Der Aa1, Gabe Sonke10, Philip Schouten4, Koen Van De Vijver2, Hugo Horlings4

1Netherlands Comprehensive Cancer Organization, Department Of Research & Development, Utrecht, Netherlands, 2Center for Gynecologic Oncology Amsterdam (CGOA), Department Of Gynecology, Amsterdam, Netherlands, 3Leiden University Medical Centre, Department Of Obstetrics And Gynecology, Leiden, Netherlands, 4The Netherlands Cancer Institute, Department Of Pathology, Amsterdam, Netherlands, 5The Netherlands Cancer Institute, Amsterdam, Division Of Tumor Biology & Immunology, Amsterdam, Netherlands, 6University of Groningen, Department Of Obstetrics And Gynecology, Groningen, Netherlands, 7Maastricht University Medical Center, Pathology, Maastricht, Netherlands, 8The Netherlands Cancer Institute, Core Facility Molecular Pathology & Biobanking, Amsterdam, Netherlands, 9Maastricht University Medical Center (MUMC), Department Of Obstetrics And Gynecology, Maastricht, Netherlands, 10The Netherlands Cancer Institute - Antoni van Leeuwenhoek, Department Of Medical Oncology, Amsterdam, Netherlands

Objectives: How molecular profiles are associated with tumor microenvironment (TME) in high-grade serous ovarian cancer (HGSOC) is incompletely understood, while this influences survival. Therefore, we analyzed the TME and molecular profiles (homologous recombination deficiency (HRD) and Cyclin E1 (CCNE1) amplification) of HGSOC and assessed their associations with overall survival (OS).

Methods: Patients with advanced-stage HGSOC treated in three Dutch hospitals between 2008-2015 were included. Patient, treatment, and outcome data were collected from medical records. BRCA1/2 mutation, BRCA1 promotor methylation analyses, and copy number variations were used to define the molecular profiles. Immune cell infiltration was assessed with immunohistochemical staining.

Results: 348 patients were categorized as BRCA mutation (BRCAm) profile (BRCAm or promotor methylation)(30%), non-BRCA mutated HRD(19%), CCNE1-amplification(13%), non-BRCAmut HRD and CCNE1-amplification (double classifier)(20%), and no specific molecular profile (NSMP)(18%). BRCAm profile tumors showed highest immune cell densities and CCNE1 amplification lowest. BRCAm profile showed the most favorable OS (52.5 months), compared to non-BRCAmut HRD (41.0 months), CCNE1-amplification (28.0 months), double classifier (27.8 months), and NSMP (35.4 months). CCNE1-amplification and double classifier remained to have a significantly worse OS in multivariable analysis. Higher immune cell densities showed a favorable OS compared to lower densities, also within the molecular profiles. CD8+, CD20+, and CD103+ cells remained associated with OS in multivariable analysis.

Conclusions: Molecular profiles and TME are associated with OS. TME differs per profile, with higher immune cell densities showing a favorable OS, even within the profiles. HGSOC does not reflect one entity but comprises different entities based on molecular profile and TME which could assist with patient-tailored treatment in the future.
OBJECTIVES: Single-agent chemotherapy is a mainstay of platinum-resistant ovarian cancer treatment. However, most patients eventually face chemotherapy resistance, which might be driven by endogenous cortisol suppressing apoptotic pathways utilized by chemotherapies. A phase 2 study of nab-paclitaxel (NP) with/without the glucocorticoid receptor modulator relacorilant (RELA) in patients with ovarian cancer showed improved progression-free survival (PFS), overall survival (OS), and duration of response (DOR) with addition of RELA. We present a post-hoc subgroup analysis in patients with/without prior bevacizumab.

METHODS: 178 women with recurrent, platinum-resistant/refractory ovarian, primary peritoneal, or fallopian tube cancer or ovarian carcinosarcoma with ≤4 prior lines of chemotherapy (105 with; 73 without prior bevacizumab) were enrolled in a phase 2, open-label, randomized study (NCT03776812). Data for patients receiving either NP (80 mg/m²) + intermittent RELA (150 mg QD the day before, of, and after NP) (n=60) or NP alone (100 mg/m²) (n=60) are reported.

RESULTS: Baseline characteristics in the 2 groups were generally balanced. While patients without prior bevacizumab were balanced between North America and Europe, 70% of patients who received prior bevacizumab were in Europe. PFS, OS, ORR, and DOR are shown in Table
### Table 1.

<table>
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<tr>
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<th>Prior bevacizumab</th>
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<tr>
<td></td>
<td>Intermittent RELA + NP (n=31)</td>
<td>NP alone (n=37)</td>
<td>Intermittent RELA + NP (n=29)</td>
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<tr>
<td><strong>PFS</strong></td>
<td>Median PFS (95% CI), mo</td>
<td>7.2 (2.96, 7.39)</td>
<td>3.7 (3.48, 5.49)</td>
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<tr>
<td></td>
<td>HR* (95% CI)</td>
<td>0.44 (0.24, 0.78)</td>
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<td></td>
<td>2-sided P-value</td>
<td>0.0046</td>
<td>N/A</td>
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<td><strong>OS</strong></td>
<td>Median OS (95% CI), mo</td>
<td>17.9 (11.89, NR)</td>
<td>12.6 (6.93, 15.87)</td>
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<td></td>
<td>HR* (95% CI)</td>
<td>0.47 (0.24, 0.94)</td>
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<td>2-sided P-value</td>
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<td><strong>ORR</strong></td>
<td>Patients with measurable disease at baseline, n</td>
<td>n=27</td>
<td>n=30</td>
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<td></td>
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<td>11 (40.7%)</td>
<td>10 (33.3%)</td>
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<tr>
<td><strong>DOR</strong></td>
<td>Patients with response, n</td>
<td>n=11</td>
<td>n=10</td>
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<tr>
<td></td>
<td>Median DOR (95% CI), mo</td>
<td>5.6 (4.1, NR)</td>
<td>3.4 (1.28, 3.71)</td>
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<tr>
<td></td>
<td>HR* (95% CI)</td>
<td>0.25 (0.08, 0.83)</td>
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<tr>
<td></td>
<td>2-sided P-value</td>
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Data from the study arm treated with continuous, daily RELA + NP are not reported here (n=37 patients with and n=21 without prior bevacizumab). *Comparing intermittent RELA + NP vs NP alone. ORR, objective response rate

**Conclusions:** In this subgroup analysis, patients who had received prior bevacizumab had better PFS, OS, and DOR with intermittent RELA+NP vs NP alone, while ORR was similar across all groups. Numerical improvement in PFS was seen in patients without prior bevacizumab. Prior bevacizumab will be a stratification factor in the phase 3 trial of RELA+NP (ROSELLA, NCT05257408) that is planned to start in mid-2022.
FIRST-LINE MAINTENANCE AMONG ADVANCED OVARIAN CANCER PATIENTS IN THE US ONCOLOGY NETWORK: A REAL-WORLD RETROSPECTIVE COHORT STUDY

Dana Chase¹, Jinan Liu², Laura Moore-Schiltz³, Jennifer Perhanidis⁴, Purva Bulsara³, Gregory Patton³
¹Arizona Center for Cancer Care, Gynecologic Oncology, Phoenix, United States of America, ²GlaxoSmithKline, Veo, Philadelphia, United States of America, ³Onctara, Oncology, Woodlands, United States of America, ⁴GlaxoSmithKline, Veo, Waltham, United States of America

Objectives: We investigated patient characteristics and treatment patterns among patients with stage III/IV ovarian cancer (OC) who received first-line (1L) platinum-based chemotherapy (PBC) in The US Oncology Network.

Methods: This retrospective study leveraged structured data from the iKnowMed electronic health record. Patients with initial diagnosis of stage III/IV OC who initiated PBC in 1L setting between January 1, 2016, and December 31, 2020, were followed until September 30, 2021.

Results: The study included 1428 patients; 1087 (76%) received active surveillance (AS), 341 (24%) received maintenance after 1L PBC. Median age was 65 y in AS vs. 63 y in the maintenance group. In AS, 23% were stage IV vs. 28% in the maintenance group. Overall, 10% received bevacizumab monotherapy, 13% poly(ADP-ribose) polymerase inhibitor (PARPi) monotherapy, and 1% PARPi+bevacizumab. Among 206 patients who received bevacizumab in 1L PBC treatment, 70% received maintenance; 48% received bevacizumab monotherapy, 17% PARPi monotherapy, and 6% PARPi+bevacizumab. Among 1222 patients who did not receive bevacizumab in 1L PBC treatment, 16% received maintenance; 4% received bevacizumab monotherapy, 12% PARPi monotherapy. From 2016 to 2021, 1L maintenance use increased from 2% to 52%. Specifically, bevacizumab monotherapy increased from 2% to 12%, PARPi monotherapy from 0% to 31%, and PARPi+bevacizumab from 0% to 9%.

Conclusions: Despite increased use of OC maintenance therapy within The US Oncology Network, 48% of patients received AS in 2021. Further research is warranted to understand barriers of adopting 1L maintenance use in the community oncology setting considering its availability regardless of biomarker
status.

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<th>Active surveillance N=1067</th>
<th>Maintenance N=341</th>
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<th>PARPi monotherapy N=183</th>
<th>Bevacizumab + PARPi combination N=13</th>
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<td>Patients receiving after 1L PBC, %</td>
<td>76.1</td>
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<td>Median age at initial stage III/IV OC diagnosis (range), years</td>
<td>65 (18-90+)</td>
<td>63 (21-90+)</td>
<td>64 (25-90+)</td>
<td>63 (21-87)</td>
<td>52 (41-74)</td>
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<td>Race, n (%)</td>
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<td>Caucasian</td>
<td>811 (74.8)</td>
<td>221 (54.8)</td>
<td>91 (52.8)</td>
<td>120 (65.6)</td>
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<td>171 (15.7)</td>
<td>85 (24.9)</td>
<td>36 (24.8)</td>
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<td>Time from initial stage III/IV OC diagnosis to initiation of platinum-based chemotherapy, mo</td>
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<tr>
<td>Mean (StDev)</td>
<td>1.6 (3.0)</td>
<td>2.6 (5.3)</td>
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<td>2.7 (5.6)</td>
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<td>Median (range)</td>
<td>1.2 (0.0-35.6)</td>
<td>1.1 (0.1-41.5)</td>
<td>1.2 (0.1-25.7)</td>
<td>1.2 (0.2-41.5)</td>
<td>0.9 (0.1-1.9)</td>
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<td>Stage at diagnosis, n (%)</td>
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<td>III</td>
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<td>46 (13.5)</td>
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*77 patients who were maintenance eligible were not included in this analysis.
NR, not reported.
MIRVETUXIMAB SORAVTANSINE AND CARBOPLATIN FOR TREATMENT OF PATIENTS WITH RECURRENT FOLATE RECEPTOR ALPHA-POSITIVE PLATINUM-SENSITIVE OVARIAN CANCER: A FINAL ANALYSIS

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Objectives: Mirvetuximab soravtansine (MIRV) is a first-in-class ADC comprising a folate receptor-α (FRα)-binding antibody, cleavable linker, and maytansinoid DM4 payload. As part of the phase 1b/2 trial (NCT02606305), efficacy and safety of MIRV and carboplatin (carbo) were evaluated in patients with recurrent FRα-positive platinum sensitive ovarian cancer (PSOC) measured by immunohistochemistry (PS2+ ≥25%; Table
Methods: Eighteen patients received MIRV and carbo intravenously on Day 1 of a 3-week cycle using a standard 3 + 3 design, with a starting dose of MIRV 5 mg/kg adjusted ideal body weight (AIBW) and carbo AUC4. FRα positivity by immunohistochemistry (PS2+ ≥25%) was required. Primary endpoint was confirmed ORR by RECIST v1.1.

Results: Ten patients received MIRV 6 mg/kg AIBW and carbo AUC5. Anti-tumor activity was observed in all dose escalation cohorts with varying levels of FRα expression. Patients receiving MIRV 6 mg/kg AIBW and carbo AUC5 had an ORR of 89%, mDOR of 12.1, and mPFS of 16.5 months. Patients with medium/high FRα-expressing tumors had an ORR of 80%, mDOR of 24.2, and mPFS of 15.0 months across all escalation cohorts (Table 2). The most frequent treatment-emergent adverse events (all, grade 3+) included nausea (72%, 0%), diarrhea (67%, 6%), blurred vision (67%, 0%), thrombocytopenia (61%, 17%), fatigue (61%, 11%), and neutropenia (56%).
Conclusions: MIRV and carbo demonstrated anti-tumor activity in patients with recurrent FRα-positive PSOC. MIRV 6 mg/kg AIBW and carbo AUC5 was selected as the phase 2 dose. This combination is being evaluated in one planned and two ongoing (NCT04606914 and NCT04274426) studies.
THE IMPACT OF UTILIZATION INDOCYANINE GREEN FOR ANASTOMOTIC PERFUSION ASSESSMENT ON THE RATE OF DIVERTING ILEOSTOMY IN PATIENTS WITH ADVANCED OVARIAN CANCER

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Objectives: To compare rates of diverting ileostomy in patients with epithelial ovarian cancer (EOC), undergoing surgical cytoreduction with bowel resection before and after the acquisition of surgical innovative tool for anastomotic perfusion assessment using indocyanine green (ICG-FA).

Methods: A retrospective cohort study of patients with EOC undergoing bowel resection during primary or interval cytoreductive surgery, at Princess Margaret Hospital between 2010-2021. We evaluated whether utilizing the ICG-FA surgical tool, without integrating it into a systematic decision-making diversion protocol, impacted surgeons’ decision on performing diverting ileostomy.

Results: Overall 181 patients met inclusion criteria. Of whom, 84 (46%) underwent ICG-FA assessment after bowel resection, and 97 (54%) had bowel resection without ICG-FA assessment. Mean age of the cohort was 58.2. There was no significant difference between groups in the rates of diverting ileostomy (40.5% in the ICG-FA group vs 41.2% in the no ICG group, p=1.0). In a univariable logistic regression, the odds of having an ileostomy were 2.92 times higher in patients undergoing primary surgery as compared to patients undergoing interval cytoreductive surgery (95% CI 1.25-6.85, p=0.013). The use of ICG-FA did not predict performing or omitting a diverting ileostomy (OR 0.97, 95% CI (0.53-1.76), p=0.92).

Table 1 – Baseline characteristics of the study cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>All cohort (n=181)</th>
<th>No ICG (n=97)</th>
<th>ICG (n=84)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at diagnosis, years, mean (SD)</strong></td>
<td>58.2 (11.6)</td>
<td>58 (12.2)</td>
<td>58.4 (11)</td>
<td>0.73</td>
</tr>
<tr>
<td><strong>Stage, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I/II</td>
<td>8 (4.4)</td>
<td>5 (5.2)</td>
<td>3 (3.6)</td>
<td>0.71</td>
</tr>
<tr>
<td>III</td>
<td>132 (72.9)</td>
<td>72 (74.2)</td>
<td>60 (71.4)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>41 (22.7)</td>
<td>20 (20.6)</td>
<td>21 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Primary Treatment:</td>
<td></td>
<td></td>
<td></td>
<td>0.3</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy</td>
<td>36 (19.9)</td>
<td>16 (16.5)</td>
<td>20 (23.8)</td>
<td></td>
</tr>
<tr>
<td>Primary Surgery</td>
<td>145 (80.1)</td>
<td>81 (83.5)</td>
<td>64 (76.2)</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions: In this cohort, the introduction of ICG-FA technology had no impact on the rates of diverting ileostomy. A systematic, quality-based decision-making protocol for bowel diversion that includes ICG-FA assessment is needed to prospectively assess the potential impact of this surgical innovative tool on the surgeon's decision-making and the rates of bowel diversion in patients with EOC.
FP045 / #729

POSTER ROUNDS WITH THE PROFESSORS: GROUP O5
01-10-2022 2:05 PM - 2:35 PM

FIRST CLINICAL STUDY REPORTING ADOPTION OF ERAS IN CRS HIPEC AS PER PUBLISHED GUIDELINES: TIME TO ADOPT, EVOLVE & IMPROVE

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Objectives: We report our experience of implementation of ERAS protocol in CRS and HIPEC for peritoneal carcinomatosis as per guidelines published in december 2020.

Methods: ERAS protocol for CRS± HIPEC was implemented in 80 patients from January 2021 to March 2022. We documented compliance rate and analysed the reason for non-compliance, effect of compliance on length of hospital stay, postoperative complications and readmission rate and compared the same with the 95 patients who had CRS HIPEC before adopting ERAS protocol from January 2019 to December 2020

Results: Of 175 patients in the study, 95 were in pre eras group and 80 in ERAS group. Demography, pre-operative and operative parameters were comparable between the groups. The average compliance rate achieved for entire cohort was 78.5%. Lowest compliance rates were seen for post-operative elements especially, early feeding and early mobilization. After implementation of ERAS, median length of hospital stay reduced from 12 to 9 days, length of ICU stay reduced from 4 to 2 days and postoperative complications sepsis reduced from 14.7% to 7%, respiratory complications 15.7% to 7%, surgical complications 10.5% to 2.9%, resurgery from 6.3% to 1.4% and in hospital mortality reduced from 5.3% to 1.4%. The ERAS group didn’t receive any long acting opioids, less usage of intraoperative crystalloids(7ml/kg/hr vs 13ml/kg/hr, p = 0.0001), early extubation and less readmission rates.

Conclusions: The implementation of ERAS protocol is safe and feasible for CRS and HIPEC patients. Implementation of ERAS program has significantly reduced the length of hospital stay, length of ICU stay and postoperative morbidity.
PREDICTION OF PLATINUM-BASED CHEMOTHERAPY RESISTANCE IN EPITHELIAL OVARIAN CANCER USING APPARENT DIFFUSION COEFFICIENT OF MAGNETIC RESONANCE IMAGE AND MACHINE LEARNING ALGORITHM

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Objectives: To investigate the role of a preoperative apparent diffusion coefficient (ADC) of magnetic resonance imaging (MRI) and machine learning for the prediction of platinum-based chemotherapy resistance in patients with epithelial ovarian cancer (EOC).

Methods: The ADC of MRI was preoperatively evaluated on the largest solid portion of the ovarian mass on the axial MRI maps. All patients underwent platinum-based chemotherapy after cytoreductive surgery. Logistic regression and machine learning applications were used to investigate the role of the ADC and clinical factors for the prediction of platinum-based chemotherapy resistance in ovarian cancer.

Results: Of the 168 patients, 97 had high-grade serous ovarian cancer (HGSOC) and 71 had non-HGSOC patients; 33 clear cell carcinoma, 18 mucinous carcinoma, 15 endometrioid carcinoma, 5 low-grade serous carcinoma. The patients were divided into the platinum-sensitive group (n=146) and the platinum-resistance group (n=22). The gradient boosting machine algorithm showed the highest accuracy in differentiating histologic types of ovarian cancers (accuracy: 0.91, AUC: 0.93). In the ROC curve, CA 125 and the ratio of solid to the total area were significantly associated with platinum-based chemotherapy resistance (AUC: 0.758, AUC: 0.687, respectively). The deep learning algorithm demonstrated increased accuracy (AUC: 0.814). In cox regression analysis, the area of the solid portion was significantly related to the resistance to chemotherapy (hazard ratio: 1.033, p=0.014).

Conclusions: The ADC and area of the solid portion on MRI using machine learning can be helpful to predict histologic types and resistance of platinum-based chemotherapy in EOC.
Objectives: Cytoreductive surgery with HIPEC has shown promising results in interval setting in advanced epithelial ovarian cancer. Its role in upfront setting has not yet been established.

Methods: All eligible patients underwent CRS HIPEC as per institution protocol. Relevant data was entered prospectively in institutional HIPEC registry and analysed retrospectively for study period from February 2014 – February 2019.

Results: Out of 190 patients, 80 underwent CRS HIPEC in upfront setting and 110 in interval setting. Median age was 54±7.45 years, upfront group had higher PCI (14.1±8.75 VS. 9.6±5.2, 2), and required longer duration of surgery (10.6±1.73 vs. 8.4±1.71 hrs) had more blood loss (1025±668.76 vs.680±302.23 ml). Upfront group required more diaphragmatic resections, bowel resections and multivisceral resections. The overall G3-G4 morbidity was comparable (25.4%vs. 27.3%), upfront group had more surgical morbidity (20%vs.9.1%) whereas interval group had more medical morbidity i.e. electrolyte imbalance and haematological. After a median follow up of 43 months, median DFS was 33 months in upfront vs. 30 months in interval group, p=0.75, median OS was 46 months interval group and was not yet achieved in upfront group.(p=0.13). 4 year OS was 85%vs 60%. Performance status (P =0.025 C.I 1.190-12.80) was the only factor predicting morbidity on multivariate analysis.

Conclusions: In patients of advanced EOC upfront CRS HIPEC showed promising outcomes and better survival with similar morbidity and mortality. Upfront group had more surgical morbidity whereas interval group had more medical morbidity. Multi-institutional randomised studies are needed to define patient selection and study morbidity patterns.