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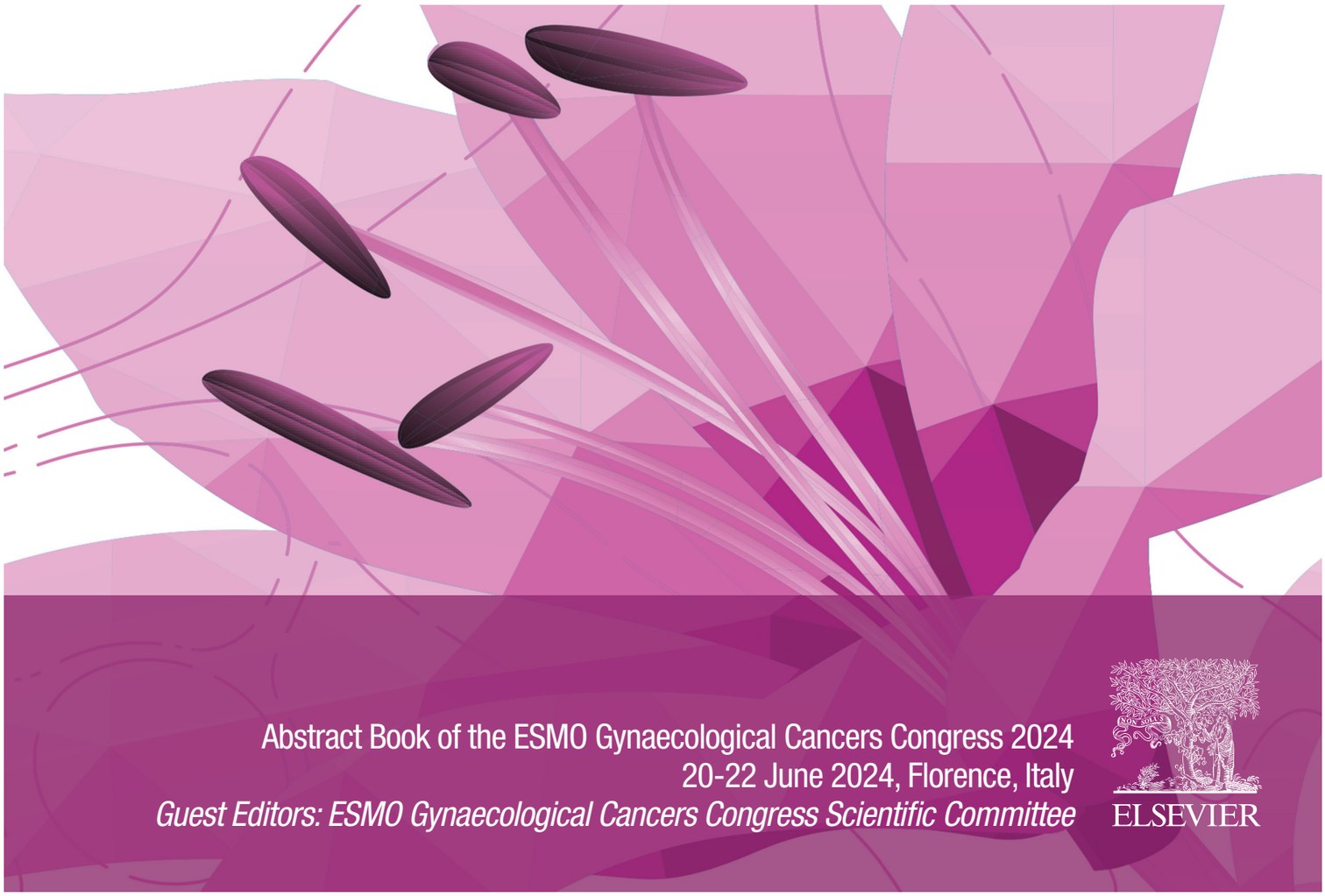

Abstract Book of the ESMO Gynaecological Cancers Congress 2024
20-22 June 2024, Florence, Italy
Guest Editors: ESMO Gynaecological Cancers Congress Scientific Committee

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ABSTRACT BOOK

Guest Editors:
ESMO Gynaecological Cancers Congress 2024 Scientific Committee

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Note:
Abstract suffixes

"O" indicated a submitted abstract accepted for proffered paper presentation
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BASIC AND TRANSLATIONAL RESEARCH

2P Integrated analysis of DNA and RNA revealed PARPi resistant mechanism of ovarian cancer: A paired tissue analysis of pre and post PARPi therapy

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Background: PARP inhibitors (PARPi) maintenance has become standard therapy in ovarian cancer. Strong anti-tumor effect was demonstrated especially in homologous recombination defects (HRD) tumors. However, systematic clinical study on PARPi resistance mechanisms and molecular changes of tumor is still lacking.

Methods: In this study (ethics number: 20200076), 14 ovarian cancer patients who were treated with PARPi at West China Second University Hospital were enrolled. PARPi treatment-naive samples (PNS, n = 12) and post-PARPi progression samples (PPS, n = 14) were acquired. Two next-generation sequencing (NGS) panels (Master panel, 563 genes for exons of DNA plus 1831 genes for RNA; HRD panel, 70,000 SNPs for HRD score evaluation, Amoydx) were used to analyze gene variation, expression, and HRD score changes in tumors.

Results: Total 14 resistant-related DNA alternation were identified. In 12 BRCA1/2 deficient cases, 4 (25%) BRCA1/2 restoration mutation were observed in PPS. Other resistant-related gene alternation included FGFR AMP (amplification, 16.7%) MYC AMP (16.7%), CCND1 AMP (16.7%), and RB1 loss (8.3%). 21.4% (3/14) cases harbored 2 or more resistance-related mutation. Upregulation of PIK3CA, MAPK, and Wnt signaling was observed at the RNA level in four cases lacking resistance-related DNA alterations. When compared with PNS, HRD scores and tumor mutation burden (TMB) were significantly elevated in PPS. Patients with high HRD scores in PPS had shorter PFS in PARPi rechallenge. DNA repair was up regulated in PPS. JAK, Apoptosis and MAPK pathways were down regulated in PPS. Cell cycle and other cancer related pathways upregulated after PARPi resistance. NK-cell/ T-cell and B-cell scores were up regulated in PPS.

Conclusions: Resistance mechanism of PARPi is complex. BRCA restoration mutation is a frequent cause of PARPi resistance. PARPi resistance could be driven without DNA mutation. Up regulating DNA damage repair and down regulating of apotosis could promotes tumor survival. The predictive value of HRD score for PARPi response was not applicable in the PARPi-treated samples. Tumor microenvironment could be changed and beneficial to immunotherapy after PARPi.

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3P The validation of a homologous recombination deficiency assay into clinical practice within the NHS

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Background: Homologous Recombination Deficiency (HRD) testing has been available for all NHS patients with newly diagnosed, advanced high-grade epithelial ovarian cancer to determine eligibility for PARP inhibitors Olaparib/Bevacizumab as an option for maintenance treatment. HRD status is determined by combining BRCA1/2 mutation status and a genomic instability score (GIS). Patients with HRD-positive tumours show an increased sensitivity to PARP inhibitors leading to significant improvements in progression-free survival.

Methods: HRD referrals were previously sent to Myriad, but from April 2024 testing will be taken over by NHS England at each NHS Genomic Laboratory Hub (GLH). The Royal Marsden, as part of NT-GLH, surveyed wet-lab and bioinformatic solutions in a product evaluation for the replacement of this service. 23 FFPE samples were assessed across four assays, including GIS positive/negative and tBRCA positive/negative clinical cases and compared to the original reported results. Following a product performance review, two bioinformatic solutions were tested with a larger dataset of 59 FFPE samples before a final decision was made on the solution for routine service.

Results: The NT-GLH selected The SOPHiA DDM™ solution, which utilises low amplification WGS in conjunction with a deep learning algorithm called GIInger™ to produce a Genomic Integrity Index (GII). The GII is then paired with the Royal Marsden's in-house somatic DNA NGS panel (RMH200, Roche) to generate tBRCA status for a complete HRD status. The validation of the GIInger pipeline showed 88% overall percentage agreement (OPA) to previously reported samples (Myriad, AZ), increasing to 97.7% when samples +/- 10% of positivity threshold were excluded. The pipeline reproducibility and repeatability exhibited 100% concordance.

Conclusions: The SOPHiA GIInger bioinformatics Pipeline for GI status, alongside our in-house RMH200 panel for tBRCA status provides a suitable HRD solution for testing patients with newly diagnosed, advanced high-grade epithelial ovarian cancer to determine PARP inhibitor eligibility. The pipeline was implemented at The Royal Marsden in December 2023, with 73 samples tested internally by March 2024.

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4P Mutational landscape of ovarian cancer patients (pts) by homologous recombination deficiency (HRD) status

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Background: Concomitant assessment of HRD and BRCA1/2 status provides critical information on platinum and poly-ADP ribose polymerase inhibitors (PARPi) sensitivity. HRD tests, in addition to evaluating genomic scars, can provide information on potential targetable genes.

Methods: We included 75 pts with high-grade serous ovarian cancer from Area Vasta Romagna (AVR). The DNA obtained from FFPE tissue samples of patients were processed using the SOPHiA HRD Solutionenrichment protocol (SOPHiA GENETICS, Saint-Sulpice, Switzerland). Sequencing was performed through the NextSeq500/550 sequencer platform (Illumina) and output files (FASTQ) were uploaded on the SOPHiA DDM Platform for the analysis. Sequencing results included SNP/INDEL and gene amplifications of 28 targeted genes, BRCA status and a HRD value, obtained by combining BRCA status with genomic integrity (GI) index.

Results: Among our 75 patients (median age 67, range 36-88), 6 pts were BRCA1 mutated (7.9%) and 9 pts were BRCA2 mutated (11.8%). BRCA variants with uncertain significance (VUS) were found in 14 pts, 7 for both BRCA1 and BRCA2 (9.2% for each). Of these, 3 pts (21.4%) were HRD positive, 5 pts (35.7%) were HRD negative, and 5 pts (35.7%) were HRD indeterminate. Among 47 (61.8%) BRCA WT pts, 15 pts (20%) were HRD positive, 34 pts (45.3%) were HRD negative and for 10 pts (13.3%) HRD status was not evaluable. In the BRCA WT HRD negative group, 14 pts (41.2%) harbored at least one other mutation, with the most frequent alteration in PIK3CA (20.6%), BARD1 (17.7%), RAD51B (11.8%) and FANCA (8.8%). In the BRCA WT HRD positive group, 8 pts (44.4%) had at least one other mutation, most frequently BRIP1 (25%) and RAD51B (25%). In the BRCA mutated group, 6 pts (40%) harbored at least one other mutation, most frequently RAD51B (26.7%), FANCD2 (20%) and BARD1 (13.3%).

Conclusions: Our test is able to discriminate HRD status in the vast majority of our patients with low number of indeterminate pts. BRCA1/2 VUS does not correlate with HRD status. Interestingly, PIK3CA mutations were found only in the HRD negative group, given the rationale for considering PIK3CA inhibitors (alone or in combination) as an investigational therapy for this population.

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5P Ovarian cancer ESCAT gene actionability: Cinderella wears the gown

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Background: In recent years, the prognosis of several malignancies has been positively influenced by the introduction of target therapy. In this context, ovarian cancer (OC) has played a minor role and chemotherapy still represents the backbone of standard treatment both in first and in subsequent lines. In 2023, BRCA1-2 and Homologous recombination deficit (HRD) status were included as Tier IA in the European Society of Medical Oncology Scale for Clinical Actionability (ESCAT) for OC.

Methods: In January 2022 our institution launched a comprehensive cancer genome profiling (CGP) (FPG500 IRB approval 3837; NCT06020625) enrolling patients with several neoplasms including OC, regardless of stage and histology except for mucinous and borderline tumors. Oncogenic and likely oncogenic alterations were reported according to OncoKB and classified as Tier I-II-III according to ESCAT classification. The aim of the current analysis was to count the rate of ESCAT I-II-III actionable and potentially actionable alterations.

Results: From January 1st 2022 to December 31st 2023, 832 patients with OC (72% high grade serous ovarian cancer, 9% endometroid cancer, 7% clear cells histology and 12% other histologies) underwent CGP, 338 of whom were also characterized for HRD. Overall, 47% showed at least one actionable or potentially actionable genomic alteration according to the ESCAT classification (level I, II, III). Concerning level IA, 15% and 9% were BRCA1 and BRCA 2 mutated, respectively, 53% were HRD. FGFR2 mutations were 2% (Tier IC). The most frequently found level II-III ESCAT genomic alterations were: PIK3CA mutations (13%), PTEN (mutations 4,7%, homdel 2,3%), ATM mutations (3%) and ERBB2 mutations (2%).

Conclusions: In the era of chemo free treatment, a wide genomic profiling in OC could pave the way to potential targeted approaches expanding therapeutic opportunities especially for BRCA 1/2 WT and HR proficient population.

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6P An innovative evidence-based laboratory medicine (EBLM) test to help doctors in the screening of ovarian cancer

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Background: Ovarian ranks seventh in women's cancers and eighth in female cancer-related deaths. Despite its low incidence, its impact is substantial due to late detection and limited treatment options. Named the 'silent killer' for its vague symptoms, it often leads to delayed diagnosis and metastasis. Hence, early detection remains challenging. Thus, we present Venient Sx Ovarian Basic (Kience Inc., Wilmington, US) a novel non-invasive test for ovarian cancer early detection. This diagnostic tool aims to accurately detect ovarian cancer, even in early stages, before symptoms appear and when treatment is most likely to succeed.

Methods: Venient Sx Ovarian Basic, designed specifically around serum biomarkers for ovarian cancer screening. It primarily relies on the tumor markers CA 19.9, CEA, and the ROMA score, which incorporates key factors such as age, menopausal status, and serum levels of CA 125 and HE4, to generate the likelihood of ovarian cancer, distinguishing between mucinous and serous epithelial ovarian cancer. To assess the estimated accuracy of our test, we conducted an extensive literature review of diagnostic accuracy studies about constituent algorithms, calculations, and combinations of analytes included within it. Parallel approximations were conducted to optimize overall sensitivity (Se), followed by serial approximations to enhance specificity (Sp), a process performed by our own machine learning (ML) algorithm.

Results: We obtained a final sample size (n) of 9,324 individuals and achieved a Se of 0.97 and a Sp of 0.93. Subsequently, we conducted an approximation of the area under the receiver operating characteristic (AUROC) curve, as well as estimations for the positive predictive value (PPV) and the negative predictive value (NPV) based on these results, yielding values of 0.92, 0.93, and 0.97, respectively.

Conclusions: This data suggests that the innovative non-invasive blood-based biomarker algorithm, Venient Sx Ovarian Basic, holds promise in providing timely ovarian cancer screening, particularly among individuals aged 40 and above. We are conducting an extensive parallel study with additional ovarian analytes to increase the Se of the test and offer the physicians a tool with minimum false negatives (FN).

Legal entity responsible for the study: Kience Inc..

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7P Unveiling the prognostic significance of protein expression in advanced high-grade serous ovarian cancer: A comparative study between long-term survivors and early mortal patients

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Background: High-grade serous ovarian cancer, despite its high lethality, lacks reliable biomarkers for predicting poor prognosis, and Limited progression has been made in personalized treatment. Genomic profile-based targeted therapy has not met

expectations, as genomic alterations alone do not exclusively determine cancer cell phenotypes. Protein expression critically influences cellular processes. Recognizing proteomic alterations is even more crucial. This study proposes a novel technique, utilizing statistical deviation and machine- learning to select protein factors determining ovarian cancer prognosis.

Methods: In advanced high-grade serous ovarian cancer patients, divided into two groups with very good (n=23) and poor prognoses (n=24), proteins were extracted from fresh frozen tissue and subjected to proximity extension assay (PEA). We explored a novel approach called AI-based machine learning to identify key proteins that could distinguish between groups with good and poor prognoses. Proteins were validated by immunohistochemistry (IHC) staining and cell proliferation assay, transwell migration assay, and Boyden chamber invasion assay.

Results: We explored a novel approach called AI-based machine learning to identify key proteins that could distinguish between groups with good and poor prognoses. By developing a model, we found that high levels of NPTN and PPM1A indicated a poor prognosis group, demonstrating remarkably high efficacy (Precision 0.857, Recall 0.818, F1-score 0.893). After IHC of NPTN and PPM1A in a tissue microarray (TMA), survival analysis showed that survival decreased when the expression was high. In vitro experiments with NPTN and PPM1A knockdown showed reduced cell proliferation, migration, and invasion.

Conclusions: Our results suggest that it is feasible to select factors with significant differences between prognostic groups, particularly those that are amenable to clustering based on identified proteins. The research highlights the potential of proteomic markers to guide personalized therapeutic strategies to improve patient outcomes.

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8P Biomarkers to predict chemotherapy response in low-grade serous ovarian carcinoma

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Background: Low-grade serous ovarian carcinoma (LGSC) is a rare subtype with distinctive genomic characteristics and low response to platinum chemotherapy. Outcomes for advanced LGSC are poor, therefore treatment options, including non-platinum chemotherapy need to be explored. Importantly, predictive biomarkers are needed to avoid exposure to toxic ineffective treatments. We aimed to identify molecular features predictive of response to docetaxel, paclitaxel and gemcitabine in well-defined LGSC cell line models.

Methods: Cell viability was assessed following docetaxel, paclitaxel and gemcitabine exposure in eight LGSC lines (CellTiter 96™ MTS Assay, Promega). RNA was sequenced (RNAseq, Illumina HiSeq2000) and analysed using EdgeR & clusterProfiler.

Results: The LGSC cell lines had MAPK pathway variants that are reflective of clinical samples (Table). HOC7 was relatively sensitive to all three agents. MPSC1 was sensitive to docetaxel and gemcitabine, and HO433 was only sensitive to gemcitabine. WMINV10, WMOV24 and WMINV13 were relatively resistant to all agents. There was no association between RAS/RAF mutation and drug response.

Table: 8P IC_{50} (nM) of LGSC cell lines, ordered by docetaxel IC_{50}

Cell Line	RAS/RAF Mutation	Docetaxel IC_{50}	Paclitaxel IC_{50}	Gemcitabine IC_{50}
MPSC1	$BRAF^{V600L}$, $NRAS^{Q61R}$	1.8	6.1	10
HCC5075	$KRAS^{G12V}$	2	1.5	18
HOC7	$KRAS^{G12A}$	2.1	1.7	5
AOCS2	WT	6.6	11.4	29
WMINV10	$KRAS^{G12V}$	38.2	NR	1669
WMOV24	$KRAS^{G12D}$	95	NR	1038
HO433	WT	103	113.8	5.1
WMINV13	$NRAS^{Q61R}$	NR	NR	3451

WT = wild type; NR= not reached.

Transcriptome analysis showed epithelial to mesenchymal transition genes to be strongly associated with resistance to docetaxel (Gene Set Enrichment Analysis, GSEA $q=2.1x10^{-10}$) and paclitaxel (GSEA $q=1.1x10^{-10}$) whereas pathways involving DNA replication were upregulated in cell lines sensitive to docetaxel (p-adj=0.0004). Neuronal system pathways were upregulated in cell lines resistant to gemcitabine (p-adj=$9.4x10^{-11}$) and docetaxel (p-adj=$2.8x10^{-12}$).

Conclusions: Our pre-clinical data suggests that non-platinum chemotherapy may be a viable option in selected LGSC patients. Gene expression profiles associated with response to specific agents were identified. However, these findings need further validation in patient samples.

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9P Synergistic potential of vitamin D receptor and cancer stem cells markers expression in ovarian tumors

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Background: Ovarian cancer (OC) is the most aggressive gynecological malignancy. Vitamin D actions mediated by its receptor (VDR) showed significant antitumor activity. Cancer stem cells (CSC) that are characterized by specific surface markers CD44 and CD133, are responsible for the tumor resistance to various treatment modalities.

This study aimed to analyze the association of CD44, CD133, and VDR expression in epithelial ovarian tumors (EOT).

Methods: Our cohort comprised 218 patients with EOT of which 131 were OC, 42 atypical proliferative tumors (APT), and 45 benign tumors. A set of histopathology parameters were correlated with CD44, CD133, and VDR immunohistochemical expressions, using the tissue microarray method. We used extensive scoring method (IR score, Remmele's score) as a more validate than basic one. It considered multiplied staining intensity (0- absent, 1- low, 2- moderate, 3- strong) and the percentage of positive cancer cells (0 = 0%, 1 ≤ 10%, 2 = 11—50%, 3 = 51—80%, 4 ≥ 81% of the cells). High expression was defined as IR score >2, while low expression was with IR score 0-2.

Results: There was a positive correlation between CD44, CD133, and VDR markers in all groups ($p<0.05$). CD44 and cytoplasmic VDR expression showed higher levels in OC than in other groups, while CD133 expression was most prominent in the APT ($p<0.05$). Significant CD44 and VDR expression was evident in high grade serous carcinoma (HGSC) in advanced stages. CD133 marker did not show a correlation with these histopathology parameters. This study indicates very important and complex relationships between CSCs and VDR-mediated calcitriol function, which certainly is one of the very crucial regulation mechanisms in CSC. High VDR expression point to possible effective antitumor (calcitriol) therapy in HGSC ovarian cancer cells. Calcitriol treatment could activate the VDR signaling pathway in CSCs, which further disrupts the CSC's stemness, leading to a reduction of the CSC population.

Conclusions: Significant CD44 and cytoplasmic VDR expressions were demonstrated in ovarian CSC in aggressive types as HGSC, at advanced stages. It indicates the possible benefits of target therapy in patients with high expression levels of these markers.

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10P Human papillomavirus integration testing and high-grade cytology improve diagnostic performance of colposcopy-guided biopsy

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Background: Our objective was to investigate the diagnostic efficacy of colposcopy-guided biopsy (CGB) and to explore new strategies to increase the accuracy for detecting cervical intraepithelial neoplasia grade 2 or more severe lesions.

Methods: We conducted a retrospective cohort study of 550 women who underwent both CGB and surgery to assess the consistency of their pathological findings. Using surgical pathology as the gold standard, we evaluated the diagnostic accuracy of CGB in detecting high-grade lesions. Univariate and multivariate logistic regression analyses were used to identify independent predictors for CIN2+ and CIN3+ lesions on definitive pathology. The AUC was utilized to evaluate the diagnostic performance of detecting CIN2+ and CIN3+ lesions on surgical pathology with various variables.

Results: Among 550 women with paired CGB/surgical pathology, 53.5% (294/550) had perfect agreement, with 17.1% (94/550) underestimations and 29.5% (162/550) overestimations. The sensitivity and specificity of CGB for detecting CIN2+ lesions were 86.3% (276/320) and 51.3% (118/230), respectively. Multivariate logistic analysis revealed that CGB confirming CIN2+ (OR, 6.0; 95% CI, 3.9-9.1; $P < 0.001$), high-grade cytology (OR, 2.6; 95% CI, 1.4-4.9; $P = 0.003$), and HPV integration-positive (OR, 2.2; 95% CI, 1.3-3.5; $P < 0.001$) were significant predictors for CIN2+ on surgical pathology. For identifying CIN3+, CGB confirming CIN2+ (OR, 5.3; 95% CI, 3.4-8.3; $P < 0.001$), high-grade cytology (OR, 2.6; 95% CI, 1.5-4.7; $P = 0.001$), HPV integration-positive (OR, 2.0; 95% CI, 1.3-3.1; $P = 0.003$) were independent predictors. The AUCs increased when incorporating several variables to predict high-grade lesions. For 27 patients with both high-grade-cytology and HPV integration-positive results, 25 (92.6%) of them confirmed CIN2+ on definitive pathology.

Conclusions: CGB's accuracy is limited, leading to underestimations and overestimations. Combining CGB with HPV integration and cytology enhances CIN2+ and CIN3+ diagnosis. Diagnostic conisation may be considered for patients with high-grade cytology and HPV integration-positive results.

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11P Human papillomavirus integration: A novel biomarker for prediction of overtreatment in cervical intraepithelial neoplasia grade 2 or 3 patients with non-high-grade cytology abnormalities

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Background: We aimed to establish a predictive model enabling gynecologists to assess risk and minimize overtreatment among cervical intraepithelial neoplasia (CIN) 2 or 3 patients.

Methods: We conducted a retrospective cohort study of 311 women diagnosed with CIN2 or CIN3 by colposcopy-directed biopsy before surgical treatment. Univariate and multivariate logistic regression analyses were performed to identify independent overtreatment-associated predictors. We also employed E-value analysis to evaluate the effect of unmeasured confounding variables. Overtreatment was defined as surgical specimens diagnosed with negative or CIN1 pathology.

Results: Among the 311 CIN2/3 women, 103 patients (33.1%) showed CIN 1 or less in the surgical specimens. In multivariate analysis, CIN2 biopsy (odds ratio [OR], 3.1; 95% confidence interval, [CI], 1.9 - 5.2; $P < 0.001$) and non-high-grade cytology (OR, 3.3; 95% CI, 1.5 - 7.2; $P = 0.003$) were independent predictors for overtreatment. Furthermore, in 258 patients with non-high-grade cytology, overtreatment occurred in 95 (36.8%) patients, where CIN2 biopsy (OR, 2.8; 95% CI, 1.7 - 4.9; $P < 0.001$) and human papillomavirus (HPV) integration-negative or low-grade HPV integration-positive results (OR, 4.9; 95% CI, 1.1 - 21.7; $P = 0.039$) were independent indicators for overtreatment. Based on E-value analysis, our study findings were robust to potential unmeasured confounding variables.

Conclusions: HPV integration status may serve as a good predictor for overtreatment in women with non-high-grade cytology. In women with non-high-grade cytology, HPV integration status may be a good predictor for overtreatment.

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12P Exploring the prognostic value of circulating tumor HPV DNA in cervical cancer

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Background: Persistent infection with high-risk HPV is a known cause of cervical cancer. Minimal residual disease (MRD) is increasingly well recognized in guiding adjuvant therapy for colorectal and lung cancer, and exploring its role in cervical cancer is essential for improving patient outcomes. This study investigates the prognostic potential of circulating tumor HPV DNA (ctHPV-DNA) in monitoring treatment response and predicting recurrence in cervical cancer.

Methods: The prospective, observational clinical study (NCT05602831) enrolled patients undergoing radical radiotherapy or surgery. Blood samples were collected for HPV digital droplet PCR (ddPCR) testing, targeting HPV16/18/33/52/58, at baseline, post-surgery, and the day after radical radiotherapy, at 1 and 3 months to assess HPV clearance in relation to treatment efficacy and prognosis.

Results: From August 2022 to March 2024, 43 patients were enrolled, with 27 completing sequential blood collections and 23 undergoing baseline tissue and ctHPV-DNA testing. Among the 23 patients, all are squamous cervical cancer, with a mean age of 55 years and 82.6% (19/23) at stage III. The majority (95.7%) received radical radiotherapy, with a 73.9% complete remission rate. Concordance between baseline ctHPV-DNA and tissue HPV testing was 100%. The 18 tissue-confirmed HPV-positive patients were analyzed for ctHPV-DNA dynamic surveillance: 13 HPV16+, 3 HPV58+, 1 HPV52+, and 1 HPV18+. A positive correlation existed between baseline tissue HPV copy number and ctHPV-DNA copy number ($r=0.4718$, $p=0.0615$). Notably, patients with stage IIIC had higher ctHPV-DNA copy numbers than those with IIIB. Post-radiation, 4 patients (22.22%) tested positive for ctHPV-DNA, with two experiencing relapse. Detailed case studies highlighted the prognostic value of ctHPV-DNA, with early detection of recurrence possible 105 days ahead of imaging and 90 days ahead of tumor marker SCC-Ag elevation.

Conclusions: The study demonstrates a strong correlation between ctHPV-DNA and tissue HPV testing, positioning ctHPV-DNA as a valuable prognostic tool for cervical cancer. Future research with increased enrollment and extended follow-up period will further validate these promising results.

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13P HPV integration status conversion and risk stratification by HPV integration levels in HPV integration-positive women: A 1-year follow-up

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Background: To evaluate the risk stratification by HPV-integration levels and HPV integration status conversion in HPV integration-positive women after 1-year follow-up.

Methods: This prospective cohort study conducted in Tongji hospital between June 2020 to August 2022 with 1297 consecutive HPV-positive women. The level of integration reads was stratified for risk assessment.

Results: A total of 194 women were HPV integration-positive and followed-up for at least 1 year. The immediate risk of cervical intraepithelial neoplasia grade 2 or worse (CIN2+) increased from 36.2% (25/69) in women with 6-20 integration reads to 93.8% (30/32) in women with more than 1000 integration reads ($P_{trend} < 0.001$). The 1-year cumulative risk of CIN2+ increased from 39.1% (27/64) in women with 6-20 integration reads to 96.9% (31/32) in women with more than 1000 integration reads ($P_{trend} < 0.001$). The 1-year cumulative risk of CIN2+ with HPV integration reads more than 40 was 93.8% (90/96), which was significantly higher than that of HPV integration reads less than 40 (38/85, $P < 0.001$). At one-year follow-up, in women with HPV integration reads more than 40, 99.0% (95/96) of women progressed with positive outcomes (persistent integration at the same site, immediate CIN2+ and 1-year CIN2+). The progression rate of women with persistent integration at the same site was 41.6% (5/12), which was significantly higher than those of HPV-integration negative conversion (0/41, 0%, $P < 0.001$).

Conclusions: The number of HPV integration reads may have the potential in CIN2+ risk stratification to facilitate the clinical management of high-risk patients.

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14P Evaluation of PAX1/JAM3 gene methylation detection for cervical cancer screening: A prospective multi-center study

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Background: Cervical cancer presents a significant health and economic threat to women. Efficient and accurate screening strategies are crucial for achieving "cervical cancer elimination". This study is a multi-center prospective study aimed at evaluating the application value of PAX1/JAM3 gene methylation ($PAX1^m/JAM3^m$) detection in cervical cancer screening.

Methods: The research included a total of over 6000 women in gynecological outpatient clinics from May to October 2022. Cervical scraping cells were collected for $PAX1^m/JAM3^m$ testing and compared with liquid-based thin-layer cytology testing (TCT) and high-risk human papillomavirus (hrHPV) DNA testing. Ethics registration number of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences: KS2021211 (approved on April 25, 2021).

Results: The results showed that $PAX1^m/JAM3^m$ detection has high AUC, sensitivity, and specificity in identifying CIN2+ (cervical intraepithelial neoplasia 2 or more severe) at 0.85, 74.1%, and 95.9%, and CIN3+ at 0.87, 87.6%, and 86.8%. The study also indicated that $PAX1^m/JAM3^m$ detection has significant advantages over TCT or hrHPV testing in identifying CIN3+. Therefore, the study concluded that $PAX1^m/JAM3^m$ detection has excellent accuracy in cervical cancer screening and is expected to replace cytology screening as a triage option for hrHPV-positive women in opportunistic cervical cancer screening in hospitals.

Conclusions: Overall, the large-scale study highlights the high accuracy of $PAX1^m/JAM3^m$ detection in opportunistic cervical cancer screening in hospitals, especially in the detection of CIN2+ and CIN3+. The results suggest that $PAX1^m/JAM3^m$ detection has the potential to become a precise tool for cervical cancer screening in the future, which is of great significance for optimizing cervical cancer screening strategies. This method may become a promising alternative to traditional screening methods and provide a more accurate screening option for hrHPV-positive women in the future.

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15P Loss of vimentin expression in preoperative biopsies independently predicts lymph node metastasis in endometrial cancer

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Background: Precise preoperative risk classification of endometrial cancer is crucial to guide selection of treatment. Still, 15-20% of tumors classified as low-risk recur. Loss of expression of vimentin was recently identified as a marker of recurrence in patients with low stage disease. We aimed to investigate if vimentin expression in preoperative biopsies could predict poor prognosis and lymph-node metastasis in a large, prospectively collected multicentre endometrial cancer cohort.

Methods: Preoperative biopsies were collected from 1483 patients diagnosed and treated for endometrial cancer in 10 hospitals in Norway, Sweden, Belgium and Polen. Vimentin expression was investigated by immunohistochemistry and evaluated using the staining index method. Expression levels were analysed for association with clinical characteristics, and in uni- and multivariate analyses to predict disease-specific survival (DSS) and lymph node metastases.

Results: Loss of vimentin expression was significantly associated with histopathological parameters of aggressive disease and poor disease-specific survival. Vimentin expression had independent prognostic value in multivariate survival analysis, both when including all patients (hazard ratio (HR) 1.82, 95% CI 1.31-2.55, P<.001), in the subgroup of endometrioid patients (HR 3.59, 95% CI 2.19-5.88, P<.001) and for patients with FIGO stage 1 disease (HR 3.24, 95% CI 2.04-5.75, P<.001). Lymph node metastases were more frequent in patients with loss of vimentin expression compared to patients with positive vimentin expression (26% vs 13%, P<.001), and loss of vimentin expression independently predicted lymph node metastases (HR 1.91, 95% CI 1.10-3.34, P=0.021).

Conclusions: Loss of vimentin expression in preoperative endometrial cancer biopsies independently predicts poor disease-specific survival and lymph node metastases and may aid in identifying high-risk patients otherwise classified as low risk.

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16P Homologous recombination deficiency in endometrial cancer: Association with clinical and molecular characteristics

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Background: The frequency of homologous recombination deficiency (HRD) and the clinical relevance of these alterations in patients with endometrial cancer (EC) are unknown. The aim of this study was to assess the incidence of HRD and its impact on the clinical characteristics and prognosis in patients with EC.

Methods: Tumors with pathogenic and/or potentially pathogenic mutations in 10 genes (BRCA1, BRCA2, ATM, BARD1, BRIP1, PALB2, RAD51C, RAD51D, CHEK2, and CDK12) involved in the homologous recombination pathway in the MSK-MET and The

Cancer Genome Atlas (TCGA) EC cohorts were considered to have HRD, and the others were considered to be homologous recombination proficient (HRP). The correlation between HRD status and the clinical characteristics of patients with EC was evaluated. The analyses were conducted in microsatellite stable (MSS) and microsatellite instability-high (MSI-H) populations, respectively.

Results: Of the 1315 patients with EC enrolled in the MSK-MET cohort, 163 (12.4%) patients had HRD and 1152 (87.6%) patients were HRP. HRD occurred more frequently in MSI-H patients than in MSS patients (28.7% vs. 9.8%, $P < 0.001$). Among patients with MSS, compared to patients in the HRP group, patients in the HRD group had a younger median age at EC diagnosis (60.4 vs. 64.6 years, $P < 0.001$), and were more likely to have endometrioid carcinoma (73.0% vs. 56.0%, $P = 0.003$), POLE mutation (40.5% vs. 1.4%, $P < 0.001$), or high tumor mutational burden (62.2% vs. 11.3%, $P < 0.001$). Tumors with HRD had a significantly lower rate of TP53 mutation than HRP tumors (30.6% vs. 49.4%, $P < 0.001$). HRD did not significantly alter the overall survival of patients with MSS tumors in either the MSK-MET cohort or the TCGA cohort.

Conclusions: Tumors with HRD are a subtype of MSS EC with unique clinical and molecular characteristics. The evaluation of HRD in patients with MSS EC may help clinicians select patients who may benefit from targeted therapies. The potential clinical efficacy of agents targeting the homologous recombination system in this subgroup is worthy of study.

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17P Hormone receptor expression outperforms molecular class in predicting endometrial cancer risk pre-operatively

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Background: Pre-operative histologic subtype and deep myometrial infiltration at magnetic resonance imaging are strong predictors of high-risk disease in endometrial cancer (EC). Whether molecular subtype in combination with hormone receptor status can refine conventional risk stratification is uncertain.

Methods: A prospectively collected EC cohort including 446 patients was molecularly subtyped using surrogate markers and the WHO-endorsed classification algorithm. Median follow-up was 6.4 years. Estrogen- and progesterone receptor (ER and PR) status was investigated by IHC and scored using the staining index method. Uni- and multivariate analyses to predict disease-specific survival (DSS) were performed. The multivariate model included patient age, preoperative risk groups, molecular subtypes and combined ER/PR status.

Results: Patients were classified as POLE (9%), MMR-D (29%), copy-number low (46%) and copy-number high (16%). Loss of ER and/or PR expression was found in 36% of the tumors. Both molecular type and dichotomized ER/PR expression associated with DSS in univariate analyses ($p < 0.001$). However, after adjusting for preoperative risk group, loss of ER/PR outperforms molecular class for predicting poor DSS (ER/PR: $p = 0.004$, MolClass: $p > 0.05$).

Conclusions: Preoperative loss of ER/PR predicts poor prognosis and outperforms molecular class for improving risk stratification of EC patients.

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18P PIK3CA mutations in relapse risk stratification of stage I endometrial cancers with no special molecular profile

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Background: The Cancer Genome Atlas (TCGA) current molecular classification has established four categories with prognostic and predictive values in endometrial cancer (EC): POLE mutated, microsatellite instable (MSI), no specific molecular profile (NSMP), and p53 abnormal. In this context, NSMP represents the most heterogeneous subgroup, underlying several molecular alterations with unknown clinical value. The aim of this study is to evaluate how PIK3CA mutations could affect the prognosis of NSMP subgroup.

Methods: Formalin-fixed paraffin-embedded (FFPE) tumour samples of 112 stage I EC patients treated at Careggi University Hospital, Florence (Italy) were gathered. p53 status by immunochemistry (IHC), microsatellite status by IHC and/or real time PCR, PIK3CA mutations by real time PCR, and POLE status by NGS sequencing were assessed. The primary endpoint was disease-free survival (DFS).

Results: Among 112 patients analyzed, 39 patients were p53 wild-type. Among them, a statistically significant difference in DFS between PIK3CA mutated and not mutated patients was found ($p=0.029$). 20 patients out of 39 (51%) were p53 wild-type/MSS. 9 of 20 (45%) p53 wild-type/MSS patients had POLE status known and they were all wild-type, however POLE status was not known for the remaining 11 patients. In the subgroup of 20 patients p53 wild-type/MSS, PIK3CA mutated patients showed a statistically significant worse DFS compared to PIK3CA wild-type ($p=0.032$).

Conclusions: PIK3CA mutations negatively influence the outcomes of stage I EC patients with NSMP as the p53 wild-type/MSS. Therefore, PIK3CA testing might be implemented in clinical practice to further stratify the risk of EC patients without a specific molecular mark according to the current TCGA molecular classification, such as NSMP subgroup, in order to optimize adjuvant treatments.

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19P Molecular characteristics of rare gynecological mesonephric(like) adenocarcinoma: A comprehensive analysis using whole exon sequencing and mRNA sequencing

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Background: Gynecological mesonephric-like adenocarcinoma (MLA) is a rare tumor type. Its morphology is similar to mesonephric adenocarcinoma but histological origin is unknown. The molecular pathological study of MLA is still in its preliminary stage. Poor prognosis and lack of diagnostic and therapeutic standards are the major challenges of this disease.

Methods: The medical records of patients admitted to West China Second University Hospital between January 1, 2010 and December 30, 2022 were retrospectively reviewed (Ethics number: 20220305). Total DNA and RNA were extracted from formalin-fixed paraffin-embedded (FFPE) tumor samples and peritumoral samples. Whole exon sequencing and mRNA sequencing were performed using AmoyDx® Tumor panoramic genetic testing kits (AmoyDx, Xiamen, China) and AmoyDx® Human transcription genetic testing kits (AmoyDx, Xiamen, China) respectively.

Results: A total of 17 cases of gynecological MLAs were identified, originating from three sites (cervix n=2, ovary n=5, uterus n=10). Median follow up time, progression free survival (PFS), and overall survival were 19 months, 14.5 months, and18.5 months respectively. High frequency of KRAS mutation was observed (82.4%). Enrichment of KRAS signaling was observed simultaneously at the RNA level. Mutations in PIK3CA and SPOP are also present at moderate frequencies (47.1% and 23.5%) and mutually exclusive. Signature 15 and NNAT CNV gain were associated with poor prognosis. Upregulating of G2M checkpoint, E2F targets, and epithelial-mesenchymal transition (EMT) were main tumor-associated features of MLA. 16 kidney development related genes were identified upregulate in MLA, which was also

significantly highly expressed when compared to TCGA UCEC/CESC/OV datasets. MLA exhibited a lower immune response potential, including lower lymphocyte infiltration and IFN scores when compared with peritumoral samples and UCEC/CESC/OV.

Conclusions: KRAS mutation is a key driver event in MLA. Kidney development related genes are important transcriptomic differences between MLA and other gynecologic tumors. Low immune response may limit the efficacy of PD-1/L1 therapy in MLA.

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20P Unexpected germline pathogenic variants in gynaecologic cancers identified through a comprehensive cancer genome profiling programme

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Background: There is a growing utilization of comprehensive cancer genome profiling (CGP) to assess patients' eligibility for target therapies. Potential pathogenic germline variants (PPGVs) may be identified via CGP. Large series indicate that PPGVs in cancer risk genes are found in 10-23% of patients tested by CGP and 3-7% were confirmed to be germline. The present study reports the frequency of PGVs in a cohort of gynaecologic cancers patients on a prospective CGP programme.

Methods: PPGVs were indicated for 1.069 tumor samples of ovarian (OC, n=632) and endometrial (EC, n=437) cancer patients analyzed by TruSight Oncology 500 High-Throughput (TSO500HT) solution from January 2022 to June 2023. PPGVs focused on 40 cancer risk genes as indicated by the European Society for Medical Oncology recommendations.

Results: Overall, 22.5% of patients (29.3% of OC and 12.8% of EC) had at least one PPGVs in cancer risk genes; in detail, 71 PPGVs were identified for EC and 206 for OC. Considering the association between variants and tumor type, 46.5% of PPGVs in EC and 65% in OC were referred to genes involved in well-known hereditary conditions (MLH1, MSH2, MSH6, PMS2 in EC and BRCA 1/2 in OC). Data on germinal confirmation are available for 207/277 variants (74.7%). 153 out of 207 variants (73.9%, of which 64.4% for EC and 76.5% for OC) were confirmed of germline origin. 30.7% (9/29 of EC and 38/124 of OC) of the confirmed PGVs were not related to Lynch syndrome and BRCA1/2 genes in EC and OC, respectively (Table).

Table: 20P

Gene	OC		EC	
	PPGV (n)	Confirmed PGV (n)	PPGV (n)	Confirmed PGV (n)
ATM	5	4	7	1
BRCA1	97	59	3	0
BRCA2	37	27	5	1
BRIP1	5	3	1	1
CHEK2	1	1	4	0
DICER1	2	0	1	0
MLH1	4	3	6	2
MSH2	3	1	18	10
MSH6	6	3	8	7
MUTYH	11	6	5	3
NF1	8	0	1	0
PALB2	7	6	2	1
PMS2	1	1	1	1
POLD1	1	0	1	0
POLE	1	1	3	0
PTCH1	2	0	1	0
PTEN	0	0	1	0
RAD51C	9	6	0	0
RAD51D	3	2	1	1
RET	0	0	1	0
SDHA	2	1	1	1
SMARCB1	1	0	0	0
Total	206	124	71	29

Conclusions: Besides therapeutic and prognostic implications, CGP can identify variants related to hereditary cancer predisposition conditions allowing cascade prevention and identification of affected relatives. Approximately one-third of gynecological cancer patients were discovered to have PGVs in genes other than those commonly recommended.

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ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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CERVICAL CANCER

21O Coformulated vibostolimab/pembrolizumab in advanced cervical cancer: KEYVIBE-005

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Background: Vibostolimab (vibo) (anti-TIGIT) + pembrolizumab (pembro) has shown promising efficacy in cervical cancer. KEYVIBE-005 (NCT05007106) evaluated coformulated vibo/pembro in previously treated cervical cancer (cohort A).

Methods: This open-label phase 2 trial enrolled patients (pts) aged ≥ 18 years with previously treated, anti- PD-[L]1 naïve, unresectable or metastatic cervical cancer, by PD-L1 status to cohort A1 (CPS ≥1) or A2 (CPS<1). Cohort A1 was randomized 1:1 to coformulated vibo 200 mg/pembro 200mg or pembro 200 mg Q3W. Cohort A2 received coformulated vibo 200 mg/pembro 200mg Q3W. Primary endpoints were PFS and ORR per RECIST 1.1 by BICR (cohort A1), and ORR per RECIST 1.1 by INV (cohort A2). Secondary endpoints were DOR (RECIST 1.1, BICR), OS and safety (cohort A1), and PFS and DOR (RECIST 1.1, INV), OS and safety (cohort A2). Data cut-off was October 24, 2023.

Results: At data cut-off, 169 pts were enrolled in cohort A1 (85 vibo/pembro, 84 pembro) and 31 in cohort A2. Median follow-up was 18.2 months (mo) for cohort A1 and 15.7 mo for cohort A2. The ORR was 20% for vibo/pembro vs 15.5% for pembro (p=0.2215). The ORR was 16.1% for cohort A2. Median PFS was 2.2 mo with vibo/pembro vs 2.1 mo with pembro (HR=0.99, p=0.4787). Median PFS was 2.2 mo for cohort A2 (Table). Drug-related adverse events (AEs) occurred in 64 pts (75%) with vibo/pembro, 48 (58%) with pembro (cohort A1), and 24 (77%) in cohort A2. Grade ≥3 drug-related AEs occurred in 15 (18%) pts with vibo/pembro, 10 (12%) with pembro (cohort A1), and 9 (29%) in cohort A2. One pt died due to a drug-related AE (septic shock) with vibo/pembro (cohort A1). Immune-mediated AEs occurred in 30 pts (35%) with vibo/pembro, 26 (31%) with pembro (cohort A1), and in 12 pts (39%) in cohort A2.

Conclusions: Efficacy outcomes with coformulated vibo/pembro were not superior to pembro in pts with previously treated PD-L1+ cervical cancer, consistent with that observed in other anti-TIGIT trials. No new safety signals were identified.

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Table: 21O

	CPS≥1		CPS<1
	vibo/pembro N=85	pembro N=84	vibo/pembro N=31
ORR, n (%) [95% CI]	17 (20.0) [12.1-30.1]	13 (15.5) [8.5-25.0]	5 (16.1) [5.5-33.7]*
CR	6 (7.1)	6 (7.1)	0
PR	11 (12.9)	7 (8.3)	5 (16.1)
Median DOR, mo (range)	10.9 (5.3-NR)	NR (NR-NR)	10.8 (9.6-NR)*
Median PFS, mo (95% CI)	2.2 (2.1- 4.2)	2.1 (2.1-2.3)	2.2 (2.0-4.2)*
12-mo PFS rate, %	16.8	19.8	19.4
Median OS, mo (95% CI)	10.2 (7.2-15.2)	10.3 (8.4-14.7)	12.8 (7.9-17.0)
12-mo OS rate, %	48.2	42.1	50.6

CPS= combine positive score, CR= complete response, mo= months NR= not reached, PR= partial response. *Per RECIST 1.1 by INV.

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22O Association of biomarkers with response to coformulated vibostolimab/pembrolizumab (vibo/pembro) in metastatic cervical cancer (CC): Exploratory analysis from the phase II KEYVIBE-005 study

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Background: In the multicohort KEYVIBE-005 study (NCT05007106), vibo/pembro (n = 85) showed antitumor activity similar to pembro (n = 84; ORR, 20.0% vs 15.5%) with a manageable safety profile in patients (pts) with previously untreated metastatic CC with PD-L1 CPS ≥1. We evaluated the association between biomarkers and response to treatment in this cohort.

Methods: Using tumor samples, expression of TIGIT on immune cells (clone SP410, FLA assay) and PD-L1 CPS (PD-L1 22C3 pharmDx) were evaluated by IHC, T-cell–inflamed gene expression profile ($Tcell_{inf}GEP$) by NanoString, and TMB by WES. ORR and PFS were evaluated. Significance of continuous biomarkers was prespecified at 0.05 for 1-sided P values from logistic (ORR) and Cox proportional hazard (PFS) regression. ctDNA was isolated from pretreatment plasma samples collected on day 1 at cycle 1 (C1), C2, and C3 and sequenced using a personalized tumor-informed assay (Invitae PCM); quantity was expressed as maximum somatic allele frequency (MSAF).

Results: The association of biomarkers with ORR and PFS is reported in the table. The AUROCs (95% CI) for discriminating response to vibo/pembro were as follows: TIGIT, 0.64 (0.48-0.80); PD-L1, 0.72 (0.61-0.83); $Tcell_{inf}GEP$, 0.71 (0.56-0.86); and TMB, 0.74 (0.58-0.91). The AUROCs (95% CI) for discriminating response to pembro were as follows: TIGIT, 0.63 (0.47-0.79); PD-L1, 0.68 (0.50-0.86); $Tcell_{inf}GEP$, 0.65 (0.46-0.84); and TMB, 0.71 (0.46-0.95). Median ctDNA MSAF was reduced by 21% at C2 and by 32% at C3 with vibo/pembro (from C1) compared with 4% and 6% reductions, respectively, with pembro.

Table: 22O P values of the association analysis between biomarkers and clinical outcomes

Biomarker	Vibo/pembro			Pembro monotherapy		
	n	ORR	PFS	n	ORR	PFS
TIGIT	81	0.0740	0.0700	80	0.076	0.0270
PD-L1 CPS	85	0.0070	0.0002	83	0.011	0.2200
$Tcell_{inf}GEP$	74	0.0050	0.0003	66	0.060	0.0020
TMB	57	0.0120	0.1470	53	0.021	0.0004

Conclusions: In pts with CC with PD-L1 CPS ≥1, all biomarkers trended towards a positive association with response to vibo/pembro; the strongest associations were observed for PD-L1 and $Tcell_{inf}GEP$. Trends towards larger ctDNA decreases were observed with vibo/pembro vs pembro.

Clinical trial identification: NCT05007106 (study start date: 2021-09-16).

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23O A randomized, phase III, double-blind study of chemoradiotherapy with or without pembrolizumab in patients with high-risk, locally advanced, cervical cancer (KEYNOTE-A18/ENGOT-cx11/GOG-3047): Results for patients enrolled in Asia

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Background: In the global, randomized, phase 3 ENGOT-cx11/GOG-3047/KEYNOTE-A18 (NCT04221945) study, pembrolizumab (pembro) + concurrent chemoradiotherapy (CCRT) showed a statistically significant improvement over placebo (pbo) + CCRT in PFS (median PFS, not reached in either group; hazard ratio [HR], 0.70 [95% CI, 0.55—0.89]; P=0.0020) and a favorable trend for improved OS vs pbo + CCRT (median OS not reached in either group; HR, 0.73 [95% CI, 0.49—1.07]) in patients with high-risk locally advanced cervical cancer (LACC) at the first interim analysis. We present results for patients enrolled in East Asia.

Methods: Eligible patients had newly diagnosed, previously untreated, high-risk LACC (FIGO 2014 stage IB2-IIB with node-positive disease or stage III-IVA regardless of lymph node status). Patients were randomly assigned (1:1) to receive 5 cycles of pembro 200 mg or pbo Q3W + CCRT, followed by 15 cycles of pembro 400 mg or pbo Q6W. CCRT included 5 cycles (with optional 6th dose) of cisplatin 40 mg/m^2 QW + external beam radiotherapy, then brachytherapy. Primary endpoints were PFS per RECIST v1.1 by investigator assessment and OS. No alpha was allocated to this exploratory analysis in the East Asia subgroup.

Results: 299 patients were enrolled in East Asia (China, n=149; Japan, n=90; Republic of Korea, n=26; Thailand, n=20; Taiwan, n=14): pembro + CCRT, n=153; pbo + CCRT, n=146. Median follow-up at database cutoff (Jan 9, 2023) was 19.3 (range, 0.9—31.0) months. Median PFS was not reached in either treatment group (HR, 0.55 [95% CI, 0.35—0.88]); 24-month PFS rate was 77.6% in the pembro + CCRT group and 59.8% in the pbo + CCRT group. Grade ≥3 treatment-related AEs occurred in 78.3% of patients in the pembro + CCRT group and 77.4% in the pbo + CCRT group; none were grade 5. Immune-mediated AEs occurred in 43.4% and 10.3% of patients, respectively.

Conclusions: Consistent with the global analysis, pembro + CCRT demonstrated PFS benefit vs pbo + CCRT, with manageable safety in patients with high-risk LACC enrolled in East Asia. These results suggest pembro + CCRT may be considered as a new treatment option for patients with high-risk LACC in East Asia.

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24MO TROP-2, TF and NECTIN4 as targets for ADC treatment in cervical cancer

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Background: If detected early, most cervical cancers associate with good prognosis. However, survival rates drop significantly for late stage or recurrent disease, and treatment options are limited. Antibody drug conjugates (ADCs) represents a new group of cancer drugs providing promising response rates across multiple cancer types. However, only the ADC tisotumab vedotin (TV) is approved by the Food and Drug Administration (FDA) for use in cervical cancer. The aim of this study was to assess the expression of the ADC target proteins TROP2, Tissue factor (TF) and NECTIN4 by immunohistochemistry (IHC) in a population based cervical cancer cohort.

Methods: A prospectively collected cohort of 525 cervical cancer patients with extensive clinicopathological data including follow-up was investigated. Membrane expression of TROP2, TF, and NECTIN4 was assessed by IHC on tumor sections assembled on tissue microarrays (TMAs). TMAs were scored according to the HercepTest criteria applied for HER2 detection in breast cancer diagnostics.

Results: All ADC targets had tumor-specific membranous expression. TROP2, TF and NECTIN4 were highly expressed (i.e., HercepTest 3+), in 37%, 29% and 4% of the tumor, respectively. Furthermore, 68%, 48% and 12% of the tumors had high to medium (i.e., HercepTest ≥2+) TROP2, TF and NECTIN4 expression, respectively. High TROP2 expression associated with vascular space invasion (p=0.009) and squamous, adenosquamous and undifferentiated histology (p<0.001). High to medium TF expression associated with low histologic grade (p=0.042) and squamous and adenosquamous histology (p<0.001). High NECTIN4 expression associated with low histological grade (p=0.03) and squamous histology (p<0.001).

Conclusions: TROP2, TF and NECTIN4 are highly expressed in cervical cancer. Clinical trials evaluating the safety and efficacy of ADCs are highly relevant in cervical cancer.

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25P Patient-reported outcomes (PROs) with coformulated vibostolimab/pembrolizumab (vibo/pembro) for metastatic cervical cancer (CC): Results from the KEYVIBE-005 study

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Background: In the multicohort phase 2 KEYVIBE-005 study (NCT05007106), first-line vibo/pembro (n = 85) showed antitumor activity similar to pembro (n = 84; ORR, 20.0% vs 15.5%) with a manageable safety profile in patients (pts) with metastatic CC with PD-L1 CPS ≥1. We report prespecified PRO end points.

Methods: Pts ≥18 y with previously untreated locally recurrent or metastatic CC with PD-L1 CPS ≥1 were randomly assigned 1:1 to vibo 200 mg/pembro 200 mg or pembro 200 mg IV Q3W for ≤35 cycles. Prespecified PRO end points were least squares mean (LSM) change from baseline (BL) to wk 12 in EORTC QLQ-C30 global health status/quality of life (GHS/QoL) and physical functioning (PF) subscales, EORTC QLQ-CX24 symptom experience subscale, and EQ-5D-5L VAS health status score; within-pt changes of 10 points were considered clinically meaningful for QLQ-C30 and QLQ-CX24 measures. PRO assessments were performed at every cycle before treatment and evaluated in pts who received ≥1 dose of study treatment and completed ≥1 postbaseline PRO assessment.

Results: The PRO population comprised 166 pts (n = 85; vibo/pembro; n = 81; pembro). At wk 12, completion and compliance rates for both treatment groups were ≥64% and ≥86%, respectively, for all assessments. LSM change and 95% CIs from BL to wk 12 for all scales are reported in the table. Pts in both groups experienced small changes in EORTC QLQ-C30 GHS/QoL and PF, EORTC QLQ-CX24 symptom experience, and EQ-5D-5L scores, with overlapping CIs. None of the group differences were clinically meaningful.

Conclusions: These are the first PRO results from the KEYVIBE-005 study in which pts with previously untreated metastatic CC with PD-L1 CPS ≥1 were randomly assigned to vibo/pembro vs pembro. For all PRO assessments, the change from BL to wk 12 with vibo/pembro was similar to pembro alone; thus, vibo/pembro did not negatively impact health-related QoL in this pt population.

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Table: 25P Least squares mean change from baseline to week 12

PRO Scale	Vibo/pembro n = 85 LSM (95% CI)	Pembro n = 81 LSM (95% CI)	Difference (95% CI)
EORTC QLQ-C30			
Global health status/quality of life[a]	0.77 (−3.84 to 5.38)	3.53 (−1.13 to 8.20)	−2.76 (−8.81 to 3.29)
Physical functioning[a]	−3.58 (−8.29 to 1.14)	−3.14 (−7.96 to 1.68)	−0.44 (−7.07 to 6.19)
EORTC QLQ-CX24			
Symptom experience[b]	0.27 (−2.74 to 3.27)	−2.99 (−6.04 to 0.05)	3.26 (−0.61 to 7.13)
EuroQol 5D-5L VAS[a]	1.86 (−2.52 to 6.24)	2.23 (−2.18 to 6.64)	−0.37 (−6.20 to 5.46)

[a]Higher values indicate improvement. [b]Higher values indicate worsening.

26P Efficacy and safety of tislelizumab combined with concurrent chemoradiotherapy for high risk locally advanced cervical cancer

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Background: Concurrent chemoradiotherapy (CRT) is the standard treatment for new diagnosis locally advanced cervical cancer (LACC). However, local recurrence and distant metastasis are the main modes of CRT failure in LACC, especially for the patient with high risk such as stage IIIA ～IVA, tumour with large masses (>4cm) or regional lymph node metastasis. Here is a prospective, single-arm, phase II study aims to evaluate the efficacy and safety of tislelizumab (anti-pd-1 antibodies) combined with concurrent chemoradiotherapy for high risk LACC.

Methods: Eligible patients were age 18-75 years with ECOG PS 0-1, histologically confirmed cervical cancer with 2018 FIGO stage IIIA, IIIB, IVA or cervical tumors > 4cm with regional lymph node metastasis, or paracervical invasion with regional lymph node metastasis, and without received prior systemic therapy, surgery or radiation. All patients received CRT combined with tislelizumab 200mg Q3W for 1 year or until disease progression or intolerable toxicity. The CRT includes at least 4 cycles of cisplatin 40mg/m^2/W + EBRT 45～50Gy/25f then BT 28～30Gy/4～5f. The primary endpoint was tumor regression ratio after EBRT. Secondary endpoints were 3-month and 6-month ORR after CRT, 1-year and 3-year OS and PFS, safety.

Results: Until Feb,28, 2024, 30 patients were enrolled. 25 patients completed CRT and were available for evaluation. The median age was 59 years (range 40-75). The tumor regression ratio after EBRT was 90.6%. The 3 and 6-months ORR after CRT were 100% and 100%. The 1-year PFS rate was 100%. The main adverse effect was neutropenia including 36% for grades 3-4 and 20% for grades 1-2. Radiation enteritis incidence was 64% and were grade 1-2. Other adverse effect such as nausea, vomiting, and dizziness occurred during CRT and could be alleviated after symptomatic treatment. No immune-related adverse events were observed.

Conclusions: Our results suggest that Tislelizumab combined with concurrent chemoradiotherapy showed valuable antitumor activity and controllable safety in high risk LACC. The combination regimens can be one of the treatment options for these patients.

Clinical trial identification: NCT05588219.

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27P Concurrent chemoradiotherapy and immunotherapy for locally advanced cervical cancer: A cost-effectiveness analysis based on the KEYNOTE-A18 trial

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Background: Immunotherapy administration can improve chemoradiotherapy (CCRT) efficacy in newly diagnosed, high-risk, locally advanced cervical cancer (LACC). Given the importance of balancing the costs of innovative therapeutics against their efficacy, this study was developed to assess the cost-effectiveness from the perspective of payers in America, Europe, and Asia.

Methods: The main survival and other relevant parameters of 1,060 LACC patients from the KEYNOTE-A18 trial were collected to establish a lifetime three-state Markov model to evaluate the cost and effectiveness of pembrolizumab-CCRT and CCRT. Primary outcome measures included total cost, life-years (LYs), quality-adjusted LYs (QALYs), incremental cost-effectiveness ratio (ICER), incremental net monetary benefit (INMB), and incremental net health benefits (INHB) at countries' traditional willingness-to-pay (WTP) thresholds. Model stability was also examined through sensitivity analyses.

Results: The USA, Italy, and China are selected as representative countries for each of the three continents, assuming that their WTP thresholds were $150,000, $43,749, and $37,766 per QALY. The increased efficacy and costs of pembrolizumab-CCRT versus CCRT were 2.52 QALYs (3.11 LYs) and $346,479, 2.30 QALYs (2.81 LYs) and $236,776, 1.79 QALYs (2.12 LYs) and $29,027, calculating the ICER for the three countries as $137,500/QALY ($111,499/LY), $102,758/QALY ($84,192/LY), and $16,217/QALY ($13,726/LY), respectively. The respective INHBs were 0.21 QALY, -3.11 QALY, and 1.02 QALY, and pembrolizumab-CCRT was exhibited cost-effectiveness opportunities of 62.68%, 12.53%, and 75.23% at the selected WTP threshold, respectively.

Conclusions: At current prices, pembrolizumab-CCRT represents a cost-effective alternative for patients with LACC in the USA and China, but not in Italy.

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28P Real-life efficacy and safety of cemiplimab in advanced cervical cancer from a nominal use program in Italy: The MITO 44 study

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Background: Cemiplimab is an immunoglobulin G4 monoclonal antibody targeting the programmed cell death-1 receptor. A nominal use program is available in Italy for advanced cervical cancer (CC) patients treated with platinum-based chemotherapy based on the results of the EMPOWER-Cervical 1/GOG-3016/ENGOTcx9 trial. This real-world, retrospective cohort, multicenter study aimed at describing the clinical outcomes of patients with advanced CC treated with cemiplimab in Italy.

Methods: The primary objective of the study was to assess the feasibility and replicability of the initial results in a real-world setting of cemiplimab. The primary endpoint of our analysis was progression-free survival (PFS). Secondary endpoints included overall response rate (ORR), overall survival (OS) and safety data.

Results: From March 2022 to December 2023, 135 patients were treated in 12 Multicenter Italian Trials in Ovarian cancer and gynecologic malignancies (MITO) Centers. Forty-two percent of patients had one or more comorbidities, hypertension being the most common (23.4%). Median PFS was 4.0 months (range 3.0-6.0) and median OS was 12.0 months (12.0- NR) with no differences according to PD-L1 status. Complete response (CR) or no evidence of disease (NED) were observed in 8.6%; partial response (PR) in 21.1%, stable disease (SD) in 14.8% and progression was recorded in 44.5% of patients. Most common drug related adverse events (AEs) were anemia (39.1%) and fatigue (27.8%). Immune related AEs occurred in 18.0%.

Conclusions: This study confirms the feasibility and the replicability of the cemiplimab nominal use in advanced CC, in a real-world practice in Italy.

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29P fT3/fT4 ratio, systemic inflammation and skeletal muscle indexes in advanced cervical cancer (aCC) treated with cemiplimab in the MITO44 study

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Background: Peripheral conversion of thyroid hormones is key in regulating a wide range of functions, including central metabolism. Low fT3/fT4 ratio is a negative prognosticator in other cancers. Skeletal muscle index (SMI) calculated by CT scan at L3 level estimates commonly sarcopenia. Inflammation indexes (i.e., SII, SIRI, N/L) showed their prognostic values in CC. Correlation between those features and their independent contribution to prognosis of aCC is unclear. Cemiplimab is a new IO option in aCC.

Methods: 135 aCC pts treated with cemiplimab at 12 centers from the MITO group were included. Data on fT3/fT4 were available for N=109 pts, 8 were excluded for thyroidal comorbidities. Of those, CBC values were available for 89 pts for calculating SII, SIRI and N/L. Baseline CT scans from 25 pts were available for SMI calculation. Pts characteristics resembled those reported by Tuninetti et al., *EJC* 2024. At first, variables were categorized as follows: ECOG PS: 0-1 vs 2, fT3/fT4 ratio, SII, SIRI and N/L: low vs high, (cut-off median) and SMI (sarcopenic vs not, cut-off 34 cm2/m2). Additional optimal cut-offs were explored by means of ROC analyses.

Results: at a mFUP of 6.9 mos, mPFS of ECOG PS 0-1 vs 2 was 4.5 vs 2.5 mos, HR 0.64; p=0.004, low vs high SII: 5.1 vs 2.7 mos, HR 0.53; p=0.019, low vs high fT3/fT4 ratio: 2.9 vs 5.3 mos, HR 1.44; p=0.150. mOS of ECOG PS 0-1 vs 2 was 15.8 vs 4.3 mos, HR 0.46; p<0.001, low vs high SII: NR vs 8.9 mos, HR 0.26; p=0.004, low vs high fT3/fT4 ratio: 8.9 mos vs NR, HR 2.95; p=0.008. At MV analyses, ECOG PS and fT3/fT4 ratio retained their prognostic impact (HR 0.50, p=0.002 and HR 3.13, p=0.011) while SII did not. SII values were higher in ECOG PS 2 vs 0-1, p=0.025. fT3/fT4 ratio as a continuous variable confirmed its prognostic value. No associations with other variables nor prognostic effects were found for SIRI, N/L or SMI, the latter limited by low numbers.

Conclusions: fT3/fT4 ratio, SII and ECOG PS predicted prognosis of aCC pts receiving cemiplimab. Independent impact on OS at MV analyses was found only for fT3/fT4 and ECOG PS, coherently with the finding that SII and PS are associated. These data provide new insights for valuable prognostic nomograms useful to optimize clinical use of innovative treatment in aCC.

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30P Cemiplimab in treatment of metastatic and recurrent cervical cancer

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Background: Patients with recurrent cervical cancer have a poor prognosis. Cemiplimab, the fully human programmed cell death 1 (PD-1)-blocking antibody approved to treat lung and skin cancers, has been shown to have preliminary clinical activity in this population.

Methods: Our research included patients who had disease progression after first-line platinum-containing chemotherapy, regardless of their combined positive score (CPS) status. Women were randomly assigned (1:1) to receive cemiplimab (350 mg every 3 weeks) or the physician's choice of single-agent chemotherapy. The primary end point was overall survival. Progression-free survival and safety were also assessed.

Results: A total of 180 women were included in our research (90 in each group). Overall median overall survival was longer in the cemiplimab group than in the chemotherapy group (12.4 months vs. 7.5 months; hazard ratio for death, 0.69; 95% confidence interval [CI], 0.56 to 0.84; two-sided P<0.001). The overall survival benefit was consistent in both histologic subgroups (squamous-cell carcinoma and adenocarcinoma [including adenosquamous carcinoma]). Progression-free survival was also longer in the cemiplimab group than in the chemotherapy group in the overall population (hazard ratio for disease progression or death, 0.75; 95% CI, 0.63 to 0.89; two-sided P<0.001). In the overall population, an objective response occurred in 16.1% (95% CI, 12.5 to 21.1) of the patients in the cemiplimab group, as compared with 6.3% (95% CI, 3.8 to 9.6) in the chemotherapy group. An objective response occurred in 18% (95% CI, 11 to 28) of the cemiplimab-treated patients with PD-L1 expression greater than or equal to 1% and in 11% (95% CI, 4 to 25) of those with PD-L1 expression of less than 1%. Overall, grade 3 or higher adverse events occurred in 45.0% of the patients who received cemiplimab and in 53.4% of those who received chemotherapy.

Conclusions: Survival was significantly longer with cemiplimab than with single-agent chemotherapy among patients with recurrent cervical cancer after first-line platinum-containing chemotherapy.

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31P Risk and prognosis for brain metastasis in primary metastatic cervical cancer patients: A population-based study

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Background: The purpose of this study was to evaluate the risk and prognostic factors of stage IVB cervical cancer with brain metastasis from the Surveillance, Epidemiology and End Results (SEER) population-based database.

Methods: Cervical cancer patients initially diagnosed with brain metastasis between 2010-2019 were included in this study. The risk factors of developing brain metastasis were evaluated by logistic regression model with corresponding 95% confidence interval (95% CI). Survival analysis was performed through the Kaplan—Meier method, log-rank test, and Cox proportional hazards model.

Results: A total of 88 (88/25476, 0.35%) cervical cancer patients initially diagnosed with brain metastasis between 2010-2019 were retrieved. The presence of lung, bone or liver metastasis (all P<0.001) were shown to be independent risk factors for developing brain metastasis. Patients with brain metastasis showed a poor prognosis (P<0.001, HR=2.84, 95%CI = 1.71-4.72) with a median survival of 6 months, which is much shorter than with the lung (9 months), liver (8.5 months) or bone (11 months) metastasis groups. Patients with lower tumor grade (P=0.001, HR=0.27, 95% CI=0.09-0.76) and with bone metastasis (P=0.007, HR=2.74, 95% CI=1.33-5.67) also demonstrated poor overall survival outcomes in patients with brain metastasis. In terms of treatment modality, chemoradiotherapy tended to prolong the survival of stage IVB cervical cancer patients with brain metastasis (P=0.001, HR=0.17 95%CI = 0.06-0.48).

Conclusions: In conclusion, the prognosis of stage IVB cervical cancer patients with brain metastasis remains poor. Chemoradiotherapy may provide survival benefits, which deserves large scale prospective clinical trials to confirm.

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32P Cervical cancer: Barriers and smears to prevention

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Background: Regular cervical screening, crucial for preventing cervical cancer, detects high-risk HPV, linked to over 99% of cases. The NHS England screening program reports to save 5,000 lives yearly. However, NHS data shows a decline in screening attendance, from over 72% in March 2020 to 69.9% in March 2022 for those aged 25 to 64. This study aims to understand barriers preventing females from taking the cervical smear test. A secondary aim was to improve the rate of cervical smear update of female patients in a family medicine or general practitioner (GP) clinic.

Methods: All females in a GP practice in NorthWest of England that were overdue a smear test (479/1150) in August 2023 were phoned enquiring about their overdue smear. A subsequent follow-up after three months gauged the impact of the intervention on screening rates. The same individual phoned everyone in the cohort with a written script to avoid risk of bias and individuals were only called once. Rush hour and school pick up times were avoided.

Results: 197 (41.1%) responded to the phone call of which 155 (78.6%) were accurately eligible for a smear test. 32 (17.3%) stated they were too busy with other commitments to book the test, mentioning the need for more out of hours appointments. 20 (12.9%) mentioned they were uncomfortable or anxious about the process. 18 individuals (11.2%) struggled with a language barrier during the conversation and had their family translate. Overall, 141 (91.0%) of patients agreed to receiving a booking link for the smear test. Upon review in December 2023, only 16 (11.3%) had undergone a smear test.

Conclusions: This study highlights various reasons for which women may not attend their smear test, most commonly being busy with work and children alongside procedural anxieties and language barriers. This can be reflected nationally due to all women in the inclusion criteria being of working age, pre-menopausal and around 1 million residents of the UK self-reporting poor English language skills. Whilst, phone calls didn't appear to be a useful way to increase cervical smear uptake other interventions such as weekend and out of hours smear test services; in person consultations to address concerns and multilingual forms of communications involving local cultural communities may be tried to improve uptake.

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33P Impact of age in survival of Peruvian patients with cervical cancer

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Background: Cervical cancer (CC) is one of leading causes of cancer-related deaths among women, particularly in low-income countries. The age at diagnosis has been associated with contradictory outcomes in different CC cohorts worldwide. We evaluated the impact of age at diagnosis in overall survival (OS).

Methods: Retrospective analysis of CC patients between 2008 and 2012. Patients were divided in two groups: $\leq$ 40 yo (from 36 to 40) and $>$ 40 yo. Clinical-pathological data was retrieved from clinical files. T test and Mann-Whitney test were performed to evaluate differences between both groups. Kaplan-Meier survival curves and log-rank tests were used to compare OS. Cox proportional hazards regression models were used to identify independent variables with significant influence on the OS.

Results: A total of 448 CC patients were included. 54% were $\leq$ 40 yo. Significant differences were observed between $\leq$40yo and older $>$40yo as follows: age at first pregnancy (18 vs 18.5yo, p=0.016), absence of symptoms (4.1% vs. 0.5%, p=0.038), creatinine levels $\geq$65 umol/L (26.4% vs. 39.1%, p=0.004), tumor size $\geq$ 4 cm (84.4% vs. 75.7%, p=0.0027), vaginal involvement (52.3% vs. 41.4%, p=0.034), and FIGO stage I (15.8% vs. 6.9%, p=0.023). With a median follow up of 5yo, the median OS was 172 months and not reached in patients $\leq$ 40 yo and $>$ 40 yo, respectively. 5-yo OS rate was lower in patients $\leq$ 40 yo compared with $>$ 40 yo (63.4% vs. 79.3%, p=0.0019). No significant association was detected between OS and the presence of symptoms, Hb levels, parametrial involvement, vaginal involvement, hydronephrosis, and primary treatment. In the multivariate analysis, age $>$ 40 yo shows a significant lower risk of death (HR: 0.37, 0.22-0.62, p=0.0001), while FIGO stage III (HR: 9.36, 2.72-32.34, p=0.0004) and stage IV (HR: 16.44, 3.97-68.10, p=0.0001) showed higher risk of death.

Conclusions: Although patients younger than 40 years old often present with earlier disease, they demonstrate statistically and clinically inferior survival outcomes. Staging and younger age at diagnosis are independently associated with a higher risk of death. The prognostic significance of these findings warrants validation in prospective series, as it suggests that this population may require intensified treatment strategies.

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ENDOMETRIAL CANCER

34O ROCSAN: A multicentric randomized phase II/III evaluating dostarlimab in combination with niraparib versus niraparib alone compared to chemotherapy in the treatment of endometrial/ovarian carcinosarcoma after at least one line of platinum-based chemotherapy – Preliminary results

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Background: Carcinosarcomas (CS) are rare and highly aggressive gynecological carcinomas with poor outcome. The median Progression-Free-Survival (PFS) in relapse after platinum-based chemotherapies (CT) is less than 4 months. CS were excluded from Keynote755 trial. Since CS show high DNA damage response activity and potentially a high tumor mutational load resulting in neo-antigens, a synergy between PARPi and anti-PD1 is expected.

Methods: This is an open-label (NCT03651206) study with a two-stage design. In step 1, patients (pts) were randomized (2:2:1) to receive either niraparib (N), niraparib and dostarlimab (ND) or chemotherapy (CT). Randomization was stratified by number of previous CT lines, FIGO stage, localization, and performance status. The primary objective was to select the best experimental strategy between N and ND using Response Rate (RR) at 16 weeks (RECIST1.1). Secondary endpoints included best Objective RR, disease control rate (DCR), safety, OS & QoL. After an interim analysis at the end of phase II, data will be reviewed by an Independent Data Monitoring Committee, and eventually allow the enrolment in subsequent phase III (part 2).

Results: 64 pts with recurrent or progressing endometrial or ovarian CS after at least one line of platinum-based CT were randomized in the phase II (N=26, ND=25, CT=13). Median age was 70 years (range 34-84). The 16w-RR was 3.8%, 12.0% and 15.4% respectively. The ORR was 3.8%, 20% and 15.4% and the 8w-DCR was 26.9%, 52% and 30.8% in arm N, ND and CT, respectively. With a median follow-up of 11.2 months, median PFS (months) was 2.0 (95%CI, 1.9-2.2), 2.7 (95%CI, 1.9-3.7), 1.9 (95%CI, 1.7-3.6) and median OS (months) was 6.7 (95%CI, 3.8-9.6), 6.3 (95%CI, 3.9-12.4), 4.5 (95%CI, 3.0-NE) in arm N, ND and CT respectively. %AE grade >3 were 69.2%, 68% and 69.2% respectively.

Conclusions: ROCSAN step 1 did not met primary endpoint for 16W RR (> 20%), however the DCR, median OS and safety suggest some benefice for ND compared to CT in this very rare and poor prognostic population.

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35MO Quality-adjusted survival in patients with advanced or recurrent endometrial carcinoma treated with atezolizumab in combination with carboplatin-paclitaxel versus carboplatin-paclitaxel in the AtTEnd/ENGOT-EN7 trial

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Background: In the phase III randomized international multicentric academic AtTEnd trial, the addition of atezolizumab (atezo) to standard carboplatin and paclitaxel chemotherapy (CP) demonstrated a statistically significant improvement in progression free survival versus CP alone for patients (pts) with advanced/recurrent endometrial carcinomas (EC) with a substantial benefit in pts with a mismatch repair deficient (dMMR) carcinoma. This is a post-hoc analysis of the quality-adjusted time without symptoms of disease progression or toxicity of treatment (Q-TWiST) in dMMR and all comer population.

Methods: Pts were randomized (2:1 ratio) to receive either CP and atezo (N=360) or placebo (N=189), followed by atezo or placebo until disease progression. In safety population (356 pts in atezo arm and 185 pts in placebo arm), overall survival was partitioned into three health status: the time without symptoms of progression or toxicity (TWiST), the time before progression with Grade ≥ 3 adverse events (TOX), and the time from progression to death (REL). The restricted mean survival time (measured up to 36 months for the all-comers population and 23 months for the dMMR population) of each health status were adjusted using EQ-5D-5L questionnaire. Q-TWiST was calculated using the utility values for TOX and REL defined relative to TWiST.

Results: Overall, median follow-up duration was 28.3 months. In pts receiving atezo a significantly longer Q-TWiST was detected compared to pts receiving placebo (25.9 versus 24.0 months, p=0.0144). Q-TWiST was also significantly longer in atezo arm compared to placebo arm (20.3 versus 16.2 months, p<0.0001) for patients with a dMMR carcinoma (Table).

Table: 35MO

	TOX	TWiST	REL	Q-TWiST
All-comers				
ATEZOLIZUMAB				
Estimate (95%CI)	3.0 (2.7 to 3.2)	13.4 (12.3 to 14.6)	9.8 (8.7 to 10.9)	25.9 (24.6 to 27.2)
PLACEBO				
Estimate (95%CI)	2.1 (1.9 to 2.3)	11.2 (9.8 to 12.7)	11.5 (9.9 to 13.1)	24.0 (22.2 to 25.8)
DIFFERENCE				
Estimate (95%CI)	0.9 (0.6 to 1.2)	2.2 (0.4 to 4.1)	-1.6 (-3.5 to 0.3)	1.9 (0.4 to 3.5)
p	<0.001	0.018	0.092	0.014
Patients with dMMR carcinoma				
ATEZOLIZUMAB				
Estimate (95%CI)	1.6 (1.4 to 1.7)	14.4 (12.7 to 16.1)	4.5 (3.1 to 6.0)	20.3 (19.1 to 21.5)
PLACEBO				
Estimate (95%CI)	1.9 (1.6 to 2.2)	7.7 (6.0 to 9.7)	7.3 (5.3 to 9.2)	16.2 (14.0 to 18.5)
DIFFERENCE				
Estimate (95%CI)	-0.3 (-0.7 to <-0.1)	6.7 (4.1 to 9.1)	-2.7 (-5.1 to -0.4)	5.5 (3.3 to 7.6)
p	0.034	<0.001	0.022	<0.001

Conclusions: In pts with advanced/recurrent EC, the addition of atezo to CP improved the quality-adjusted survival compared to CP alone.

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Legal entity responsible for the study: Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Via Mario Negri 2, Milan.

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36MO Patient-reported outcomes in primary advanced or recurrent endometrial carcinoma treated with atezolizumab or placebo in combination with carboplatin-paclitaxel in the AtTEnd/ENGOT-EN7 trial

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Background: The AtTEnd trial showed that adding atezolizumab (atezo) to carboplatin-paclitaxel chemotherapy (CP) improved progression free survival (PFS) in patients (pts) with advanced/recurrent endometrial carcinomas (EC), especially those with mismatch repair deficient tumours. Here we report the patient-reported outcomes (PROs).

Methods: Pts were randomized (2:1) to receive CP plus atezo (N=360) or placebo (N=189), followed by maintenance atezo or placebo until disease progression. EORTC QLQ-C30, QLQ-EN24 and EQ-5D-5L questionnaires were analysed at baseline (BL), cycle 6 (C6) of treatment phase, and cycle 8 (M8) of maintenance phase. Mixed models were used to analyze score trends over time, with individual pts treated as random effects to account for intra-patient variability, and trial treatment and baseline values treated as fixed effects.

Results: PROs completed were evaluable for 89% pts (atezo arm, N=323; placebo arm, N=170). Although no statistically differences were detected, global health status scores decreased at C6 but improved by M8 above BL in atezo arm, remaining lower than BL in placebo arm (Table). At C6, pts reported lower scores in most functional scales except for emotional functioning. By M8, all functional scales showed improvement, with social functioning increased above BL in both arms and role functioning increased above BL in atezo arm only. No differences in symptom scales were reported between two arms, except for back/pelvic pain score where a significant reduction in severity from BL was observed in favour of atezo vs placebo arm (p=0.023). Mean scores on the EQ-5D-5L were similar at all time points in both arms.

Table: 36MO				
	Atezo		Placebo	
	C6-BL	M8-BL	C6-BL	M8-BL
QLQ-C30				
Global health status	-1.8 (22)	3.8 (19)	-5.5 (21)	-2.5 (21)
Functional scales				
Physical	-5.1 (19)	-2.8 (16)	-7.3 (18)	-3.5 (15)
Role	-6.4 (30)	0.6 (24)	-8.1 (33)	-1.4 (27)
Emotional	4.6 (22)	8.0 (18)	3.8 (19)	6.2 (18)
Social	-4.7 (26)	2.4 (23)	-5.1 (24)	1.7 (22)
Symptom scales*				
Fatigue	8.6 (26)	1.3 (18)	9.6 (25)	0.2 (21)
Pain	-2.5 (30)	-0.6 (24)	-2.6 (31)	-4.4 (23)
Nausea/vomiting	2.6 (17)	-0.2 (11)	3.7 (20)	1.0 (15)
Dyspnoea	4.9 (26)	2.6 (19)	8.3 (28)	3.5 (22)
Appetite loss	-2.7 (33)	-7.8 (24)	1.9 (30)	-3.4 (26)
QLQ EN24 Symptom scales*				
Pain in back-pelvis	-7.1 (31)	-4.7 (28)	-2.7 (28)	-0.0 (18)

Numbers are mean (SD), *lower scores indicate reduced symptom severity.

Conclusions: Quality of life was maintained over time in both arms, even if an initially reduction could not be excluded. Coupled with the significantly improved PFS, these findings support the use of CP plus atezo in advanced/recurrent EC.

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37MO Dostarlimab plus chemotherapy in primary advanced or recurrent endometrial cancer (pA/rEC) in the RUBY trial: Overall survival (OS) by MMR status and molecular subgroups

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Background: At interim analysis (IA) 1 of Part 1 of the RUBY trial (NCT03981796), statistically significant benefit in PFS was observed with dostarlimab+carboplatin-paclitaxel (D+CP) vs placebo (PBO)+CP in the overall and mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) populations of pts with pA/rEC. Here we report OS from IA2.

Methods: Pts with pA/rEC were randomized 1:1 to D+CP or PBO+CP followed by D or PBO for ≤3 years or until progression. OS was a dual-primary endpoint in the overall population and a prespecified, exploratory analysis in the dMMR/MSI-H and mismatch repair proficient/microsatellite stable (MMRp/MSS) populations. OS by molecular subgroup was a post-hoc analysis. Safety was a secondary endpoint.

Results: 494 pts were randomized (245 D+CP; 249 PBO+CP). In the overall population, there was a significant reduction in the risk of death by 31% and clinically meaningful improvement of 16.4 mo in median OS (mOS) for D+CP vs PBO+CP (Table). In the dMMR/MSI-H population, hazard ratio (HR) for OS was 0.32; mOS was not reached for D+CP and was 31.4 mo for PBO+CP. In the MMRp/MSS population, HR for OS was 0.79; mOS was 34.0 mo for D+CP and 27.0 mo for PBO+CP. At IA2, in 400 pts with whole exome sequencing, a trend towards clinical benefit with D+CP was observed in the dMMR/MSI-H, TP53 mutated, and no specific molecular profile subgroups.

Table: 37MO Safety at IA2 was similar to IA1			
	Dostarlimab+CP	Placebo+CP	OS, HR (95% CI)
Overall, N	245	249	0.69 (0.54—0.89) P=0.002
OS, median (95% CI), mo	44.6 (32.6—NR)	28.2 (22.1—35.6)	—
dMMR/MSI-H, n	53	65	0.32 (0.17—0.63)
OS, median (95% CI), mo	NR (NR—NR)	31.4 (20.3—NR)	—
MMRp/MSS, n	192	184	0.79 (0.60—1.04)
OS, median (95% CI), mo	34.0 (28.6—NR)	27.0 (21.5—35.6)	—
Post hoc exploratory molecular subgroup analysis of OS[a]			
POLEmut, n	2	3	No events in either arm
dMMR/MSI-H, n	39	52	0.40 (0.19—0.83)
TP53mut, n	47	41	0.59 (0.33—1.03)
NSMP, n	103	113	0.89 (0.61—1.29)

[a]Analyses were conducted in 400 patients with whole exome sequencing results. Mut, mutant; NR, not reached; NSMP, no specific molecular profile.

Conclusions: D+CP showed statistically significant and clinically relevant OS benefit in the overall population compared with CP alone. A substantial survival difference was seen in the dMMR/MSI-H population. In the MMRp/MSS population, there was a 7 mo difference in median OS vs CP alone, with a 21% risk reduction for death. OS by molecular subgroup at IA2 was consistent with IA1. RUBY is the only trial to

demonstrate a statistically significant OS benefit in pts with pA/rEC and supports the use of dostarlimab+CP as a standard of care in the 1L setting.

Clinical trial identification: NCT03981796.

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38MO Progression-free survival (PFS) in primary advanced or recurrent endometrial cancer (pA/rEC) in the overall and mismatch repair proficient (MMR/MSS) populations and in histological and molecular subgroups: Results from part 2 of the RUBY trial

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Background: In Part 1 of the phase 3 RUBY trial (NCT03981796) in pA/rEC, patients (pts) receiving dostarlimab (dostar)/carboplatin-paclitaxel (CP) exhibited significant benefits in PFS and overall survival versus CP alone. Outcomes may be further improved by adding a poly(ADP-ribose) polymerase inhibitor (PARPi). Here we report results from Part 2 of RUBY of dostar/CP followed by dostar/niraparib (nira; a PARPi) maintenance therapy in pts with pA/rEC.

Methods: Pts were randomized 2:1 to dostar 500 mg IV + CP Q3W for 6 cycles followed by dostar 1000 mg IV Q6W + nira (individualized starting dose of 200 or 300 mg) PO daily for ≤3 years from randomization or to placebo (PBO) + CP Q3W for 6 cycles followed by PBOs for ≤3 years. The primary endpoint was PFS in the overall and MMRp/MSS populations.

Results: 291 pts were randomized (192 dostar/CP + dostar/nira; 99 PBO/CP). PFS was significantly improved in pts receiving dostar/CP + dostar/nira vs PBO/CP in the overall and MMRp/MSS populations (Table). In pts with endometrioid carcinoma, pts with other histologies, and across most biomarker subgroups (eg, TP53mut), the hazard ratio (HR) directionally favored dostar/CP + dostar/nira in the overall and MMRp/MSS populations. The safety profile observed was consistent with those of the individual agents.

Table: 38MO PFS

	Dostar/ CP+dostar/nira	PBO/CP+PBO	HR (95% CI)
Overall, n	192	99	0.60 (0.43—0.82) P=0.0007
Median (95% CI), mo	14.5 (11.8—17.4)	8.3 (7.6—9.8)	-
MMRp/MSS, n	142	74	0.63 (0.44—0.91) P=0.0060
Median (95% CI), mo	14.3 (9.7—16.9)	8.3 (7.6-9.8)	-
Pre-specified exploratory analyses			
	No. of pts with events/No. of pts		
All pts	95/192	69/99	-
Endometrioid carcinoma	52/114	46/67	0.58 (0.39—0.87)
Other histologies	42/76	23/32	0.53 (0.32—0.88)
Molecular subgroup[b]			
POLεmut	0/3	1/2	-[a]
dMMR/MSI-H	12/37	10/17	0.45 (0.20—1.05)
TP53mut	27/39	10/10	0.29 (0.13—0.63)
No specific molecular profile	37/75	31/46	0.61 (0.38—0.99)
Not evaluable	19/38	17/24	0.71 (0.37—1.37)

[a]<20 events. [b]Based on whole exome sequencing.

Conclusions: RUBY Part 2 met its primary endpoint and is the first study to show significant and clinically meaningful improvement in PFS in the MMRp/MSS and overall populations. The trial is ongoing for OS follow-up. The safety profile observed was generally consistent with the known safety profiles of the individual agents.

These data demonstrate a potential role for PARPi maintenance in pts receiving dostar/CP, especially for MMRp/MSS tumors.

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39MO Phase III ENGOT-En9/LEAP-001 study: Lenvatinib + pembrolizumab (LEN/PEMBRO) vs chemotherapy (chemo) as first-line (1L) therapy for advanced or recurrent endometrial cancer

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Background: LEN/PEMBRO following prior systemic therapy in any setting, including neo/adjuvant, is a standard of care for advanced endometrial cancer (EC). The phase 3 ENGOT-en9/LEAP-001 trial (NCT03884101) compared 1L LEN/PEMBRO vs chemo in patients (pts) with advanced/recurrent EC.

Methods: Eligible pts had stage III—IV or recurrent, measurable/non-measurable, radiographically apparent EC, with no prior chemo or PD ≥6 mo after neo/adjuvant platinum-based chemo. Pts were randomized 1:1 (stratified by proficient vs deficient mismatch repair status [pMMR/dMMR] and, in the pMMR stratum, by ECOG PS [0/1], measurable disease [yes/no], and chemo/chemoradiation [yes/no]) to lenvatinib 20 mg QD plus pembrolizumab 200 mg Q3W or paclitaxel 175 mg/m^2 Q3W plus carboplatin AUC 6 Q3W. Dual primary endpoints were PFS (RECIST v1.1, blinded independent central review) and OS in the pMMR population and among all-comers. Secondary endpoints included ORR and safety; duration of response (DOR) was an exploratory endpoint; and efficacy outcomes assessed by tumor histology was a prespecified exploratory analysis.

Results: 842 pts were randomized. At final analysis (data cutoff, 2 Oct 2023), after median follow-up of 38.4 (range, 30.3—52.9) mo, statistical significance for non-inferiority (NI) OS endpoint was not achieved for LEN/PEMBRO vs chemo in the pMMR population (HR, 1.02 [95% CI, 0.83—1.26]; NI P = 0.2459875; Table). PFS and OS results for LEN/PEMBRO vs chemo by histological subtype will be presented for the pMMR population and all-comers. Treatment-related AEs occurred in 411/420 (97.9%) vs 398/411 (96.8%) treated pts in the LEN/PEMBRO vs chemo groups.

Table: 39MO

	pMMR		All-comers	
	LEN/PEMBRO n = 320	Chemo n = 322	LEN/PEMBRO n = 420	Chemo n = 422
OS HR (95% CI)	1.02 (0.83—1.26)[a]		0.93 (0.77—1.12)	
PFS HR (95% CI)	0.99 (0.82—1.21)		0.91 (0.76—1.09)	
ORR (95% CI), %	50.6 (45.0—56.2)	54.7 (49.0—60.2)	55.7 (50.8—60.5)	55.5 (50.6—60.3)
Median DOR (range), mo	16.1 (1.0+ to 48.7+)	10.6 (1.1+ to 43.8+)	23.2 (1.0+ to 49.0+)	10.9 (1.1+ to 46.9+)

[a]1-sided NI P = 0.2459875 (nonsignificant), not crossing prespecified OS NI boundary, P = 0.0158890, so no further statistical testing of efficacy endpoints was performed per prespecified multiplicity strategy for type 1 error control.

Conclusions: The prespecified statistical criteria for OS and PFS in pts with pMMR IL advanced/recurrent EC were not met. Subgroup analyses identifying pts who may benefit most from LEN/PEMBRO will be presented. The safety profile was manageable and consistent with prior experience.

Clinical trial identification: NCT03884101.

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40MO First-line (1L) durvalumab + carboplatin/paclitaxel (CP) followed by durvalumab ± olaparib for endometrial cancer (EC) (DUO-E): Objective response rate (ORR), duration of response (DoR) and time to treatment discontinuation or death (TDT) by mismatch repair (MMR) status

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Background: DUO-E showed statistically significant and clinically meaningful PFS benefit with CP + durvalumab followed by durvalumab ± olaparib v CP alone (primary endpoints); addition of olaparib conferred enhanced benefit in MMR proficient (pMMR) patients (pts).

Methods: Pts with newly diagnosed FIGO Stage III (measurable disease [RECIST 1.1] before randomization) or IV, or recurrent EC, and naïve to systemic 1L treatment were randomized 1:1:1 to CP + durvalumab placebo (pbo; 6 cycles) followed by durvalumab pbo + olaparib pbo (CP arm); CP + durvalumab (1120 mg IV q3w) followed by durvalumab (1500 mg IV q4w) + olaparib pbo (CP+D arm); or CP + durvalumab followed by durvalumab + olaparib (300 mg bid; CP+D+O arm). ORR, DoR and TDT were assessed in ITT and MMR populations (exploratory).

Results: In the ITT at primary data cutoff (12 Apr 2023), ORRs with CP+D and CP+D+O were improved v CP (62 and 64 v 55%); median (m)DoR and mTDT were longer for CP+D v CP (mDoR: 13.1 [95% CI 6.0—NR] v 7.7 [5.1—13.5] months [mo]; mTDT: 9.9 [8.8—11.2] v 8.8 [7.6—9.7] mo) and further increased with CP+D+O (mDoR: 21.3 [8.1—29.9] mo; mTDT: 15.1 [12.5—18.6] mo; Table). In MMR deficient (dMMR) pts, CP+D and CP+D+O v CP improved ORRs (71 and 73 v 40%), mDoR (NR and 29.9 [95% CI 9.7—29.9] v 10.5 [4.6—NR] mo) and mTDT (21.2 [9.3—NR] and 20.6 [13.4—NR] v 6.7 [5.1—7.9] mo). In pMMR pts, ORRs were similar across arms but mDoR and mTDT were longer with CP+D v CP (mDoR: 10.6 [95% CI 5.6—NR] v 7.6 [5.1—13.1] mo; mTDT: 9.6 [8.1—10.6] v 9.3 [8.0—9.9] mo) and further extended with CP+D+O (mDoR: 18.7 [8.0—NR] mo; mTDT: 13.4 [10.6—15.6] mo).

Table: 40MO

	ITT			dMMR			pMMR		
	CP n=241	CP+D n=238	CP+D+O n=239	CP n=49	CP+D n=46	CP+D+O n=48	CP n=192	CP+D n=192	CP+D+O n=191
mTDT, mo (95% CI)	8.8 (7.6—9.7)	9.9 (8.8—11.2)	15.1 (12.5—18.6)	6.7 (5.1—7.9)	21.2 (9.3—NR)	20.6 (13.4—NR)	9.3 (8.0—9.9)	9.6 (8.1—10.6)	13.4 (10.6—15.6)
Pts with measurable disease at baseline, n	198	202	184	42	42	37	156	160	147
Objective response, n (%)*	109 (55)	125 (62)	117 (64)	17 (40)	30 (71)	27 (73)	92 (59)	95 (59)	90 (61)
mDoR, mo (IQR)	7.7 (5.1—13.5)	13.1 (6.0—NR)	21.3 (8.1—29.9)	10.5 (4.6—NR)	NR (22.0—NR)	29.9 (9.7—29.9)	7.6 (5.1—13.1)	10.6 (5.6—NR)	18.7 (8.0—NR)

*In pts with measurable disease at baseline. CI, confidence interval; IQR, interquartile range; ITT, intent to treat; NR, not reached.

Conclusions: CP + durvalumab followed by durvalumab ± olaparib improved ORR, DoR and TDT v CP (ITT population). In dMMR pts, CP+D consistently improved ORR, DoR and TDT v CP. In pMMR pts, CP+D improved mDoR v CP and adding olaparib further extended mDoR and mTDT v CP+D.

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41MO ESR1 mutation in untreated endometrial cancer: Prevalence, characteristics and prognostic implications from the UTOLA trial

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Background: Aromatase inhibitors (AIs) are a therapeutic option for estrogen receptor (ER)-positive endometrial cancer (EC) especially for low-grade endometrioid EC. ESR1 somatic mutations result in constitutive ligand-independent activation of ER and resistance to AIs in pts with breast cancer (BC). In BC, these mutations are rare at diagnosis (<1%) but are acquired in up to 36% of cases that become resistant to AIs. Here, we aimed to describe the prevalence of ESR1 mutations (ESR1m) in a cohort of treatment naïve EC samples and correlate it with molecular profile, ER expression and outcomes.

Methods: 147 patients (pts) with relapsed/metastatic EC and controlled after first-line platinum chemotherapy were recruited into the academic UTOLA trial. Archival EC FFPE tumor tissues were subjected to large panel sequencing encompassing 127 genes and including the ESR1 gene. Only hotspot mutations in the ligand-binding domain (LBD) and reported in BC were considered. All tumors were defined as POLE, MMRd, TP53mut or NSMP according to the PROMISE classification.

Results: 137/147 (93%) pts had enough tumor material for sequencing. Eight tumors (6%) harbored a pathogenic ESR1m, including Y537S/C/N (N=4), L536H/P (N=2) and E380Q (N=2). All ESR1m cases had low grade endometrioid histology, were ER-positive and classified as NSMP. Among the 43 pts with metastatic endometrioid NSMP EC, 19% (8/43) were ESR1m in archival treatment naïve tumor tissue. When comparing outcomes, overall survival was similar in pts with ESR1m EC compared to pts with ESR1-wt NSMP EC (median not achieved versus 25.3 months, p=0.114).

Conclusions: Our data suggest that activating mutations in the LBD of ESR1 are frequent among EC tumors traditionally considered good candidates for hormonal therapy, detected in almost 20% of pts with relapsed/metastatic low grade endometrioid NSMP EC. Importantly, these ESR1 mutations were found in treatment naïve archival tissue. ESR1-mutated EC are unlikely to benefit from AIs, thus we would advocate that ESR1 mutational status should be considered in the selection of a hormonal agent and a stratification factor in trials of AIs.

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42MO Interpreting somatic POLE mutations in endometrial cancer emerging from comprehensive genomic profiling

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Background: Endometrial cancer (EC) patients harbouring recognized POLE gene mutations have exceptional survival outcomes. Considering the TCGA data and a pragmatic score provided by Leon-Castillo et al., 11 POLE mutations have been recognized as "hotspots". While international guidelines encourage molecular testing and de-escalation of adjuvant treatment in early-stage EC, there's ongoing debate on whether POLE status should be prioritized over established prognostic factors in clinical decision-making. Moreover, the spread of comprehensive genome profiling programs (CGP) has underscored the need to interpret variants to date not considered hotspots. Here, we provide a genomic and clinical characterization of a large, prospective, EC population to better characterize POLE variants.

Methods: Patients diagnosed with epithelial EC who underwent surgery at Fondazione Policlinico Universitario A. Gemelli IRCCS were profiled with the Institutional CGP programme (ID: FPG500, NCT 06020625) using TruSight Oncology 500 high throughput. A mutational and signature analysis was then performed and integrated with clinical data.

Results: 387 cases were included and categorized into four groups according to POLE status: A: hotspots mutations (n=40); B: mutation in the exonuclease domain (EDM) non-recognized as hotspots (n=7); C: mutations outside the EDM (n=14); D: non-pathogenic variants (n=326). Genomic features of the four groups are summarized in the table. Furthermore, we analyzed the most frequent co-altered genes with hotspot POLE mutations, identifying RASA1 and LRP1B. Adapting Leon-Castillo's score in our cohort, we identified four patients who displayed different clinical and molecular characteristics compared to their supposed belonging Group.

Conclusions: Our results raise the question that additional features may be considered to better interpret the value of POLE status.

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Table: 42MO Medians (range) are reported for each value

Group	TMB (mut/MB)	C>A	C>G	T>G	Indels
Group A	137.75 (28.3-714.5)	9.54 (4.69-16.04)	3.87 (2.31-5.52)	4.95 (2.74-7.37)	3.2 (2.31-4.46)
Group B	35.5 (2.4-301.4)	4.26 (3.22-12.48)	5.04 (2.09-6.01)	3.15 (2.46-3.69)	4.45 (2.31-6.39)
Group C	30.1 (2.4-148.3)	4 (3.29-4.56)	5.39 (4.05-5.89)	3.29 (2.71-4.16)	5.02 (4.19-11.45)
Group D	7.1 (0-147.9)	3.89 (2.82-12.7)	5.35 (3.49-6.46)	3.35 (2.35-4.31)	4.47 (2.81-8.33)

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43O Durvalumab (D) + carboplatin/paclitaxel (CP) + bevacizumab (B) followed by D, B + olaparib (O) maintenance (mtx) for newly diagnosed advanced ovarian cancer (AOC) without a tumour BRCA1/BRCA2 mutation (non-tBRCAm): Updated results from DUO-O

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Background: DUO-O, a phase III, placebo-controlled study, showed statistically significant and clinically meaningful PFS benefit with D + CP + B followed by D + B + O mtx vs CP + B followed by B in non-tBRCAm HRD+ and non-tBRCAm ITT populations (primary endpoint; Harter *JCO* 2023;41:17; LBA5506). We report updated data.

Methods: Patients (pts) had newly diagnosed high-grade epithelial AOC and primary, or planned interval, debulking surgery. After 1 cycle of CP ± B, pts with non-tBRCAm AOC were randomized 1:1:1, stratified by timing and outcome of cytoreductive surgery (no macroscopic residual disease after upfront primary surgery and all others), and geographic region (North America, Europe, and other regions), to Arm 1 (control): CP + B followed by B; Arm 2: D + CP + B followed by D + B; or Arm 3: D + CP + B followed by D + B + O mtx. We present final descriptive PFS and subgroup analyses (Arm 3 vs 1); secondary endpoints of PFS (Arm 2 vs 1; non-tBRCAm ITT) and interim OS (both formally tested per the predefined multiple testing procedure); and PFS2.

Results: At DCO2 (18 Sep 2023), PFS benefit for Arm 3 vs 1 was sustained in both the non-tBRCAm HRD+ and non-tBRCAm ITT populations (Table), and was consistent across pre-planned subgroups, including for the stratification factors. The interim OS analysis for Arm 3 vs 1 (non-tBRCAm ITT) was not statistically significant. A favourable OS trend was shown for Arm 3 vs 1 in the non-tBRCAm HRD+ population. In both populations, PFS2 was improved for Arm 3 vs 1 and Arm 2 vs 1 (Table). DCO2 safety findings were similar to DCO1.

Conclusions: D + CP + B followed by D + B + O mtx continued to improve PFS vs control, including by subgroup; in the non-tBRCAm HRD+ population, median PFS was 45.1 mo, the longest seen for these pts in the first-line setting to date, with an associated favourable OS trend. PFS2 was improved in both the non-tBRCAm HRD+ and non-tBRCAm ITT populations.

Clinical trial identification: NCT03737643.

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Table: 43O

		Non-tBRCAm					
		HRD+*			ITT		
Arm		1 n=143	2 n=148	3 n=140	1 n=378	2 n=374	3 n=378
PFS							
	Median, mo	23.3	25.1	45.1	19.3	20.6	25.1
	HR (95% CI)†		0.89 (0.67–1.19)	0.46 (0.33–0.65)		0.87 (0.74–1.03) P=0.11	0.61 (0.51–0.73)
OS	HR (95% CI)†		0.69 (0.41–1.15)	0.84 (0.51–1.37)		0.92 (0.73–1.16)	0.95 (0.76–1.20) P=0.68
PFS2	HR (95% CI)†		0.91 (0.60–1.36)	0.62 (0.40–0.95)		0.91 (0.75–1.12)	0.82 (0.67–1.01)

*Myriad MyChoice® CDx assay, genomic instability score ≥42.
†vs Arm 1. Estimated from a stratified Cox model (stratified by timing and outcome of cytoreductive surgery [HRD+: PFS, OS, PFS2] or by timing and outcome of cytoreductive surgery and geographic region [ITT: PFS]) or an unstratified Cox model (ITT: OS, PFS2).

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44O Safety and efficacy results in patients who received dose modifications in the phase III MIRASOL (GOG 3045/ENGOT-ov55) trial of mirvetuximab soravtansine vs investigator's choice chemotherapy (ICC) in platinum-resistant ovarian cancer (PROC) with high folate receptor-alpha expression

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Background: Mirvetuximab soravtansine (MIRV), an antibody-drug conjugate targeting folate receptor alpha (FRα), demonstrated an improvement in progression-free survival (PFS), overall response rate (ORR), and overall survival (OS) in patients (pts) with high-grade serous PROC compared to ICC (Moore K et al. *N Engl J Med* 2023;389:2162-74). Here, we present safety and efficacy data in pts who received dose modifications, which are defined as dose delays, reductions, or interruptions.

Methods: 453 PROC pts with high FRα expression (VENTANA FOLR1 [FOLR1-2.1] RxDx Assay) with 1-3 prior therapies were randomized 1:1 to MIRV 6 mg/kg, adjusted ideal body weight, Day 1 of a 21-day cycle or ICC: paclitaxel, pegylated liposomal doxorubicin, or topotecan. The primary efficacy endpoint was PFS by investigator, with key secondary endpoints ORR, OS, and patient-reported outcomes in hierarchical order; other endpoints included safety, tolerability, and duration of response.

Results: With a data cutoff of March 6, 2023, 124 (57%) pts in the MIRV arm and 114 (55%) pts in the ICC arm received dose modifications. The median age was 63 for MIRV and 64 for ICC. In the MIRV arm, 36% had prior bevacizumab vs. 45% in the ICC arm, and 55% had prior PARPi vs 59% in the ICC. The PFS HR was 0.58 (0.43, 0.78), OS HR was 0.45 (0.30, 0.69), favoring MIRV, and the overall response rate was 59.7% for MIRV vs. 26.3% for ICC. Compared with ICC, pts on MIRV were associated with lower rates of grade 3+ treatment-emergent AEs (53% vs 72%) and serious AEs (24% vs 39%). Treatment discontinuations occurred in 12 (10%) pts on MIRV arm vs. 25 (22%) on ICC. Ocular, gastrointestinal, and neurosensory adverse events were comparable to the intent to treat population in the respective treatment arms.

Conclusions: Dose modifications occurred at similar rates in both treatment arms. MIRV demonstrated a longer PFS, OS, and higher ORR vs ICC in patients with dose modifications. The efficacy data and the well-characterized safety profile support MIRV as the standard of care for pts with FRα positive PROC.

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45MO Management of stage I ovarian Sertoli-Leydig cell tumors: Prognostic factors from a multicenter international retrospective study

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Background: Sertoli-Leydig cell tumors (SLCT) are extremely rare, thus evidence regarding optimal management is limited. According to European guidelines, fertility sparing surgery (FSS) is recommended for stage IA and adjuvant chemotherapy in stage >IA or in G3. The aim of this study was to assess the prognostic factors in the management of SLCT.

Methods: Retrospective data on patients diagnosed with stage I SCLT between January 1980 and March 2024 within MITO group (Multicenter Italian Trials in Ovarian cancer) and Charing Cross Hospital, London were collected. Statistical analyses were carried out using the SPSS Statistics. Clinicopathological variables were evaluated for association with relapse.

Results: 72 patients were included. Median age was 36.4 years (range 5-81). Stage was IA in 59 (81.9%), IB in 1(1.3%) and IC in 12 patients (16.7%). Tumor grade was G1, G2 and G3 in 20 (27.8%), 33 (45.8 %) and 19 (26.4%) patients, respectively. FSS was performed in 49 patients (68.0%), with laparoscopic approach in 56.9%. Peritoneal staging was done in 63.9% of patients. Most patients (86.1%) received surveillance postoperatively. After a median follow up time of 87 months (range 70-103), 12 patients (16.7%) recurred and 4 (5.5%) died of disease. Relapse rates in G1,2,3 tumors were 5%, 24.2% and 31.6%, respectively. Among patients with stage IA and IC, relapse rate was 17% and 41.7% (p=0.06). There was no statistically significant difference in relapse rates between FSS and non-FSS (24.5% vs 13%, p=0.26), nor between laparoscopic and open surgery (19.5% vs 22.6%, p=0.75). No statistically significant difference in recurrence rate was detected between G3 cases receiving or not chemotherapy (33% vs 30%). At multivariable analysis, the only factors associated with relapse were grade (G2-3 vs G1, OR 9.08 [95%CI 1.04-79.23]) and absence of peritoneal surgical staging (OR 3.58 [95% CI 1.03-12.45]).

Conclusions: These findings support conservative surgery as a safe approach for patients affected by stage I SLCT, provided that surgical staging is performed. More data deriving from international multicenter collaborations are needed to clarify the role of adjuvant chemotherapy in this setting.

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46MO What are the predictors of the success of interval debulking surgery (CC0-IDS) in patients with advanced ovarian cancers? Consistent data from two large independent datasets

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Background: Over 50% of advanced epithelial ovarian cancer patients undergo neoadjuvant chemotherapy (NACT), aiming to achieve a complete interval debulking surgery (IDS). Understanding the factors that can predict IDS success is crucial.

Methods: The French GINECO and the Gemelli (Italy) groups analyzed two independent datasets, separately. The French dataset included 133 patients from the CHIVA (C) randomized phase II trial (NCT01583322). The Italian dataset was built with the Policlinico GEMELLI (G) real-life registry with 357 patients (ID5936—ProtN45). Univariate/multivariate logistic regression models were performed to examine the clinical and biological covariates associated with: 1) low peritoneal carcinomatosis index (PCI) after 3/4 NACT cycles (Sugarbaker PCI $\leq$ 10 or Fagotti score at IDS $\leq$ 2); 2) IDS with no macroscopic residual lesion (CC0), 3) Complete or near-complete pathological response according to chemotherapy response score (CRS3). The assessed predictor factors were the modeled CA-125 longitudinal kinetics parameter KELIM, considered as a continuous (KCont) value or as Favorable ($\geq$ 1; FavK) vs Unfavorable ($<$1; UnFavK); best radiological response according to RECIST 1.1; and BRCA mutation/homologous recombination deficiency (HRD) status (C: Shallow HRD; G: Myriad&AmoyDx).

Results: Higher KELIM, was the only factor in both the datasets that consistently predicted: - lower PCI after NACT: Odd Ratios (O.R.) KCont: (C) 4.08 [1.78-10.10] - (G) 4.44 [2.09-9.40]; O.R. FavK vs UnFavK: (C) 4.19 [1.76-10.71] - (G) 2.92 [1.58-.39] - higher rates of complete IDS-CC0: O.R. KCont: (C) 7.29 [3.38-17.13] - (G) 4.66 [1.89-11.48]; O.R. FavK vs UnFavK: (C) 4.24 [2.07-8.99] - (G) 3.66 [1.67-8.01] - higher probability of CRS3: O.R. KCont: (C) 12.43 [3.75-55.5] - (G) 2.97 [1.82-4.84]; O.R. FavK vs UnFavK: (C) 21.44 [4.15-394.01] - (G) 2.36 [1.51-3.70]. The best radiological response was inconsistently significant. The BRCA/HRD status was not predictive of IDS success.

Conclusions: Across 2 independent international datasets, the primary tumor's chemosensitivity, assessed by CA-125 KELIM, was the sole consistent predictor of IDS success after NACT.

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47MO The risk index of early relapse defined by MiROvaR, a miRNA-based classifier, is a potential predictive marker for bevacizumab benefit: A MITO-MANGO-ENGOT study

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Background: The introduction of PARP inhibitors (PARPi) has greatly changed Ovarian Cancer (OC) patients' journey. Nonetheless, subgroups of patients still benefit of Bevacizumab (Bev) particularly those at clinical high risk or proficient for BRCA and/or Homologous Recombination. We developed, and validated, a robust and independent

miRNA-based molecular predictor, MiROvaR, successfully identifying patients at high risk of early relapse. MiROvaR may contribute in refining poor-prognosis patients predicting those who could greatly benefit from Bev treatment.

Methods: Samples used for the analyses were from two clinical trials: MITO16A-MANGO-Ov2 (MITO16A), single arm including Bev treatment/maintenance in front-line and MITO16B-MANGO-Ov2-ENGOT-Ov17 (MITO16B), randomized phase III including or not Bev treatment/maintenance in platinum sensitive patients relapsing after receiving Bev in front-line. RNA of adequate quality from patient enrolled in MITO16A (n=197) and MITO16B (n=102 standard arm; n=108 experimental arm) was profiled for miRNA expression (Agilent 8x60K miRBase21 version). MiROvaR-Index was derived to classify patients for being at high/low risk of relapse and assess association with clinical/pathological parameters and prognostic/predictive impact.

Results: The biomarker-evaluable populations comprising 49.5% and 51.7% of the intent-to-treat populations of MITO16A and MITO16B respectively had representative baseline characteristics and outcomes. In MITO16A, MiROvaR confirmed its performance in progression-free survival (PFS) and maintained an independent prognostic power in multivariable analysis with residual disease and FIGO stage (HR 1.74, 95% CI 1.131−2.67; P=0.011). In MITO16B, high MiROvaR-Index was predictive of a therapeutic advantage with Bev for PFS ($P_{interaction} = 0.00754$) but not for Overall Survival. Patients with high MiROvaR-Index treated with Bev had longer PFS (13 vs. 8 months; log-rank P<0.0001) compared to those in the control arm.

Conclusions: High MiROvaR-Index confirmed its prognostic power of early relapse independently of the treatment schedule and suggested a predictive potential of Bev response.

Clinical trial identification: MITO16A-MANGO-Ov2: EudraCT 2012-003043-29; NCT01706120. MITO16B-MANGO-Ov2-ENGOT-Ov17: NCT01802749 and EudraCT 2012-004362-17.

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48MO Treatment and outcome of elderly patients with advanced ovarian cancer in Germany: QS-OVAR of the AGO Study Group

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Background: Treatment of elderly ovarian cancer (OC) patients follows a fine line between risk and benefit and is often below recommended standards. The German quality assurance program QS Ovar provides a deep and representative insight into the treatment of elderly OC patients and their outcome during the past decade.

Methods: All German hospitals with OC patients were asked to document patient characteristics, treatment and outcome of all patients with first diagnosis in the third quarter of 2012, 2016 and 2021, respectively. This analysis is focusing on patients with age =/>75 years and OC FIGO III/IV.

Results: A total of 1951 OC patients were analyzed, 539 (28%) =/> 75 years and 1412 (72%) < 75 years. Elderly and younger showed significant differences in ECOG (ECOG =/> 2: 39% vs 17%), surgical outcome (residual tumor (RT) = 0 cm: 32 vs 54%; RT> 1cm: 37% vs. 22%), chemotherapy (CTX) use (platinum/taxane (TC) + maintenance (M) (31 vs 66%), Carboplatin-mono (C) (15 vs 3%) and survival (PFS: 13 vs 22, HR 1.7 and OS: 21 vs 44 months, HR 2.29). Among elderly, 15% received no surgery and 34% no CTX. Optimal treatment in terms of surgery and/or CTX translated into improved survival and was influenced by numerical age, ECOG, comorbidities and FIGO stage. Subgroup analysis showed no benefit for TC +/-M vs C+/-M in elderly with no RT after surgery (PFS 29 vs 32 months, p= 0.77; OS 52 vs 39 months, p= 0.23) but in pts with RT > 0 cm (PFS 16 vs 10 months, p=0.065; OS 28 vs 20 months, p= 0.032). Incomplete cytoreductive surgery without postoperative CTX (n= 102 (19%)) had no beneficial effect on survival. Median PFS and OS for elderly patients who received no or incomplete (TR> 0cm) surgery without CTX was 3.2 and 2.9 months, resp. 3.2 and 3.4 months, but with subsequent CTX 12 and 14 months, resp. 17 and 26 months (p<0.001).

Conclusions: Treatment decisions in elderly are critical. Treatment patterns offer a potential for de-escalation. The triage for or against surgery should be done with respect to subsequent CTX, whose omission seems to be the worst prognostic factor among the therapeutic modalities. Survival of OC patients with tumor but without CTX was 3 months.

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49MO Updated progression-free survival (PFS) in patients (pts) with newly diagnosed advanced ovarian cancer (OC) treated with rucaparib (RUC) in ATHENA-MONO

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Background: RUC provided a sustained PFS benefit in pts with newly diagnosed advanced OC after first-line (1L) treatment in the ATHENA-MONO study (NCT03522246). We report updated PFS analyses (data cutoff 01 March 2024).

Methods: Pts with high-grade, FIGO stage III-IV OC with response to 1L treatment were randomized 4:1 to treatment with 600 mg BID RUC (N = 427) or placebo (PBO, N = 111) for up to 2 y. An exploratory analysis was done to evaluate updated investigator-assessed PFS (INV). It included the primary populations (homologous recombination deficiency [HRD] and intent to treat [ITT]), non-nested HRD subgroups, and low/high-risk pts according to FIGO stage/surgical outcome and surgery timing. For pts in complete response (CR) at baseline, recurrence-free survival was defined as time from randomization to disease recurrence (new lesions by imaging) or death.

Results: After a median of 4.0 and 3.5 y of follow-up, an additional 1.9 and 1.6 y of follow-up, respectively, median PFS was consistently longer or not reached (NR) in pts treated with RUC than with PBO in ITT populations as well as in the HRD subgroup and the non-nested HRD subgroups (Table). In the higher-risk subgroup 27.7% of RUC vs 8.6% of PBO-arm pts were progression-free at 4 y; in the lower-risk subgroup 41.9% vs 37.2% of pts, respectively, were progression free at this time point. Among pts in CR at baseline, risk of disease recurrence or death was reduced by 51%. The safety profile of RUC was consistent with that from the primary endpoint analysis (23 March 2022). Three new cases of myelodysplastic syndrome or acute myeloid leukemia were reported since the primary analysis; the incidence was the same in the RUC and PBO arms (<1%).

Table: 49MO

	RUC vs PBO		
	23 Mar 2022		1 Mar 2024
	Blinded independent central review	INV	INV
	Median PFS, mo, HR (95% CI)		
Overall	25.9 vs 9.1 0.47 (0.36-0.63)	20.2 vs 9.2 0.52 (0.40-0.68)	20.2 vs 9.2 0.53 (0.41-0.68)
HRD	NR vs 9.9 0.44 (0.28-0.70)	28.7 vs 11.3 0.47 (0.31-0.72)	31.4 vs 12.0 0.49 (0.33-0.73)
BRCA	NR vs NR 0.48 (0.23-1.00)	NR vs 14.7 0.40 (0.21-0.75)	NR vs 16.7 0.47 (0.26-0.84)
Non-BRCA LOH^{high}	27.8 vs 9.1 0.46 (0.26-0.81)	20.3 vs 9.2 0.58 (0.33-1.01)	22.3 vs 9.2 0.56 (0.33-0.92)
Non-BRCA LOH^{low}	12.0 vs 6.4 0.60 (0.40-0.89)	12.1 vs 9.1 0.65 (0.45-0.95)	12.1 vs 9.1 0.66 (0.46-0.96)
Non-BRCA^{unknown}	17.4 vs 6.5 0.33 (0.16-0.68)	17.5 vs 8.9 0.39 (0.20-0.78)	17.5 vs 8.9 0.38 (0.19-0.76)

LOH, loss of heterozygosity.

Conclusions: RUC maintained a clinically significant improvement in PFS with 4.0 y of follow-up in pts with newly diagnosed advanced OC in pts with both low and high risk of progression. No new safety signals were identified.

Clinical trial identification: NCT03522246.

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50P Vididencel, a cell-based cancer vaccine, induces tumor-directed immune responses in high-grade serous ovarian carcinoma patients

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Background: Improving disease free and overall survival in advanced high grade serous ovarian carcinoma (HGSC) after primary treatment remains challenging. This phase 1 trial (NCT04739527) evaluated vididencel, a cell-based cancer vaccine, to prime or boost immune responses and prevent disease recurrence after primary treatment. Vididencel is highly immunogenic and expresses tumor associated antigens (TAA), such as WT1 and PRAME, which are also frequently upregulated in HGSC.

Methods: Patients with advanced HGSC (n=17) after primary treatment, were given vididencel four times biweekly, followed by 2 booster injections. Peripheral blood mononuclear cells (PBMC) were obtained at week 0, 4, 10, 14, 18 and 22. At week 22 patients were assessed for their disease status, both clinically and by CA125 levels in peripheral blood. IFNγ ELISpot was performed on PBMC for WT1, PRAME, MAGEA3/4 and NY-ESO1. Vaccine induced T-cell response (VIR) were calculated as ≥2-fold increase of the mock-corrected baseline response.

Results: As of April 2024, all 17 planned patients have completed treatment phase up to week 22 or end of treatment. One patient prematurely discontinued study treatment due to disease progression. Ten patients had stable disease and 7 patients had imaging confirmed recurrence at week 22 or end of treatment. The safety profile aligns with prior reports in AML patients, indicating the vaccine only gives mild adverse reactions, predominantly at the site of injection. VIR to any of the antigens tested were observed in 9/12 (75%) analyzed patients, with 3 patients not reaching a VIR due to high baseline responses. Notably, most immune responses were observed to WT1 (5/9 patients) and NY-ESO (4/9 patients). In 3 out of 9 patients responses to more than one antigen were observed.

Conclusions: The use of vididencel in this phase 1 trial for HGSC patients is feasible, well-tolerated, and results in a T-cell response against TAA in the majority of patients. The observed immune responses to a wide range of antigens provides a potential basis for an effective anti-tumor response. Long-term follow-up is ongoing to evaluate clinical benefit of this active immunotherapy approach.

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51P Efficacy and safety by time to maintenance therapy treatment initiation in PRIMA/ENGOT-OV26/GOG-3012

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Background: To help delay cancer recurrence, maintenance treatment (MT) with PARP inhibitors is recommended in patients (pts) with advanced ovarian cancer (OC) that responded to 1L platinum-based chemotherapy (PBCT). Because PARP inhibitors, including niraparib, are associated with early hematologic adverse events, understanding when to initiate MT after 1L PBCT to best optimize safety and efficacy is vital.

Methods: In the phase 3 PRIMA study, eligible pts had newly diagnosed advanced epithelial OC that responded to 1L PBCT. Pts were randomized 2:1 to receive either niraparib (nir) or placebo (PBO) MT within 12 wks after completion of the last dose of 1L PBCT. This post hoc analysis grouped pts by time from end of 1L PBCT to randomization (<8 vs ≥8 wks) and evaluated investigator-assessed progression-free survival (PFS) and safety outcomes (17 Nov 2021 clinical cutoff date; median follow-up, 3.5 years).

Results: Overall, 356 pts (nir, 236; PBO, 120) were randomized <8 wks after 1L PBCT and 377 pts (nir, 251; PBO, 126) were randomized ≥8 wks after 1L PBCT. Median time from the end of 1L PBCT to randomization (range): <8 wks subgroup, nir, 6.1 wks (0.3—7.9 wks) and PBO, 5.7 wks (1.1—7.9 wks); ≥8 wks subgroup, nir, 10.6 wks (8.0—28.0 wks) and PBO, 10.8 wks (8.0—26.14 wks). The PFS benefit of nir was similar in pts randomized <8 wks and ≥8 wks after the end of 1L PBCT (Table). The percentages of pts who experienced any-grade treatment-emergent adverse events (TEAEs) were similar across subgroups in both treatment arms (Table). In the nir arm, the percentages of pts who experienced TEAEs leading to dose interruptions and reductions were slightly higher in pts randomized <8 wks than in pts randomized ≥8 wks after the end 1L PBCT.

Table: 51P

	Time from end of 1L PBCT to randomization			
	<8 wks		≥8 wks	
	Nir	PBO	Nir	PBO
PFS[a]	n=236	n=120	n=251	n=126
Median PFS, mo	13.8	8.2	13.9	8.4
Hazard ratio (95% CI)	0.64 (0.50−0.83)		0.67 (0.52−0.86)	
TEAE, n (%)[b]	n=236	n=119	n=248	n=125
Any-grade	233 (98.7)	109 (91.6)	246 (99.2)	120 (96.0)
Leading to dose interruption	197 (83.5)	22 (18.5)	192 (77.4)	29 (23.2)
Leading to dose reduction	177 (75.0)	8 (6.7)	170 (68.5)	15 (12.0)
Leading to treatment discontinuation	31 (13.1)	2 (1.7)	36 (14.5)	5 (4.0)

[a]Efficacy evaluable pts. [b]Safety evaluable pts. 1L, first-line; nir, niraparib; PBCT, platinum-based chemotherapy; PBO, placebo; PFS, progression-free survival; pts, patients; TEAE, treatment-emergent adverse event.

Conclusions: Within the allowable 12-wk interval, efficacy and safety outcomes were generally similar regardless of time to MT initiation in PRIMA. Pt safety should be considered when beginning nir MT soon after 1L PBCT to allow for recovery from chemotherapy-induced myelosuppression.

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52P MONITOR-UK: An initial analysis of a multi-centre, observational study of maintenance niraparib in ovarian cancer

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Background: Niraparib (PARP inhibitor) is approved in advanced ovarian cancer (OC) as maintenance therapy in the first line and recurrent platinum-sensitive settings. The MONITOR-UK study was designed to report real-world niraparib experience in UK clinical practice.

Methods: In this national, multi-centre, observational study (NCT04295577), patients with newly diagnosed or recurrent OC treated with maintenance niraparib were enrolled. The primary endpoint is the incidence of grade ≥3 treatment emergent adverse events (TEAEs). Secondary endpoints include PFS and quality of life. Recruitment is ongoing (n=375 planned). We report an initial, descriptive analysis of subjects enrolled with at least 6 months (mo) follow up.

Results: Between 12/2019 and 8/2023, 319 eligible patients were enrolled from 14 centres; median age 68 years (IQR 59-74); 166/319 (52%) first line (139/166 (84%) prospective); 153/319 (48%) recurrent OC (110/153 (72%) prospective); 300mg initial dose 24%. Median follow-up 17.3 mo (IQR 8.7 - 27.8). Among first line patients, 111/166 (67%) stage III at initial diagnosis; 59/166 (36%) neoadjuvant chemotherapy; 126/166 (76%) cytoreductive surgery; 103/126 (82%) no residual disease. 106 (33%) patients experienced a grade ≥3 TEAE: hypertension (n=44, 14%), anaemia (n=27, 8%), low neutrophil (n=20, 6%) and low platelet count (n=20, 6%). Adverse events of special interest included secondary cancer diagnosis (n=6), pneumonitis (n=2), AML (n=1) and MDS (n=1). Discontinuation rate due to TEAEs was 5%. 47% patients had dose reductions. In the first line, median PFS for all-comers was 12.5 mo (95% CI, 9.7 - 15.8); median PFS for stage III without residual disease 14.6 mo (95% CI, 11.3 - 17.3) and 8.5 mo (95% CI, 5.6 - 10.8) for stage III with residual disease. In patients with recurrent disease, the PFS was 15.4 (95% CI, 8.5 - 40.9) and 7.1 (95% CI, 5.4 - 8.5) mo in BRCA-mutated (n=17, 11%) and all-comers, respectively.

Conclusions: In this real-world, ongoing, observational study, which included first line patients without residual disease, the occurrence of treatment-related adverse events graded ≥3 reported is lower than reported in phase III clinical trials. Clinical outcomes and biomarker status will be updated.

Clinical trial identification: NCT04295577.

Legal entity responsible for the study: The authors.

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53P Description of BRCA mutated high-grade ovarian cancer demonstrating primary resistance to first-line platinum in the French national multicenter ESME database

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Background: High-grade epithelial ovarian cancer (HGOC) harboring a BRCA mutation (BRCAm) are the proof of concept for a homologous recombination deficient tumor. As a result of this defect in a crucial DNA repair pathway, most BRCAm OC are sensitive to first-line platinum-based chemotherapy. However, a small subset of patients (pts) with BRCAm OC demonstrate primary chemo-resistance. We aimed to describe the prevalence, clinico-pathological characteristics, and disease evolution of pts with primary resistant/refractory BRCAm OC (PROC).

Methods: We conducted a retrospective observational cohort study based on OC data from the Epidemiological Strategy and Medical Economics (ESME) platform which centralizes real-life data of pts aged $\geq$ 18 years treated for OC in France between 2011 and 2022. PROC was defined as pts who received non-platinum chemotherapy in second-line for progression.

Results: Out of the 13,032 pts included in the ESME database, 1505 pts with BRCAm HGOC were identified. The prevalence of PROC among pts with BRCAm OC was 3.3% (43/1302). When comparing BRCAm PROC and BRCAm platinum sensitive OC (PSOC) pts, there were no significant differences in age at diagnosis (p=0.1798), but there was a trend in distribution of BRCA1(77 vs 66%) vs BRCA2 (21 vs 34%) mutations (p=0.0687). BRCAm PROC was more frequently associated with non-serous histology (29% vs 16%, p=0.042), with higher FIGO stage at diagnosis (85% vs 41% stage IV, p=0.0003), and non-operable disease at diagnosis (77% vs 55%, p= 0.004). Pts with BRCAm PROC had higher ca125 values at diagnosis and at last platinum than PSOC patients (mean 3364 vs 2090, p=0.04, and 562 vs 51U/mL, p<0.0001, respectively). Median PFS and OS were 10.2 [7.6-11.7] and 29.2 months [19.0-43.2] respectively in BRCAm PROC pts, and 34.0 [31.9-36.8] and 95.1 months [88.0-104.9] in PSOC pts.

Conclusions: PROC is rare among pts with BRCAm OC but their prognosis is catastrophic. BRCAm PROC pts were more likely to have non-serous histology and exhibited more advanced disease at diagnosis than PSOC pts. We did not identify any other predominant features distinguishing PROC pts. These results suggest the importance of early cancer screening in BRCAm pts.

Legal entity responsible for the study: Unicancer manages independently ESME OC database (i.e., data collection, analyses and publication) and is the sole data controller for data processing. This study was specifically conducted by Alexandra Leary (Gustave Roussy).

Funding: The ESME Ovarian Cancer database (NCT03275298) received financial support from industrial partners. Unicancer manages the database (i.e., data collection, analyses and publication) independently.

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54P Real-world data of patients with recurrent BRCA-mutated platinum-sensitive ovarian cancer treated with olaparib maintenance: Surgical outcome subgroup analysis from the C-PATROL study

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Background: Maintenance monotherapy with the poly-(ADP-ribose)-polymerase inhibitor olaparib has previously shown good effectiveness and tolerability in patients with platinum-sensitive relapsed ovarian cancer (PSROC) who are in response to platinum-based chemotherapy (PBC) in the C-PATROL study. Cytoreductive surgery followed by PBC has the potential to improve survival in PSROC if a complete resection can be achieved.

Methods: The prospective German non-interventional study C-PATROL (NCT02503436) captured routine clinical data of patients with BRCA-mutated PSROC treated with PBC and receiving olaparib maintenance according to label. This predefined subgroup analysis compares patients based on surgery details for the current relapse and its outcome: patients who were macroscopic tumour-free (MTF) versus no surgery/non-MTF (non-MTF). Data were analysed by descriptive statistics.

Results: The study enrolled 277 patients between 10/2015 and 10/2019. Within the ITT set (study selection criteria fulfilled; N=267), 66 patients were included in the MTF vs 201 in the non-MTF subgroup (182 had no surgery and 19 were non-MTF). Median age was 59 vs 61 years, 58% vs 60% had an ECOG performance status of 0, 82% vs 63% were tumour-free after primary surgery, 27% vs 34% had $\geq$2 relapses, and 65% vs 20% had a complete response (CR) to the current PBC. Median follow-up was 42.8 (range: 0.3—80.5) vs 20.3 months (0.0—79.4). Median progression-free survival (PFS) was 43.2 (95% CI 21.9—nr) vs 12.1 months (10.7—14.1). Median overall survival (OS) was not reached (nr) (95% CI 60.8—nr) vs 27.4 months (24.4—33.6). Adverse events (AEs) were consistent with the known tolerability profile of olaparib (safety set: n=274; any AE: 96% vs 95%, AE of CTCAE grade $\geq$3: 34% vs 42%, olaparib discontinuation due to AE: 9% vs 12%).

Conclusions: Patients with PSROC for whom in the real-world a macroscopic complete (recurrence)tumour-resection was achieved before receiving PBC and olaparib maintenance, have a beneficial prognosis concerning PFS and OS.

Clinical trial identification: NCT02503436.

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55P Long-term responders (LTR) with niraparib maintenance in platinum-sensitive recurrent high-grade serous ovarian cancer (PSROC) focusing on subsequent therapies and post-progression outcomes (GEICO-88R study)

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Background: The GEICO-88R study evaluated the real-world use of niraparib (NIR) as maintenance treatment in patients (pts) with PSROC (Cueva et al, *EJC* 2023). A subanalysis of the LTR subgroup (NIR exposure ≥12 mo) was also communicated (Cueva et al, ESMO 2023,795-P).

Methods: In this study across 57 Spanish sites, pts received NIR at fixed 300 mg/day or individualized starting dose. Now, an extended follow-up (FU) analysis of LTR has been performed, focused on subsequent systemic lines.

Results: The characteristics of 107 LTR were previously reported describing a high-risk population, mostly BRCAwt (81.3%), with a median of 2 prior treatment lines and significant concomitant comorbidities (46.7%). Of note, 58.3% ORR was observed in the 48 pts with pre-NIR measurable disease. 61 pts (62.8%) had at least 1 post-NIR systemic line, with 53 pts (86.9%) having a platinum-based treatment (PBT). The proportion of pts receiving subsequent lines was: 1-2L, 55.7%; 3-4L, 24.6%; ≥5L, 19.7%. 31 (29%) pts remained on NIR therapy upon analysis. 61 pts (57%) had very long maintenance (>24 mo) and 68.9% of them remained alive. With a median FU of 49.1 mo, the median PFS, PFS2 and OS were 26.4 (95% CI 21.3-28.8), 33.5 (95% CI 28.5-NA) and 56.9 mo (95% CI 48.2-NA) respectively. Median PFS of first and second post-NIR lines were 8.2 (95% CI 6-12) and 7 mo (95% CI 4.7-10.4) respectively. The ORR with the first subsequent line was 34.9%. 2 pts had AML (1.8%) and 1 MDS (0.9%).

Table: 55P First and second lines after niraparib (NIR)

LTR (N = 97)	N (%)		N (%)
First-line after NIR	61 (62.8)	Second-line after NIR	45 (46.4)
PBT + bev	12 (19.7)	PBT + bev	1 (2.2)
PBT w/o bev	31 (50.8)	PBT w/o bev	11 (24.4)
Pac + bev	1 (1.6)	Pac + bev	4 (8.9)
PARPi	2 (3.3)	Pac w/o bev	6 (13.3)
Other	15 (24.6)	PRS + bev	1 (2.2)
None	36 (37.1)	PRS w/o bev	5 (11.1)
		PARPi	2 (4.4)
		Other	15 (33.3)
		None	52 (53.6)

PBT: Platinum-based treatment. PRS: Platinum-resistant scheme (other than paclitaxel). Bev: Bevacizumab. Pac: Paclitaxel.

Conclusions: This subanalysis of LTR to NIR maintenance in real life focusing on post-NIR treatment shows a significant proportion of pts with NIR therapy >24 mo; that most pts received a PBT as next line; and a remarkable median OS (56.9 mo).

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56P Real-life data for HRD testing from the only French platform using the Myriad MyChoice test

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Background: HRD is correlated with increased survival of patients with advanced ovarian cancer treated with maintenance olaparib + bevacizumab. HRD is defined by pathogenic or likely pathogenic mutations of BRCA1/BRCA2 and/or a genomic instability.

Methods: Our lab is the only one performing the Myriad MyChoice test in France. The Genomic Instability Score (GIS) is calculated with the Myriad's bioinformatics pipeline, while alterations of 11 genes are internally analyzed.

Results: From October 2022 to November 2023, we received 1009 samples from all over France. Fifty-two percent were for complete HRD testing (BRCA+GIS), whereas 48% were for GIS testing only. The mean turnaround time was 13 calendar days. The mean time between tissue sampling and receipt at our lab was 17 days for an HRD test (5.9% were over 50 days) and 35 days for a GIS testing only (20.6% were over 50 days). For a complete HRD test, only 2.3 % of samples could not be analyzed due to the lack of tumor in the sample, while for GIS more than 11% of samples did not have enough tumor material. We observed the number of GIS+ tumors decreased with the age at cancer diagnosis. More than 50% of tumors from patients younger than 50 yo were GIS+, whereas 35% of tumors were positive for patients between 50 and 75, less than 30% of tumors were positive for patients older than 75, and only 25% for patients older than 85. Of the 1009 analyses, 22.5% had inconclusive results. This was due to low/no tumor content (80.2%), low sample quality (16.3%), or consanguinity (3.5%). This thorough selection avoids false negative results. In tumors with TP53 Mutant Allele Frequency between 20-80% (good tumor content), 38% were GIS+. When TP53 MAF $<$ 20%, meaning low tumor content, 55% were inconclusive and less than 10% were GIS+. Surprisingly, in case of high tumor ploidy (TP53 MAF $>$ 80%), only 23% were GIS+.

Conclusions: The Myriad MyChoice test allows the analysis of BRCA variations and the GIS at the same time for a complete and faster molecular diagnosis, which is suitable for the majority of patients. Moreover, the thorough quality selection of tissue samples during the bioinformatics analysis leads to a strong reliability and a confidence in the results by dramatically reducing the rate of false negative results.

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57P Prognostic impact of functional domain of BRCA1/2 mutation in platinum-sensitive recurrent epithelial ovarian cancer patients receiving PARP inhibitors

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Background: PARP inhibitors (PARPi) have revolutionized the management of epithelial ovarian cancer (EOC). In this context, BRCA1/2 mutations represent the main predictor of benefit from PARPi. However, little is known regarding the impact of the type of BRCA mutation on benefit derived from PARPi and on prognosis.

Methods: This retrospective observational study included patients treated with PARPi for platinum-sensitive recurrent EOC at our Institution between 2015-2023. Progression-free survival (PFS) and overall survival (OS) from start of PARPi were evaluated according to the involved BRCA functional domain (DNA-binding domain [DBD], really interesting new gene [RING], RAD51-binding domain [RAD51-BD], BRCA1 C Terminus [BRCT]) and the type of alteration (missense, nonsense, large rearrangements, frameshift, in-frame, splicing, synonymous).

Results: Of 113 patients identified, 33.6% (n=38) presented a BRCA mutated tumour (germline=34, somatic=4; BRCA1=22, BRCA2=16). Mutations were more frequently located in the DBD for BRCA1 (n=6) and in the RAD51-BD for BRCA2 (n=4); most mutations were non-sense (n=14) and frameshift (n=13). At a median follow-up of 56.7 months, BRCA functional domains were significantly associated with OS, with a median OS not reached for DBD (95%CI NR-NR), 8.5 months (95%CI NE-NE) for RING, 21.6 months (95%CI 5.2-38.1) for RAD51-BD, 23.4 months (95%CI 20.6-26.3) for BRCT and 51.7 months (95%CI 20.1-83.3) for other domains (p=0.01). Mutations in DBD or other domains were also associated with a numerically longer PFS from start of PARPi as compared to RING, RAD51-BD, and BRCT (median PFS 66.7, 30.8, 7.4, 5.2, 13.3 months, respectively; p=0.22). On the contrary, the type of alteration observed in BRCA1/2 genes was not significantly associated with PFS and OS from start of PARPi (p=0.60 and p=0.64, respectively).

Conclusions: In platinum-sensitive recurrent EOC treated with PARPi, BRCA1/2 mutations carry a different prognostic impact in terms of PFS and OS from start of PARPi according to the functional domain of the gene involved. If confirmed, this might be used in clinical practice to further optimize prognostic assessment of these patients.

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58P A multicenter, prospective, non-interventional drug intensive monitoring study of olaparib in real-world Chinese patients with ovarian cancer (DIM-OC)

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Background: In China, ovarian cancer (OC) is the leading cause of death among gynecological cancers. Clinical trials showed that olaparib maintenance therapy was effective and well-tolerated in OC patients (pts). Yet, real-world safety data of olaparib in a broad Chinese population are limited. DIM-OC aims to intensively monitor the safety of olaparib in the largest Chinese OC cohort.

Methods: This multicenter, prospective, observational study enrolled OC pts who had received $\geq$1 dose of olaparib. Primary endpoints included the incidences of adverse events (AEs), serious AEs (SAEs) and AEs of special interest (AESIs) during the follow-up (up to 30 days after olaparib discontinuation or maximally for 6 months after enrolment), and were reported with the Clopper-Pearson 95% CIs.

Results: 799 pts from 33 sites were enrolled by 30 Jun 2023, and 796 pts treated with olaparib were analyzed by data cut-off (29 Dec 2023). At baseline, the mean age was 56$\pm$9 years. 490 (61.6%) and 306 (38.4%) pts had newly diagnosed and platinum-sensitive relapsed OC, respectively. 343 (43.1%, 95% CI [39.6%, 46.6%]) reported $\geq$1 AEs and 257 (32.3%, 95% CI [29.0%, 35.7%]) had $\geq$1 treatment-related AEs (TRAEs) as per investigator assessment (Table). Most common TRAEs included anemia (n=137, 17.2%), white blood cell count decreased (n=79, 9.9%) and neutrophil count decreased (n=59, 7.4%). Grade $\geq$3 AEs occurred in 68 (8.5%, 95% CI [6.7%, 10.7%]) pts, grade $\geq$3 TRAEs in 52 (6.5%, 95% CI [4.9%, 8.5%]), SAEs in 27 (3.4%, 95% CI [2.2%, 4.9%]), and AESIs in 3 (0.4%, 95% CI [0.1%, 1.1%]). For AESIs, myelodysplastic

syndrome, breast cancer and pneumonitis each occurred in 1 pt (0.1%, 95% CI [0.0%, 0.7%]). 21 (2.6%, 95% CI [1.6%, 4.0%]) pts discontinued treatment due to AEs. No new safety signals were detected.

Table: 58P

n (%)	Olaparib (N = 796)	95% CI
≥1 AEs	343 (43.1)	39.6%, 46.6%
≥1 treatment-related AEs	257 (32.3)	29.0%, 35.7%
Grade ≥3 AEs	68 (8.5)	6.7%, 10.7%
Grade ≥3 treatment-related AEs	52 (6.5)	4.9%, 8.5%
SAEs	27 (3.4)	2.2%, 4.9%
Treatment-related SAEs	10 (1.3)	0.6%, 2.3%
AEs leading to treatment discontinuation	21 (2.6)	1.6%, 4.0%
Treatment-related AEs leading to treatment discontinuation	16 (2.0)	1.2%, 3.2%

AEs occurring in >5% of patients	Overall	Grade 1 or 2	Grade 3 or 4
Anemia	153 (19.2)	110 (13.8)	43 (5.4)
White blood cell count decreased	88 (11.1)	81 (10.2)	7 (0.9)
Neutrophil count decreased	67 (8.4)	59 (7.4)	8 (1.0)
Platelet count decreased	49 (6.2)	45 (5.7)	4 (0.5)

Conclusions: Olaparib showed acceptable and tolerable safety profile in this largest to date, real-world Chinese OC cohort, regardless of treatment lines. No new safety signals were detected.

Clinical trial identification: NCT04560452.

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59P Real-world effectiveness of niraparib in recurrent ovarian cancer patients in France: Impact of starting dose and timing of the maintenance initiation

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Background: Niraparib is a PARP inhibitor first approved by EMA in 2017 as maintenance monotherapy in patients (pts) with platinum-sensitive relapsed high grade serous epithelial ovarian cancer (OC) who are in response to platinum-based chemotherapy (PBCT), based on the NOVA study. It is reimbursed in France since May 2019.

Methods: This study aimed to retrospectively analyze the ESME French real-world dataset of OC pts to describe the clinical characteristics, treatment patterns and survival outcomes of pts who initiated niraparib in second-line or beyond (2L+) between May 2019 and Jul 2021. Subgroup analyses on pts eligible per the main criteria of the NOVA trial were explored.

Results: 389 pts were eligible (including 139 NOVA-like pts; 36%), with a median follow-up of 12 months. Mean age was 63 years, mean weight was 68kg. 93% of pts with available results were BRCAwt. Niraparib was mostly initiated in complete or partial PBCT responders (73%), at a dose of 200mg (72%), between 4-8 weeks after PBCT (57%) and in 2L (62%). Median exposure to niraparib was of 97 days and 76% of patients discontinued niraparib during the observational period. Among the 295 pts who discontinued niraparib, 56% discontinued for progression and 32% for toxicity. Median progression-free survival (mPFS) was estimated at 7.2 [95% CI 6.2-8.5] months (mo) in the main population. Unadjusted analyses in the NOVA like population showed comparable efficacy regardless the timing of initiation: median PFS of 8.7 [6.4-13.0] mo after 8 weeks (w) vs mPFS of 6.8 [6.0-8.5] mo before 8 w; as well as regardless of the dose, mPFS 8.7 [6.7—12.0] mo for patients who initiated niraparib at 300 mg vs mPFS of 6.8 [6.2-8.2] m for those who initiated niraparib at a lower dose. However, mPFS was higher for pts who initiated niraparib in 2L (8.7 [7.3-9.8] mo) compared to 3L+ (5.2 [4.0-6.2]).

Conclusions: First study providing real-word data on the use of niraparib in French OC patients shows efficacy results (PFS) consistent with the randomized NOVA trial results. Niraparib can be introduced more than 8 w after end of PBCT without loss of efficacy; as well as initiated at the recommended dose depending on the pts features. The main reason for niraparib discontinuation was progression.

Clinical trial identification: NCT03275298.

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60P Exploration of homologous recombination deficiency testing in ovarian cancer: Insight from an Italian referral center

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Background: PAOLA 1 trial reported an unprecedented benefit of 66% 5-year rate survival increase with olaparib + bevacizumab in Homologous Repairs Recombination (HRR) deficient population (HRD). Literature data report an HRD prevalence of 50% in patients with high-grade serous carcinoma (HGSOC) and endometrioid high grade carcinoma (HGEOC). In this scenario HRD testing should be offered to any HGSOC and HGEOC patients. Here we present a descriptive analysis of an Italian referral center.

Methods: Patients respecting PAOLA-1 criteria were profiled adopting SOPHiA DDM™ HRD solution. The assay encompasses somatic mutations in 26 HRR genes (including BRCA1 and BRCA2), identifying pathogenic variants, such as SNPs and Indels. Report's result includes: a) HRR status (negative/positive), b) Genomic instability (GI) value (ranging from -20 to 20), c) BRCA status.

Results: From January 1st 2023 to December 31st 2023, 338 patients were evaluated and only in 7 patients (2%) HRD test was indeterminate. Among patients' characteristics, summarized in the table, RT <0 and primary debulking surgery (PDS) were

more observed in HRD group. At data cut off, 22 patients experienced disease progression (14 HRR proficient (HRP), 7 HRD, 1 indeterminate). Data on maintenance therapy is under collection and will be integrated.

Table: 60P

	HRD 179 (53%)	HRP 152 (45%)	Indeterminate 7 (2%)
Histology			
HGSOC	173	127	7
HGEOC	0	7	0
Others	6	18	0
FIGO STAGE			
IIIA	15	9	0
IIIB	20	17	0
IIIC	70	60	5
IV	70	60	2
Others	4	6	0
Surgery			
Primary debulking	103	65	7
Interval debulking	76	87	0
Residual Tumor (RT)			
0	81	65	0
>0	84	68	5
Not available	14	19	2
Status GI			
positive	171	0	0
negative	8	152	0
indeterminate	0	0	7
Indice GI			
Range (min-max)	-6.8 to 18.9	-20 to 0	Not available
BRCA			
mutated	77	0	0
Wild Type	100	150	7
indeterminate	2	2	0

Conclusions: Our data confirm current literature on HRD prevalence in HGOSC and HGEOC patients. Despite the limited follow-up, the dimension of the cohort will provide valuable real world data insights.

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61P Prognostic impact in ovarian cancer carriers of mutations located in cluster with higher risk of ovarian cancer in BRCA

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Background: The information between the phenotype and genotype in ovarian cancer (OC) carrying a BRCA mutation (BRCAmut) has been the subject of some publications in recent years. Rebbeck's work reports a mapping of the BRCA1 and 2 genes in which several areas are found that function as association clusters with a greater risk of suffering from OC. To date, it has not been reported whether the mutations that affect these areas have a prognostic impact on patients affected by BRCAmut CO or on the results of treatment with IPARP.

Methods: 283 patients with ovarian cancer treated in our unit between 2011 and 2023 with a mutational study that includes the BRCA genes are reviewed. The clusters with higher risk of ovarian cancer are defined as follows: BRCA1: c.1380-4062aa BRCA2: c.3249-5681aa and c.6645-7471aa.

Results: In the log-rank test, there is a tendency towards significance (p: 0.071) of a worse prognosis of patients carrying mutations in the association cluster with OC. Among the patients who received iPARP, there were no statistically significant differences between both groups (p:0.69), although the number of patients in the group with mutations in the CO cluster was only 3 patients.

Table: 61P Patients' clinical data

Number of patients	49
Median age (years)	55
Histological types (N, %)	
High grade serous carcinoma	42 (85,8%)
High grade endometrioid carcinoma	4 (8,2%)
Mucinous carcinoma	1 (2%)
Carcinosarcoma	1 (2%)
Undifferentiated carcinoma	1 (2%)
Stage at diagnosis	
I	4 (8,2%)
II	2 (4.1%)
III	29 (59,2%)
IV	14 (28,5%)
BRCAmut	
BRCA1	27 (55,2%)
Ovarian cluster	6 (22,2%)
BRCA2	22 (44,8%)
Ovarian cluster	1 (4,5%)
iPARP treatment	33 (67.3%)
Olaparib	28 (84.8%)
Niraparib	5 (15,2%)

Conclusions: A trend towards significance is seen regarding the worse prognosis conferred by the BRCA mutation located in the OC association cluster. Treatment with iPARP seems to compensate for this point, at least partially. A larger number of patients is necessary to validate this hypothesis, for which national registry work launched in various countries, or even collaboration between them, can be a very useful tool.

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62P A multi-center real-world study of the efficacy and safety of PARP inhibitors in patients with ovarian cancer in Spain

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Background: PARP inhibitors (PARPi) have changed the treatment paradigm in ovarian cancer. The objective of this collaborative study among 21 Spanish hospitals is to collect real-world data on the efficacy and safety of ovarian cancer patients treated with PARPi.

Methods: We conducted a post-authorization observational study with the three available PARP inhibitors (olaparib, niraparib, and rucaparib) in each of their indications. Data were collected from medical records. Clinical-pathological variables, treatment, and survival were recorded. The primary endpoint was progression-free survival (PFS) in the first-line setting and maintenance after platinum-sensitive (PS)

relapse. Secondary endpoints included PFS in relevant clinical and molecular subgroups (FIGO stage, type of surgery, BRCAm, HR status). Patients were included from November 2022 to March 2024. Medians and proportions were used for descriptive analysis, and PFS and overall survival (OS) were estimated using Kaplan-Meier method.

Results: A total of 391 patients were enrolled in the study, with a median age of 59 years. High-grade serous carcinoma was the most frequent histology (95%). According to FIGO stage at diagnosis, 65% had stage III, and 35% had stage IV. Primary debulking surgery was performed in 50% of the patients (40% optimal), interval debulking surgery in 40%, and 10% were irresectable. Germline BRCA1/2 mutations were present in 25% of the sample. Homologous recombination (HR) testing in first-line was available in 107 patients, and 49% were classified as HR deficient. The median follow-up was 46 months. The table shows the estimated median PFS in both first-line and PS relapse. The hematological adverse events were the most frequent grade 3 events, with an overall discontinuation rate due to adverse events of 10%.

Table: 62P Median PFS in months (95% confidence interval) in the overall cohort

First-line		Platinum-sensitive relapse	
Niraparib (n=63)	17.0 (4.9-NR)	Niraparib (n=153)	8.5 (4.0-21.3)
Olaparib (n=46)	NR (16.3-NR)	Olaparib (n=60)	19.3 (7.8-NR)
Olaparib + bevacizumab (n=10)	25.0 (25.0-NR)	Rucaparib (n=23)	6.5 (3.0-26.8)
Bevacizumab (n=76)	19.1 (8.0-68.4)		

Conclusions: This multicenter real-world study shows meaningful clinical benefits in PFS with PARPi in advanced ovarian cancer. Safety analyses were consistent with clinical trials.

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63P A real-world comparison of the tolerability and toxicity of niraparib in older and younger women with high-grade serous ovarian carcinoma

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Background: Patients with newly diagnosed or recurrent platinum-sensitive advanced ovarian cancer benefit from maintenance Niraparib as per the PRIMA and NOVA trials. These trials recruited younger patients (median age 57 and 63 respectively) as compared to real-world clinical practice.

Methods: A single centre retrospective analysis was carried out on all high grade serous ovarian cancer patients commenced on Niraparib in the first or subsequent line setting between January 2020 and June 2022 in the Edinburgh Cancer Centre.

Results: 111 patients were included in this study; 61 patients $\geq$70 years and 50 patients $<$70 years. The median number of cycles in both groups was 7 and median follow up time was 28.9 and 26.9 months in the older and younger groups respectively. A significantly greater proportion of older than younger patients started on the lowest dose of Niraparib (100mg) (13.1% vs 2.0%, P=0.0361). The 3 most common toxicities experienced in the older and younger groups were nausea/vomiting, haematological toxicity and fatigue (59.0% vs 60.0%, 52.5% vs 54.0%, 59.0% vs 50.0%). All incidences of nausea/vomiting and fatigue were Grade 1-2 in severity. Grade 3-4 haematological toxicity was seen in 19.6% and 30.0% of the older and younger groups respectively (P=0.184). Dose interruptions and reductions were seen similarly in the older and younger groups (85.2% vs 82.0%, 60.7% vs 62.0%). Haematological toxicity was the main reason for both. More older than younger patients stopped Niraparib due to toxicity (20.4% vs 7.5%, P=0.0948). No significant difference in median PFS was seen across the older and younger groups (7.0 vs 6.0 months, P=0.33). This median PFS is shorter than reported in clinical trials.

Conclusions: There was no significant difference in incidence of toxicities, dose interruptions or reductions across the older and younger groups. This may be confounded by a significantly larger proportion of older patients initiated on the lowest dose of Niraparib to improve tolerability. There was also a trend to more older than younger patients stopping treatment due to toxicity. This may reflect a distinction in management due to patient fitness and wishes as well as treatment intent.

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64P Response to PARPi in advanced high-grade serous ovarian cancer (HGSOC) based on the location and type of BRCA mutation: Real-world data from a Spanish tertiary university hospital

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Background: The presence of a BRCA mutation (BRCAm) is the only biomarker of response to treatment with platinum and PARP inhibitors (PARPi) validated in HGSOC. However, the location of the BRCAm and whether it is germline (gBRCAm) or somatic (sBRCAm) can affect the response to treatment and progression-free survival (PFS). Determining the influence of these factors is necessary to optimize treatment strategies.

Methods: Retrospective observational study of stage III-IV BRCAm or HRD+ HGSOC patients (pts) diagnosed in our institution from 01/2015 to 06/2023. Functional domains (FD) of BRCA1 were defined as RING, DNA-BD or BRCA1 C terminus (BRCT) and FD of BRCA2 were PALB2, RAD51-BD and DNA-BD. Presence of BRCA1/2 mutation was determined using NGS.

Results: Eighty-one pts were included: 32 BRCA1m (21 germline), 29 BRCA2m (12 germline) and 20 BRCAwt/HRD+ (7 germline: 2 PALB2m, 2 RAD51Cm, 2 RAD51Dm, 1 BRIP1m). 42 pts received first-line PARPi (24 olaparib, 8 niraparib and 10 bevacizumab/olaparib). Of the pts who received olaparib, 11 had disease progression/relapse (2 after the end of treatment, 2 after stopping treatment due to toxicity and 7 during it). Pts with a shortest time to progression (3-11 months (m)) had sBRCA1m and/or mutations in the RING or BRCT domains of BRCA1, and they achieved lower overall survival (OS) than expected in BRCAm pts due to poor response to successive treatments. Four pts who received niraparib progressed to treatment, all of them during it (1 BRCAwt/HRD+), and sBRCA1m pts showed worse prognosis. Statistical analysis indicates a positive trend in OS for pts with a missense BRCAm. 12 pts received olaparib in second line of treatment, and 5 of them showed disease progression (2 pts during treatment: 1 with BRCA1 nonsense mutation showed PFS of 3 m). Pts in response reached a median treatment time of 81'5 m. 1 of 3 pts who received niraparib progressed during treatment (showing mutation in the RING domain of BRCA1). Median follow-up was 32'5 m (1-123).

Conclusions: In our study, mutation on BRCA1 RING or BRCT showed a poor response to PARPi and lower survival consistently with previous reports, highlighting among them somatic mutations.

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65P Chemotherapy response score (CRS) and efficacy of PARP inhibitor (PARPi) treatment in advanced epithelial ovarian cancer (AEOC)

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Background: BRCA 1/2 mutations (BRCAmut) and homologous recombination deficient (HRD) status are well-established prognostic and predictive factors of the magnitude of response to PARPi. CRS is also known as a prognostic value in patients with AEOC undergoing interval debulking surgery after neoadjuvant chemotherapy (NACT). The role of CRS in predicting PARPi response in AEOC is unclear and is the aim of this analysis.

Methods: We conducted a retrospective study of 45 patients diagnosed AEOC, FIGO stage III-IV, treated with platinum-based NACT followed by interval debulking surgery, from April 2018 to June 2023. Somatic mutations and HR status were detected by BRCA MASTR Plus Dx, Myriad myChoice CDx Plus, Foundation One Medicine or SOPHiA Genetics and germline mutations were detected by Hereditary OncokitDx. Pathologic tumor response was evaluated using CRS (CRS1=no/minimal response; CRS2=appreciable response; CRS3=complete/near-complete response). Primary end point was Progression Free Survival (PFS) according to CRS (CRS1/2 vs 3) in patients receiving PARPi.

Results: 43 patients had high grade serous AOC and 2 had high grade endometroid AOC. 32 were stage III and 13 stage IV. 13 had CRS3 and 31 had CRS1/2, 1 undetermined. 36 (80%) had complete resection. Considering the entire population, 24.4% of tumors were BRCAmut and 37% had HRD status. 22 patients (48%) received PARPi (2 olaparib, 10 niraparib). Out of this 22: 12 had CRS3 and 10 had CRS1/2. PFS according to CRS in patients receiving PARPi were: BRCAmut & CRS3 23 months versus 43 months for the BRCAmut & CRS1/2 (p=0.49); HRD & CRS3 24 months versus 43 months for the HRD & CRS1/2 (p=0.47); HR proficient (HRP) & CRS3 25 months versus 13 months for the HRP & CRS1/2 (p=0.19).

Conclusions: Due to small sample, we did not find any statistical differences on PFS in the different subgroups. Contrary to expectations, we did observe a tendency of longer PFS in CRS1/2 versus CRS3 for BRCAmut and HRD tumors, indicating no added value for CRS in these situations. In contrast, a tendency of better PARPi response in the CRS3 versus CRS1/2 was noticed in HRP subgroup, suggesting that platinum sensitivity according to CRS could predict a better PARPi response in HRP population.

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66P PARPi and myeloid neoplasia: The Italian MITO-MaNGO experience based on a multicentric survey

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Background: The risk of PARPi related myeloid neoplasias (PrMN) in PARPi treated patients has been a growing concern. Morice's metanalyses, taking into consideration the trials and the World Health Organization (WHO) Vigibase, has shown a significant elevation of the risk (Peto OR 2,63 [95% CI 1,13—6,14], p=0,026) with no inter study heterogeneity. While few mono-centric studies have been published, data on a wider scale is lacking. Our aim was to gauge the incidence of PrMN in a real-life setting.

Methods: A survey of 71 items was proposed to 17 MITO and MaNGO centers. Each center counted all patients ever treated with PARPi within the standard of care. Details on the choice of PARPi, line of treatment, length of therapy and BRCA mutational status were collected. Data cutoff was December 2023.

Results: A total of 2320 patients were collected (1254 BRCA mutated). Out of this number, 56 myeloid neoplasias were diagnosed, 35 MDS and 21 AML respectively (2.55%). Two patients had both MSD and AML. Thirty-two were BRCA 1 or 2 mutated, (2.5% of the total). Thirty-two had received Olaparib (resulting in an incidence of 2.5% in the total of patients treated with Olaparib at any line), 19 had received Niraparb (2%) and 4 (3.4%) had received Rucaparib respectively. The length of PARPi therapy before the diagnoses did not show a direct link between a longer exposure to PARPi and a higher risk of PrMN, with 7.4% of patients developing MSD or AML before six months and 20.4% after 6 to 12 months of maintenance therapy. Of all patients treated at each line, 0.52% developed a myeloid neoplasia after receiving PARPi in the first line, 4.2% in the 2°, 1.8% in the 3°, 10.8% in the 4° and 12.2% over the 4° line. Regarding the outcome there were 4 remissions, 4 partial responses, 8 progressions and 37 deaths.

Conclusions: While still considered a rare collateral effect, PrMN have a much worse clinical outcome than non-therapy related MN which was confirmed. While PrMN did not seem more present in BRCA mutated patients than in BRCA wild type (2.5% vs 2.6%), the second, fourth and over the fourth lines of treatment had higher percentages of incidence. No difference in risk among PARPi was noted. As we move towards a better outcome for OC patients, it is paramount to identify higher risk cases and understand how to treat them accordingly.

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67P Factors that may influence physicians' perceptions of "cure" in ovarian cancer: A discrete choice experiment

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Background: Novel therapies increase optimism for a cure for ovarian cancer (OC). Yet, physicians remain reticent towards discussing "cure" as a treatment outcome and the factors associated with physicians' perceptions of "cure" in OC are poorly understood. We evaluated the influence of patient characteristics, including treatment outcomes, on oncologists' perceptions of better prognosis and "cure" in OC.

Methods: US oncologists (N=150) completed a cross-sectional survey in spring 2023 which included a discrete choice experiment (DCE) that iteratively presented 2 hypothetical patient profiles varying on 8 attributes (Table). Physicians select the profile they associated with a better prognosis. Attribute-level preference weights were estimated with hierarchical Bayesian models; a larger absolute difference between the most- and least preferred attribute levels indicated greater influence on preferences. Differences in relative attribute importance (RI) estimates were evaluated by practice setting, specialty and 12-month OC case volume.

Results: Factors that most influenced optimism for better prognosis were: increasing patients' progression-free years from 2 to 10 (RI=22.0%), reducing cancer stage from IV to II (RI=20.0%), and changing CA125 from rising to low/normal (RI=17.7%). Younger age was more important to academic versus community oncologists ($p<0.01$) and to oncologists with >50 epithelial OC cases in the past 12 months ($p<0.01$). The absence of ascites influenced gynecological oncologists' likelihood of giving a better prognosis than medical/hematological oncologists ($p=0.02$).

Table: 67P Attributes, levels & preference weights from the DCE

Attribute	Level	Preference Weight
Patient age (years)	45	0.45
	60	0.09
	75	-0.54
Received anti-vascular endothelial growth factor-(VEGF) therapy in first line	Yes	-0.03
	No	0.03
Cancer stage	II	1.5
	III	-0.11
	IV	-1.39
BReast CAncer gene (BRCA)/Homologous Recombination Deficiency (HRD) status	BRCA wild type/HRD-test (-)	-0.08
	BRCA wild type/HRD-test (+)	-0.44
	BRCA mutation	0.52
Cytoreduction	Complete gross resection	0.22
	≤ 1cm residual tumor	0.17
	>1cm residual tumor	-0.4
Ascites present	Yes	-0.57
	No	0.57
Progression free years	2	-1.7
	5	-0.03
	10	1.73
Cancer antigen (CA)125 status	Low/normal	1.41
	Rising	-1.41

Conclusions: Oncologists' perceptions of better prognosis and potential for cure in OC may be influenced by several patient and treatment outcomes, such as longer PFS, lower stage, and CA125 status. Use of therapies that improve factors linked to better prognosis may increase oncologists' willingness to discuss "cure" with OC patients.

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68P The effectiveness of treatment of ascites due to recurrence of platinum-refractory ovarian cancer using metronomic chemotherapy

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Background: The growth rate of this indicator compared to 2020 was 16.4%, and among the female population: breast cancer (24.0), cervical cancer (10.6), and ovarian cancer (5.7 per 100,000 population). The incidence of ovarian cancer (RY) throughout the world and in Uzbekistan tends to constantly increase. In Uzbekistan, the incidence was 5.7 per 100,000 population in 2021; in 2015, this figure was 4.7.

Methods: The object of the study was 116 female patients with a verified diagnosis of ovarian cancer complicated by ascites (OCA) who were treated at the Russian National Medical Research Center for Medical and Radiological Research as well as at the Samarkand branch from 2017 to 2023. Patients were randomized as follows: Group 1 received standard palliative therapy: gemcitabine 1000 mg/m2 on days 1, 8, 15, and bevacizumab at a dose of 7.5—15 mg/kg once every 3 weeks (n = 42); Group 2 patients receiving metronomic chemotherapy:cyclophosphamide 50 mg/day orally daily without a break (n = 33); and Group 3 patients receiving metronomic chemotherapy: cyclophosphamide 50 mg/day. orally daily without interruption, and pazopanib 400 mg days 1—28 (n = 41).

Results: Please see the table below.

Table: 68P

	Study Groups								
	Group 1, n=42			Group 2, n=33			Group 3, n=41		
	abs	M (%)	m	abs	M (%)	m	abs	M (%)	m
Full effect	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Partial effect	14	33.33	7.27	14	42.42	8.60	18	43.90	7.75
Stabilization	10	23.81	5.57	10	30.30	8.00	14	35.15*	4.41
Progression	18	42.86	7.64	9	27.27*	7.75	9	21.95*	6.4

Conclusions: Was developed a new method of metronomic maintenance chemotherapy, which is the use of cyclophosphamide and pazopanib in low doses in patients with ascites caused by platinum-resistant recurrent ovarian cancer after completion of second-line chemotherapy. This method helps to achieve disease control in 65.7% of patients and increase the median time to progression from 7.4 to 9.1 months. (plog-rank <0.0001), median overall survival observed from 15.0 to 22.7 months. (plog-rank = 0.0005).

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69P Use of bevacizumab for patients with FIGO stage IIIB to IV epithelial ovarian cancer undergoing primary debulking surgery and its association with oncologic outcomes: A German cancer registry study

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Background: We aimed to evaluate the use of bevacizumab for patients with FIGO stage IIIB to IV advanced epithelial ovarian cancer (EOC) undergoing primary debulking surgery (PDS) in the primary disease setting using real-world data from a German cancer registry.

Methods: We identified patients with the initial diagnosis of FIGO stage IIIB to IV EOC, reported between 2009 and 2022 from the clinical cancer registry of Baden-Wuerttemberg, Germany. We excluded patients with recurrent disease, neoadjuvant chemotherapy, inoperable disease, or with insufficient information on systemic treatment or follow-up. The influence of Bevacizumab in addition to Carboplatin and Paclitaxel (Cb+T+Bev vs. Cb+T) on progression-free survival (PFS) and overall survival (OS) was assessed using Kaplan- Meier statistics and multivariate Cox regression models, adjusted for age, grading, stage, tumor histology, use of poly (adenosine diphosphate [ADP]—ribose) polymerase (PARP) inhibitor, and PDS outcome (macroscopic complete gross resection, residual disease ≤1cm and >1cm).

Results: A total of 835 patients with a median follow-up of 25.1 months were identified: 542 patients (64.9%) had FIGO stage IIIB/C disease, 293 (35.1%) had FIGO stage IV disease. Post-operative residual disease was complete gross resection in 468 (56.0%), ≤1cm in 181 (21.7%), and >1cm in 186 (22.3%). Median age was 63.8 years

(SD 11.1). Use of Cb+T+Bev was 40.1% (335/835) overall, 43.8% (205/468) for patients with complete gross resection, 38.7% (70/181) for patients with ≤1cm residual disease, and 32.3% (60/186) for patients with >1cm residual disease. Cb+T+Bev was not associated with improved OS (HR 0.88, 95% CI 0.73-1.07, P=0.216) or PFS (HR 0.95, 95% CI 0.79-1.10, P=0.610). Also in the subgroup of patients with >1cm residual disease, Cb+T+Bev was not associated with improved OS (HR 0.90, 95% CI 0.61-1.31, P=0.565) or PFS (HR 0.86, 95% CI 0.56-1.32, P=0.483).

Conclusions: This data suggests that bevacizumab is often used for patients with primary FIGO stage IIIB to IV EOC undergoing PDS although it does not provide an OS or PFS benefit.

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70P Tumor biomarkers contribute to the clinical management of the O-RADS MRI risk stratification system in epithelial ovarian tumors

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Background: This retrospective study aimed to evaluate the accuracy of the O-RADS MRI risk stratification system for characterising EOTs, especially the BEOTs. More importantly, the efficiency of tumor biomarkers in distinguishing the nature of EOTs and guiding clinical management for each O-RADS MRI risk category was explored in Department.

Methods: 54 benign, 104 borderline and 203 malignant EOTs were enrolled and retrospectively assigned risk scores. The diagnostic efficacy of CA125, HE4 and ROMA index in distinguishing EOTs within each risk category was evaluated using ROC curves. Clinical management recommendations were made for EOTs across all risk categories by integrating tumor biomarkers.

Results: No MEOTs were assigned a risk score of 2, while 0.96% BEOTs and 29.63% benign EOTs scored O-RADS MRI 2. Therefore, EOTs assigned a score of 2 are eligible for minimally invasive or conservative, or elective surgery. 66.67% of benign, 50.96% of borderline, and 13.80% of malignant EOTs were assigned a score of 3. Among EOTs with O-RADS MRI 3, 96.43% MEOTs and 98.11% BEOTs had the feature of a low-risk time-intensity curve (TIC), compared to only 16.67% in benign EOTs. CA125 ≥ 60.39 U/ml helped screen MEOTs from EOTs with a low-risk TIC and O-RADS MRI 3 for timely surgical evaluation. Only 3.7% (2/54) benign EOTs were assigned as O-RADS MRI 4/5, while BEOTs and MEOTs were 48.08% and 86.2%, respectively. Overall, EOTs with a score of 4/5 should refer to semi-elective surgery due to the low probability of benign lesions. Specifically, minimally invasive surgery is recommended for EOTs with a ROMA index < 20.14% (premenopausal)/29.9% (postmenopausal), while comprehensive staging or cytoreductive surgery is recommended for the remaining. It is worth mentioning that there was a high proportion of fertility preservation needs and a high possibility of conducting fertility preservation surgery among premenopausal EOT patients assigned as O-RADS MRI 4/5 with a ROMA index < 20.14%.

Conclusions: The O-RADS MRI risk score accurately distinguished between benign EOTs and BEOTs/MEOTs. CA125 and the ROMA index helped further determine EOTs and facilitate clinical management in the O-RADS MRI 3/4/5 categories.

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71P Pre- and post-polyphenol intake and ovarian cancer survival: Evidence from a prospective cohort study

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Background: Although polyphenols have shown potential in anti-cancer activities, their impact on improving ovarian cancer (OC) survival remains unknown. Therefore, we aim to first investigate the association between dietary polyphenol intake and OC survival, providing valuable insights into potential interventions.

Methods: The prospective cohort recruited 560 patients with OC to assess the association of polyphenol intake, not only pre- and post-diagnosis but also the change from pre- to post-diagnosis with OC survival. Dietary intakes of total polyphenols and their five groups (flavonoids, phenolic acids, lignans, stilbenes, and other polyphenols) were assessed using a validated 111-item food frequency questionnaire. Overall survival (OS) was tracked through active follow-up and medical records until February 16th, 2023. Cox proportional hazard regression models were applied to calculate the hazard ratios (HR) and 95% confidence intervals (CI).

Results: During a median follow-up of 44.4 months, 211 all-cause deaths were identified. We observed an improved OS with the highest compared with the lowest tertile of dietary flavonoids for both pre-and post-diagnosis ($HR_{T3\ vs\ T1}$=0.60, 95% CI=0.39−0.94 for pre-diagnosis; and $HR_{T3\ vs\ T1}$=0.58, 95%CI=0.36-0.93 for post-diagnosis). Consistently, an evident linear trend was observed for polyphenol and flavonoid intake with OC survival. Of note, compared to the stable group (change within 10%), the decreased intake (change of more than 10%) of total polyphenols and five polyphenol groups was significantly associated with worse OS in patients with OC. Additionally, significant associations were generally consistent across sensitivity and stratified analyses.

Conclusions: The consumption of dietary polyphenols, as well as its five groups, has a protective association with OC survival.

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72P Real-world data of treatment and outcome of patients with advanced ovarian cancer (AOC) in Germany: QS OVAR of the AGO Study Group

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Background: Recent and detailed data regarding treatment quality of patients with AOC in the era of precision medicine are largely unknown in Germany.

Methods: All German hospitals treating patients with ovarian cancer were asked to document prospectively all patients with first diagnosis in the third quarter in 2021. Details of tumor, treatment and outcome were documented. Here, we report tumor and treatment characteristics.

Results: In total, 598 pts with AOC were documented. The primary debulking surgery (PDS) rate was 429/598 (71.7%) and complete resection (CR) at PDS was achieved in 252/429 pts (58.7%), 92/598 pts (15.4%) had interval debulking surgery and 77/598 pts (12.9%) had no surgery. In total, 514/598 pts (86.0%) were treated with chemotherapy. 490/514 (95.3%) received carboplatin/paclitaxel and 401/514 (78.0%) received additional maintenance therapy. 470 patients had high-grade histology and were treated with chemotherapy. The BRCA testing rate in this population was 390/470 (83.0%) and HRD testing rate was 245/470 (52.1%). In total, 90 of 390 tested patients were BRCA-positive (23.1%) and 101/245 patients were HR deficient (41.2%). BRCA+ patients were treated with bevacizumab/PARPi in 58.9%, PARPi single agent in 31.1%. The rates in BRCAwt/HRd were 62.9% and 12.0%, respectively. HRp tumors were treated mainly with bevacizumab (70.8%) or by PARPi in 15.4%. BRCAwt/HRD unknown patients were treated mainly with bevacizumab (35.8%) or PARPi (30.5%). Patients who were not tested (15.8%) were mainly treated with chemotherapy only (58.0%) and bevacizumab (35.8%). The rates of chemo only patients in the other subgroups varied between 2.2% and 22.1%.

Conclusions: Most patients in Germany with AOC are treated with primary surgery followed by chemotherapy including a maintenance therapy. The rates of BRCA and HRD testing are high and PARPi in primary OC are often used already after a short period after approval in Germany.

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73P Association between pre- and post-diagnosis Healthy Eating Index 2020 and ovarian cancer survival: Evidence from a prospective cohort study

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Background: Previous studies on the association between diet quality and ovarian cancer (OC) survival are limited and inconsistent. We evaluated the relationship between pre- and post-diagnosis diet quality based on the Healthy Eating Index-2020 (HEI-2020), as well as their changes and OC survival.

Methods: HEI-2020 was evaluated using validated food frequency questionnaires. Overall survival (OS) was followed up until February 16th, 2023. Cox proportional hazards regression models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).

Results: We included 549 OC cases with a median follow-up of 44.9 months, representing 206 total deaths. Higher HEI scores were associated with better OS (pre-diagnosis: $HR_{T3\ vs.\ T1}$ 0.66, 95%CI: 0.46-0.95, HR_{1-SD} 0.84, 95%CI: 0.73-0.96; post-diagnosis: $HR_{T3\ vs.\ T1}$ 0.71, 95%CI: 0.51-1.00, HR_{1-SD} 0.79, 95%CI: 0.68-0.92). Compared to the stable group, the group with decreased HEI scores (>3%) from pre- to post-diagnosis had worse OS (HR 2.11, 95%CI: 1.36-3.26). Compared to patients with consistently high HEI scores, individuals with decreased HEI scores after diagnosis had a lower OS (HR 1.71, 95%CI: 1.09-2.68).

Conclusions: High pre- and post-diagnosis diet quality was associated with improved OC survival, whereas deterioration in diet quality after diagnosis was associated with decreased OC survival.

Legal entity responsible for the study: The authors.

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74P The association of dietary fat and fatty acid intake with ovarian cancer survival: Findings from the OOPS — A prospective cohort study

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Background: Dietary fat and fatty acid intakes impact the occurrence and development of several cancers. However, the evidence regarding dietary fat and fatty acid intake and ovarian cancer (OC) survival is limited. We, thus, aimed to provide a report on the associations between fat and fatty acid intake and OC survival.

Methods: This prospective cohort study analyzed data collected between 2015 and 2020 from 703 newly diagnosed OC patients, aged 18—79 years. Deaths were ascertained until March 31, 2021, via medical records and active follow-up. Dietary intake was derived from a validated food frequency questionnaire. Cox proportional hazard models were used to explore associations. Furthermore, several subgroup and sensitivity analyses were also performed.

Results: A total of 130 patients died during a median follow-up of 37.17 (interquartile: 24.73—50.17) months. Relative to the lowest tertile of intake, patients with the highest tertile of pre-diagnosis total fatty acid, total saturated fatty acid (SFA), shorter-chain SFA, long-chain SFA, total monounsaturated fatty acid (MUFA), and animal-based MUFA intake had worse overall survival. Additionally, poor survival associated with several common fatty acid intakes, including capric acid, palmitic acid, stearic acid, and oleic acid, was also observed. Furthermore, results from numerous subgroup and sensitivity analyses were consistent with the main finding.

Conclusions: We provide evidence linking pre-diagnosis consumption of total fatty acid, SFA, shorter-chain SFA, long-chain SFA, total MUFA, and animal-based MUFA with worse overall survival of OC patients.

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Disclosure: All authors have declared no conflicts of interest.

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75P Association between pre-diagnosis screen time and ovarian cancer survival: Findings from the ovarian cancer follow-up study — A prospective cohort study

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Background: Screening time (ST), a highly prevalent sedentary behaviour, may affect a variety of health outcomes. However, the relationship with ovarian cancer (OC) survival is relatively unknown. The objective of our study was to firstly clarify the association between ST and OC survival based on the Ovarian Cancer Follow-Up Study, a prospective cohort study in China.

Methods: We assessed the association between ST and OC survival based on a prospective cohort study of 590 newly diagnosed OC patients aged 18-79 years. Deaths were ascertained until March 31, 2021, via medical records and active follow-up. Multivariable-adjusted Cox proportional hazards regression was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) with pre-diagnosis ST and all-cause mortality of OC. The isotemporal substitution analysis was used to examine the risk of OC mortality associated with ST with alternative activities. Additionally, we explored the interaction between ST and demographic and clinical characteristics including immunohistochemical biomarkers.

Results: During a median follow-up of 42.00 (interquartile: 31.00-52.73 months), 130 deaths were identified. Patients who reported ≥5, compared with <2, hours/day of pre-diagnosis ST had higher risk of OC mortality (HR=2.58, 95%CI: 1.40-4.77, P trend<0.05). Similar adverse effect was found in phone and computer viewing ($HR_{\geq 3\ vs.\ <1\ hours/day}$ =2.24, 95%CI: 1.30-3.84, P trend<0.05), whereas finding was non-significant for TV viewing time ($HR_{\geq 3\ vs.\ <1\ hours/day}$ =1.61, 95%CI: 0.77-3.38, P trend=0.10). Additionally, isotemporal substitution models showed reduced risk of OC mortality when replacing 2-hour/day of ST with 2-hour of walking (HR=0.50, 95% CI: 0.26-0.97) or sleeping (HR=0.52, 95%CI: 0.38-0.71). Furthermore, we observed curvilinear association between ST and OC survival. Interestingly, there were

significant interactions between ST and WT-1, estrogen receptor, and progesterone receptor expression ($P<0.05$).

Conclusions: Our findings firstly indicated that high level of pre-diagnosis ST potentially contributed to increasing all-cause mortality among OC patients. Further studies are warranted to confirm our findings.

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76P Association of long-term particulate matter exposure with all-cause mortality among patients with ovarian cancer: A prospective cohort

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Background: Evidence of the association between particles with a diameter of 2.5 μm or less ($PM_{2.5}$) in long term and ovarian cancer (OC) mortality is limited.

Methods: This prospective cohort study analyzed data collected between 2015 and 2020 from 610 newly diagnosed OC patients, aged 18—79 years. The residential average PM2.5 concentrations 10 years before the date of OC diagnosis were assessed by random forest models at a 1 km × 1 km resolution. Cox proportional hazard models fully adjusted for the covariates (including age at diagnosis, education, physical activity, kitchen ventilation, FIGO stage, and comorbidities) and distributed lag non-linear models were used to estimate the hazard ratios (HRs) and 95 % confidence intervals (CIs) of $PM_{2.5}$ and all-cause mortality of OC.

Results: During a median follow-up of 37.6 months (interquartile: 24.8—50.5 months), 118 (19.34 %) deaths were confirmed among 610 OC patients. One-year $PM_{2.5}$ exposure levels before OC diagnosis was significantly associated with an increase in all-cause mortality among OC patients (single-pollutant model: HR = 1.22, 95 % CI: 1.02—1.46; multi-pollutant models: HR = 1.38, 95 % CI: 1.10—1.72). Furthermore, during 1 to 10 years prior to diagnosis, the lag-specific effect of long-term $PM_{2.5}$ exposure on the all-cause mortality of OC had a risk increase for lag 1—6 years, and the exposure-response relationship was linear. Of note, significant interactions between several immunological indicators as well as solid fuel use for cooking and ambient $PM_{2.5}$ concentrations were observed.

Conclusions: Higher ambient $PM_{2.5}$ concentrations were associated with an increased risk of all-cause mortality among OC patients, and there was a lag effect in long-term $PM_{2.5}$ exposure.

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Disclosure: All authors have declared no conflicts of interest.

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77P The association between chlamydia trachomatis infection and epithelial ovarian cancer risk using mendelian randomisation

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Background: History of Chlamydia trachomatis infection has previously been associated with epithelial ovarian cancer (EOC) in observational studies. The existing evidence base is deficient due to challenges in study design, influenced by residual confounding factors and small study populations, and it has not been possible to determine whether observed associations are causal. Mendelian randomisation (MR) is an epidemiological strategy aimed at removing potential biases which exist within conventional observational studies. This method uses single nucleotide polymorphisms (SNPs) as instrumental variables, enabling potential causal relationships between an exposure and outcome to be determined. To our knowledge, MR has never been used to explore this association.

Methods: We used a two-sample univariable MR approach to investigate the causal relationship between seropositivity to the C. trachomatis major outer membrane protein (momp) D antibody and EOC. MR analyses employed genetic associations derived from the UK Biobank as proxies for momp D seropositivity in 25 509 EOC cases and 40 941 controls that participated in the Ovarian Cancer Association Consortium (OCAC). Findings were replicated using a GWAS meta-analyses of global biobanks including the UK Biobank and FinnGen.

Results: Ten SNPs were identified to be associated with momp D seropositivity using the UK Biobank as the reference panel. Genetically-predicted momp D risk was associated with overall and high-grade serous EOC in inverse-variance weighted MR analysis using OCAC data (odds ratio (OR) 1.06; 95% confidence interval (CI) 1.02—1.10, and OR 1.08; 95%CI 1.01—1.16, respectively). Replication using UK Biobank and FinnGen yielded similar results for overall EOC (OR 1.11; 95%CI 1.01—1.22).

Conclusions: This MR study confirms the causative link between C. trachomatis infection and overall and high-grade serous EOC. As a key modifiable risk factor for future serous EOC, primary prevention of C. trachomatis infection is a crucial public health target and may help reduce burden of EOC.

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78P Age-adjusted trends of malignant ovarian granulosa cell tumor

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Background: Granulosa cell tumor (GCT) is a rare ovarian neoplasm characterized by its distinct histological features and variable clinical presentation. Despite being one of the most common sex cord-stromal tumors of the ovary, granulosa cell tumors remain relatively rare, contributing to a limited understanding of their incidence rates and trends, genetic predisposition, and clinical behavior which has resulted in underdeveloped guidelines for its screening and treatment. So, this study aims to add more evidence and data about this rare type.

Methods: Data of 1627 patients were extracted from the Surveillance, Epidemiological, and End Results (SEER) database diagnosed from 2000-2020. We analyzed age-adjusted trends and age-adjusted incidence rates. Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130) standard; confidence intervals are 95% for rates (Tiwari mod) and trends. Percent changes were calculated using 1 year for each endpoint; APCs were calculated using weighted least squares method.

Results: The overall incidence rate was 0.1. The age-adjusted trends showed an annual percent change (APC) of 0.4 (95% CI -0.6 to 1.4), and percentage change (PC) of -4.7 with. This increase was among all ages, and races. When stratified by race from 2000 to 2020, Black, White, and Asian populations exhibited PCs of 21.7, -11.8, -79.6 respectively and APCs of 1.7 (95% CI: -0.4 to 3.8), -0.1 (95% CI -1 to 0.8), -0.7 (95% CI -4.6 to 3.3), and respectively.

Conclusions: Granulosa cell tumors showed poor overall survival. It showed an overall low incidence rate however, there is an expected increase in the next years as demonstrated by APC result. While the Black race exhibited an increasing incidence rate, Asian and White races showed decreasing rates. This expected increase in the incidence rate combined with poor survival outcomes of Granulosa cell tumors warrants the development of screening guidelines. We recommend focusing on the black race as they have the highest incidence rate.

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79P Plant-based diet indices and their interaction with ambient air pollution on the ovarian cancer survival: A prospective cohort study

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Background: Ambient air pollution might serve as a prognostic factor for ovarian cancer (OC) survival, yet the relationships between plant-based diet indices (PDIs) and OC survival remained unclear. We aimed to investigate the associations of comprehensive air pollution and PDIs with OC survival and explored the effects of air pollution-diet interactions.

Methods: The present study encompassed 658 patients diagnosed with OC. The overall plant-based diet index (PDI), the healthful PDI, and the unhealthful PDI (uPDI) were evaluated by a self-reported validated food frequency questionnaire. In addition, an air pollution score (APS) was formulated by summing the concentrations of particulate matter with a diameter of 2.5 microns or less, ozone, and nitrogen dioxide. Cox proportional hazard models were applied to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) of overall survival (OS). The modifying effect of PDIs on the relationships between APS and OS was further examined by incorporating interaction terms.

Results: Throughout a median follow-up of 37.60 (interquartile: 24.77—50.70) months, 123 deaths were confirmed. Comparing extreme tertiles, higher uPDI was associated with lower OS of OC (HR=2.06, 95%CI=1.30, 3.28; P-trend<0.01), whereas no significant association was found between overall PDI as well as hPDI and OC survival (P-trend > 0.05 for both). Higher APS ($HR_{\text{for per interquartile range}}$=1.27, 95% CI=1.01, 1.60) were significantly associated with worse OC survival, and the associations could be exacerbated by adhering to uPDI. Notably, an additive interaction was identified between combined air pollution and uPDI ($P < 0.005$ for high APS and high uPDI). We also found that adherence to overall PDI aggravated associations of air pollution with OC survival (P-interaction=0.006).

Conclusions: Joint exposure to various ambient air pollutants was significantly associated with lower survival among patients with OC, particularly for those who predominantly consumed unhealthy plant-based food.

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80TiP A phase III randomized controlled trial in primary stage three and four ovarian cancer after interval cytoreductive surgery (FOCUS)

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Background: The addition of hyperthermic intraperitoneal chemotherapy (HIPEC) during interval cytoreductive surgery increases progression-free and overall survival for patients with stage III ovarian cancer in two randomized controlled trials (OV-HIPEC-01 and KOV-HIPEC-01) in the era of platinum. The aim of this trial is to identify the survival benefit of HIPEC in stage III & IV ovarian cancer with maintenance therapy of bevacizumab and/or PARP inhibitor.

Trial Design: The KOV-HIPEC-04 trial is an international, multicenter, 1:1 randomized, phase III trial that will enroll 520 patients with stage III & IV ovarian cancer who received neoadjuvant chemotherapy. Patients with residual tumor < 2.5mm after interval cytoreductive surgery will be randomized to the trial arm (HIPEC, 41.0-42.0°C cisplatin 75mg/m^2, 90 minutes) or control arm. After recovery from surgery, patients will receive postoperative platinum-based adjuvant chemotherapy followed by maintenance therapy with PARP inhibitor or bevacizumab following the institutional guideline based on BRCA/HRD status. The primary endpoint is to evaluate overall survival (OS); secondary objectives are progression-free survival (PFS), cancer-specific survival, time to the first subsequent therapy, safety, and quality of life. Assuming that the enrollment period is 5 years and the follow-up period is 3 years, the total number of events required is 263. Based on the log-rank test, the total number of subjects required to prove HR 0.67 with a two-sided alpha of 0.05 and 90% power is 494. Considering 5% drop-out, 520 patients will be finally enrolled.

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81TiP Rationale and study design of the KOV-HIPEC-02 trial: A randomized, multicenter, open-label phase III trial of hyperthermic intraperitoneal chemotherapy in platinum-resistant recurrent ovarian cancer

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Background: Hyperthermic intraperitoneal chemotherapy (HIPEC) during cytoreductive surgery has emerged to achieve a higher concentration of chemotherapeutic agents and treat micro-metastases on peritoneal surfaces. At advanced staged ovarian cancer treated with neoadjuvant chemotherapy, HIPEC during interval cytoreductive surgery with cisplatin 75-100mg/m^2 increases progression-free survival and overall survival (OV-HIPEC-01 and KOV-HIPEC-01). In chemotherapy-naïve ovarian cancer patients, survival benefit is not identified with HIPEC (KOV-HIPEC-01). And the meta-analysis revealed the survival benefit after recent exposure of chemotherapy. In ovarian cancer, HIPEC is thought to overcome chemotherapy resistance.

Trial Design: This trial (KOV-02) is currently actively enrolling, a multicenter, open-label, 1:1 randomized, phase III trial that will enroll 140 patients in platinum-resistant recurrent epithelial ovarian cancer. The trial is registered on ClinicalTrials.gov (NCT05316181). Institutional review board approval was obtained. The first patient was enrolled on April 07, 2022. The experimental arm will receive cytoreductive surgery and HIPEC (Doxorubicin 35mg/m^2 and mitomycin 15mg/m^2, 41.5-42.0°C) followed by physician-choice chemotherapy, and the control arm will receive physician-choice chemotherapy until disease progression or intolerable toxicity. The primary objective of the trial is to evaluate progression-free survival (PFS) between the HIPEC group and the control group. Secondary objectives are overall survival (OS), cancer-specific survival, safety, and quality of life. Assuming that the enrollment period is three years and the follow-up period is two years, the total number of events required is 121. Based on the log-rank test, the total number of subjects required to prove HR 0.6 with a two-sided alpha of 0.05 and 80% power is 126. Considering 10% drop-out, 140 patients are finally studied.

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ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

GENERAL INTEREST

82MO European multi-disciplinary tumor boards within the EURACAN network increasingly support management of patients with rare gynaecological tumors: 6-year activity results

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Background: The European Reference Network for Rare Adult Cancers (EURACAN) G2 domain deals with rare gynaecological cancers. Within this domain, virtual multidisciplinary tumor boards (MDTs) were implemented to advise on clinical management of complex cases. Here, we present the 6-year activity outcomes.

Methods: EURACAN G2 MDTs were organized monthly since November 2017 by Karolinska University Hospital, Stockholm. From March 2021 to March 2023, the MDTs were coordinated by Ospedale San Raffaele, Milan and since April 2023 by Hospital Clinico San Carlos, Madrid. A summary of cases was circulated to participants prior to MDTs and recommendations were distributed following each MDT. Background data and outcomes were registered prospectively. Follow up data were collected until March 2024.

Results: Between November 2017 and October 2023, 67 MDTs were held with participants from 18 countries and 20 centers. 260 patients were discussed (median 4 patients/session, range 1-12). Background data are shown in the table. The number of annual cases discussed has increased over time (+182% from 2017 to 2022), as is the median number of participants (+27% from 2020 to 2022). The MDTs resulted in a recommendation for pathological review and genetic sequencing in 24% and 9.6% of cases. Surveillance was recommended for 17% of cases. Alternative treatment opportunities were suggested for 58.7% of patients compared to the initial proposed management. Follow up data were available for 155 patients. Adherence to treatment recommendation was 94%. As a consequence of MDT recommendations, access to off-label therapies was achieved in 37 patients (23.8%) and 4 patients (2.5%) were enrolled in clinical trials abroad.

Table: 82MO

Patients N = 260	
DIAGNOSIS	
Gestational trophoblastic disease	51 (19.6%)
Malignant ovarian germ cell tumors	51 (19.6%)
Sex cord stromal tumors	38 (14.6%)
Other Rare ovarian histologies	76 (29.2%)
Rare uterine tumors	20 (7.8%)
Rare cervical tumors	11 (4.2%)
Other	13 (5%)
PREVIOUS LINES OF TREATMENT (median, range)	1 (0-10)
INDICATIONS FOR DISCUSSION*	
Initial management	117 (42.5%)
Relapse/disease Progression	133 (48.4%)
Other (follow up, further investigation)	25 (9.1%)

* N= 275 case discussions.

Conclusions: EURACAN G2 domain MDTs increasingly offer opportunity for clinical support and access to treatment alternatives for patients with complex rare gynecological cancers.

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83P Does the most common gynaecological cancer have an awareness blind spot? An Israeli preliminary study

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Background: We aimed to assess the awareness of healthy women who present online to endometrial cancer (EC) symptoms and risk factors among the Israeli population.

Methods: A survey regarding awareness of EC symptoms and risk factors was published in secure link on popular Israeli feminine social-media groups (>20,000 users), for accurate reach. The survey was conducted during May 2023 just before establishing June as Uterine Cancer Awareness Month. 1161 healthy women completed the survey voluntarily and anonymously.

Results: Thousand-fifty-six women met the survey's inclusion criteria. About 90% graduated college, all graduated high-school. The respondents were predominantly non-orthodox Jewish. More than quarter had a healthcare background. About two-thirds visit gynecologist at least once a year and about three-quarters had a gynecological examination in the last year. Most respondents were aware of other gynecological cancers, mainly cervical and ovarian cancers. Only about a quarter of the survey population had some awareness of EC symptoms. Nearly half of study population had some idea about signs and symptoms of any gynecological cancer. Regarding EC, more than a quarter were unaware of vaginal bleeding as an EC symptom and about 90% were unaware of any EC risk factors. More than three-quarters were defined as unaware at all. Only about 1% were fully aware. A statistical trend was observed as women older than 45 were more aware than younger. If a symptom occurs, most declared they would visit a gynecologist and only about 8% would refer to their general practitioner.

Conclusions: In our study population, we observed an extremely low awareness of the most common gynecological cancer in the industrial world (EC) which has easily diagnosed symptoms and risk factors. These striking findings, in a highly-educated and media-exposed group, are a wakeup-call for policymakers and regulators to take further action in order to achieve earlier diagnosis and curative prognosis in EC patients.

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84P Lack of diversity in clinical trials leading to Food and Drug Administration (FDA) approvals for gynaecological cancers

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Background: Clinical trials (CTs) leading to FDA approvals should give an estimation of investigational drugs' effect on enrolled patients (pts); however, enrollment criteria do not always accurately reflect a real-world population. As such, demographics and baseline characteristics of enrolled pts are essential to evaluating the applicability and safety of study drugs in the intended use population, particularly underrepresented minorities (URMs).

Methods: We searched "Drugs@FDA" to identify CTs that led to FDA drug approvals for gynecological cancers (GynC) between 2006 and 2024. We assessed the demographics and baseline characteristics, including ECOG Performance Status (PS), older adults (OA), race, and ethnicity in the published CTs.

Results: Out of 437 FDA approvals for solid tumors, 30 (4.6%) were for GynC based on 23 CTs: 73.9% phase 3, 21.8% phase 2, and 4.3% phase 1. Of note, 91.2% (21/23) of CTs led to approvals granted after 2014. ECOG PS was reported in 82.6% (19/23) CTs, with only 26.1% (6/23) CTs allowing the enrollment of pts with ECOG PS up to 2; the median proportion of enrolled pts with ECOG PS of 2 was 6.4 % (IQR 5.6-7.1%). The proportion of enrolled OA was reported in 30% (7/23) of CTs, all of which were published on or after 2014. The median proportion of enrolled OA was 36.8% (IQR 16.9-43.7%). Race was reported in 52.2% (12/23) of CTs, with a median proportion of 78.9% white pts enrolled (IQR 72.3-85.5). Ethnicity was reported in 30.4% (7/23) trials, but only in 13% (3/23) of CTs was reported separately from the race.

Conclusions: After years of limited therapeutic advancement, 2014 marked a new era for GynC treatment, with many FDA approvals. Despite the FDA's recommendations regarding data collection, demographics and baseline characteristics are still underreported. Data on traditionally URMs (non-white race, Hispanic or Latino ethnicity, and pts with a non-optimal PS) are often lacking and deserve further inclusion in future CTs to assess the applicability of new drugs in the real world. Actionable first steps to achieve this goal include expanding eligibility criteria, establishing engagement and partnerships with communities and institutions, and prioritizing diversity.

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85P Real-world molecular profiling in gynaecologic oncology: Shaping tailored treatments and leveraging genetic insights to provide personalized care

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Background: In the last years, diagnostic and therapeutic algorithms in gynecologic oncology have been dramatically revolutionized. Today, molecular diagnostic is mandatory to reach a complete histological diagnosis and to guide the oncologist through the most appropriate treatment. However, data from genomic analysis are extremely complex and multidisciplinary approach to interpret them is crucial, especially in high volume gynecologic cancer centers.

Methods: We retrospectively collected the records of 639 women with gynecologic tumors molecularly profiled at the National Cancer Institute of Milan (INT) between May 2020 and March 2024. All patients underwent molecular profiling using next generation sequencing test. ESMO Scale for Clinical Actionability of Molecular Targets (ESCAT) was used to select patients for targeted therapies.

Results: 74.6% patients had diagnosis of epithelial ovarian cancer (OC); 16.4% had endometrial carcinoma; 5.9% had cervical cancer and 2.9% had rare gynecological tumors (including vulvar carcinoma, non-epithelial OC, uterine leyomiosarcoma and others). For 437 (68.4%) patients we identified a pathogenic variant; 165 (25.8 %) patients had at least one actionable alteration with ESCAT scale I-II (21.1 % and 4.7 %, respectively). After MTB discussion, 22 received a personalized treatment: 13 received drugs as off-label request and 9 in clinical trials. Moreover, among patients with HGSOC, 103 (24.1%) had BRCA1/2 mutation and, from March 2023, we identified 44 (6.9%) patients BRCA 1/2 wild type but with genomic instability score (GIS) $>$ 42, eligible for olaparib+bevacizumab.

Conclusions: Comprehensive Genomic Profiling by NGS and ESCAT scale allow to identify several pathogenic variants, in addition to BRCA, and stratify actionable alterations guiding their therapeutic relevance other than genetic counseling for hereditary syndromes.

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86P Clinicopathological characteristics and oncologic outcomes of patients with gestational trophoblastic neoplasia initially manifesting as isolated pulmonary lesion

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Background: Gestational trophoblastic neoplasia (GTN) represents a group of gynecological malignancies related to pregnancy, which originates from placental trophoblasts, including choriocarcinoma, malignant invasive mole, epithelioid trophoblastic tumor (ETT) as well as placental site trophoblastic tumor (PSTT). In clinical practice, a typical group of patients with GTN were identified that initially manifesting as isolated pulmonary lesion. Previous studies were mainly case reports of that, and no cohort study was conducted to capture the clinical features of these patients and recognize the prognostic factors. Therefore, it is the first study of isolated GTN of the lung to provide guidance to manage these patients for favorable prognosis.

Methods: A number of 2358 GTN patients between 2000～2023 were retrospectively reviewed in our hospital, and 40 patients were eventually enrolled. The primary outcome was progression free survival (PFS). The Kaplan-Meier (KM) analysis,

univariate and multivariate Cox proportional hazard analysis were utilized to recognize risk factors.

Results: Among the cohort of 40 patients, 95.0% of patients manifested as solitary lung lesion, with a median size of 1.9cm. There were 85.0% of patients showing the HCGmax lower than 1000 (mIU/mL) during the whole disease course. And 72.5% of patients were confirmed as ETT. The initial treatment mainly included simple chemotherapy (20.0%), and lung operation±chemotherapy (80.0%). With a median follow-up period of 53.5months (range, 2～143), 11 patients experienced recurrence and no death case was observed. The univariate and multivariate cox analysis identified that chemotherapy as the initial treatment (HR=7.738, 95%CI 1.698～35.269, P=0.008) and the antecedent pregnancy as abortion (HR=5.650, 95%CI 1.030～31.004, P=0.046) were the independent risk factors of recurrence.

Conclusions: Isolated GTN of the lung is featured as initially presenting with lung lesion (mostly solitary), elevated HCG (mostly <1000), and unobserved pelvic lesion, and mostly is ETT. Lung surgery is considered as the radical therapy and the adjuvant chemotherapy is recommended as EMA/CO or FAEV.

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87P Characteristics and prognostic factors of high-grade uterine sarcomas: Unmet need of new therapeutic approaches

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Background: Uterine sarcomas (US) represent a rare group of malignancies characterized by diverse histopathological subtypes. Due to their infrequency, scientific evidence is limited, leaving many treatment approaches open-ended. This study aims to elucidate the experience of our cancer center.

Methods: This retrospective study enrolled patients diagnosed with high-grade US between 2008 and 2024. The study objectives included evaluating population demographics and treatment modalities. Survival analyses were conducted using the Kaplan-Meier method and prognostic factors were assessed using Cox regression.

Results: Eighty-one patients with US were evaluated, of whom 53 presented with localized disease at diagnosis. The median age was 51.8 years (interquartile range [IQR] 22.3-80.9). The majority of patients had Eastern Cooperative Oncology Group Performance Status (ECOG-PS) scores of 0-1 (74%) and were diagnosed with leiomyosarcoma (92.2%). FIGO staging revealed 39.5% at stage I, 7.8% at stage II, 6.5% at stage III, 1.3% at stage IVA, and 36.4% at stage IVB. Among patients with localized disease, 67.9% underwent hysterectomy and bilateral salpingo-oophorectomy, with 86.7% achieving R0 resection. Regarding adjuvant therapy, 17% received adjuvant chemotherapy (predominantly Doxorubicin + Ifosfamide), 22.6% radiotherapy, and 13.2% brachytherapy. With a median follow-up of 52 months, 54.7% of pts recurred, primarily at distant sites (86%), notably the lungs. Median disease-free survival and overall survival were 58.5 months (IQR 9.73-154.83) and 105.17 months (IQR 37.4-121.33), respectively. Only FIGO stage was significantly associated with increased recurrence risk (HR 5.2 for stage III-IVA vs. I-II, 95% CI 1.86-14.49, P=0.002), while lymphadenectomy, adjuvant chemotherapy, or adjuvant radiotherapy did not impact recurrence risk.

Conclusions: Despite achieving high rates of R0 resection in patients with localized disease, more than half experienced recurrence, particularly at distant sites. Strategies such as lymphadenectomy and conventional adjuvant therapies (chemotherapy or radiotherapy) did not mitigate recurrence risk, highlighting the need for novel therapeutic approaches to improve outcomes.

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88P Can we improve the FIGO risk score? Developing the inFIGO score for patients with gestational trophoblastic neoplasia

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Background: Gestational trophoblastic neoplasia (GTN) is a rare tumor with excellent prognosis. Besides the FIGO risk score, factors related to immune nutritional status have not been studied. We proposed the immune nutritional FIGO (inFIGO) risk score based on the association of pretreatment body mass index (BMI), hemoglobin (Hb), prognostic nutritional index (PNI), and neutrophil-to-lymphocyte ratio (NLR) with response to chemotherapy (rCT) and overall survival (OS).

Methods: This is a retrospective analysis of women newly diagnosed with GTN between 2005 and 2019 who received CT. Wilcoxon test, univariate and multivariate analysis were performed to evaluate the association with rCT. Cox proportional hazards regression models were used to identify independent significantly influencing OS. ROC curve was used to determine the cutoff point of variables significantly predicting rCT and OS. The inFIGO risk score was calculated based on the FIGO score and variables with significant association; and was compared with the original FIGO score.

Results: A total of 160 GTN patients were included. There was a positive association between rCT, PNI (p <0.0001) and NLR (p <0.001). In multivariate analysis, only PNI had significant association (p= 0.001), with an optimal cutoff of 35.005 (sensitivity 66.3% and specificity 72.7%) and AUC=0.722. A significant association was found between higher PNI (HR 0.95-IC 0.91-0.99, p= 0.019) and OS. The optimal cutoff was 30.005 (sensitivity 57.7% and specificity 78.8%) and AUC=0.704. The inFIGO score was obtained by summing the logarithm of the FIGO HR plus the PNI HR, and was calculated for all patients. For rCT, the inFIGO score had higher sensitivity (71.6 vs. 61.5%), specificity (74.3 vs. 62.9%), and AUC (0.719 vs. 0.633) than the original FIGO score. For OS, the inFIGO score demonstrated higher sensitivity (96.6% vs. 72.4%) but lower specificity (45.0% vs. 61.8%) and AUC (0.691 vs. 0.710).

Conclusions: PNI impacts in rCT and OS. Patients with low PNI may require additional interventions to improve outcomes. The inFIGO score demonstrated improved sensitivity and specificity in predicting rCT compared to the original FIGO score. Further research is warranted to assess its applicability in clinical practice.

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89P A single-centre retrospective study of patients with brain metastases and gynaecologic cancers

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Background: Brain metastases (BrM) among patients (pts) with gynecological cancers (GC) have historically been considered rare events. We aimed to characterize treatment patterns and outcomes of pts with GC and BrM.

Methods: We conducted a retrospective analysis of pts with GC and BrM who were treated with whole brain radiotherapy (WBRT) or stereotactic radiation (SRS) to the brain at the Sunnybrook Odette Cancer Centre, Toronto between 2010 and 2022. Analyses were performed using R software. Median follow up from time of BrM development was 7.5 (range 2.9 - 15) months.

Results: We identified 94 pts with BrM who had primary GC. Median age at time of BrM diagnosis was 66 (range 30-85) years. Median time from primary GC cancer diagnosis to BrM development was 28.5 (range 0 - 218) months. Presentation of BrM was with neurologic symptoms (96%, n=90) and multiple BrM (62%, n=58). All patients received radiotherapy; 63% (n=59) underwent SRS delivered in 1 to 5 fractions, and 36% (n=34) received WBRT; 40% (n=38) also had surgery for BrM. Patients with endometrial cancer (EC) accounted for 54% (n=51) of cases, ovarian cancer (OC) 26% (n=24), cervical cancer 17% (n=16). Among pts with EC, 41% had endometrioid (n=21) histology, 24% serous (n=12), 14% carcinosarcoma (n=7) and sarcoma 7.8% (n=4). Where status was known, BrM occurred in 33% (n=4/12) of patients with mismatch repair protein deficiency and 84% (n=10/12) of patients with protein TP53

overexpression. High grade serous (HGSC) was the most common subtype of OC, (83%, n=20). Both squamous 44% (n=7) and adenosquamous 31% (n=5) histology were observed among pts with cervical cancer (CC). Two pts with neuroendocrine CC developed BrM. Median overall survival (OS) from the time of BrM diagnosis was 10.6 months (0.1-143). The median OS among pts with OC and BrM (27.2 months) was longer than for those with EC (7.6 months) or CC (5.8 months), p=0.0034.

Conclusions: Among pts with GC and BrM in our cohort, the most common primary malignancy was EC and about two thirds of pts were treated with SRS. Patients with OC and BrM lived longer than those with other primary GC. Investigation of molecular events that "drive" the development of BrM among pts with GC is warranted.

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