LBA5500 **Oral Abstract Session**

TRUST: Trial of radical upfront surgical therapy in advanced ovarian cancer (ENGOT ov33/AGO-OVAR OP7).

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The full, final text of this abstract will be available at meetings.asco.org on the day of presentation and in the online supplement to the June 10, 2025, issue of the *Journal of Clinical Oncology*.

LBA5501 **Oral Abstract Session**

Sentinel lymph node biopsy versus pelvic lymphadenectomy in cervical cancer: The PHENIX trial.

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Ultrasensitive detection and tracking of circulating tumor DNA (ctDNA) and association with relapse and survival in locally advanced cervical cancer (LACC): Phase 3 CALLA trial analyses.

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Background: In LACC, there is an unmet need for prognostic biomarkers as about 1/3 of patients (pts) relapse after chemoradiotherapy (CRT). The global randomized CALLA trial (NCT03830866) of durvalumab (D) in combination with CRT followed by D (D+CRT arm) vs CRT (CRT arm) did not significantly improve progression-free survival (PFS) in a biomarker unselected intent-to-treat (ITT) population. We analyzed the association of ultrasensitive ctDNA detection with relapse and survival in the largest ctDNA data set in LACC to date. **Methods:** Adult women with Stage IB2-IIB node positive (N+) or IIIA-IVA any N LACC (ITT) were randomized 1:1 to D+CRT or CRT alone. NeXT Personal (Personalis, Fremont, CA), an ultrasensitive tumor-informed MRD assay with up to 1,800 patient-specific variants from WGS, was used for ctDNA analysis from Cycle 1 Day 1 (C1D1; baseline [BL]), C3D1, and 6 mo post treatment initiation. Correlations were analyzed between ctDNA detection and outcomes (PFS, overall survival [OS]). **Results:** Of 770 pts randomized, the biomarker-evaluable population (BEP) comprised 185, 186, and 130 pts at BL, C3D1, and 6 mo, respectively. BL pt characteristics, PD-L1, PFS, and OS between BEP and ITT populations were generally similar. ctDNA was detected in 99% of pts at BL and decreased after treatment, reaching 23% in the D+CRT and 36% in the CRT arm at 6 mo. The lower detection rate in the D+CRT arm was associated with the PD-L1 tumor area positivity (TAP) ≥20% subpopulation. At BL, pts with low (<BL median [5268.2 ppm]) ctDNA levels had a reduced risk of progression vs pts with high (≥median) ctDNA levels (PFS hazard ratio [HR] D+CRT 0.58 [95% CI, 0.27-1.24]; CRT 0.66 [0.34-1.28]). Pts with detectable ctDNA at C3D1 or 6 mo had a higher risk of progression independent of treatment arm (Table). No differences in risk of progression between the D+CRT vs CRT arms were observed based on ctDNA detection. Correlations between ctDNA and OS will be presented. **Conclusions:** This pre-planned analysis of a large, global LACC population from CALLA demonstrates the high sensitivity of a personalized ctDNA assay. High ctDNA levels at BL were associated with higher risk of progression or death. Lower ctDNA detection rates after treatment with D+CRT and CRT correlated with improved survival and highlight increased tumor control by D, especially in the PD-L1 TAP ≥20% subpopulation. This analysis supports the potential utility of ultrasensitive ctDNA analysis to guide treatment decisions in LACC. Clinical trial information: NCT03830866. Research Sponsor: AstraZeneca.

	D+CRT		CRT	
	Not detected	Detected	Not detected	Detected
C3D1	n=60	n=33	n=56	n=37
Median PFS (95% CI), mo	NC (37.52-NC)	14.03 (7.49-NC)	NC (NC-NC)	10.68 (7.39-19.61)
HR (95% CI)	0.25 (0.12-0.53)		0.16 (0.08-0.34)	
6 mo	n=49	n=15	n=42	n=24
Median PFS (95% CI), mo	NC (NC-NC)	10.35 (7.49-NC)	NC (NC-NC)	12.98 (10.38-NC)
HR (95% CI)	0.04 (0.01-0.16)		0.05 (0.02-0.16)	

NC, not computed.

Patient-reported outcomes (PROs) in locally advanced cervical cancer (LACC): Insights from the OUTBACK trial.

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Background: OUTBACK (ACTRN12610000732088), an open-label, international, randomized phase 3 trial of 919 participants (pts) with LACC, showed that adding adjuvant chemotherapy (ACT) after chemoradiotherapy (CRT) increased adverse events without improving overall survival compared to CRT alone. PRO objectives of OUTBACK were to determine the: 1) prevalence of patient-reported moderate-severe symptom issues at years 1-3 post-randomisation 2) duration of common issues; 3) long-term psycho-sexual health. **Methods:** Pts completed the EORTC core questionnaire QLQ-C30; cervical cancer module QLQ-CX24 (questions 50-54 only for sexually active pts); EORTC Item Library questions on abdominal, urinary, bowel and chemotherapy side-effects; & FACT-GOG-NTX4 neurotoxicity over 36 months. A moderate-severe long-term symptom issue was defined as a score in the worst 2 response categories (EORTC items), a total score ≤8/16 on FACT-GOG-NTX4 at years 1, 2 or 3 for Objectives 1-2, or equivalent subscale score for Objective 3. The availability of PROs for analysis was not related to 11 pre-specified demographic/clinical variables so no imputation for missing data was performed. **Results:** PRO completion rates were 94% at baseline, 64% at year 1 & 37% by year 3. Table 1 shows the 10 top-ranked issues at year 1 & their persistence or resolution by years 2-3. These may be underestimates, due to lower PRO completion rates at years 2-3. Issues and frequencies were similar across treatment arms by year 1. Moderate-severe peripheral neuropathy affected 24% post CRT+ACT & 18% post CRT (year 1); 19% post CRT+ACT & 12% post CRT (year 3). At baseline, 77% reported no sexual activity in the past 4 weeks. Overall, 92% of pts reported low sexual activity at years 1, 2 or 3; 68% reported low enjoyment, 40% moderate-severe vaginal tightness, 37% vaginal dryness during sex and 32% were moderately-severely worried sex would be painful. **Conclusions:** Long-term symptom issues & sexual health concerns are common & persistent following CRT +/-ACT for LACC and need dedicated survivorship care. Clinical trial information: 12610000732088. Research Sponsor: National Health and Medical Research Council; National Cancer Institute; SHCC MU NCORP Grant.

Frequency and duration of top-ranked moderate-severe symptoms.

Item	CRT + ACT n (%)	CRT alone n (%)	All participants n (%)		
	Issue rated moderate-severe at Year 1	Issue rated moderate-severe at Year 1	Issue rated moderate-severe at Year 1	Issue from Year 1 resolved by Year 2 or 3	Issue from Year 1 persistent at Year 2 or 3
Worried future health	76 (50)	59 (38)	135 (44)	14 (10)	49 (36)
Hot flushes/ sweats	68 (39)	64 (35)	132 (37)	24 (18)	49 (37)
Frequent urination	67 (38)	59 (32)	126 (35)	24 (19)	45 (36)
Sexual activity (not) enjoyable	59 (63)	66 (65)	125 (64)	11 (9)	43 (34)
Trouble sleeping	62 (35)	55 (30)	117 (32)	19 (16)	37 (32)
Tired	53 (30)	51 (28)	104 (29)	22 (21)	33 (32)
Changed bowel habit	56 (32)	46 (25)	102 (28)	22 (22)	41 (40)
Financial difficulties	51 (27)	50 (28)	101 (28)	17 (17)	32 (32)
Pain	54 (29)	42 (24)	96 (27)	21 (22)	23 (24)
Dissatisfied with body	48 (26)	47 (27)	95 (26)	21 (22)	27 (28)

LBA5504 **Oral Abstract Session**

Pembrolizumab with chemoradiotherapy in patients with high-risk locally advanced cervical cancer: Final analysis results of the phase 3, randomized, double-blind ENGOT-cx11/GOG-3047/KEYNOTE-A18 study.

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LBA5506 **Oral Abstract Session**

FIRST/ENGOT-OV44: A phase 3 clinical trial of dostarlimab (dost) and niraparib (nira) in first-line (1L) advanced ovarian cancer (aOC).

Anne-Claire Hardy-Bessard, Eric Pujade-Lauraine, Richard G. Moore, François Montestruc, Andres Redondo, Mansoor Raza Mirza, Nataliya Volodko, Tudor-Eliade Ciuleanu, Lucy Gilbert, Ram Eitan, Flora Zagouri, Sandro Pignata, Rosalind Glasspool, Jacobus Pfisterer, Rebecca Phaeton, Charles K. Anderson, Manuel Rodrigues, Fernanda Musa, Isabelle Laure Ray-Coquard, Kathleen N. Moore; Centre Armoricain d'Oncologie, CARIO-HPCA, and GINECO, Plérin, France; ARCAGY-GINECO, Paris, France; Wilmont Cancer Institute, University of Rochester, Rochester, NY; Statistician GINECO Committee, Paris, France; Hospital Universitario La Paz and GEICO, Madrid, Spain; Rigshospitalet – Copenhagen University Hospital, Department of Cancer Treatment, Copenhagen, Denmark; Department of Oncology and Radiology, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine; Institutul Oncologic Prof. Dr. Ion Chiricuță, Cluj-Napoca, Romania; Division of Gynecologic Oncology, Research Institute, McGill University Health Centre, Gerald Bronfman Department of Oncology, McGill University, Montreal, QC, Canada; Rabin Medical Center, Tel Aviv University, Tel Aviv, Israel; Alexandra Hospital, Athens, Greece; Istituto Nazionale Tumori di Napoli IRCCS - Fondazione G. Pascale and MITO, Naples, Italy; Beatson West of Scotland Cancer Centre and School of Cancer Sciences, University of Glasgow, Glasgow, United Kingdom; AGO Study Group, Wiesbaden, Germany & Gynecologic Oncology Center, Kiel, Germany; GSK, Collegeville, PA; Willamette Valley Cancer Institute and Research Center, Eugene, OR; Institut Curie and GINECO, Paris, France; Providence-Swedish Cancer Institute, Seattle, WA; Centre Léon Bérard and GINECO, Lyon, France; Stephenson Cancer Center at The University of Oklahoma Health Sciences Center, Oklahoma City, OK

LBA5507 **Oral Abstract Session**

ROSELLA: A phase 3 study of relacorilant in combination with nab-paclitaxel versus nab-paclitaxel monotherapy in patients with platinum-resistant ovarian cancer (GOG-3073, ENGOT-ov72).

Alexander Olawaiye, Laurence Gladieff, Lucy Gilbert, Jae-Weon Kim, Mariana Scaranti, Vanda Salutari, Elizabeth Hopp, Linda R. Mileshkin, Alix Devaux, Michael McCollum, Ana Oaknin, Aliza L. Leiser, Nicoletta Colombo, Andrew R. Clamp, Boglarka Balazs, Giuseppa Scandurra, Emilie Kaczmarek, Hristina I. Pashova, Sachin Gopalkrishna Pai, Domenica Lorusso; University of Pittsburgh School of Medicine and Magee-Women's Hospital, Gynecologic Oncology Group, Pittsburgh, PA; Oncopole Claudius Regaud IUCT-Oncopole, Toulouse, France; Division of Gynecologic Oncology, Research Institute, McGill University Health Centre, Gerald Bronfman Department of Oncology, McGill University, Montreal, QC, Canada; Department of Obstetrics and Gynecology, Seoul National University, College of Medicine, Seoul, South Korea; DASA Oncologia, Hospital 9 de Julho, São Paulo, Brazil; Department of Woman, Child and Public Health, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy; Medical College of Wisconsin, Milwaukee, WI; Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; Oncology Department of Grand Hôpital de Charleroi, Charleroi, Belgium; Virginia Oncology Associates, Norfolk, VA; Medical Oncology Service, Vall d'Hebron Institute of Oncology, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; University of Milan Bicocca, European Institute of Oncology, Milan, Italy; The Christie NHS Foundation Trust and University of Manchester, Manchester, United Kingdom; Department of Gynecology, Hungarian National Institute of Oncology, Budapest, Hungary; Medical Oncology Unit, Cannizzaro Hospital, Catania, Italy; Centre Oscar Lambret, Lille, France; Corcept Therapeutics Incorporated, Redwood City, CA; Department of Biomedical Science, Humanitas University, Pieve Emanuele, Milan and Humanitas San Pio X Hospital, Milan, Italy

Benmelstobart plus carboplatin/paclitaxel with or without anlotinib, followed by maintenance benmelstobart with or without anlotinib, as first-line treatment for advanced or recurrent endometrial cancer: A randomized, open-label, phase II trial.

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Background: Immunotherapy combined with chemotherapy has demonstrated efficacy in treating endometrial cancer (EC), with greater benefit in mismatch repair (MMR)–deficient (dMMR) tumors compared to MMR-proficient (pMMR) disease. Adding an anti-angiogenic inhibitor could potentially enhance treatment outcomes, particularly in patients with pMMR tumors. Benmelstobart (BMSB, TQB2450) is a humanized monoclonal antibody against PD-L1 and Anlotinib (ALTN) is an anti-angiogenic oral multi-target tyrosine kinase inhibitor. Here, we report the results of a randomized, open-label, phase 2 trial comparing BMSB plus carboplatin/paclitaxel ± ALTN followed by maintenance BMSB ± ALTN as first-line treatment for advanced or recurrent EC patients. **Methods:** Eligible patients with primary advanced stage III/IV or recurrent EC, who had not received first-line systemic anticancer therapy, were randomized in a 1:1 ratio to receive either BMSB 1200mg, Carboplatin (CBP, AUC=5 mg/ml.min) and Paclitaxel (PTX, 175mg/m^2) every 3 weeks for 6-8 cycles plus ALTN 8mg orally once daily (2-week on/1-week off), followed by maintenance BMSB 1200mg every 3 weeks and ALTN 10mg once daily (2-week on/1-week off) (BMSB + ALTN arm); or BMSB 1200mg, CBP (AUC=5 mg/ml.min) and PTX 175mg/m^2 every 3 weeks for 6-8 cycles followed by maintenance BMSB 1200mg every 3 weeks (BMSB arm). Stratification factors included MMR status (dMMR or pMMR). The primary endpoint was objective response rate (ORR) as assessed by investigator according to RECIST 1.1. **Results:** As of November 1, 2024, a total of 71 patients were enrolled: 38 in the BMSB + ALTN arm, and 33 in the BMSB arm. The median duration of follow-up was 16.2 mo vs. 14.2 mo in the two arms respectively. The ORR was 86.1% (95% CI: 70.5-95.3) in the BMSB + ALTN arm and 80.6% (95% CI: 62.5-92.5) in the BMSB arm. A significant PFS benefit was observed in the BMSB + ALTN arm (HR 0.38 [95% CI 0.18-0.81]; median not reached (NR) vs. 8.41 mo) compared to the BMSB arm. The median overall survival (OS) was not reached in either arm (HR=0.29 [95% CI: 0.07-1.16]). PFS benefit was also observed in subgroups with pMMR tumors (HR 0.35 [95% CI 0.15-0.79]). The incidence of Grade ≥3 TEAEs was similar between the two arms (81.58% vs 75.76%). The most frequent Grade ≥3 TEAEs(≥20%) were decreased white blood cell count (52.63% vs 60.61%), thrombocytopenia (28.9% vs 27.2%) and anemia (26.3% vs 27.7%). **Conclusions:** Benmelstobart combined with carboplatin/paclitaxel and anlotinib, followed by maintenance benmelstobart and anlotinib, demonstrated clinically meaningful ORR and PFS benefits in patients with previously untreated advanced or recurrent EC. The regimen was particularly helpful in improving outcomes for patients with pMMR tumors, potentially providing a new treatment option. Clinical trial information: NCT05481645. Research Sponsor: None.

Cadonilimab plus platinum-based chemotherapy ± bevacizumab for persistent, recurrent, or metastatic cervical cancer: Subgroup analyses of COMPASSION-16.

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Background: The phase 3 COMPASSION-16 trial demonstrated statistically significant progression-free survival (PFS) and overall survival (OS) benefits with cadonilimab plus chemotherapy ± bevacizumab in patients with persistent, recurrent, or metastatic cervical cancer (R/M CC). This analysis assessed efficacy in several key clinical subgroups. **Methods:** R/M CC pts who had no prior systemic treatment were randomized 1:1 to receive cadonilimab (10 mg/kg) or placebo Q3W plus platinum-based chemotherapy ± bevacizumab (15 mg/kg). The dual primary endpoints were PFS per RECIST v1.1 assessed by blind independent central review and OS in the ITT population. Treatment effects on PFS and OS were evaluated in subgroups including age (<65 or ≥65 years), bevacizumab use (yes or no), prior concurrent chemoradiotherapy (CCRT; yes or no), metastatic disease at baseline (yes or no), PD-L1 CPS (<1, ≥1, or ≥10), and platinum use (cisplatin or carboplatin). Hazard ratios (HRs) and 95% CIs were estimated from an unstratified Cox model. **Results:** 445 patients were randomized (222 to the cadonilimab group and 223 to the placebo group). At the Apr 30, 2024 data cutoff, the median follow-up was 26 months. The addition of cadonilimab prolonged PFS and OS in all investigated subgroups (Table). **Conclusions:** Subgroup analyses of COMPASSION-16 showed that the addition of cadonilimab to chemotherapy ± bevacizumab improved PFS and OS across subgroups defined by age, bevacizumab use, prior CCRT, metastatic disease, PD-L1 CPS, and platinum use, consistent with results for the overall population. Cadonilimab plus standard treatment is a potential treatment option for patients with R/M CC. Clinical trial information: NCT04982237. Research Sponsor: Akeso Biopharma.

Subgroup (N)	Median PFS (mo) Cadonilimab	Median PFS (mo) Placebo	PFS, HR (95% CI)	Median OS (mo) Cadonilimab	Median OS (mo) Placebo	OS, HR (95% CI)
<65 yrs (369)	13.5	9.5	0.68 (0.52, 0.88)	NR	25.3	0.69 (0.50, 0.95)
≥65 yrs (74)	12.0	7.4	0.39 (0.22, 0.68)	26.6	15.5	0.49 (0.27, 0.91)
With bevacizumab (265)	15.1	11.5	0.78 (0.57, 1.06)	NR	NR	0.84 (0.56, 1.26)
Without bevacizumab (180)	11.7	6.7	0.44 (0.31, 0.63)	28.8	15.1	0.50 (0.33, 0.75)
CCRT, yes (215)	16.1	7.9	0.55 (0.39, 0.78)	NR	22.8	0.54 (0.35, 0.82)
CCRT, no (230)	12.0	8.5	0.67 (0.49, 0.93)	27.0	24.5	0.76 (0.52, 1.12)
Metastatic, yes (323)	12.0	8.3	0.70 (0.54, 0.92)	28.8	25.3	0.73 (0.52, 1.02)
Metastatic, no (122)	NR	8.0	0.42 (0.25, 0.70)	NR	17.6	0.48 (0.27, 0.86)
PD-L1 CPS<1 (116)	12.0	8.2	0.65 (0.42, 1.03)	NR	25.3	0.77 (0.44, 1.34)
PD-L1 CPS≥1 (312)	14.7	8.3	0.62 (0.47, 0.83)	NR	22.7	0.69 (0.49, 0.97)
PD-L1 CPS≥10 (180)	17.1	8.1	0.54 (0.37, 0.79)	NR	29.0	0.68 (0.42, 1.08)
Cisplatin (192)	14.7	8.1	0.49 (0.34, 0.72)	NR	23.9	0.43 (0.27, 0.70)
Carboplatin (253)	12.0	8.2	0.72 (0.53, 0.97)	27.8	22.8	0.82 (0.57, 1.18)

Nimotuzumab combined with chemotherapy in the first-line treatment for patients with stage IVB, recurrent or persistent cervical squamous cell carcinoma: A multi-center, randomized, double-blind, and controlled study.

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Background: Stage IVb, recurrent or persistent cervical cancer patients have limited treatment options and poor survival prognosis. Additionally, 70-90% of cervical cancers have over-expression of EGFR (epidermal growth factor receptor), a promising therapeutic target. Nimotuzumab (nimo), an EGFR antibody, 95% humanization degree, had applied in the treatment of various advanced solid tumors. So, we conducted the study to investigate its efficacy and safety. **Methods:** This trial is a prospective study with a total of 118 patients enrolled. There were 55 patients (pts) in the experimental group (nimo+chemotherapy) and 63 pts in the control group (chemotherapy alone). Primary efficacy endpoint is overall survival (OS). Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), quality of life (QoL) and exploratory endpoints including the relationship between EGFR expression level and clinical efficacy and prognosis. The study of NCT approval number is 06781073. **Results:** The median age of the study population was 51.3 (range, 24.7-69.5) years. The average number of organs involved in the lesion was 2. The disease stage at initial diagnosis (2018 FIGO stage) was Ia-IVb. According to the disease status at the time of enrollment, IVB/ recurrence/persistence accounted for 14.4%, 92.4%, and 9.3%, respectively. The results showed that the median OS was 15.7 (95% CI, 11.8-26.9) months in the nimo arm and 12.4 (95% CI, 7.9-21.0) months in the control arm. For recurrence pts, median OS was 21.7 (95% CI, 21.1-32.9) months vs. 12.4 (95% CI, 8.0-21.4) months for both groups. Median PFS was 7.4 (95% CI, 4.9-8.9) months in the nimo arm and 5.6 (95% CI, 4.1-6.1) months in the control arm. For recurrence pts, median PFS was 7.9 (95% CI, 5.6-12.0) months vs. 5.2 (95% CI, 3.7-8.0) months for both groups. In terms of safety, SAEs occur as follows. There were 8 pts (14.5%) in the nimo and 13 pts (23.6%) in the control group, respectively. For AEs above grade 3, there were 43 pts in the nimo and 45 pts in the control group. Adverse events related to the study drug, there were 6 cases in the nimo group with neutropenia. Among all AEs, the highest frequency was in the nimo group with 20 cases of leukopenia, 16 cases of nausea, 23 cases of anemia, and 11 cases of alopecia. In the control group, there were 17 cases of leukopenia, 21 cases of nausea, 23 cases of vomiting and 20 cases of alopecia. There was no significant difference between the two groups for adverse events. **Conclusions:** Adding nimotuzumab to chemotherapy in the first-line treatment for stage IVB, recurrent or persistent cervical squamous cell carcinoma could have an improvement trend on progression-free and overall survival with well tolerated toxicity, and should be considered as a new first-line therapy option. Research Sponsor: None.

5511 Rapid Oral Abstract Session

Primary results of a phase 2 study of cisplatin-sensitized radiation therapy and pembrolizumab for unresectable vulvar cancer.

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Background: Locally advanced vulvar cancer is a rare but lethal disease more common in underserved populations. In contrast to other gynecologic cancers, the incidence and mortality of this disease has increased over the past decade. Treatment for locoregional disease involves surgery and chemoradiation, while systemic chemotherapy and immunotherapy are reserved for patients with distant metastases. Cisplatin and radiation (cis-RT) have been reported to have anti-tumor immunomodulatory properties in addition to their cytotoxic effects. We hypothesized that immune checkpoint inhibitors could synergize with chemotherapy and improve outcomes for this disease. **Methods:** In this single-arm phase II trial (NCT04430699), patients with primary unresectable, incompletely resected, recurrent, or metastatic squamous cell carcinoma of the vulva undergoing RT were eligible. Patients who had received prior chemotherapy were also eligible. Patients received cisplatin 40 mg/m2 weekly concurrently with intensity modulated (IM) RT, and pembrolizumab 200 mg was administered every three weeks for a total of 12 cycles. The primary endpoint was overall response rate (ORR), and the secondary objective was six-month recurrence free survival (RFS). PD-L1 expression and T-cell receptor beta clonality were assessed among other translational endpoints. An ORR $\geq$ 60% was considered worthy of further study. **Results:** The study closed to accrual on 10/11/2024 after 24 patients had enrolled. Twenty-two patients (92%) had primary unresectable disease and two (8%) had recurrent disease. All patients were treated with definitive intent RT, with a median dose to the primary of 68.4 Gy (range, 26.2, 70.2) and 45 Gy to pelvic, inguinal, vulva CTV (range, 21.6, 50.4). One patient stopped RT early due to disease progression. At the data cutoff on 01/22/2025, the ORR (CR+PR) was 75%. The 6-month RFS rate was 70% (95% CI: 48 – 85%). The median PFS has not been reached. Any grade adverse events (AE) occurred in all patients. Grade (G) 3 or 4 AEs occurred in 19 (78.6%) patients, most of which were related to cisplatin. The most common treatment-emergent adverse events were nausea (88%), diarrhea (71%), fatigue (67%) and anemia (50%). There were 6 serious AEs, only 2 of which were related the treatment (both AKI). Most immune related toxicities were G1/2, except for G3 diarrhea (4%). Immune mediated colitis led to discontinuation in 1 patient (4%). PD-L1 (CPS $\geq$ 1) was positive in all patients. There was an increase in mean TCR clonality after 2 cycles. **Conclusions:** The study met its primary endpoint. Concurrent treatment with chemo-radiation and pembrolizumab improved ORR and 6-month RFS in vulvar cancer. The addition of pembrolizumab did not lead to any unexpected AEs. Chemoradiation with pembrolizumab could be considered in patients with primary unresectable or incompletely resected vulvar cancer. Clinical trial information: NCT04430699. Research Sponsor: Merck Sharp & Dohme Corp.

Durvalumab plus carboplatin/paclitaxel followed by durvalumab with or without olaparib as first-line treatment for endometrial cancer: Longitudinal changes in circulating tumor DNA.

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Background: DUO-E (NCT04269200) showed statistically significant and clinically meaningful progression-free survival (PFS) with carboplatin/paclitaxel (CP) plus durvalumab (D) followed by D (CP+D) ± maintenance olaparib (O) vs CP in endometrial cancer (intent-to-treat [ITT] population; primary endpoints). The greatest benefit for CP+D was in mismatch repair deficient (dMMR) patients (pts); addition of O (CP+D+O) further enhanced PFS in MMR proficient (pMMR) pts (prespecified exploratory analyses). We present exploratory longitudinal circulating tumor (ct)DNA analyses. **Methods:** Pts were randomized 1:1:1 to CP (CP alone), CP+D, or CP+D+O arms. ctDNA was analyzed in plasma at baseline (BL; Cycle 1 Day 1 [C1D1]), during the chemotherapy phase (C3D1), prior to maintenance initiation (C7D1), and during the maintenance phase (C9D1) using the methylation-based Guardant Infinity assay (Guardant Health, Palo Alto, CA). **Results:** Of 718 pts randomized, the biomarker-evaluable population (BEP) comprised 347, 349, 350, and 349 pts at BL, C3D1, C7D1, and C9D1, respectively. Pt characteristics were similar to the ITT population but fewer pts had Eastern Cooperative Oncology Group status 1. ctDNA was detectable in 80% (278/347) of C1D1 samples, and presence of BL ctDNA was associated with shorter PFS across treatment arms. In both dMMR and pMMR pts, CP+D treatment during the chemotherapy phase led to numerically greater reductions in detectable ctDNA vs CP at C3D1; continued treatment with D led to lower ctDNA detection at C9D1 (Table) due to a lower proportion of pts switching from no detectable ctDNA to detectable (re-emergence) ctDNA between C7D1 and C9D1. The addition of maintenance O to CP+D had limited effect on ctDNA levels in dMMR pts; however, in pMMR pts, the ctDNA detection rate was lower at C9D1 vs CP or CP+D due to increased ctDNA clearance from C7D1 to C9D1 (CP+D+O vs CP+D: 48% vs 17%). **Conclusions:** In this post hoc exploratory analysis, BL ctDNA was associated with shorter PFS. The addition of D was associated with rapid reductions in ctDNA detection during chemotherapy and less re-emergence of ctDNA during maintenance. The addition of maintenance O was associated with further reduction of detectable ctDNA and increased ctDNA clearance in pMMR pts, reflecting an additional activity of the combination. Clinical trial information: NCT04269200. Research Sponsor: AstraZeneca.

ctDNA detection rates (% [n/N]).

Population	Treatment arm	C1D1	C3D1	C7D1	C9D1
BEP	CP	80 (94/118)	44 (51/117)	35 (41/117)	50 (58/117)
	CP+D	86 (96/112)	26 (29/112)	27 (30/112)	33 (37/112)
	CP+D+O	75 (88/117)	31 (37/120)	21 (26/121)	25 (30/120)
dMMR	CP	79 (11/14)	57 (8/14)	21 (3/14)	43 (6/14)
	CP+D	91 (21/23)	23 (5/22)	32 (7/22)	22 (5/23)
	CP+D+O	85 (22/26)	41 (11/27)	18 (5/28)	22 (6/27)
pMMR	CP	80 (83/104)	42 (43/103)	37 (38/103)	50 (52/103)
	CP+D	84 (75/89)	27 (24/90)	26 (23/90)	36 (32/89)
	CP+D+O	73 (66/91)	28 (26/93)	23 (21/93)	26 (24/93)

5513 Rapid Oral Abstract Session

Phase 2 study of letrozole, abemaciclib, and metformin in estrogen receptor (ER)–positive recurrent endometrial cancer (EC).

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Background: Preclinical studies have demonstrated synergism with simultaneous inhibition of the estrogen receptor (ER), CDK4/6 and PI3K pathways. Metformin suppresses PI3K signaling directly via activation of the AMP-activated protein kinase (AMPK) and indirectly via down-regulating the insulin/IGF-1 signaling pathway. We conducted a phase 2 study of letrozole/abemaciclib/metformin in ER positive EC. **Methods:** Patients (pts) with recurrent ER positive (≥1% immunoreactive tumor nuclei) endometrioid EC, measurable disease, any number of prior therapies and any prior hormonal therapy but no prior CDK4/6 inhibitor received abemaciclib 150 mg PO bid, metformin 500mg PO qd and letrozole 2.5 mg PO qd until progression or unacceptable toxicity. Primary endpoints were objective response (OR) rate (ORR) and progression-free survival (PFS) rate at 6 months (PFS6). A safety lead-in was included, and target accrual was 25 pts; if there were ≥6 ORs or ≥9 pts without disease progression or death at 6 months, letrozole/abemaciclib/metformin would be considered worthy of further investigation. Correlative studies included pharmacokinetic (PK) analyses of metformin alone and in combination with letrozole/abemaciclib, molecular profiling using Oncopanel targeted NGS, and progesterone receptor (PrgR) expression by IHC. **Results:** As of 10/4/2024, all 25 pts received protocol therapy. Median follow up was 17 months, median number of prior lines was 2 and 18 (72%) pts had previously received hormonal therapy. Eight pts exhibited OR: 3 complete responses (CRs) and 5 partial responses (PRs),ORR 32% (95% CI 14.9% to 53.5%). Sixteen (64%) pts had stable disease (SD) and 1(4%) pt progressive disease (PD) as best response. Kaplan Meier estimate of PFS6 was 69.7% and median PFS was beyond 19.3 months. Most common G3+ treatment-related toxicities were G3 neutropenia (24%) and G3 fatigue (16%). No pts discontinued therapy because of toxicity. PK analyses demonstrated that metformin plasma concentrations were ~3-fold higher when combined with letrozole/abemaciclib compared to metformin monotherapy. Molecular profiling showed no objective responses in *TP53* mutated ECs and no objective responses in pts with NSMP ECs with *RB1* or *CCNE1* alterations; median PFS was only 3.8 months in these tumors. All objective responses were observed in pts with NSMP ECs without *RB1* and *CCNE1* alterations; these pts exhibited an ORR of 50% and PFS6 of 87.5%. There were no MMRD and no *POLE*-mutated tumors. Responses were observed regardless of PrgR expression. **Conclusions:** Addition of metformin (at plasma concentrations sufficient to inhibit the PI3K pathway) to letrozole/abemaciclib is feasible and safe, and appears to induce deeper responses (including complete responses) and more prolonged PFS than letrozole/abemaciclib alone. NSMP tumors without *RB1* and *CCNE1* alterations derive the most benefit from this regimen. Clinical trial information: NCT03675893. Research Sponsor: None.

5514 Rapid Oral Abstract Session

Safety and preliminary efficacy from a phase 1 study of INCB123667, a selective CDK2 inhibitor, in patients with advanced platinum-resistant and refractory ovarian cancer (OC).

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Background: Inhibition of cyclin-dependent kinase 2 (CDK2), the binding partner of cyclin E1 (CCNE1), is a potential therapeutic approach for cancers with increased CCNE1 activity. In an ongoing phase 1 study, the potent and selective CDK2 inhibitor, INCB123667, has shown acceptable safety and preliminary efficacy in patients (pts) with advanced solid tumors (NCT05238922). Here, we present safety and preliminary efficacy data for enrolled pts with OC. **Methods:** Eligible pts had ECOG PS ≤1 and measurable disease (RECIST V1.1). Part 1A (dose escalation) enrolled pts with advanced/metastatic solid tumors with no maximum prior lines of treatment; *CCNE1* amp (locally tested) was not mandatory. INCB123667 dosing started at 50 mg and escalated up to 150 mg daily. In part 1B (dose expansion), selected RDEs from part 1A were expanded in 6 tumor cohorts, including platinum-refractory/resistant (r/r) OC with ≤4 prior lines of systemic treatment; pts must have had locally tested *CCNE1* amp or centrally confirmed CCNE1 overexpression. Blood samples were collected for ctDNA analysis. **Results:** As of Dec 19, 2024, 90 pts with advanced/metastatic platinum-r/r OC received INCB123667: 45 in part 1A (50 mg qd, n=1; 50 mg bid, n=4; 75 mg qd, n=12; 75 mg bid, n=4; 125 mg qd, n=18; 150 mg qd continuous or intermittent, n=6) and 45 in part 1B (RDEs: 50 mg bid, n=16; 100 mg qd, n=14; 125 mg qd, n=15). Sixty one pts (67.8%) had prior PARPi. Median number of prior systemic therapies was 4 (1-12). Median duration of treatment was 4.9 months (0.1-13.6), with 17 pts (18.9%) still on treatment. Overall, 88 pts (97.8%) had treatment-emergent adverse events (TEAEs), predominantly nausea (n=51 [56.7%]), anemia (n=34 [37.8%]), and vomiting (n=33 [36.7%]). Of 38 pts (42.2%) with grade ≥3 TEAEs, most common were intestinal obstruction (n=8 [8.9%]), anemia (n=6 [6.7%]), neutropenia (n=5 [5.6%]), and thrombocytopenia (n=5 [5.6%]). Treatment was discontinued due to TEAEs in 3 pts (3.3%). Overall response rate (ORR) among all pts in parts 1A and 1B was 21.1% (19/90; complete response, n=4; partial response, n=15) and 43 (51.2%) achieved stable disease, with an ORR of 33.3% (10/30) at selected RDEs of 100 mg daily (ie, 50 mg bid and 100 mg qd) in part 1B. All but 1 responder had CCNE1 overexpression (18/19); responses were observed in pts with *CCNE1*-amp (6/19) and in pts without *CCNE1*-amp but with CCNE1 overexpression (13/19). Consistent decreases in ctDNA were observed on treatment compared with baseline. **Conclusions:** In this phase 1 study of pts with heavily pretreated advanced/metastatic platinum-r/r OC, single agent INCB123667 at various doses showed an acceptable safety profile including expected cytopenia and nausea. The encouraging antitumor activity in this difficult-to-treat population support the advancement of INCB123667 into pivotal studies in pts with platinum-resistant OC. Clinical trial information: NCT05238922. Research Sponsor: Incyte Corporation.

A phase II trial of pembrolizumab and lenvatinib in recurrent or persistent clear cell ovarian carcinoma (NCT05296512).

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Background: Clear cell ovarian carcinoma (CCOC) is a chemoresistant subtype of ovarian cancer. Immune checkpoint inhibitors have been reported to have clinical activity in CCOC. Additionally, CCOC harbors molecular alterations suggesting a role for anti-angiogenic agents. We therefore conducted a single-arm two-stage phase 2 trial to investigate the clinical activity of the combination of the PD-1 inhibitor pembrolizumab with the anti-angiogenic tyrosine kinase inhibitor lenvatinib in patients (pts) with CCOC. **Methods:** Pts with CCOC and measurable disease received pembrolizumab 200 mg IV every 3 weeks and lenvatinib 20 mg daily. Pts could have received an unlimited number of prior therapies; prior bevacizumab and immune checkpoint inhibitors were allowed, but prior lenvatinib was exclusionary. Malignant bowel involvement was not allowed. Co-primary endpoints were objective response rate (H_o 5%; H_a 25%) and rate of PFS at 6 months (mo) per RECIST v1.1 (H_o 10%; H_a 30%), restricting the probabilities of type I and type II errors to 10% and 10%, respectively. Two pts with objective responses or 3 pts progression-free and alive at 6 mos were needed to proceed from stage 1 (n=18) to stage 2 (n=13); 5 pts with objective responses or 6 pts progression-free and alive at 6 mos were needed to declare the combination worthy of further study. **Results:** Data cut-off occurred 22-Oct-2024. Of 30 enrolled pts, 83.3% were white; the mean age among all pts was 54.1 years. 30% of pts (9/30) experienced a confirmed response (2 CR, 7 PR); an additional 3 pts (10%) experienced unconfirmed PRs and 4 pts (13.3%) had SD ≥6 mo. As of data cut-off, 3 pts (10%) had not yet reached their first radiographic assessments, and 17 pts were still receiving study therapy. With a median of 9.72 mo of follow up, 16 pts were alive and progression-free at 6 months. The estimated 6-month PFS was 75.96% (95% CI 53.82-88.51%). Median PFS was 10.9 mo. The estimated 12-month PFS was 48.86% (95% CI 23.67-70.04%). The most common any-grade TRAEs were hypertension (71%), hypothyroidism (66%), and fatigue (60%). There were no unanticipated TRAEs. **Conclusions:** The combination of pembrolizumab/lenvatinib demonstrates encouraging evidence of clinical activity in CCOC, with 9 pts experiencing a confirmed response and 16 pts alive and progression-free at 6 months. As both co-primary endpoints of the study were met, enrollment closed with 30 pts. Updated data for all pts will be reported. There were no new safety signals. Clinical trial information: NCT05296512. Research Sponsor: Merck.

A phase I/II study of the safety and efficacy of intraperitoneal IMNN-001 in combination with neoadjuvant chemotherapy (NACT) of paclitaxel and carboplatin in patients newly diagnosed with advanced epithelial ovarian cancer (EOC): Updated survival analysis from OVATION-2 trial.

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Background: OVATION-2 (NCT03393884) is a randomized, controlled phase I/II study evaluating IMNN-001 in newly diagnosed advanced epithelial ovarian cancer (EOC) patients. The study's purpose was to assess safety and efficacy of IMNN-001, an interleukin-12 (IL-12) gene therapy in combination with standard of care (SoC) chemotherapy. **Methods:** Patients were randomized 1:1 to NACT alone or NACT +IMNN-001. Carboplatin/paclitaxel IV was administered every 21 days for 3 cycles before and after interval debulking surgery (IDS) in the control arm, and concurrently with intraperitoneal IMNN-001 given weekly for 8 weeks prior to and for 9 weeks after IDS in the experimental arm. PFS was the primary endpoint with secondaries of OS, chemotherapy response score (CRS), surgical response score (SRS) and overall response rate (ORR). Hazard ratios are reported for PFS and OS as the study was not powered for statistical significance. Additional statistical methods quantified Totality of Evidence (ToE, Wang et al 2023, Claggett 2022) by considering PFS and OS outcomes simultaneously. Data lock was June 2024, with OS updated with data through November 2024. **Results:** 112 patients were enrolled with a median follow-up 31 months. Stage IV disease (31.0% vs 22.2%) and ECOG PS≥1 (48.3% vs 35.2%) were more common in the experimental arm. PARPi maintenance was less frequent in the experimental arm (32.8% vs 44.4%) despite balanced HRD status. IMNN-001 was well-tolerated with common adverse events (AEs) primarily including abdominal pain, nausea, and vomiting. There was no report of cytokine release syndrome or elevated risk of immune-related adverse events. Median PFS was 14.9 vs 11.9 months (HR:0.79, 95% CI: 0.51-1.23), and median OS was 46.0 vs 33.0 months (HR:0.69, 95% CI: 0.4-1.19) favoring the experimental arm. Rates of CRS with CRS3 outcome (complete or near complete response) and SRS R0 Section outcome were higher in the experimental arm; ORR was similar. In investigator choice PARPi subgroups, median PFS was 33.8 vs 22.1 months favoring the experimental arm (HR:0.79, 95% CI: 0.51-1.23), median OS was not reached in the experimental arm vs 37.1 months in the control arm (HR:0.38, 95% CI: 0.13-1.06). By simultaneously considering individual patients' progression and death times (ToE), the experimental arm shows 6.5 months improvement (less time lost) compared to the control arm with one-sided p = 0.375. **Conclusions:** IMNN-001 demonstrated trends towards material improvement in overall survival and acceptable safety in advanced EOC, especially in HRD+ patients. These results are supportive of further development in the upcoming pivotal phase 3 study. Clinical trial information: NCT03393884. Research Sponsor: None.

Safety and efficacy of BAT8006, a folate receptor α (FRα) antibody drug conjugate, in patients with platinum-resistant ovarian cancer: Update on the dose optimization/expansion cohort of BAT-8006-001-CR trial.

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Background: This report presents an update results of the BAT-8006-001-CR trial, which evaluated the safety and clinical activity of BAT8006, an antibody drug conjugate (ADC) consisting of a humanized anti-folate receptor alpha (FRα) monoclonal antibody linked to the topoisomerase I inhibitor exatecan, in patients with platinum-resistant ovarian cancer (PROC). **Methods:** Patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer received BAT8006 monotherapy every 3 weeks. The adverse events, incidence of dose interruptions or reductions, tumor response, progression-free survival (PFS) and overall survival (OS) were determined. **Results:** As of January 1st, 2025, 131 PROC patients were enrolled across various cohorts: 1.8 mg/kg (n=2), 2.1 mg/kg (n=16), 2.4mg/kg(n=15), 84 mg/m^2 (n=50) or 93mg/m^2(n=48) cohorts during the dose escalation and dose optimization/expansion study. The most common treatment-emergent adverse events (TEAEs) were anemia (82%), leukopenia (80%), neutropenia (77%), vomiting (67%), nausea (60%) and thrombocytopenia (55%). The most frequent grade ≥3 treatment related adverse events (TRAEs) were neutropenia (42%), leukopenia (33%), anemia (30%) and thrombocytopenia (26%). Notably, no cases of interstitial lung disease (ILD), ocular toxicities, or treatment-related deaths were reported. In the 84 and 93 mg/m^2 dose cohorts, selected for further exploration in the dose optimization/expansion study, the incidences of grade ≥3 neutropenia, anemia and thrombocytopenia were 35% vs 45% ,20% vs 32% and 18% vs 32%, respectively. Among 108 efficacy-evaluable patients with PROC (regardless the FRα expression and prior lines of treatments), the objective response rate (ORR) was 32.4% (35/108) and disease control rate (DCR) was 75.9% (82/108). The median PFS was 6.9 months (95% CI: 4.3-7.9), while the median OS was not reached (NR). In cohort 1 (n = 77), PROC patients with ≤3 lines of prior systemic anti-tumor therapies and FRα expression ≥1% were randomly assigned to received BAT8006 at 84 mg/m^2 (n=40) or 93mg/m^2 (n=37) every 3 weeks. Among 64 efficacy-evaluable patients in this cohort, the ORRs were 30.6% (11/36) and 32.1% (9/28) for the 84 mg/m^2 and 93mg/m^2 doses, respectively, while the DCRs were 75.0% (27/36) and 78.6% (22/28). The median PFS were 7.5 months (95% CI: 4.0-NR) and 5.5 months (95% CI: 2.9-NR), respectively. The median OS were NR. **Conclusions:** The safety profile is consistent with previous results, with no reports of ILD or ocular toxicity. The preliminary efficacy of BAT8006 appears promising in PROC patients with FRα expression ≥1%. On the basis of these findings, the target population, dose and schedule have been identified for a phase III trial of BAT8006 monotherapy in PROC patients. Clinical trial information: NCT05378737. Research Sponsor: Bio-Thera Solutions.

A phase II study of tumor microenvironment profiling at single cell level in patients with locally advanced cervical cancer (LACC) treated with immunotherapy combined with concurrent chemoradiotherapy (CICRT).

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Background: Concurrent chemoradiotherapy (CCRT) followed by intrauterine brachytherapy is the standard treatment for LACC, while the therapeutic efficacy can be limited by an immunosuppressive tumor microenvironment (TME). PD-1 inhibition has displayed efficacy and a clinically manageable safety profile in patients with cervical cancer. Single-cell RNA sequencing (scRNA-seq) of paired pre-treatment and on treatment samples offers a dynamic and detailed examination of the transcriptomic changes in the TME under different treatment conditions. Here, we present the results of patients with LACC treated with either CCRT or CICRT, along with the paired analysis of various cellular components in the TME from pre-treatment and on-treatment samples through scRNA-seq. **Methods:** Patients with untreated, high-risk stage III–IVA and stage IVB cervical cancer (limited to groin lymph nodes metastasis) according to FIGO 2018, with measurable disease per RECIST 1.1 and ECOG performance status ≤1, were included and randomly assigned (1:1) to receive either tislelizumab combined with chemoradiotherapy, followed by tislelizumab (200mg, Q3W for 6 cycles), or chemoradiotherapy alone (cisplatin 40 mg/m^2, Q1W for 3-5 cycles; pelvic external beam radiation therapy 50.4 Gy in 28 fractions; brachytherapy 28 Gy in 4 fractions). Single-cell transcriptomic profiles were obtained from paired biopsies at two time points: pre-treatment and on-treatment. **Results:** A total of 18 patients were included, with 12 single-cell analysis samples collected (6 CCRT and 6 CICRT). At the end of pelvic radiotherapy, the CICRT group exhibited a trend toward a greater reduction in tumor volume compared to the CCRT group (7.4% vs. 3.0%; p = 0.08), albeit not reaching statistical significance. Cancer cells in CICRT group exhibited with an increased expression of MHCII genes and chemotaxis-related genes on treatment. CICRT reduced the proportion of immunosuppressive regulatory CD4+ T cells and exhausted CD8+ T cells compared to CCRT. In myeloid cells, TNF-α signaling via NF-κB and inflammatory response pathways were enriched following CICRT, and tumor-associated macrophages were reprogrammed to a relatively pro-tumorigenic phenotype. The cancer-associated fibroblast (CAF) subset CAF_FTH1, characterized by a pro-inflammatory gene signature, was increased during CICRT. Moreover, CICRT induced higher expression of MHC-II-related molecules and chemotaxis-associated genes in CAFs compared to CCRT. **Conclusions:** The CICRT treatment group demonstrated a trend toward improved local control during the early phase of treatment compared to the CCRT group. Single-cell profiling revealed the differences in the potential to reshape the TME between CCRT and CICRT, with CICRT showing a greater ability to reduce immune suppression. Clinical trial information: ChiCTR2200067166. Research Sponsor: None.

Impact of pre-treatment counseling on uptake of hormone replacement therapy in patients undergoing chemoradiation for cervical cancer.

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Background: Chemoradiation therapy (CRT) for cervical cancer can lead to premature ovarian insufficiency (POI) in premenopausal women, accelerating the onset of menopause and its related symptoms, and adversely affecting sexual health. This study aimed to assess the impact of pre-CRT counseling on the initiation of hormone replacement therapy (HRT) in patients with cervical cancer, and to describe common practice patterns in the management CRT-related side effects. **Methods:** This retrospective cohort study included patients treated for cervical cancer at four New York City hospitals (one public and three private) from 2010 to 2024. Patients were included if they underwent CRT as first-line treatment and were premenopausal before treatment initiation. Data were extracted from medical records including demographics, pre-treatment counseling, CRT side effects, and HRT use. Descriptive statistics and chi-square were used for analysis, with $p<0.05$ as significant. **Results:** Of the 2,009 patients identified with a history of cervical cancer at our institutions, 81 premenopausal patients who underwent CRT were included, with a median age of 41.9 years at diagnosis. Prior to CRT, 69.1% of patients (n=56/81) were counseled on potential vaginal toxicity (e.g., stenosis/shortening), 63% (n=51/81) on the risk of POI, and 11.3% (n=9/81) on CRT's impacts on sexual health. Following treatment, 46.9% of patients (n=38/81) experienced menopausal symptoms, including vasomotor symptoms (84.2%, 32/38), vaginal dryness (36.8%, 14/38), and mood alternations (18.4%, 7/38). Among symptomatic patients, 55.3% (n=21/38) were prescribed HRT. Common regimens included vaginal estrogen (33.3%, 7/21) and combined estrogen/progestin pills (28.6%, n=6/21) followed by systemic estrogen patches (19%, n=4/21) and systemic estrogen pills (19%, n=4/21). Factors statistically significantly associated with HRT use after CRT included pre-treatment counseling on vaginal toxicity ($X^2=13.77$, $p=0.008$) and POI ($X^2=13$, $p=0.011$), as well as vaginal dilator use after CRT ($X^2=31.68$, $p<0.01$). Compared to patients at the public hospital, private hospital patients were more likely to be prescribed HRT (18.5% vs 40%, $p=0.046$). No significant differences were noted in HRT initiation rates by language ($p=0.201$), insurance type ($p=0.234$), or race ($p=0.617$). **Conclusions:** In this study we demonstrate that pre-CRT counseling on risks of vaginal toxicity and POI leads to a significant increase in HRT uptake after treatment. Further, we highlight a notable gap in counseling, as only two-thirds of premenopausal patients at our institutions undergoing CRT were counseled on side effects. To enhance patient care, vigilant screening on vaginal toxicity and vasomotor symptoms should be performed with each surveillance visit to ensure rapid treatment initiation and reduce morbidity from CRT. Research Sponsor: None.

Toripalimab with chemoradiotherapy followed by toripalimab maintenance therapy for newly diagnosed, high-risk, locally advanced cervical cancer (TorCH-CC): A single-arm phase II study.

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Background: Despite concurrent chemoradiation (CRT) being the standard treatment, patients with high-risk locally advanced cervical cancer (FIGO 2018 III-IVA, HR-LACC) experience suboptimal survival outcomes. This phase II clinical trial aimed to evaluate the efficacy and safety of toripalimab, an innovative and cost-effective PD-1 inhibitor, combined with CRT and followed by toripalimab maintenance, in patients with HR-LACC. **Methods:** Patients with untreated HR-LACC were enrolled. All patients were treated with cisplatin-based CRT combined with toripalimab, and followed by toripalimab maintenance therapy. Toripalimab is administered at a fixed dose of 240mg every 3 weeks intravenously, with the concurrent CRT and immunotherapy phase not exceeding 8 weeks. The primary endpoint was 2-year PFS rate, with secondary endpoints including overall response rate (ORR), duration of response (DoR), treatment-related adverse events (TRAEs), immune-related adverse events (iRAEs), 2-year OS, and quality of life. **Results:** From October 2023 to December 2024, 43 patients were enrolled, with a median age of 52 years (range: 28–72). Most patients (79%) were at stage IIIC, while others were stage IIIB (16.3%) or IVB (with inguinal or supraclavicular lymph node metastasis, 4.7%). PD-L1 expression was CPS $<$10 in 32.6% and CPS $\geq$10 in 67.4%. All received VMAT radiotherapy and image-guided high-dose-rate intracavitary/interstitial brachytherapy, with 74.4% receiving 5-6 cycles of concurrent chemotherapy and 90.7% receiving 3 cycles of concurrent toripalimab. The median CRT duration was 52.7 days (range: 43–62), and the median D90 HR-CTV was 93.9 Gy (EQD2, range: 84–114). With a median follow-up of 8 months (range: 3–15 months), the ORR was 97.1% at 3 months post-treatment, with 32 complete and 2 partial responses, and 1 stable disease. The best ORR after CRT was 100%, with 41 complete and 2 partial responses. Grade 3 or 4 hematologic TRAEs occurred in 27.9% of patients, and non-hematologic in 2.3%, with no discontinuations or deaths. Grade 3 or 4 hematologic irAEs occurred in 7% of patients. **Conclusions:** Toripalimab combined with cisplatin-based CRT followed by toripalimab maintenance was well-tolerable and demonstrated promising anti-tumor efficacy in patients with HR-LACC. Trial registration: The study was registered at ClinicalTrials.gov, NCT06416696. Clinical trial information: NCT06416696. Research Sponsor: None.

Nimotuzumab with chemoradiotherapy for newly diagnosed, high-risk, locally advanced squamous cervical cancer (CC11): A prospective single-arm phase II study.

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Background: Cervical cancer ranks as the fourth most common cancer, with 32% of cases being locally advanced (stage IIB-IVA, LACC). The standard treatment is concurrent chemoradiotherapy (CCRT) with platinum drugs, but many patients only achieve partial or short-term remission. Nimotuzumab has shown promise in treating LACC, but few studies focus on high-risk cases (FIGO 2018 III-IVA). This study aims to evaluate the efficacy and safety of combining nimotuzumab with CCRT for high-risk LACC. (NCT06771596). **Methods:** Patients aged 18-75 with confirmed cervical squamous cell carcinoma, an ECOG status of 0-2, and at least one measurable lesion were eligible. All patients received nimotuzumab 400 mg weekly for 4-6 weeks combined with CCRT. CCRT included external beam radiotherapy (45 Gy/1.8Gy/25 fractions) using volumetric modulated arc therapy (VMAT), concurrent with weekly cisplatin (40mg/m^2 for 4-6 weeks), followed by image-guided high-dose-rate brachytherapy, aiming for a cumulative dose ≥87 Gy (EQD2). The primary endpoint was 1-, 2-year progression free survival (PFS) per RECIST 1.1. The secondary endpoints were 1-, 2-year overall survival (OS), objective response rate (ORR), disease control rate (DCR) rate per RECIST v1.1, and safety per CTCAE v5.0. **Results:** In total, 40 patients were enrolled. The baseline characteristics are shown in the table. 36 (90%) patients had CR, 3 (7.5%) patients had PR, ORR was 97.5% (95% CI: 86.84%-99.94%), and DCR was 97.5% (95% CI: 86.84%-99.94%). The median follow-up time was 21.32 months (95% CI: 20.01~24.34) months, with mPFS and mOS not yet reached. The 1-, 2-year PFS rates were 79.11% (95% CI: 62.53%-88.97%) and 76.29% (95% CI: 59.33%-86.91%), respectively, and 1-, 2-year OS rate were 100% (95% CI: 100%~100%) and 85.27% (95% CI: 64.8%~94.32%). The most common AEs were leukopenia (42.5%), myelosuppression (40%), and anemia (37.5%), all of which were graded 1-2. **Conclusions:** Nimotuzumab combined with chemoradiotherapy in the treatment of high-risk squamous LACC demonstrated prolonged PFS and favorable safety profile. Clinical trial information: NCT06771596. Research Sponsor: None.

Baseline characteristics.

Characteristic	All patients (n=40)
Age (mean ± SD, years)	53.9±11.69
FIGO stage	
IIIA-IIIB	6(15.0%)
IIIC1R-IIIC2R	33(82.5%)
IVA	1(2.5%)
Tumor differentiation	
Low differentiation	8(20.0%)
Medium differentiation	1(2.5%)
Highly differentiation	31(77.5%)

Enlonstobart in patients with PD-L1 positive recurrent/metastatic cervical cancer: Updated survival results of the phase II study.

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Background: Enlonstobart is a PD-1 inhibitor that has demonstrated durable anti-tumor activity and acceptable safety in patients with PD-L1 positive recurrent/metastatic cervical cancer in a multicenter, single-arm, open-label, phase II study. At primary cutoff date (May 27, 2023), the overall survival (OS) was not reached. Here, we report results from a pre-planned further follow-up (August 20, 2024). **Methods:** Eligible patients were ≥18 years old with PD-L1-positive (combined positive score ≥ 1) cervical cancer who had progression during or after or intolerance to the first-line platinum-based therapy. A total of 107 patients received enlonstobart 240 mg every two weeks for up to 24 months or until disease progression, intolerable toxicities, or other study discontinuation criteria were met. At the updated cutoff date, analyses of progression-free survival (PFS) and OS in the full analysis set (FAS), which consisted of all patients who had received at least one dose of enlonstobart treatment, and the per protocol set (PPS), which consisted of all patients in the FAS who had at least one available postbaseline tumor assessment were conducted. **Results:** At the cutoff date of August 20 2024, the median follow-up time was 15.84 months (range 0.4 ~ 35.6 months). In FAS, the median PFS was 3.06 (95 % CI 2.23–6.90) months. The median OS was 19.38 (95 % CI 14.95–25.40) months and the estimated OS rate was 68.14 % (95 %CI 58.20–76.19) at 12 months, 50.78 % (95 % CI 40.46–60.20) at 18 months, and 42.84 % (95 % CI 32.76–52.53) at 24 months. In PPS, the median PFS was 3.81 (95 % CI 2.63–7.49) months. The median OS was 21.26 (95 % CI 15.44–27.66) months and the estimated OS rate was 71.53 % (95 %CI 61.48–79.40) at 12 months, 53.32 % (95 % CI 42.64–62.87) at 18 months, and 44.98 % (95 % CI 34.50–54.89) at 24 months. **Conclusions:** Enlonstobart monotherapy showed a promising survival in patients with PD-L1 positive recurrent/metastatic cervical cancer, whose disease experienced progression after first-line platinum-based therapy. Clinical trial information: NCT04886700. Research Sponsor: CSPC Zhongqi Pharmaceutical Technology Co., Ltd.

miRNA(s) expression as predictive biomarkers in recurrent/metastatic cervical cancer: The NRG Oncology/GOG-0240 NIH Cancer Moonshot.

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Background: Chemotherapy + pembrolizumab +/- bevacizumab (BEV) is the standard treatment for recurrent/metastatic (R/M) cervical cancer (CC). GOG-0240 was a predecessor registration trial demonstrating survival benefit with incorporation of BEV with chemotherapy in R/M CC. In the wake of KEYNOTE A18, prior exposure to immunotherapy (I-O) via incorporation of pembrolizumab with ChemoRT for frontline therapy (FIGO stage III-IVA) may limit I-O use in 1st-line R/M CC. The need for new agents and predictive biomarkers to guide BEV use is implicit. Aberrant expression of miRNAs in CC can drive oncogenic pathways and/or suppress tumor suppressor genes, highlighting their potential as therapeutic targets. Here we present miRNA differential expression from the NIH Cancer Moonshot, which aims to identify biomarkers and predictors of survival outcomes in R/M CC through evaluation of miRNA differential expression among patients treated with Chemotherapy +/- BEV. **Methods:** miRNA-sequencing of R/M CC tumors from GOG-0240 was performed. miRNA expression was profiled and correlated with overall survival across all cohorts and differentials among tumors treated with ChemoRx+BEV or ChemoRx-alone were compared. **Results:** In the ChemoRx-alone group, lower expression of miR443 was associated with improved survival. miR-4443 may play a role in modulating tumor progression and metastasis through its impact on cell migration/invasion mechanisms. In the ChemoRx+BEV group, lower miR-196b-3p was associated with better overall survival. MiR-196b-3p has been implicated in the progression of various cancers, acting as an oncogene by regulating gene expression pathways that promote cell proliferation, inhibit apoptosis, and enhance metastatic potential. In the overall study population, higher expression of miR-10a and miR-1307 was associated with better survival. miR-1307 is thought to down-regulate ING5, which in turn may regulate the PIK3A pathway. In contrast, higher expression of several miRNAs, notably miR-584, mi-223, miR-144 was associated with worse survival. Multiple miRNAs that interact with ARID1A, VEGFA, and PIK3A were implicated. Higher expression of miR-223-5p was associated with worse outcomes. miR-223-5p is hypothesized to inhibit ARID1A expression and has been suggested to affect inflammatory response. Similarly, miR-144-5p and miR-144-3p are thought to affect both ARID1A and VEGFA. expression. Higher miR-144-3p expression was associated with lower survival, which may imply that more suppression of ARID1A expression by miR-144-3p results in a worse outcome. Finally, miR-193-5p negatively effects survival and is suggested to affect PIK3CA. **Conclusions:** Low expression of miR443 (ChemoRx-alone group) and miR196b-3p (ChemoRx+BEV group) track with survival in R/M CC and may serve as biomarkers to guide bevacizumab use in this orphan disease. Research Sponsor: National Cancer Institute/U.S. National Institutes of Health; 75N91019D00024.

An NCDB study examining disparities in the administration of immunotherapy among advanced cervical cancer patients.

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Background: The addition of immunotherapy (IO) to standard therapy has demonstrated substantial survival benefits in the upfront treatment of advanced cervical cancer. Our primary objective was to investigate the role of race on the administration of IO among patients with stage IV cervical cancer, following the publication of KEYNOTE-826 in 2021. Secondarily, we aimed to describe additional factors that may be associated with disproportionate administration. **Methods:** This was a retrospective cohort study utilizing the National Cancer Database (NCDB). We included all patients diagnosed in 2022 with stage IV adenocarcinoma, adenosquamous carcinoma, and squamous cell carcinoma of the cervix. Proportions were used to estimate the administration of IO. Multivariable models adjusted for age, insurance, education, Charlson-Deyo comorbidity scores, geography, distance to treatment center, as well as treatment facility type, location, and volume. **Results:** There were 937 cases identified, of which 368 (39.3%) received IO and 569 (60.7%) did not. A higher proportion of patients received IO at age < 65 compared to > 65 (74.5% vs 25.5%). Patients with Medicaid received IO at similar rates compared to privately-insured patients, at 33.4% verses 34.5%, respectively. When controlling for all other variables, higher education was associated with a greater likelihood of receiving IO (RR 1.46, CI 1.10 – 1.95, p=0.01). Patients with comorbidity scores > 2 were less likely to receive IO than those with lower scores (RR 0.71, CI 0.52 – 0.98, p=0.038). Proportions of patients receiving IO in urban verses rural communities was also similar, at 33.3% and 39.4%, respectively. There were no significant differences in administration of IO associated with treatment center type (RR 1.05, CI 0.89 – 1.23, p=0.55) or volume (RR 0.95, CI 0.79 – 1.13, p=0.55). Mean distances to treatment centers were similar between patients who did and did not receive IO (29.31 vs 30.0 miles). Hispanic patients received IO at higher rates than non-Hispanic White, non-Hispanic Black, and Asian patients at a rate of 47.2% compared to 37.6%, 38.5%, and 38.1%, respectively. Even after adjusting for demographic and tumor factors, the increased receipt of IO among Hispanic patients could not be explained. **Conclusions:** Not only were there no racial disparities observed in the administration of IO among racial groups, but there were no disparities recognized among traditionally marginalized groups. Interestingly, the overall administration IO was lower than expected. The population included in KEYNOTE-826 had a PD-L1 combined positivity score of >1 among approximately 88% of participants. This difference in overall IO administration may be explained by PD-L1 positivity, however our study was limited by the lack of this data. Further investigation is warranted to understand trends in IO administration. Research Sponsor: None.

Clinicopathological and prognostic characteristics of gastric-type endocervical adenocarcinoma: A single-center retrospective study.

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Background: Gastric-type endocervical adenocarcinoma (G-EAC) is a rare and highly aggressive subtype of cervical cancer. Limited screening methods often lead to late-stage diagnosis, contributing to its poor prognosis. This study reviews cases of G-EAC managed at a tertiary gynecological oncology center over the past six years, focusing on prognostic characteristics and responses to adjuvant therapies. **Methods:** We reviewed demographic, pathological, clinical, and prognostic data from patients diagnosed with cervical adenocarcinoma and treated surgically at Obstetrics and Gynecology Hospital Fudan University from January 1, 2018, to December 31, 2023. G-EAC patients were assigned to the study group, while those with usual endocervical adenocarcinoma (UEA) served as the control. The groups were matched 1:1 using propensity score matching to compare prognosis. Primary endpoints were 3-year progression-free survival (PFS) and overall survival (OS). Kaplan-Meier and Cox regression analyses were used to assess survival, and univariate and multivariate analyses were conducted to identify risk factors for G-EAC. **Results:** A total of 960 patients were included in this study, comprising 195 cases of G-EAC and 765 cases of UEA. After matching, the G-EAC group exhibited significantly lower 3-year OS and PFS compared to the UEA group (OS: 74.9% vs. 84.6%, PFS: 66.1% vs. 79.8%, χ^2 = 4.59/6.04, p = 0.032/0.014). Parametrial involvement (OS/PFS: HR = 3.19/2.54, p = 0.003/0.009) and pelvic lymph node metastasis (OS/PFS: HR = 2.64/2.26, p = 0.012/0.013) as independent risk factors for death and recurrence in G-EAC patients. G-EAC patients treated with combined radiotherapy and chemotherapy had significantly better 3-year OS and PFS than those receiving either modality alone (OS: 74.3% vs. 54.5%, PFS: 65.2% vs. 43.6%, χ^2 = 4.86/4.23, p = 0.028/0.039). Cox regression analysis showed that G-EAC patients receiving radiotherapy or chemotherapy alone had significantly higher risks of death and recurrence compared to UEA patients (OS/PFS HR: 5.88/8.37, p = 0.037/0.009). Similarly, G-EAC patients treated with combined radiotherapy and chemotherapy exhibited slightly higher risks of death and recurrence than UEA patients (OS HR: 2.61 vs. 1.63, PFS HR: 3.91 vs. 2.66). **Conclusions:** G-EAC is a rare pathological subtype of cervical cancer with an exceptionally poor prognosis, significantly worse than that of UEA. Parametrial involvement and pelvic lymph node metastasis are independent risk factors for recurrence and death in G-EAC patients. Postoperative combined radiotherapy and chemotherapy reduce the risks of recurrence and death compared to single-modality treatments. However, G-EAC remains less responsive to adjuvant chemoradiotherapy than UEA. Further research to develop more effective therapeutic strategies for this rare and aggressive subtype. Research Sponsor: Shanghai Shenkang Hospital Development Center's Promotion of Clinical Skills and Clinical Innovationin Municipal Hospitals Three-Year Action Plan (2020–2023) Major Clinical Research Project; SHDC2020CR1048B; the shanghai Hospital Development Center Foundation of Clinical Technology Promotion and Management Optimization Project of Shanghai municipal hospitals in 2024; SHDC12024105; the General Program of National Natural Science Foundation of China; 82271654; the Public Welfare Project "JiShiQiYi" of Beijing Health Alliance Charitable Foundation; KM-JSQY-002; the "ZaiDing-Le" Foundation from Beijing Kanghua Foundation for the Development of Traditional Chinese and Western Medicine; KH-2020- LJJ-008.

Adjuvant, neoadjuvant and surgical treatment for locally advanced cervical cancer: A network meta-analysis.

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Background: Concurrent chemoradiotherapy (CCRT) is the standard treatment for locally advanced cervical cancer (LACC). Alternative strategies, including induction chemotherapy followed by CCRT (IC + CRRT) and CCRT with immune checkpoint inhibitors (CCRT + ICI), have shown promising yet conflicting results. This study used a network meta-analysis (NMA) to compare the efficacy of these treatments. **Methods:** A systematic review identified RCTs published until November 25, 2024, comparing treatments for FIGO stage IB2-IVA LACC, including neoadjuvant chemotherapy, adjuvant chemotherapy (ACT), radiotherapy (RT), CCRT+ICI, surgery, or combinations. Progression-free survival (PFS) and overall survival (OS) were evaluated. Hazard ratios (HRs) were extracted or reconstructed from Kaplan–Meier curves using IPDfromKM. Bayesian NMA was conducted with random-effects models using the gemtc package. Three chains were run for 600,000 iterations, discarding the first 60,000 as burn-in. Results included 95% credible intervals (CrIs) for HRs. Treatment rankings were derived using the surface under the cumulative ranking curve (SUCRA), and probabilities of treatment superiority (SP) were calculated. **Results:** A total of 46 trials (49 reports) involving 13,895 patients were included in the analysis, with 89% having squamous cell histology. CCRT and RT were the most frequently used comparator treatments. Data from 39 trials (11,727 patients) were analyzed for OS, comparing 10 treatment regimens. CCRT significantly improved OS compared to RT (HR 0.76; 95% credible interval [CrI] 0.63–0.94) and showed a trend toward superiority over surgery (HR 0.71; 95% CrI 0.49–1.02; SP = 96.9%). However, no significant differences were observed between CCRT and either CCRT + ICI (SP = 6.2%) or IC + CCRT (SP = 28.3%). CCRT + ACT further improved OS compared to RT (HR 0.60) and surgery (HR 0.56). CCRT + ICI also demonstrated superiority over RT and surgery. Based on SUCRA scores, CCRT + ICI ranked highest for OS. For PFS, data from 37 trials (12,025 patients) were analyzed. CCRT demonstrated superiority over RT (HR 0.77; 95% CrI 0.65–0.92). No significant differences were observed between CCRT and other regimens, including CCRT + ICI (SP = 5.4%), IC + CCRT (SP = 34.1%), and CCRT + ACT (SP = 29.2%). Both CCRT + ACT and CCRT + ICI were superior to RT alone (HR 0.71 and HR 0.59, respectively). Additionally, CCRT + ICI was more effective than IC + RT. In a subgroup analysis of trials limited to squamous cell carcinoma, CCRT was superior to CCRT + ACT (HR 0.4; 95% CrI 0.2–0.85). Based on SUCRA scores, CCRT + ICI ranked highest for PFS. **Conclusions:** CCRT demonstrates consistent superiority in OS and PFS over RT and surgery, with comparable efficacy to regimens such as CCRT + ACT, IC + CCRT, and CCRT + ICI. These findings reaffirm CCRT's position as the cornerstone treatment for LACC, while supporting the potential of novel strategies in select populations. Research Sponsor: None.

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A phase II study of anlotinib plus penpulimab as first-line treatment for persistent, recurrent, or metastatic cervical cancer: Results from ALTER-GO-020 trial.

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Background: In patients with recurrent, or metastatic cervical cancer, atezolizumab combined with bevacizumab and chemotherapy has significantly enhanced progression-free survival (PFS) and overall survival (OS) regardless of PD-L1 status. ALTER-GO-020 trial was designed to evaluate the efficacy and tolerability of anlotinib (a multitarget anti-angiogenic TKI) and penpulimab (anti-PD-1 antibody) as a chemotherapy-free regimen for patients (pts) with recurrent or metastatic gynecological cancer. This report presents the latest efficacy and safety data from the completed cervical cancer cohort. **Methods:** ALTER-GO-020 is a single arm, open-label, multi-cohort, multi-center phase II clinical study. In cervical cancer cohort, 26 pts were planned to be enrolled. Eligible pts were histologically confirmed persistent, recurrent, or metastatic cervical cancer (including adenocarcinoma, adenosquamous carcinoma, or squamous-cell carcinoma), not amenable to curative treatment, and had no prior systemic treatment for metastatic, persistent, or recurrent disease. Pts were treated with anlotinib (12mg, po qd, d1-14, q3w) plus penpulimab (200mg, IV, d1, q3w) until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR) and the secondary endpoints included PFS, duration of response (DOR), disease control rate (DCR), OS and safety. **Results:** 26 pts were enrolled. The median age was 52 years (range, 31-70), 65% of pts were squamous-cell carcinoma, 88% received previous chemoradiotherapy with or without surgery, and 71% had previously received neoadjuvant/adjuvant platinum-containing chemotherapy. As of date cutoff (Dec, 2024), the median follow-up time was 11.7 months (range, 1.3-30.0 months). In the efficacy analysis (n=26), the preliminary ORR was 50% (95% CI: 32.1%-67.9%), DCR was 92.3% (95% CI: 75.9%-98.6%). The mPFS was 11.0 months (95% CI: 5.8m-16.2m months). The mOS was not reached. Treatment-related adverse events (TRAEs) of any grade occurred in all 26 pts, in which 12 (46.2%) were grade ≥3. The most common grade ≥3 TRAEs were hypertension (19.2%), hand foot syndrome (11.5%), fatigue (3.8%), and diarrhea (3.8%). TRAEs led to dose reduction and interruption were 15.4%, and 38.5% of pts, respectively. No TRAEs leading to death. **Conclusions:** Anlotinib combined with penpulimab as a chemotherapy-free regimen showed a significant improvement in ORR, a trend towards longer PFS, and favorable safety in the treatment of pts with recurrent or metastatic cervical cancer. Clinical trial information: NCT05028504. Research Sponsor: None.

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Preliminary results of ZG005, a bispecific antibody targeting PD-1 and TIGIT, as monotherapy in patients with advanced cervical cancer.

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Background: ZG005, a PD-1 and TIGIT dual-specific antibody, is a promising immunotherapy for tumors. By blocking both pathways, it can synergistically activate T cells and enhance the anti-tumor activity of NK cells. Preliminary results of this first-in-human (FIH) study were presented at ASCO 2023 and ASCO 2024. Here, we report the efficacy and safety results in patients with advanced cervical cancers. **Methods:** Following the dose-escalation phase, patients with specified tumor types were enrolled into dose-expansion stage. Within each tumor type cohort, subjects were randomized 1:1 to receive ZG005 10 mg/kg Q3W or 20 mg/kg Q3W by intravenous infusion. Efficacy was assessed by both the investigator and the independent radiology committee (IRC) according to RECIST v1.1. **Results:** As of December 05, 2024, a total of 55 patients with advanced cervical cancer had been randomized to receive at least one dose of ZG005 10 or 20 mg/kg. The median age was 52.0 years. Of these patients, 98.2% had failed to at least one prior line of therapy, and 24.7% had previously received immune checkpoint inhibitor (ICI) treatments. 87.3% patients were squamous cell carcinoma, 9.1% adenocarcinoma and 3.6% adenosquamous carcinoma. Among the total 22 patients on the 20 mg/kg group who hadn't treated any prior ICI treatments before, 3 achieved a complete response (CR) and 6 partial responses (PR) per the IRC's assessments. The confirmed objective response rate (ORR) was 40.9%, and the disease control rate (DCR) was 68.2%. The median progression free survival (mPFS) has not yet been reached. Among the 55 patients for the safety analyses, 46 (83.6%) reported treatment related adverse events (TRAEs), with 5 (9.1%) grade 3-4, including one patient each with hypocalcemia, myositis, rash, hypertension and anemia. Serious adverse events (SAEs) occurred in 8 subjects (14.5%), with one myositis case (1.8%) was the only SAE related to ZG005 and also the sole TRAE that led to treatment discontinuation. No death was attributed to ZG005. Grade 3-4 Immune-related adverse events (irAEs) were observed in 4 patients (7.3%), including myositis, rash, hypertension and anemia. No new safety signals were observed compared with other ICIs. **Conclusions:** ZG005 has demonstrated a tolerable safety profile and promising anti-tumor activity at the 20 mg/kg dose as monotherapy in patients with advanced cervical cancer. Clinical trial information: NCT06233293. Research Sponsor: None.

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Preliminary results of ZG005, a bispecific antibody targeting PD-1 and TIGIT, in combination with chemotherapy with or without bevacizumab as first-line treatment for advanced cervical cancer.

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Background: ZG005, a PD-1 and TIGIT dual-specific antibody, is a promising immunotherapy for tumors. By blocking both pathways, it can synergistically activate T cells and enhance the anti-tumor activity of NK cells. This report presents the results for the combination of ZG005 and the chemotherapy with or without bevacizumab as a first-line systematic treatment in patients (pts) with advanced cervical cancer. **Methods:** ZG005-003 was a multicenter, open-label, phase I/II clinical trial. In the Part 1, the escalating doses were 10 mg/kg and 20 mg/kg. In the Part 2, pts were randomized at 1:1 ratio to receive ZG005 at 10 mg/kg or 20 mg/kg in combination with the standard chemotherapy (paclitaxel [175 mg/m^2] plus carboplatin [AUC 5] or cisplatin [50 mg/m^2]), with or without bevacizumab (15 mg/kg) every 3 weeks for six cycles, followed by the maintenance therapy of ZG005 with or without bevacizumab for up to 2 years. Safety and efficacy (per RECIST v1.1) were assessed. **Results:** As of December 19, 2024, the Part 1 had completed and the Part 2 was ongoing, a total of 41 pts had been enrolled for the both Parts, with 12 pts in Part 1 and 29 pts in Part 2. The median age was 54 years, and 87.8% of pts were squamous carcinoma. 53.7% of pts received bevacizumab during the trial. No dose-limiting toxicity (DLT) were observed during the Part 1. Among all the 41 pts, 31 (75.6%) experienced treatment-related adverse events (TRAEs) which attribute to ZG005. Most TRAEs were grade 1-2, while 12 pts (29.3%) reported grade 3 or higher TRAEs. There was no treatment discontinuation or death due to TRAEs. Only one serious adverse event (SAE) of bilateral lung pneumonia in the 10 mg/kg group was assessed related to ZG005 by the investigator. No ZG005-related SAE was reported in the 20 mg/kg group. Of the 28 pts evaluable for efficacy, 13 on 10 mg/kg and 15 on 20 mg/kg, the unconfirmed overall response rates (ORR) was 69.2% for the 10 mg/kg group, and 80.0% for the 20 mg/kg group. **Conclusions:** ZG005 in combination with the chemotherapy, with or without bevacizumab, demonstrated favorable safety and tolerability profiles at both 10 mg/kg and 20 mg/kg dosages. Additionally, this regimen exhibited a significant antitumor activity in first-line cervical cancer pts, with the 20 mg/kg dose group showing a notably better efficacy in comparison with the 10 mg/kg dose group. Clinical trial information: NCT06241235. Research Sponsor: None.

Induction cadonilimab combined with chemotherapy followed by chemo-radiotherapy for locally advanced cervical cancer: A multicenter, single-arm, phase II trial.

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Background: Short-course weekly induction chemotherapy followed by chemoradiotherapy (CCRT) improves survival for locally advanced cervical cancer (LACC) in the CxII and INTERLACE trial. However, only 70% patients achieved objective response (CR or PR) whereas 20% grade 3-4 adverse events were reported during induction chemotherapy in the CxII study. Cadonilimab is a bi-specific antibody targeting both PD-1 and CTLA-4. The COMPASSION-16 trial has recently demonstrated the encouraging effectiveness and safety of cadonilimab combined with chemotherapy in recurrent/metastatic cervical cancer. This study was aimed to assess the combination of induction cadonilimab and chemotherapy before CCRT. **Methods:** In this multicenter, single-arm, phase 2 study, we used a Simon two-stage design. Previous studies of induction chemotherapy showed a ORR of 68.8%-80% in LACC. Null hypothesis of ORR 80% was adopted in this study. Estimating a ORR of 95% would be achieved following induction therapy, a total of 29 patients (including 9 in the first stage) were required with type I and type II errors set at 0.05 and 0.2, respectively. Eligible patients were women aged 18 years or older, newly diagnosed disease with stage IB3-IVA (International Federation of Gynecology and Obstetrics [FIGO] 2018), with histologically confirmed cervical carcinoma, and had an ECOG performance status of 0 or 1. Patients received 2 cycles of induction therapy consisting of cadonilimab at a dose of 10mg/kg plus nab-paclitaxel at a dose of 260 mg/m^2 and cisplatin at a dose of 75mg/m^2 followed by CCRT. The primary endpoint was objective response rate (ORR) at 2 weeks after the completion of induction therapy and secondary endpoints included progression-free survival (PFS) and overall survival (OS). **Results:** Between January and October 2024, 29 patients were enrolled, with a median age of 58 years (range 32–70). All patients were ECOG performance status of 1. Of these, 26 had squamous cell carcinoma, and 3 had adenocarcinoma. FIGO stages included stage II (9 [31.0%]), III (18 [62.1%]), and IVA (2 [6.9%]). As of January 19, 2025, 26 patients completed CCRT. Median PFS and OS were not reached. At 2 weeks post-induction therapy, ORR was 93.1% (27 PR, 2 SD). Thirteen patients underwent evaluation at 3 months post-CCRT, all achieving CR (100%). Grade 3–4 treatment-related adverse events occurred in 10.3% of patients (3/29), including leukopenia (n=2) and primary adrenal insufficiency (n=1) during induction therapy. **Conclusions:** Cadonilimab combined with chemotherapy as induction therapy shows promising anti-tumor activity and manageable safety profile in LACC patients. These findings suggest the potential of induction chemo-immunotherapy followed by CCRT and warrants further follow-up. Clinical trial information: NCT06511726. Research Sponsor: None.

A real-world analysis of the effectiveness of pembrolizumab by type of associated treatment in patients with metastatic cervical cancer: Added value of bevacizumab.

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Background: Pembrolizumab (pembro) showed a statistical significant survival benefit in persistent, recurrent, or metastatic cervical cancer (CC) when added to chemotherapy. In this real-world study we aimed to evaluate if the effectiveness of pembro may vary according to the type of platinum used or by the incorporation of bevacizumab (bev). **Methods:** The analysis was conducted with the TriNetX Global Collaborative Network. In our study, we defined different cohort of patients by type of platinum (cisplatin or carboplatin) and bev use (yes or no). First, we compared 597 CC patients treated cisplatin with 1.080 CC patients treated with carboplatin, in addition to paclitaxel and pembro. After this analyses, we evaluated the addition of bev (701 patients) to a platinum-based regimen compared to a cohort of patients treated without bev (562 patients). A propensity score matching (PSM) was used to balance the cohorts by age, race, previous radiotherapy, body mass index and treatment (bev for first analyses and cisplatin for the second). Subsequently, a COX analyses, adjusted for the same factors, was used in un-matched cohorts to validate our results. Hazard ratio (HR) was used to compare the overall survival (OS) and the development of fistulae, bowel perforation or pulmonary embolism (PE) in the matched cohorts. **Results:** PSM generated 583 pairs of CC patients treated with cisplatin (mean age of 50.6, +/-12.6 standard deviation, SD) or carboplatin (mean age of 50.2, +/-12.7 SD). Median OS was not statistical different between the groups (HR 0.92, 95% CI 0.75-1.28), confirmed also by the Cox model (HR 0.95, 95% CI 0.79-1.15). Among the 386 matched pairs of CC patients treated with (mean age of 53.8, +/-13.1 SD) or without bev (mean age of 53.8, +/-13.4 SD), median OS was 35.7 months versus 20.1 months (HR 0.64, 95% CI 0.49–0.84, p = 0.001), without differences in the rate of fistulae (HR 0.77, 95% CI 0.50-1.18), but an increased risk in bowel perforation (HR 3.08, 95% CI 1.01-9.38, p = 0.037) and a lower risk of PE (HR 0.57, 95% CI 0.35-0.93, p = 0.022). In multivariate analyses, bev significantly reduced the risk of death (HR 0.75, 95% CI 0.61-0.94, p = 0.01). **Conclusions:** The survival rates associated with immuno-therapy treatment in our real-world study are consistent with those reported in previous studies. Specifically, we showed that the effectiveness of pembro is not influenced by the type of platinum used. However, the addition of bev may extend OS in patients with CC, without increasing the risk of fistulae or PE. Research Sponsor: None.

A non-invasive metabolomic biomarker for detecting cervical intraepithelial neoplasia and cervical cancer.

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Background: Cervical intraepithelial neoplasia (CIN) is a precancerous lesion that can progress to cervical cancer, a leading malignancy affecting women worldwide. Although current screening strategies and diligent follow-up are essential for identifying high-grade CIN, there remains a critical need for minimally invasive tests to aid in both early detection and disease monitoring. This study evaluated the utility of a blood-based metabolomic liquid biopsy for differentiating CIN from cervical cancer and investigated the role of 2,3,6-Trichlorobenzaldehyde as a novel biomarker. **Methods:** From September 2023 to December 2024, 177 participants (cervical cancer, n=18; CIN, n=49; healthy controls, n=110) were enrolled at Soonchunhyang University Hospital in Cheonan, South Korea. All participants were adults (≥18 years) with no cancer history in the previous five years and were not receiving anticancer therapy at the time of serum collection. Serum samples underwent untargeted metabolomic profiling via headspace gas chromatography–mass spectrometry (GC–MS). Relative metabolite abundances were compared among the groups, and pairwise t-tests ($p < 0.05$) assessed statistical significance. **Results:** Six metabolites demonstrated strong detection and classification performance, with 2,3,6-Trichlorobenzaldehyde emerging as the most prominent biomarker. This metabolite effectively differentiated among cervical cancer, CIN, and healthy controls (ANOVA, $p < 0.0001$). Specifically, 2,3,6-Trichlorobenzaldehyde yielded a sensitivity of 94.5% and a specificity of 95% for detecting cervical cancer, and a sensitivity of 95.9% and a specificity of 95% for identifying CIN. It also significantly distinguished Stage I cervical cancer from CIN grades 1, 2, and 3, as well as from adenocarcinoma in situ (AIS) (t-test, $p < 0.0001$). Five additional metabolites—p-Xylene, 3,6,9,12-Tetraoxahexadecan-1-ol, Ethylbenzene, Indole, and Cyclohexanone—were significantly elevated in both the cervical cancer and CIN groups compared to healthy controls (t-test, $p < 0.0001$), although they did not differ substantially between the cancer and CIN groups (t-test, $p > 0.05$). **Conclusions:** These findings highlight 2,3,6-Trichlorobenzaldehyde as a promising candidate for a blood-based metabolomic panel aimed at distinguishing cervical cancer from CIN and healthy controls. A minimally invasive assay incorporating this biomarker may improve cervical disease screening, refine risk stratification, and support continuous disease surveillance. Further prospective validation in larger cohorts is warranted to establish its clinical applicability. Research Sponsor: None.

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GT101 autologous TIL therapy in patients with recurrent and metastatic cervical cancer: A phase 1 study.

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Background: GT101 is Grit's tumor-infiltrating lymphocyte (TIL) product. Adoptive cell therapy using autologous TILs has shown efficacy and long-term responses in patients with certain advanced solid tumors that have progressed after conventional therapies. We present data from 11 patients with recurrent or metastatic cervical cancer enrolled in a Phase 1, open-label, single-arm, multicenter trial (NCT05430373) of GT101. The study aims to investigate the safety profile, efficacy trends, and duration of response. **Methods:** Eleven patients with recurrent or metastatic cervical cancer were enrolled in the study, receiving a lymphodepletion regimen followed by GT101 infusion and IL-2 administration. The study's primary endpoints were treatment-emergent adverse events (TEAEs), including serious adverse events (SAEs) and adverse events (AEs), assessed using the CTCAE version 5.0 grading scale. Secondary endpoints included objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), duration of response (DoR), and overall survival (OS) based on RECIST version 1.1. **Results:** As of August 1, 2024, 11 patients received treatment, with a median age of 48 years and two prior therapy lines. Following FC lymphodepleting chemotherapy, patients received GT101 infusion at doses of $\geq 5\times10^9$ viable cells, with a median dose of 4.1×10^{10} viable cells, followed by high-dose IL-2 (600,000 IU/kg, up to 6 doses). Most adverse events (AEs) were Grade 1 or 2. Grade ≥ 3 AEs, primarily related to lymphodepleting chemotherapy and IL-2, included decreased lymphocyte, white blood cell, and neutrophil counts, anemia, pyrexia, and decreased platelet count. Most Grade ≥ 3 AEs resolved or downgraded to Grade ≤ 2 within 14 days. Among 11 cervical cancer patients, the objective ORR was 45.5% (5/11), with disease control in 10/11 patients (90.9%). Four patients (36.4%) had confirmed PR, one (9.1%) achieved CR, and five (45.5%) had SD; one patient had unconfirmed PD. The median PFS was 4.83 months, and median OS has not yet been reached. A patient with CR maintained this response for 14.5 months, diagnosed with stage IIIC2 cervical squamous cell carcinoma, and underwent surgical resection of metastatic lymph nodes. The SOD at baseline was 71.57 mm, reduced to 29.12 mm after 28 days. At week 12 post-GT101 treatment, imaging showed complete response of the lesion, achieving CR. **Conclusions:** In the GT101 Phase 1 study, no treatment-related SAEs or DLTs were observed. GT101, infused after FC lymphodepleting chemotherapy and high-dose IL-2, exhibited a manageable safety profile. It demonstrated clinically meaningful activity and durable responses in patients with recurrent and metastatic cervical cancer. These promising results indicate favorable long-term survival outcomes, durable responses, and no long-term safety concerns related to GT101. Clinical trial information: NCT05430373. Research Sponsor: None.

Management of loop electrosurgical excision procedure with positive margins.

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Background: Loop Electrosurgical Excision Procedure (LEEP) is a primary management for preinvasive cervical disease. While often successful, around 10% will have disease extend to the margin of the LEEP specimen, leaving the possibility of pathology extended beyond the excised region. The American Society for Colposcopy and Cervical Pathology (ASCCP) provides management options for LEEP with positive margins, which include hysterectomy, repeat LEEP, or follow-up in 6 months with either: HPV-based testing or colposcopy with endocervical curettage. Limited data exists in the comparison of management options. **Methods:** This retrospective study included patients with cervical preinvasive disease referred to a single academic institution between 1/2022 to 12/2024 who underwent LEEP found to have a positive margin. Demographics and pathology results were obtained from medical records. The primary outcome was follow-up colposcopy pathology in patients who had a positive margin from LEEP. Statistical analysis was performed using GraphPad. **Results:** 67 patients underwent follow-up colposcopy after a LEEP with a positive margin. At time of LEEP, the median age was 34.5 years with 36% Hispanic, 34% African American, 22% White, and 2% Asian. With HPV status prior to LEEP, 72% were non-genotyped high risk (HR), 6% HPV16+, 6% HPV18+, and 3% were other HR+. Positive margins were either CIN 2 (N=12) or CIN 3 (N=55) and either endocervical (N=40), peripheral (N=15), both endocervical and peripheral (N=7), or unspecified (N=5). Pathology at follow-up colposcopy was primarily negative/low-grade disease (83.6%) with a minority being high-grade disease (16.4%). CIN 2 or CIN3 at the margin was not associated with high-grade disease on follow-up colposcopy (0% vs. 26.7%; p=0.108). The median age at time of LEEP did not significantly differ between CIN 2 or CIN3 positive margins (37.5 vs 34.9y; p=0.274) and was not associated with negative/low-grade or high-grade disease at follow-up colposcopy (38.4 vs 35.7y, p=0.251). Race was not associated with high-grade disease on follow-up colposcopy (p=0.239). There was no difference between high-grade lesion on colposcopy and location LEEP positive margin (p=0.998). HPV 16+ or 18+ was not associated with high-grade pathology at follow up colposcopy (p=0.289). **Conclusions:** In our diverse population, the prevalence of high-grade disease on follow-up colposcopy is low regardless of having CIN 2 or CIN 3 at any margin at time of LEEP. Numerically, CIN 2 margins were less likely to have positive high-grade colposcopy when compared to CIN 3 margin. Race nor age were associated with high-grade disease on follow-up colposcopy. While ASCCP offers follow-up repeat colposcopy in the setting of positive margins, prospective studies could be beneficial in determining if less-invasive options, such as HPV testing are sufficient for follow-up in this population. Research Sponsor: None.

5535 Poster Session

Global cervical cancer outcomes and national cancer system characteristics.

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Background: Significant global health disparities persist in cervical cancer, with over 85% of cases and deaths occurring in low- and middle-income countries (LMICs). In many settings, access to screening, vaccination, and treatment is limited. Despite being largely preventable through HPV vaccination and early detection, many women around the world still face inadequate healthcare infrastructure, lack of awareness, cultural stigma, and gender barriers to seeking care. Therefore, we evaluated global health system metrics that may inform efforts to improve equity in access to cervical cancer care globally. **Methods:** Estimates of age-standardized mortality-to-incidence ratios (MIR) were derived from GLOBOCAN 2022 for female patients of all ages with cervical cancer. We collected health spending as a percent of gross domestic product, physicians/1000 population, nurses and midwives/1000 population, surgical workforce/1000 population, GDP per capita, Universal Health Coverage Service Coverage Index (UHC index), availability of pathology services, human development index (HDI), gender inequality index (a combined metric of health, empowerment, and economic agency), radiotherapy centers/1000 population, and out-of-pocket expenditure as percentage of current health expenditure. We evaluated the association between MIR and each metric using univariable linear regressions. Metrics with $p<0.0045$ (Bonferroni corrected) were included in multivariable models. Variation inflation factor (VIF) allowed exclusion of variables with significant multicollinearity. R2 defined goodness of fit. **Results:** On univariable analysis, all 11 metrics were significantly associated with MIR of cervical cancer (<0.001 for all). After including metrics that were significant on univariable analysis, HDI demonstrated significant collinearity (VIF=19). Therefore, after correcting for multicollinearity, the final multivariable model with 10 variables had R2 of 0.79. On multivariable analysis, the following variables were independently associated with lower (improved) MIR for cervical cancer: 1) nurses/midwives per 1000 population ($\beta=-0.0071$, $p=0.029$) and 2) UHC index ($\beta=-0.0023$, $P=0.013$). In addition, greater gender inequality was associated with greater (worse) MIR ($\beta=0.30$, $P=0.002$). **Conclusions:** This global analysis of health-system metrics suggests promoting progress towards UHC and strengthening the nursing/midwifery workforce may be independently associated with improved cervical cancer mortality-to-incidence ratio. Furthermore, greater gender inequality was associated with worse MIR. These findings may inform further efforts to improve global cervical cancer care and underscore the importance of gender equity in improving global cancer outcomes. Research Sponsor: None.

Atezolizumab and stereotactic body radiation in metastatic, recurrent, or persistent cervical cancer: Results from a phase II multi-institutional study.

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Background: Pembrolizumab is approved for PD-L1+ but not PD-L1 negative metastatic, recurrent, or persistent cervical cancer. Response rates to single agent anti-PD-1/PD-L1 therapy have been modest with no responses noted in PD-L1 negative tumors. **Methods:** The study is designed as a prospective, phase II multi-institutional trial of SBRT followed by atezolizumab (1200 mg intravenously q3 weeks). Key eligibility criteria included patients with metastatic, recurrent, or persistent cervical cancer with at least 2 distinct lesions. The primary objective was objective response rate measured at the unirradiated target lesion. Secondary endpoints included overall response, progression free survival (PFS), overall survival (OS), and adverse events. Clinical trial information: NCT03614949. **Results:** A total of 21 patients were enrolled. Median follow-up is 23.6 months. The majority of patients had adenocarcinoma (n=10; 48%) and were PD-L1 negative (n=15; 71%). The best overall response was a partial response in 5 (24%) and stable disease in 12 (57%) patients. The median duration of response was 8.6 months (95% CI: 4.5-13.6 months). An objective response at the unirradiated target lesion was observed in 8 patients (38%), meeting the study defined endpoint. Responses were noted in PD-L1 negative tumors. The median PFS was 4.7 months (95% CI: 3.9-7.4) with a 6-month PFS of 48%. The median OS was 26 months (95% CI 7.6 – 54) with a 6-month OS of 76%. No differences were noted in OS or PFS by PD-L1 status. The most common grade $\geq$ 2 toxicities at least possibly attributed to study therapy included lymphopenia (n=6; 29%), nausea/vomiting (n=3; 14%), and hyponatremia (n=3; 14%). **Conclusions:** In this first trial of SBRT and atezolizumab in metastatic cervical cancer unselected for PD-L1, combination therapy was well tolerated. Responses were noted in PD-L1 negative tumors. Combination therapy may allow for improved response rates to immune checkpoint inhibition in metastatic cervical cancer particularly in PD-L1 negative tumors. Clinical trial information: NCT03614949.
Research Sponsor: Genentech; ML40521.

Real-world efficacy and safety of cadonilimab (PD-1/CTLA-4 bispecific antibody) in patients with advanced, recurrent, and metastatic cervical cancer.

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Background: Immune checkpoint inhibitors have become one of the important treatment modalities for advanced, recurrent and metastatic cervical cancer (A/R/M CC). Cadonilimab, a PD-1 and CTL-4 bispecific antibody, has showed considerable efficacy for treatment of A/R/M CC. This study aims to investigate the real-world efficacy and adverse event profile of cadonilimab in the treatment of A/R/M CC. **Methods:** We enrolled patients with histologically confirmed CC, who had received at least two cycles of cadonilimab for A/R/M disease and had imaging evaluation at Department of Gynecologic Oncology in Shandong Cancer Hospital and Institute in China, between July 2022 and March 2024. Efficacy including objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), overall survival (OS) and adverse events (AEs) were analyzed. **Results:** 96 patients treated with cadonilimab monotherapy or cadonilimab plus chemotherapy with/without radiotherapy were enrolled. The median follow-up duration was 12.5 months. The overall ORR was 69.8%, the DCR was 89.6%. (Table 1). The median PFS was 12 months (95%CI 8.4-15.6), and the median OS was not reached. The ORR of first and second line's treatment was 77.7% and 56.6%, respectively. DCR was 91.7% and 80.0%, respectively. Among the 18 patients treated with third-line and above, four (22.2%) patients achieved CR, ORR was 72.2%, and DCR was 88.8%. Among all patients, PD-L1 positive patients had a higher ORR (74.4%, P=0.049). Comparing with non-SCC, patients with SCC had better ORR (78.6% vs.38.0%, P=0.001). It's also worth noting that, among 19 patients who had progressed on first or second line's therapy of PD-1 monospecific antibody, cadonilimab mono or combination therapy achieved an overall ORR of 63.1% (1 CR, 11 PR) and a DCR of 94.7%, and a median PFS of 15.2 months (95%CI 5.7-24.7). Among them, 16 patients with SCC had a 100% DCR and a median PFS of 15.2 months (95%CI 5.1-25.3). The incidence of immune-related adverse events (irAEs) was 33.3%, mainly including 21 hypothyroidism (21.9%), seven hyperthyroidism (7.3%), etc. Two (2.1%) had ≥ grade 3 irAEs (one pneumonia and one myocardial injury). No death was caused by irAEs. **Conclusions:** Cadonilimab showed encouraging efficacy and manageable safety in the treatment of A/R/M CC in real world, even in patients with PD-L1 negative. And it also present promising disease control in patients who have progressed on previous PD-1 monospecific antibody. Research Sponsor: None.

The best overall response, PFS and OS in first-, second-, ≥ third-line and total patients.

Best overall response, PFS and OS	First-line (n=48)	Second-line (n=30)	≥Third-line (n=18)	Total
CR (%)	16.6	16.6	22.2	17.7
PR (%)	60.4	40.0	60.0	52.0
ORR (%)	77.7	56.6	72.2	69.8
DCR (%)	91.7	80.0	88.8	89.6
mPFS (months)	12.0	8.9	18.7	12.0
6-month PFS rate (%)	87.5	66.6	88.8	81.2
6-month OS rate (%)	100.0	100.0	100.0	100.0

Integrative analysis of VB10.16 and atezolizumab in advanced HPV16-positive cervical cancer: Linking biomarker insights to clinical outcomes.

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Background: Therapeutic cancer vaccines combined with immune checkpoint inhibitors offer a promising strategy to enhance anti-tumor responses. We recently demonstrated the safety and clinical efficacy of VB10.16, a DNA-based therapeutic cancer vaccine encoding HPV16 E6/E7 oncoproteins fused to CCL3L1 for antigen-presenting cell targeting, in HPV16-positive persistent, recurrent or metastatic cervical cancer[1]. This analysis explores the association between HPV16-specific T cell responses, tumor microenvironment (TME) characteristics, and clinical outcomes in the phase 2a trial. **Methods:** In this multicenter, open-label trial, 52 patients with advanced HPV16-positive cervical cancer received VB10.16 (3 mg intramuscularly) combined with atezolizumab (1200 mg intravenously) for up to 48 weeks. Primary endpoints were safety and objective response rate per RECIST v1.1. Secondary endpoints included overall survival (OS) and HPV16-specific T cell responses via IFN-γ ELISpot (n=36). Predefined exploratory endpoints included systemic immunosuppression and TME inflammatory status in baseline tumors, assessed via myeloid cell counts (baseline to ~week 9, n=47), flow cytometry (T cell/myeloid-derived suppressor cells [MDSC] ratio, n=21), and gene expression analyses (n=29). **Results:** Patients with reduced on-treatment systemic immunosuppression demonstrated stronger HPV16-specific T cell responses than patients without (myeloid cell counts decreased in 17/47 patients; T cell/MDSC ratio increased in 12/21 patients). On-treatment reduction in systemic immunosuppression was associated with a higher clinical benefit rate (complete response [CR]/partial response [PR]/stable disease [SD] in 17/28 vs 4/19 patients by myeloid counts and 10/12 vs 2/9 by T cell/MDSC ratio), suggesting associations between T cell response, systemic immunosuppression and effect of immunotherapies. Among the 9 responders in the efficacy population (n=47; 3 CR; 6.4% and 6 PR; 12.8%), 5 patients had available gene expression data from baseline tumors. Patients with pro-inflammatory/proliferative TME signatures demonstrated higher CR/PR rates (4/14 vs. 1/15) and longer OS compared to patients with stromal/immunosuppressive signaling (mOS not reached vs 8.3 months). Clinical benefit was also observed in stromal/immunosuppressive TMEs (1/15 CR, 6/15 SD), highlighting VB10.16's potential to overcome local immunosuppression. **Conclusions:** VB10.16 combined with atezolizumab induces durable responses, mitigates local and systemic immunosuppression, and demonstrates synergy between biomarkers and clinical outcomes. High CR/PR rates with favorable immune and TME characteristics highlight the promise of this combination therapy, warranting further exploration. [1]Hillemanns P *et al*, 2025 doi:10.1136/jitc-2024-010827. Clinical trial information: NCT04405349. Research Sponsor: Nykode Therapeutics; Nykode Therapeutics was supported by the Norwegian SkatteFUNN R&D tax deduction government program; 322860; F. Hoffmann-La Roche Ltd provided atezolizumab.

5539 Poster Session

A meta-analysis of induction chemotherapy (ICT) followed by chemoradiotherapy for locally advanced cervical cancer: The role of ICT type and duration on efficacy outcomes.

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Background: The treatment of locally advanced cervical cancer (LACC) is based on concomitant chemotherapy and radiotherapy (CCRT). While the recent incorporation of pembrolizumab for stage III-IVA disease has expanded treatment options, immunotherapy remains inaccessible in many regions with high cervical cancer prevalence. The addition of induction chemotherapy (ICT) prior to CCRT is controversial, as trials have yielded conflicting results. This study aims to evaluate the impact of the type and duration of the ICT for LACC. **Methods:** We systematically searched PubMed, Embase and Cochrane for studies with patients diagnosed with LACC receiving ICT followed by CCRT. Studies that included surgery, definitive radiotherapy (without concurrent chemotherapy), or immunotherapy were excluded. We compared ICT regimens between each other based on drug type and duration, and conducted a meta-analysis of trials comparing ICT followed by CRT versus CRT alone. Meta-analyses were carried out using random-effects model, with heterogeneity assessed via I^2 statistics and Cochran's Q test. Sensitivity analyses were performed using the leave-one-out approach, and meta-analyses of proportions with subgroup analyses. **Results:** Among 5,282 screened studies, 20 met the inclusion criteria, representing 1,543 patients treated with ICT. Meta-analysis of proportions revealed a 2-year overall survival (OS) of 84.1% for studies utilizing platinum–paclitaxel compared to 72.2% for platinum–gemcitabine (p-value for subgroup difference = 0.022). Studies with ICT duration of ≤6 weeks showed a 2-year OS of 84.8% compared to 71.7% for ICT duration >6 weeks (p = 0.003). Other subgroup comparisons (cisplatin versus carboplatin, cycle duration of ≤14 days versus >14 days, and cisplatin dose intensity <25 mg/m²/week versus ≥25 mg/m²/week) did not show statistically significant differences in 2-year OS. A meta-analysis of the five controlled studies exhibited high heterogeneity in OS and progression-free survival (PFS), driven by the CIRCE trial — the only study employing a platinum–gemcitabine ICT regimen lasting >6 weeks. Sensitivity analysis excluding this trial demonstrated a significant improvement in OS (HR 0.68; 95% CI 0.47–0.99; p = 0.049) and PFS (HR 0.46; 95% CI 0.31–0.69; p = 0.0002) with the addition of ICT to CCRT, compared to CCRT alone. **Conclusions:** In patients with LACC, the addition of ICT to CCRT significantly improves PFS and OS compared to CCRT alone, provided that the ICT involves a platinum doublet with paclitaxel and is administered within ≤6 weeks. Research Sponsor: None.

A TORC1/2 inhibitor onatasertib combined with toripalimab in patients with advanced cervical cancers with prior anti-PD-(L)1 therapy.

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Background: Clinical findings on onatasertib (ATG-008), an oral TORC1/2 inhibitor, showed promising anti-tumor efficacy and manageable safety when used in combination with toripalimab, an anti-PD-1 monoclonal antibody, in treatment-naïve cervical cancer (CC) patients who had not received prior anti-PD-(L)1 therapy. Here, we present results from the anti-PD-(L)1 therapy treated CC cohort of the TORCH-2 study who had at least prior 1 line of anti-PD-(L)1 therapy with the combination of onatasertib and tori. **Methods:** The TORCH-2 study is a phase 1/2 open-label, dose escalation and expansion trial of onatasertib in combination with tori in patients (pts) with advanced solid tumours (NCT04337463). Eligibility criteria included at least one measurable lesion, ECOG 0-1 and adequate organ function. Pts with prior PI3K/AKT/mTOR inhibitor therapy were excluded. CC pts with at least prior 1 line of anti-PD-(L)1 therapy and 1 line of platinum chemotherapy regardless of PD-L1 expression, were enrolled and received onatasertib 15mg orally once a day (QD) in combination with tori 240 mg, once every 21 days (Q3W). Efficacy assessments were reported based on RECIST1.1 criteria and the endpoints included overall response rate (ORR), disease control rate (DCR), duration of response (DOR), progression free survival (PFS) and overall survival (OS). **Results:** As of Nov 25, 2024, 30 advanced CC pts who had at least prior 1 line of anti-PD-(L)1 therapy and 1 line of platinum chemotherapy were enrolled. Median age was 56.5 years. Baseline ECOG scores were 0 (26 pts) and 1 (4 pts). There were 14 and 16 pts who had received 1 and ≥2 prior lines of systemic therapy, respectively. Additionally, 16 pts had prior abraxane treatment and 11 pts had prior bevacizumab therapy. The median time since initial diagnosis was 37 months(m). The efficacy-evaluable population (27 CC pts) had an ORR of 22.2% (6/27, all confirmed). The DCR was 85.2%. The median time to response was 1.7 m (1.4, 4.2) and median DOR was 5.7 m (95% CI: 2.7, NE). Median PFS and median OS was 4.2 m (95% CI: 3.3, 5.8) and 21.4 m (95% CI: 15.5, NE), respectively. The ORRs of PD-L1 positive and PD-L1 negative populations were 30% (3/10) and 33.3% (2/6), respectively. Thirty pts (100%) had ≥ 1 TEAEs; 22 (73.3%) pts had grade ≥ 3 TRAEs. The most common all grade TRAEs included hyperglycaemia (56.7%), rash (43.3%) and white blood cell decreased (43.3 %). No TEAE led to death. **Conclusions:** Onatasertib in combination with tori is tolerable with encouraging response rate and disease stabilisation in advanced CC pts with prior anti-PD-(L)1 therapy, regardless of PD-L1 expression. The expansion cohorts are ongoing. Clinical trial information: NCT04337463. Research Sponsor: Antengene.

Evolving global burden and trend of cervical cancer in G20 countries: Age, sex, regional disparities from 1990-2021.

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Background: Cervical Cancer (CC) is the 6th leading cause of death and 4th leading cause of disability amongst all cancer in G20 countries. The G20 nations, which represent about 85% of the global GDP, hold a pivotal role in shaping the world's economic and health landscapes. This economic dominance underscores the substantial impact that public health issues, like CC, can have not only on individual countries but on global stability and productivity. **Methods:** We estimated the incidence, prevalence, deaths, disability-adjusted life years (DALYs), and years lived with disability (YLDs) attributed to CC across the G20 countries from 1990 - 2021, disaggregated by age, sex, year, and location, using the standardized methodology of the Global Burden of Disease Study 2021. Non-fatal health outcomes were modeled using DISMOD MR 2.1, a machine learning tool, while fatal health outcomes were assessed using the Cause of Death Ensemble Model (CODEm). The results are reported as absolute counts and age-standardized rates per 100,000 population. **Results:** The total prevalence count of cervical cancer increased from 1.3 (95% uncertainty interval: 1.2–1.3) million in 1990 to 2.2 (2.0–2.5) million in 2021. Deaths rose from 140,740 (128,861–152,835) to 183,343 (166,174–200,956), while disability-adjusted life years (DALYs) increased from 4.8 (4.4–5.2) million to 5.9 (5.3–6.4) million during the same period. The highest annual percentage change (APC) in the age-standardized incidence rate (ASIR) was observed in Italy (1.59%), followed by South Africa (1.14%), China (0.43%), Argentina (0.3%), Bulgaria (0.2%), and Canada (0.1%). In contrast, the majority of countries, including the United States, experienced a decline in ASIR, with the United States showing a 1.5% reduction from 1990 to 2021. For age-standardized mortality rate (ASMR), South Africa (1.12%) and Italy (0.47%) demonstrated an increase in APC, while all other countries observed a decline. Age-wise analysis revealed that for the 20–54 age group, APC in incidence increased by 1.12%, while for the 55+ age group, it rose by 1.77%. In terms of mortality, the 20–54 age group recorded a 0.26% increase in APC, and the 55+ age group experienced a 1.25% increase. Regarding DALYs, APC for the 20–54 age group increased by 1.4%, while the 55+ age group saw a rise of 2.15% from 1990 to 2021. **Conclusions:** Death due to Cervical Cancer accounted for 2.35% of all cancer causalities in 2021. Study findings underscore the need for urgent public health interventions. Disparities in incidence and mortality trends reflect unequal access to healthcare, screening, and HPV vaccination. The higher APC in older age groups (55+ years) highlight the importance of targeted healthcare access, while modest increases among younger populations (20–54 years) emphasize sustaining vaccination and screening efforts. Research Sponsor: None.

Ceralasertib (cerala) + olaparib (ola) in patients (pts) with homologous recombination repair (HRR)-deficient platinum-sensitive relapsed ovarian cancer (OC) after progression on prior PARP inhibitor (PARPi) treatment (tx).

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Background: Combining an ATR inhibitor (ATRi) and a PARPi may overcome acquired PARPi resistance based on preclinical and clinical data. We report a Phase 1 study (NCT02264678) of cerala (ATRi) + ola (PARPi) in pts with HRR-deficient OC who had progressed on prior PARPi tx. **Methods:** Pts had histologically confirmed high-grade serous/endometrioid epithelial ovarian, fallopian tube, or primary peritoneal cancer, with deleterious or suspected deleterious *BRCA* or HRR mutations (*BRCA*m; HRRm: *RAD51C/D*m, *PALB2*m) or HRR-deficiency (HRD+). Pts received oral cerala 80 mg (d 1–14 every 28 d) + ola 150 mg (throughout) twice daily without/with (Cohort [Co] 1/2) intervening platinum-based tx after initial response and subsequent progression on prior PARPi tx. Primary endpoints were safety/tolerability; ORR per RECIST v1.1 and PFS were secondary endpoints. Emergence of PARPi resistance mechanisms was analyzed in archival/pre-study tx tissue samples. **Results:** 32 pts were treated, 30 in Co1 (7 ongoing tx at data cutoff: Mar 5, 2024) and 2 in Co2 (cohort closed early). Median age was 63.0 yrs; 68.8% (22/32) had *BRCA*m/HRRm and 31.3% (10/32) HRD+/non-*BRCA*m by local assessment. All pts had adverse events (AEs); 40.6% had grade ≥3 AEs (most common were anemia and platelet count reduced, each 21.9%); 6.3% discontinued tx due to AEs. Table shows efficacy in Co1. 24 pts had post-PARPi biopsies evaluable for genomics analysis: 3 (12.5%) had *BRCA* reversions (rev; 13 pts were *BRCA*m); 3 (12.5%) had loss of function alterations in DNA damage response (DDR) rewiring genes. Of 16 pts with post-PARPi biopsies evaluable for RAD51 foci, 81.3% (13) had RAD51 high status suggesting HRR functional proficiency as a prevalent PARPi resistance mechanism; of these 13, 61.5% (8; 80% CI, 40.2–79.9) responded to cerala + ola, while no responses occurred in 3 RAD51 low pts (80% CI, 0.0–53.6). Responders included patients with *BRCA* rev or *TP53BP1*m, indicating cerala + ola activity in pts with *BRCA* rev and alterations in DDR rewiring genes. Other PARPi resistance mechanisms were rare. **Conclusions:** In this setting of high unmet need, cerala + ola had acceptable safety, a low discontinuation rate, and clinical activity in both *BRCA*m/HRRm and HRD+/non-*BRCA*m pts after progression on a prior PARPi. Exploratory analyses highlighted emerging PARPi resistance mechanisms; ongoing assessments of PARPi resistance to inform pt selection and novel combination strategies in post-PARPi settings will be presented. Clinical trial information: NCT02264678. Research Sponsor: AstraZeneca.

	*BRCA*m/HRRm n=20	HRD+/non-*BRCA*m n=10	Total N=30
ORR, % (80% CI)	45 (29.3–61.5)	30 (11.6–55.2)	40 (27.7–53.3)
Best response, n (%)			
Complete	2 (10)	1 (10)	3 (10)
Partial	7 (35)	2 (20)	9 (30)
Stable	8 (40)	4 (40)	12 (40)
PFS			
Events, n	10	8	18
Median, months (80% CI)	7.5 (5.3–not calculable)	4.5 (1.8–5.3)	5.5 (4.7–7.5)

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Hyperthermic intraperitoneal chemotherapy combined with cytoreductive surgery versus cytoreductive surgery alone for ovarian cancer: An updated meta-analysis.

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Background: Hyperthermic Intraperitoneal Chemotherapy (HIPEC) delivers high-dose chemotherapy directly to the abdominal cavity to treat cancers that have spread to the peritoneal lining. When combined with cytoreductive surgery (CRS), HIPEC has been shown to improve survival outcomes in patients with advanced and recurrent ovarian cancer. This updated meta-analysis compares the efficacy and adverse events of CRS with HIPEC to cytoreductive surgery alone. **Methods:** A comprehensive literature search was conducted across Medline, Embase, Google Scholar, Cochrane CENTRAL, Scopus, and ClinicalTrials.gov up to December 2024. Only observational studies and randomized controlled trials (RCTs) involving adult patients with advanced or recurrent ovarian cancer treated with HIPEC in combination with CRS were included. The primary outcomes assessed were overall survival and the incidence of grade 3 or higher adverse events. A meta-analysis using a fixed-effects model was performed to calculate the pooled odds ratio (OR) and pooled hazard ratio (HR), with 95% confidence intervals (CI), to estimate the overall treatment effect. **Results:** A total of twelve studies involving 1,893 participants were included, with 1,067 participants in the control group and 826 in the treatment group. Regarding overall survival, the pooled HR was 0.67 (95% CI: 0.57–0.78; $p<0.00001$; $I^2=42\%$). In subgroup analyses, the HR was 0.67 (95% CI: 0.54–0.83) for treatment-naïve patients and 0.66 (95% CI: 0.52–0.84) for patients undergoing secondary cytoreduction for recurrent ovarian cancer. The test for subgroup differences showed no significant heterogeneity ($I^2=0\%$). In terms of adverse events, the pooled OR was 1.01 (95% CI: 0.89–1.14; $p<0.00001$; $I^2=82\%$). **Conclusions:** This updated meta-analysis demonstrates that HIPEC combined with CRS significantly improves overall survival in patients with ovarian cancer. Subgroup analysis indicated that this treatment enhances survival in both treatment-naïve patients and those undergoing secondary cytoreduction for recurrent ovarian cancer, aligning with findings from previous meta-analysis. However, in contrast to earlier meta-analysis, this study shows that HIPEC plus CRS does not increase the risk of adverse events. Therefore, HIPEC combined with CRS is both an effective and safe treatment option for patients with advanced and recurrent ovarian cancer. Research Sponsor: None.

Gynecologic oncology referral rates of adnexal masses suspicious for ovarian cancer in an academic health system: A cohort study.

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Background: Ovarian-Adnexal Reporting Data System (O-RADS) is an international lexicon and risk stratification tool. O-RADS 4 or 5 lesions are complex adnexal masses that a 10-90% risk of malignancy, and national guidelines recommend gynecologic oncology referral. Our objective was to examine patient, clinician, and imaging factors associated with referral to gynecologic oncology for complex adnexal masses. **Methods:** This retrospective cohort study was exempt from IRB review. We identified all patients with O-RADS 4 or 5 lesions on ultrasound (US) or MRI from July 1, 2020 to December 31, 2023. Our primary outcome was referral to gynecologic oncology. We gathered patient demographic data and ordering clinician characteristics from electronic health records. We performed descriptive statistics and multivariate logistic regression of patient demographics and ordering clinician characteristics associated with gynecologic oncology referral. **Results:** Our cohort included 373 patients with O-RADS 4 or 5 lesions and no prior gynecologic oncology care. The referral rate to gynecologic oncology was 68%, and referral within 30 days of abnormal imaging was 43%. Time from abnormal imaging to referral ranged from 0 to 407 days (mean 15.3, median 4 days). In multivariate analyses, the likelihood of referral to gynecologic oncology was higher among patients with repeat abnormal imaging compared to those with single instance of abnormal imaging (aOR 20.61, 95%CI 2.63-161.6), O-RADS 5 lesions compared to O-RADS 4 lesions (aOR 9.15, 95%CI 3.47-24.85) and detection on MRI compared to US (aOR 7.79, 95%CI 1.57-38.65). The likelihood of referral to gynecologic oncology was lower among non-white patients (aOR 0.24, 95%CI 0.08-0.76). There were no differences by Hispanic ethnicity, rurality, insurance, or language. Referral was higher among patients whose imaging was ordered by an internal medicine clinician (aOR 3.89, 95%CI 1.48-10.20) compared to ob/gyn. **Conclusions:** One-third of patients with complex adnexal masses were not referred to gynecologic oncology. Disparities in referral to gynecologic oncology for complex adnexal masses rates based on patient race and ordering clinician specialty highlight the need for system-based approaches including clinician education or automated referrals. Research Sponsor: Conquer Cancer, the ASCO Foundation.

Gynecologic oncology referral after O-RADS 4/5.

	Multivariate OR (95%CI)
Postmenopausal (≥55 years)	1.89 (0.95-3.74)
Race	
- White	Reference
- Black	0.57 (0.27-1.21)
- Asian	1.03 (0.30-3.58)
- Some other race	0.24 (0.08-0.76)
Ordering specialty	
- Obstetrics/Gynecology	Reference
- Emergency Medicine	0.93 (0.33-2.62)
- Internal Medicine	3.89 (1.48-10.20)
- Family Medicine	1.62 (0.66-3.98)
- Other specialty	0.87 (0.27-2.76)
Has PCP	1.66 (0.81-3.42)
O-RADS	
- 4	Reference
- 5	9.15 (3.27-24.85)
Imaging	
- MRI	7.79 (1.57-38.65)
- US	Reference
Repeat abnormal imaging	20.61 (2.63-161.79)

Progression-free survival as a surrogate outcome for overall survival in ovarian cancer maintenance therapy randomized controlled trials.

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Background: A traditional primary outcome in prospective trials is progression-free survival (PFS). PFS often functions as a surrogate outcome for overall survival (OS) to speed up the translation of research findings into practice. While PFS has been validated as a surrogate for OS in contemporary therapeutic trials for patients with advanced ovarian cancer, there is little evidence to support the validity of PFS as a surrogate for OS in contemporary trials of maintenance therapies. Our objective was to evaluate whether PFS is a reliable surrogate outcome for OS in patients with ovarian cancer receiving maintenance therapy after platinum-based chemotherapy. **Methods:** In May 2024, MEDLINE was queried for all phase 3 trials evaluating poly (ADP) ribose polymerase (PARP) inhibitors and bevacizumab in the maintenance setting for ovarian, fallopian tube and primary peritoneal cancers. Included trials studied PARP inhibitors, bevacizumab or both as an intervention compared to control. Enrollment numbers, median follow up, PFS, OS and hazard ratios were abstracted. Using a meta-analytic approach, correlation analysis was performed using weighted linear regression and Pearson's correlation coefficient. Trials included contained complete survival data. Criteria for PFS surrogacy required $R^2 > 0.8$. **Results:** Sixty trials were identified, 11 of which met inclusion criteria. Six trials investigated PARP inhibitors in the maintenance setting, while 4 trials investigated bevacizumab. One trial investigated both a PARP inhibitor and bevacizumab. The pooled sample size from all trials was n=6,243. Median follow up time was 60.35 months. Across all trials, the relationship between OS and PFS HRs was approximately linear. Corresponding R^2 values were low (R^2=0.35, 95% CI 0-0.63). Pearson correlation when weighted by total study sample size, was of low strength (r=0.59, 95% CI -0.05-0.87). Four trials evaluating bevacizumab as a maintenance therapy demonstrated favorable PFS benefit with no statistically significant difference in OS, while only one PARP inhibitor trial demonstrated a statistically significant benefit in PFS and OS. Weighted Pearson correlation coefficient for bevacizumab trials demonstrated moderate correlation between PFS and OS HRs (r=0.81, 95% CI -0.75-0.99) while PARP inhibitor trials demonstrated a low strength of correlation (r=0.26, 95% CI -0.71-0.88). **Conclusions:** Phase 3 clinical trials assessing maintenance therapies for ovarian cancer demonstrate poor correlation between PFS and OS. This effect may be modulated by type of maintenance therapy and the inclusion of platinum-based chemotherapy in trial arms. PFS as a surrogate outcome in maintenance therapy ovarian cancer clinical trials must be supported by additional studies and caution should be taken prior to regulatory approval based on PFS data alone. Research Sponsor: None.

Development and validation of a proteo-metabolic panel for detection of asymptomatic ovarian cancer with minimal serum sample requirements: A multi-center prospective study.

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Background: Early diagnosis is crucial for improving the prognosis of ovarian cancer (OC). However, most patients (pts) are diagnosed at advanced stages due to subtle symptoms and traditional biomarkers' limitations. We aimed to develop an serum panel using multi-omics data for cost-effective detection of asymptomatic OC (asym-OC). **Methods:** Participants were recruited from the Shanghai Ovarian Cancer and Family Care Project (NCT06118307) involving five centers. A total of 843 individuals were included: 135 asym-OC pts and 708 non-OC individuals (290 pts with benign lesions and 418 healthy controls). Fasting serum samples (1 μL each) were analyzed using MALDI-TOF MS to generate proteo-metabolic (pro-met) data. For each sample, the original MS have ~43,900 data points from 100-13,000 Da. Preoperative data from three centers (N=680) were used to develop Light Gradient Boosting Machine (LGBM) models to identify key signals differentiating OC from non-OC. An independent external validation set (N = 163) was assembled by the other two centers. To develop a biologically interpretable and generalizable panel, the model was further refined to minimize biomarkers while maintaining efficacy. Validation of the panel was conducted using post-operative pro-met data from 42 asym-OC pts, transcriptomic data from 89 with asym-OC and 39 with benign lesions, supported by bioinformatic analyses. **Results:** Ten biomarkers, which are involved in coagulation, complement system, carcinogenesis, epithelial-mesenchymal transition, and the Warburg effect, were selected in the panel. The panel achieved an AUC of 0.90 (95% CI: 0.82-0.98) in the external validation set. The enhanced model that integrating the panel, age, BMI and HE4 achieved an AUC of 0.94 (95% CI: 0.90-0.99). In subgroup analyses, the enhanced model outperformed CA125, HE4, and ROMA, with AUCs of 0.96 (early-stage OC vs. non-OC) and 0.96 (OC vs. endometriosis) (See Table). Moreover, post-operative levels of the biomarkers in the panel approached those of the non-OC ($p < 0.05$). Transcriptomic data of the tissues corresponded to the pathophysiological alterations associated with OC development or progression. **Conclusions:** This study introduces a novel, non-invasive, and cost-effective serum panel that demonstrates high sensitivity and specificity for detecting asym-OC, offering a promising tool for early diagnosis of the disease. Research Sponsor: National Natural Science Foundation of China; 82072866 (Y.W.), 82272888 (Y.W.), 82204047 (Z.L.); Shanghai Hospital Development Center Foundation; SHDC12022106 (Y.W.).

	Early-stage OC vs. Non-OC (N=58/708)	OC vs. Endometriosis (N=135/80)
Enhanced model: 10-biomarker Pro-Met panel + BMI +age + HE4	0.96 [0.94-0.99]	0.93 [0.90-0.97]
CA125	0.87 [0.82-0.93]	0.77 [0.71-0.83]
HE4 premenopausal	0.73 [0.63-0.83]	0.91 [0.80-0.94]
postmenopausal	0.67 [0.58-0.74]	0.88 [0.76-0.86]
ROMA premenopausal	0.75 [0.60-0.81]	0.91 [0.80-0.93]
postmenopausal	0.89 [0.67-0.84]	0.87 [0.53-1.00]

Comparison of predictive models in women with advanced epithelial ovarian cancer triaged to primary debulking or neoadjuvant chemotherapy.

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Background: Triaging women with advanced epithelial ovarian cancer (AEOC) into primary debulking surgery (PDS) or neoadjuvant chemotherapy (NACT) remains largely subjective. **Methods:** This prospective observational study recruited women over 18 years with stage III-IV AEOC. Decision for PDS or NACT was based on patient-specific factors and radiological parameters. The agreement between clinical decisions and predictive models—Aletti's surgical complexity score, MSKCC Team Ovary criteria, Mayo triage algorithm, and Integrated Predictive Model (IPM) was assessed using kappa statistics. **Results:** 72 women with AEOC were included, with 17 (23.6%) assigned to the PDS and 55 (76.4%) to NACT. Amongst NACT patients, interval debulking surgery (IDS) was feasible in 30 women (54.5%), while 25 (45.5%) did not undergo surgery due to reasons such as disease progression, death, poor performance status, stable disease, or loss to follow-up. No difference was observed between the NACT and PDS groups in demographic parameters. Performance scores differed significantly, with higher scores observed in the NACT group compared to the PDS group: median ECOG (2 [1–2] vs. 1 [1–1], $p < 0.001$), ASA score (2 [2–3] vs. 2 [2–2], $p = 0.005$), and frailty index (0.26 ± 0.11 vs. 0.15 ± 0.05, $p < 0.001$). Serum albumin levels were lower (3.0 ± 0.51 vs. 3.7 ± 0.30 g/dL, $p < 0.001$), and median CA125 levels were higher (1170 [341–2637] vs. 494 [219.7–1000] U/mL, $p < 0.001$) in the NACT group. Radiological parameters, including median peritoneal carcinomatosis index (PCI) scores (16 [10–23] vs. 5 [3–8], $p < 0.001$), volume of ascites, pleural effusion, and disease at challenging operative sites, were also higher in the NACT group ($p < 0.05$). Surgical outcomes, including surgical PCI scores (5[2-6] vs 6[3-11], =0.35), residual disease rates (complete/optimal debulking: 96.6% vs. 88.2%, $p = 0.42$), surgical complexity score (4.7 ± 1.45 vs. 4.4 ± 1.33, $p = 0.82$), blood transfusion rates (80% vs. 70.6%, $p = 0.76$), and grade 2-3 complications (60% vs. 58.8%, $p = 0.58$) were similar in both groups. Baseline predictive scores were significantly higher in the NACT group compared to the PDS group: Aletti's surgical complexity score (8.4 ± 2.80 vs. 5.2 ± 1.25, $p < 0.001$), MSKCC Team Ovary criteria (6.4 ± 3.31 vs. 1.9 ± 1.49, $p < 0.001$), Mayo triage algorithm (0.87 ± 0.39 vs. 0.24 ± 0.44, $p < 0.001$), and IPM final score (high-risk: 69.1% vs. 52.8%, $p < 0.001$). Clinical decisions showed moderate concordance with the Mayo triage algorithm ($\kappa = 0.57$) and IPM score ($\kappa = 0.51$) and fair concordance with Aletti's score ($\kappa = 0.33$) and MSKCC criteria ($\kappa = 0.23$). **Conclusions:** Triage decisions based on patient performance status, nutritional factors, and disease extent demonstrated moderate concordance with predictive models. Both PDS and IDS had excellent cytoreductive outcomes with similar perioperative performance aligning with results from literature. Research Sponsor: None.

Concordance of circulating tumor DNA and tissue genomic profiling in ovarian cancer: Influencing factors and clinical significance.

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Background: Next-generation sequencing of plasma circulating tumor DNA (ctDNA) shows promise in ovarian cancer management as a minimally invasive alternative to tissue sequencing. However, concordance between genomic alterations detected in tissue and ctDNA remains incompletely characterized, with limited understanding of influencing factors and clinical implications. **Methods:** We analyzed 29 matched pretreatment tissue and plasma samples from treatment-naïve ovarian cancer patients using a customized 2365-gene panel. Overall and individual concordance rates were calculated as the ratio of total concordant mutations to total tissue mutations, with patients stratified into high concordance ($\geq$50%) and poor concordance ($<$50%) groups. Clinicopathological and tumor molecular factors influencing concordance were analyzed. Relationship between concordance rates and clinical outcomes, including chemosensitivity (KELIM score) and progression-free survival (PFS), was assessed in advanced-stage patients. **Results:** The cohort predominantly comprised FIGO III-IV disease (89.7%) and high-grade serous histology (89.7%), with median follow-up of 306 (66-570) days. Overall tissue-plasma concordance rate was 42%, with shared variants exhibiting identical abundance patterns across sample types (r=0.25, p=0.0074) and encompassing 66.1% of tissue driver mutations. Tissue-specific mutations displayed lower variant allele frequencies than shared mutations (median 4.4% vs 28.7%). Single nucleotide variants showed higher plasma detection rate than structural variants (47.3% vs 25.4%). Individual concordance rates varied substantially (0-83.3%). High concordance group exhibited higher tumor Ki-67 index (median 85% vs 70%), tissue tumor mutation burden (TMB, median 5.1 vs 4.1 muts/Mb), and plasma ctDNA fraction (median 8.1% vs 0.9%). No significant differences were observed in largest tumor diameter, CA125 levels, tumor sample locations (from primary site or metastatic site), or BRCA mutation/homologous recombination status between groups. By multivariable analysis, higher TMB (OR 1.931, 95% CI 1.064-3.504) and plasma ctDNA fraction (OR 1.416, 95% CI 1.060-1.893) independently associated with high concordance rates. In advanced-stage patients, poor concordance group showed lower KELIM scores (median 0.7 vs 1.2; 15.4% vs 69.2% of patients with score $\geq$1), indicating reduced chemosensitivity. Concordance rates strongly correlated with KELIM scores (r=0.71, $p<0.0001$). Poor concordance group demonstrated shorter PFS (median 436 days vs not reached, p=0.037). **Conclusions:** Our study revealed moderate concordance between pretreatment tumor tissue and plasma ctDNA mutation profiles in ovarian cancer, influenced by technical and biological factors. Tissue-plasma concordance may serve as a novel chemosensitivity and prognostic indicator. Research Sponsor: Beijing Xisike Clinical Oncology Research Foundation.

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Validation of the performance of Ovarian Cancer Score for diagnosing ovarian cancer in a multicenter study.

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Background: Early detection is crucial for improving survival of patients with ovarian cancer (OC), yet current diagnostic tools lack adequate sensitivity and specificity, especially for early stage disease. The Ovarian Cancer Score (OCS) is a newly developed serum extracellular based diagnosis marker for detection of ovarian cancer. The study aimed to explore the performance of OCS in detecting OC. **Methods:** This multicenter study included 1183 adult females with adnexal masses from four hospitals in China (October 2019 - April 2023). Of these, 1,024 samples were prospectively collected, and 159 were from biobanks. All serum samples were collected before surgery. The concentrations of sEV carbohydrate antigen 125 (CA125), human epididymis protein 4 (HE4) and complement component 5a protein (C5a) were quantified using chemiluminescence immunoassay and then used for calculating OCS. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. CA125, HE4, and ROMA index results were retrieved from the medical record system at each hospital. The differences was calculated using. **Results:** The OCS demonstrated high sensitivity (95.5%, 95%CI: 93.3%-97.7%) and specificity (90.2%, 95%CI: 88.2%-92.2%) in OC in the cohort (n = 1183), significantly outperforming CA125 (90.0%, 95%CI: 86.8%-93.3% and 69.1%, 95%CI: 65.9%-72.2%) and ROMA (89.2%, 95%CI: 83.2%-95.2% and 83.1%, 95%CI: 79.3%-86.8%, all $p<0.05$). OCS was superior to HE4 in sensitivity (75%, 95%CI: 70.1%-79.9%, $p<0.001$), but not specificity (94.8%, 95%CI: 93.2%-96.5%, $p<0.001$). Subgroup analysis revealed that in premenopausal women, OCS showed higher sensitivity (94.3%, 95%CI: 90.2%-98.4%) compared to HE4 (79.0%, 95%CI: 71.5%-86.4%, $p<0.001$) and ROMA (83.0%, 95%CI: 72.2%-93.7%, $p<0.05$). The specificity of OCS was higher than CA125 and ROMA, but lower than HE4 (all $p<0.05$). In postmenopausal women, OCS showed higher sensitivity (96.2%, 95%CI: 93.6%-98.8%) than CA125 (89.9%, 95%CI: 85.8%-94.0%, $p<0.05$) and HE4 (72.6%, 95%CI: 66.2%-79.0%, $p<0.001$), but there was no significant difference in sensitivity between OCS and CA125 or ROMA ($p>0.05$). In early-stage OC (FIGO I+II), OCS's sensitivity (91.4%, 95%CI: 86.8%-96.1%) was significant higher than CA125 (78.4%, 95%CI: 71.6%-85.3%, $p<0.01$), HE4 (63.5%, 95%CI: 55.1%-71.9%, $p<0.001$) and ROMA (77.8%, 95%CI: 65.6%-89.9%, $p<0.05$). Particularly in FIGO Stage I patients, OCS demonstrated significant higher sensitivity than CA125 (89.7%, 95%CI: 83.0%-96.5% vs.70.1%, 95%CI: 59.9%-80.4%, $p < 0.01$), HE4 (51.4%, 95%CI: 39.8%-62.9%, $p < 0.001$) and ROMA (74.2%, 95%CI: 58.8%-89.6%, $p < 0.05$). The specificity of OCS was higher than CA125 and ROMA (all $p<0.001$), but lower than HE4 across all stage subgroups. **Conclusions:** This multicenter study demonstrated that the OCS is a promising non-invasive diagnostic tool for the detection of OC. Clinical trial information: NCT06366997. Research Sponsor: Chongqing Science and Technology Bureau; Talent Program of Chongqing; Chongqing Municipal Education Commission; Chongqing Health Commission; Beijing Health Alliance Charitable Foundation.

Impact of disease progression on health-related quality of life (HRQOL): Updated results from the PRIMA/ENGOT-OV26/GOG-3012 trial of niraparib first-line (1L) maintenance therapy in patients with newly diagnosed advanced ovarian cancer (aOC).

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Background: The phase 3 PRIMA trial (NCT02655016) demonstrated that niraparib 1L maintenance therapy significantly extended progression-free survival (PFS) compared with placebo in patients with newly diagnosed aOC that responded to 1L platinum-based chemotherapy. Using data from the Nov 2019 cutoff (median follow-up, ≈1.7 y), pooled results from both treatment arms found that disease progression negatively affected HRQOL. Here we report updated HRQOL results from the PRIMA final analysis. **Methods:** In PRIMA, patients were randomized 2:1 to niraparib or placebo 1L maintenance once daily. HRQOL was assessed as a prespecified secondary endpoint using patient-reported responses to multiple instruments, including the European Organisation for Research and Treatment of Cancer QOL Core Questionnaire (EORTC QLQ-C30) and the EORTC QLQ Ovarian Cancer Module (EORTC QLQ-OV28). Assessments were collected at baseline, at designated intervals while on study treatment; at the end of treatment (EOT); and at 4, 8, 12, and 24 weeks after the last dose of study treatment. Post hoc analysis results are reported herein (clinical cutoff: Apr 8, 2024; median follow-up, 6.2 y). **Results:** In the overall population (niraparib, n=487; placebo, n=246), EOT survey completion rates exceeded 80% across both instruments. In both treatment arms, disease progression significantly reduced overall HRQOL per the EORTC QLQ-C30, with marked decreases from the last on-treatment visit (LOTV) for global health status/QOL that never recovered to LOTV levels (Table). Disease progression was also associated with deterioration across all 5 functional scales of the EORTC QLQ-C30 and worsening symptoms of fatigue, nausea/vomiting, pain, dyspnea, appetite loss, diarrhea, and financial difficulties. On the EORTC QLQ-OV28, progression was associated with decreased scores for body image, sexuality, and attitude toward disease/treatment functional scales and worsening abdominal/gastrointestinal symptoms. **Conclusions:** Disease progression negatively impacted HRQOL across treatment arms in PRIMA. These results support PFS as a clinically relevant endpoint in patients with aOC, as delays in disease progression help preserve HRQOL. Clinical trial information: NCT02655016. Research Sponsor: GSK.

LS mean change from LOTV (95% CI)	Niraparib (n=487)	Placebo (n=246)
EORTC QLQ-C30 global health status/QOL		
EOT	−8.6 (−10.9, −6.4)	−7.4 (−10.1, −4.7)
Week 4 post EOT	−10.0 (−12.7, −7.3)	−10.7 (−14.0, −7.4)
Week 8 post EOT	−10.1 (−12.9, −7.2)	−12.2 (−16.0, −8.5)
Week 12 post EOT	−11.5 (−14.0, −9.1)	−9.5 (−12.6, −6.3)
Week 24 post EOT	−10.7 (−13.4, −8.1)	−9.6 (−13.1, −6.2)

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer QOL Core Questionnaire; EOT, end of treatment; LOTV, last on-treatment visit; LS, least squares; QOL, quality of life.

HER2 and HER3 expression in ovarian cancer: Evolution across chemotherapy exposure and implications for targeted therapies.

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Background: HER2 and HER3 are critical members of the ERBB receptor family, playing pivotal roles in tumorigenesis across multiple cancers, including ovarian cancer (OC). While their potential as therapeutic targets is under investigation, the clinical significance of their expression in OC remain understudied. This study investigates the expression patterns of HER2 and HER3 in OC tissues and evaluates the impact of neoadjuvant chemotherapy (NACT) on their expression levels. **Methods:** Patients with advanced epithelial ovarian cancer were identified and included in this study. Tumor samples were collected at three timepoints: prior to NACT, during interval debulking surgery and at relapse. HER2 and HER3 expressions were assessed using immunohistochemistry and scored with the gastric Herceptest scoring system (1+, 2+ or 3+), where 3+ expression was considered positive. **Results:** A total of 163 patients were analyzed, of whom 73% had high-grade serous histology and 21% harbored *BRCA* mutations. Tumor samples were available for analysis at the following timepoints: 110 pre-NACT, 81 post-NACT, and 22 at relapse. HER2 expression was rare, with 2.3% of tumors exhibiting HER2 1+ expression and 3.1% exhibiting HER2 3+ before NACT. HER2 expression remained stable at interval debulking surgery and relapse. In contrast, HER3 expression was more common with 2.7% of samples exhibiting HER3 1+ expression, 1.8% with 2+ expression and 60.9% with 3+ expression. HER3 expression remained consistent across timepoints, with 65.4% at interval debulking and 63.6% at relapse. HER3-positive samples were significantly associated with high-grade serous histology (81.5% vs 65%, p = 0.005), while *BRCA* mutation rates did not differ significantly between both groups (16.2% vs 28%, p = 0.267). Progression-free survival (PFS) and overall survival (OS) were comparable between HER3-positive and negative groups. Median PFS was 11.1 months versus 11.2 months (p = 0.537) and median OS was 44.9 months versus 44.3 months (p = 0.734). **Conclusions:** This study confirms that HER2 overexpression is rare in OC and remains stable throughout the treatment timeline. Conversely, HER3 is frequently expressed, with over 60% of tumors exhibiting 3+ HER3 expression. HER3 expression is strongly associated with serous histology, is stable across NACT exposure, and does not appear to impact clinical outcomes. These findings highlight HER3's potential as a promising therapeutic target in the OC landscape. Research Sponsor: None.

Final analysis of SCORES, a phase III randomized, double-blinded, placebo-controlled study of suvemcitug combined with chemotherapy for platinum-resistant ovarian cancer.

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Background: At the SCORES interim analysis, suvemcitug (a recombinant humanized anti-VEGF rabbit monoclonal antibody) plus chemotherapy demonstrated a significant improvement of progression free survival (PFS) compared with single-agent chemotherapy (CT) in patients with platinum-resistant Ovarian Cancer (PROC). Here we present the preplanned final analysis of OS for the SCORES along with the updating analysis of safety, PFS, and other endpoints. **Methods:** This randomized, double-blind, placebo-controlled, phase 3 trial (SCORES) conducted at 55 centers in China enrolled women with histologically-confirmed epithelial ovarian, fallopian tube or primary peritoneal cancer. Patients were required to have platinum- resistant or refractory disease with at least one measurable lesion. Eligible patients were randomly assigned (2:1) to either Suvemcitug (1.5 mg/kg q2w) or placebo combined with investigators chose CT (weekly paclitaxel, topotecan or pegylated liposomal doxorubicin) until progression or unacceptable toxicity. The primary endpoint was progression-free survival (PFS) by blinded independent review committee (BIRC) according to the RECIST 1.1. And the key secondary endpoint is the overall survival (OS). **Results:** Between June 5, 2021 and October 11, 2024, 421 patients were enrolled. At the data cutoff for the final analysis (October 11, 2024), the median follow-up duration was 23.7 and 23.4 months for the suvemcitug arm and the placebo arm. A total of 279 OS events (66.3%) occurred, the median OS was 15.31 months versus 14.03 months (stratified hazard ratio, 0.768; 95% CI, 0.595-0.991; P = 0.0304). Suvemcitug plus chemotherapy led to a significant improvement of OS versus placebo plus chemotherapy, with a 23% reduction in the risk of death and a more than 10% improvement of the 24-month OS rate (33.0% vs 22.3%). The efficacy results are summarized below. The most common grade $\geq$ 3 TEAEs (treatment-emergent adverse events) in suvemcitug arm included neutrophil count decreased, white blood cell count decreased, and hypertension. No Suvemcitug-related grade 5 TEAE occurred. **Conclusions:** The addition of suvemcitug to chemotherapy significantly improved the outcomes of patients with PROC with manageable toxicities. To the best of our knowledge, this is the first phase III study demonstrated a significant OS benefit of anti-angiogenic agent in patients with PROC. Clinical trial information: NCT04908787. Research Sponsor: Shanghai Xianxiang Medical Technology Co., Ltd.

	Suvemcitug + CT (N = 281)	Placebo+CT (N = 140)
OS, month (95% CI)	15.31 (13.73,17.81)	14.03 (11.27,16.56)
Hazard Ratio (95% CI)	0.768 (0.595,0.991)	
P value (rerandomization log-rank)	0.0304	
24-month OS rate, % (95% CI)	33.0 (26.8-39.2)	22.3 (14.8-30.8)
Median PFS by BIRC, month (95% CI)	5.49 (4.93,6.64)	2.73 (1.94,3.75)
Median PFS by investigator, month (95% CI)	5.39 (4.80,5.59)	2.46 (1.94,3.65)
ORR by BIRC, %	26.0	12.1
DCR by BIRC, %	76.5	49.3

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Assessment of tumors, blood, and ascites to establish correlations with treatment benefit in platinum resistant or refractory ovarian cancer patients treated with igrelimogene litadenorepvec and pembrolizumab combination therapy.

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Background: Platinum-resistant/refractory ovarian cancer presents a significant therapeutic challenge and despite several attempts, immunotherapies have not delivered satisfactory results to be approved. Identifying biomarkers of response to novel therapies is crucial for personalizing treatments and improving patient outcomes, especially since certain patients do experience long term benefit after the treatment with pembrolizumab and igrelimogene litadenorepvec (TILT-123; an oncolytic adenovirus coding for TNF and IL-2). **Methods:** Tumor biopsies (n=62), ascites (n=8) and blood (n=234) were collected from 15 patients treated in the PROTA trial (Phase I, NCT05271318). These patients received pembrolizumab intravenously plus igrelimogene litadenorepvec intravenously, followed by local administration intratumorally or intraperitoneally. Sampling took place prior to therapy, during therapy and after it. Tumor proteome (IHC, mIF) and transcriptome was analyzed to assess immune changes and virus presence. Ascites and blood samples were assayed to measure cell counts, phenotypes, cytokine and protein counts, as well as for the presence of antiviral neutralizing antibodies (NAbs). Biological parameters were correlated with overall survival (OS), RECIST 1.1 evaluations and tumor size changes. For analysis of OS, logrank test was used. For group comparisons two-tailed Mann-Whitney U-test was used. Pearson or Spearman tests were used for correlations. **Results:** Patients experiencing a drop in circulating lymphocytes 8-24 hours after treatment were more likely to experience longer OS (p=0.044). Additionally, patients with a higher lymphocyte count at baseline experienced similar OS benefit (p=0.018) plus a positive correlation with disease control (p=0.023). Most patients (11/15) showed antiviral immunity at baseline but eventually all patients developed neutralizing activity, and the same was observed in ascites. The presence of NAbs at baseline as well as development of highest titers were positively correlated with longer OS (p=0.004) and disease control (p=0.003). **Conclusions:** Igrelimogene litadenorepvec and pembrolizumab are therapies designed to attract, activate and/or protect lymphocyte-mediated antitumor activity. These findings suggest that having a fit immune system able to mobilize effector immune cells as well as responding to immunostimulant agents increases therapeutic success. As a disease with few therapeutic options, ovarian cancer patients often receive multiple lines of chemotherapy that might decrease the efficacy of immediate immunotherapies. The potential use of these biomarkers will be studied in larger studies to validate their utility in guiding the use of immunotherapy in this challenging patient population. Clinical trial information: NCT05271318. Research Sponsor: None.

Biomarker results from the KGOG3056/NIRVANA-R trial: Maintenance niraparib plus bevacizumab in patients with platinum-sensitive, recurrent ovarian cancer previously treated with a PARP inhibitor.

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Background: While poly(ADP-ribose) polymerase inhibitors (PARPi) have demonstrated clinical success in prolonging progression-free survival (PFS) in ovarian cancer, the efficacy of subsequent chemotherapy following progression from PARPi maintenance is markedly decreased. Modest PFS benefits with PARPi rechallenge following a response to platinum-based chemotherapy has been reported, but the efficacy of PARPi rechallenge with bevacizumab remains unknown. **Methods:** NIRVANA-R, a phase 2 study, evaluated niraparib rechallenge with bevacizumab in patients with platinum-sensitive recurrent ovarian cancer previously treated with PARPi. Eligibility required a response to the most recent platinum regimen. The primary endpoint was 6-month progression-free rate. Biomarker exploration included the analysis of BRCA status, homologous recombination deficiency (HRD) status, circulating tumor DNA (ctDNA), and circulating tumor cells (CTCs) using whole-exome sequencing, as well as CA-125 levels. **Results:** Between 2019 and 2023, 44 patients were enrolled; over 65% had received≧3 lines of chemotherapy. The estimated 6-month progression-free rate was 68% [95% confidence interval (CI) 55–85%]. Key prognostic factors included treatment-free interval after penultimate platinum-based chemotherapy (TFI_P) ($TFI_P \geq 24$ months vs. $TFI_P < 24$ months; 82% vs. 56%), achieving a complete response (CR) [CR vs. partial response; 86% vs. 57%] or normal CA-125 levels (0–35 vs. >35 U/mL; 72% vs. 25%) in response to the most recent chemotherapy. Median PFS was 11·5 months [95% CI 7.9-not reached (NR)]. Ongoing biomarker analysis includes BRCA status, HRD status, ctDNA and CTCs, and these results will be updated in subsequent reports. No new safety signals were identified with niraparib rechallenge plus bevacizumab. **Conclusions:** Niraparib rechallenge with bevacizumab showed promising efficacy, particularly in patients with $TFI_P \geq 24$ months, CR, or normal CA-125 levels following previous chemotherapy, supporting further clinical research. Ongoing exploration of HRD, ctDNA, CTCs, and other biomarkers will provide further insights into treatment stratification and outcomes. Clinical trial information: NCT04734665. Research Sponsor: None.

Estimated 6-month progression-free rate according to prognostic factors.

Factors		N	6 month PFS rate (95% CI)	p-value
1. Response to most recent chemotherapy	CR	17	85% (69-100%)	0.148
	PR	27	57% (40-82%)	
2. platinum-free interval from penultimate chemotherapy	<24 months	24	56% (38-83%)	0.018
	≥24 months	20	82% (65-100%)	
3. BRCA status	BRCA wild-type	16	56% (35-90%)	0.806
	BRCA mutation	22	73% (55-96%)	
	unknown	6	80% (52-100%)	
4. Progression during/after previous PARPi therapy	Progression during previous PARPi	30	68% (52-89%)	0.846
	Progression after previous PARPi	14	68% (50-100%)	

5557 Poster Session

JSKN003, a biparatopic anti-HER2 antibody drug conjugate (ADC), in the treatment of platinum-resistant ovarian cancer (PROC): Updated findings from two clinical trials.

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Background: JSKN003 is a biparatopic HER2-targeting ADC conjugated to a topoisomerase I inhibitor with an average DAR of 4, who has preliminarily exhibited promising efficacy and safety in the treatment of PROC (QX Rao, et al. 2024 ESMO). This update presents the latest findings in patients (pts) who were not primary platinum-refractory. **Methods:** A pooled analysis of pts with PROC was performed from the phase I JSKN003-101 trial conducted in Australia (NCT05494918) and phase I/II JSKN003-102 trial conducted in China (NCT05744427), which enrolled pts with advanced solid tumors to receive JSKN003 monotherapy. Tumor tissue samples were collected for central lab assessment of HER2-expression. **Results:** As of November 29, 2024, the median follow up time was 6.9 months. A total of 46 PROC pts received JSKN003 Q3W, with 2, 2, 40, 1 and 1 pts in 4.2, 5.2, 6.3, 7.3 and 8.4 mg/kg dose groups, respectively. Median age was 59.0 years, 65.2% had ≥ 3 prior lines of systemic therapy, 80.4% and 63.0% had previously received bevacizumab and PARP inhibitor, 39.1% were classified as HER2-expressing (IHC: 1+/2+/3+), with 21.7%, 10.9% and 6.5% in 1+, 2+ and 3+, respectively; 45.7% as HER2-no-expressing (IHC: 0), and 15.2% had no tissue samples for assessment. For 45 efficacy-evaluable pts, the overall response rate (ORR) was 64.4%, the median progression-free survival (PFS) was 7.1 months, and the 9-month overall survival (OS) rate was 84.9% (Table). JSKN003 demonstrated effectiveness across various HER2 expression subgroups. Notably, for pts with HER2-expression, the ORR reached 72.2%, with a median PFS of 9.4 months. Grade 3/4 treatment-related adverse events (TRAEs) occurred in only 6 (13.0%) pts. Serious TRAE occurred in only 4 (8.7%) pts. No TRAEs led to treatment discontinuation or death. The most common TRAE was Grade 1/2 Nausea (39.1%). Additionally, Grade 1/2 Interstitial lung disease (ILD) was observed in 4 (8.7%) pts, with no cases of Grade 3/4 reported. **Conclusions:** The maturer updated efficacy data reveal that JSKN003 provided substantial improvement in ORR, as well as benefit in PFS and OS in heavily treated PROC, irrespective of HER2 expression. The well tolerated toxicity with long-term observation was consistent with prior experience. A confirmatory trial (NCT06751485) is ongoing in all comers at any HER2 expression level to further support JSKN003 as a treatment option in this population. Clinical trial information: NCT05494918 and NCT05744427. Research Sponsor: Alphamab Oncology.

Efficacy summary.

	HER2 IHC			
	1+/2+/3+ (n = 18)	0 (n = 20)	Unknown (n = 7)	Total (n = 45)
ORR, % (95% CI)	72.2 (46.5, 90.3)	55.0 (31.5, 76.9)	71.4 (29.0, 96.3)	64.4 (48.8, 78.1)
CR, n (%)	2 (11.1)	0	0	2 (4.4)
PR, n (%)	11 (61.1)	11 (55.0)	5 (71.4)	27 (60.0)
Median PFS, month (95% CI)	9.4 (5.7, NE)	5.6 (4.1, NE)	9.6 (2.6, NE)	7.1 (5.6, 9.7)
9-mo OS Rate, % (95% CI)	83.0 (45.7, 95.6)	100.0 (100.0, 100.0)	85.7 (33.4, 97.9)	84.9 (56.6, 95.4)

Analyzing the relationship between glutaminase expression and features of the immune tumor microenvironment in epithelial ovarian cancer using imaging mass cytometry.

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Background: Immunotherapy has thus far shown limited efficacy in epithelial ovarian cancer, likely driven in part by an immune suppressive tumor microenvironment (TME). Increased glutamine metabolism by cancer cells via upregulation of the drug-targetable enzyme glutaminase (GLS) may contribute to an immune suppressive TME. Inhibiting GLS may not only inhibit tumor growth but also enhance the anti-tumor immune response in patients with epithelial ovarian cancer. We investigated the relationship between GLS expression and features of the immune TME in epithelial ovarian cancer using imaging mass cytometry. **Methods:** Tissue microarrays constructed from 41 epithelial ovarian cancer (38 high-grade serous, 3 low-grade serous) surgical specimens were stained by immunohistochemistry for GLS, which was quantified using modified histologic score (H-score). Imaging mass cytometry was then performed on tissue microarrays using a panel of 43 channels, including markers for delineating tissue architecture and assessing lymphoid cells, myeloid cells, and stromal fibroblasts. Resulting multiplexed images were segmented into a single-cell dataset to quantitatively compare between specimens, according to GLS H-score, abundances of cell types and average shortest distances between cell types. **Results:** Median GLS H-score was 150. Compared to GLS-low (H-score 0-150) specimens, GLS-high specimens (H-score >150) demonstrated lower T cell abundance (9.18% vs. 16.84% of cells; p=0.010) and lower B cell abundance (1.09% vs. 6.66% of cells; p=0.022). Compared to GLS-low (H-score <130) and GLS-medium (H-score 130-150) specimens, GLS-high specimens (H-score >150) demonstrated the lowest T cell abundance (high: 9.18% < medium: 10.46% < low: 21.28% of cells; p=0.0015) with subtype analysis showing the lowest effector helper T cell abundance (high: 0.11% < medium: 0.25% < low: 3.39% of cells; p=0.040). On spatial analysis, based on average shortest distances between cell types, GLS-high specimens demonstrated longer distances between tumor cells and lymphoid/myeloid immune cells and shorter distances between tumor cells and stromal cells than GLS-low/medium specimens. **Conclusions:** In this cohort of patients with epithelial ovarian cancer, higher levels of GLS expression were associated with several features of an immune suppressive TME, including lower T cell abundance with lower effector helper T cell abundance on subtype analysis, lower B cell abundance, and decreased proximity between tumor cells and immune cells. Further clinical studies investigating the use of GLS inhibitors to modulate the immune TME in patients with epithelial ovarian cancer are warranted. Research Sponsor: ASCO Conquer Cancer, Norman & Ruth Rales Foundation; NIH/NCI Ovarian SPORE; P50CA228991.

5561 Poster Session

Re-VOLVE: Phase II clinical trial in women with ovarian cancer progressing post-PARP inhibitor with treatment adapted to real-time assessment of evolving genomic resistance.

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Background: As the use of PARPi increases in high-grade serous ovarian cancer (HGSOC) resistance mechanisms ultimately arise. Emerging therapeutic strategies to overcome PARPi resistance is a pressing concern. Re-VOLVE study is a phase II in HGSOC women post-PARPi with treatment adapted to real-time assessment of evolving genomic resistance to guide treatment decision (NCT05065021). **Methods:** It enrolled patients (pts) with HGSOC progressing post-PARPi to receive induction phase (IP) 2-3 cycles of niraparib 200-300mg/ bevacizumab 7.5mg/kg followed by personalized phase based on initial RECIST response and real-time assessment of evolving genomic resistance from baseline biopsy (whole genome RNA sequencing/WGTS) and ctDNA (12 gene panel). If progression/stable disease after IP pts were assigned to cohort A (niraparib/bevacizumab/dostarlimab 500mg) if no resistance mechanisms and to B (weekly paclitaxel 80mg/m2/bevacizumab/dostarlimab) if any present and to cohort C (continue niraparib/bevacizumab) if partial response after IP. Primary endpoint was to assess response rate of combination therapies. **Results:** 50 pts were screened; 7 were screen fail and 43 were enrolled. Of the 43, 3 pts were taken off due to progression during IP, 1 withdrew from study, 3 are on IP and 36 continued to personalized phase. Of these 36, 78% were white, 20% Asian, 2% others; 69% *BRCA* wild-type (25/36); 61% platinum-resistant (PR;22/36) and 39% platinum-sensitive (PS;14/36). Median age 62.5 years (33-87). Pts had median 2 prior therapy lines (1-5); 22% (8/36) prior bevacizumab. Median days from collection to ctDNA results were 59 days and to WGTS 54 days. Twenty-seven pts (75%) had biopsy and ctDNA to guide therapy. 36 pts were assigned to personalized phase: 78% cohort A, 14% to B (4 *CCNE1* amplification and 1 *CHEK2* mutation) and 8% to C (3 with response during IP). Of the 31/36 pts assessed for response during personalized phase (others too early) 10 achieved partial response (32.2%; 7 PR, 3 PS). Nineteen pts (61.3%; 11 PR, 8 PS) had stable disease. By cohort, 3 pts had partial response (12.5%; 3/24) cohort A, 4 partial response cohort B (100%; 4/4 all with resistance mechanisms) and 3 partial response (100%; 3/3) cohort C. Median PFS in the personalized phase was 7.8 months (m) for those in cohort A, 6.2m for B and 13.1m for C. Median PFS for PR pts was 6.9m (4.4-13.1) and for PS pts not reached. Grade (G) 3 AE related to therapy per cohort: A) 4 pts with anemia, 2 neutropenia, 1 thrombocytopenia, 1 nausea; B) 2 pts neutropenia; C) no G3. No G4 AE. No G3-G4 immune related AE. **Conclusions:** These findings highlight the potential clinical activity of a chemo-free approach and confirmed the feasibility of guiding personalized therapy in real-time in recurrent OC pts post-PARPi. This strategy was safe and provided clinical benefit to some pts. Further translational analysis is ongoing. Clinical trial information: NCT05065021. Research Sponsor: GSK; Apobiologix; Princess Margaret Cancer Foundation; OICR.

Phase I study of sustained and local delivery of intraperitoneal IL-2 using encapsulated cells in patients with platinum-resistant high-grade serous carcinoma.

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Background: Platinum-resistant high-grade serous carcinoma's (HGSC) propensity to metastasize throughout the peritoneal cavity has generated interest in the development of high-intensity locoregional treatment administered intraperitoneally. Prior efforts have been limited by administration difficulties and potential for local toxicity. We describe a phase I trial using AVB-001, a novel intraperitoneally administered, alginate-encapsulated, allogeneic cell line modified for constitutive expression of human interleukin-2 (hIL-2). Preclinically, this new platform allows self-limited anti-tumor immune-activation without the toxicities associated with systemic administration or prior intraperitoneal formulations. The primary objectives of this study were to investigate the feasibility, safety, and tolerability of treatment with AVB-001. Secondary objectives included evaluation of clinical efficacy and translational correlates. **Methods:** This was an open-label, multicenter, phase I dose escalation study. A single dose of AVB-001 was administered via laparoscopy at 1 of 4 dose levels ranging from 0.6 to 3.6 μg hIL-2/kg/day. Escalation to a higher dose was based upon Bayesian optimal interval 3+3 design. Toxicity was evaluated via NCI CTCAE v5.0 and response was assessed via RECIST v1.1. Translational analyses were performed to evaluate serum hIL-2 concentration and immunological changes in peripheral blood. **Results:** The trial enrolled 14 patients. Eleven patients had ovarian cancer, two had fallopian tube cancer, and one had peritoneal cancer. Median age was 68 (range 47-75). In terms of safety, 4 of 14 patients (28.6%) experienced a grade 3 treatment-related adverse event (TRAE). There were no grade 4 or 5 TRAEs. One patient exhibited an unconfirmed partial response lasting 29 days (ORR 1/14, 7.1%). Stable disease was observed in 7 patients with a median duration of clinical stability lasting 2.57 months (range 2.03-4.23). On translational analyses, dose-dependent immunologic changes were noted in the peripheral blood. CTLA-4 receptor expression was upregulated with increasing dose levels in both CD8+ and CD4+ T cells, however significant upregulation was not observed for either PD-1 or TIM-3. The study was terminated early due to funding limitations. **Conclusions:** The administration of AVB-001 is safe, feasible, and shows potential for meaningful clinical activity. A dose-dependent upregulation of the CTLA-4 checkpoint on CD8+ and CD4+ T cells was noted after administration, suggesting a rationale for combination therapies involving cytokines as "priming agents" to engage checkpoint inhibition. Finally, we demonstrate feasibility of this approach for delivery of hIL-2 and other future biologics via our ability to reproducibly manufacture multiple clinical batches of AVB-001 and deliver at point of patient care. Clinical trial information: NCT05538624. Research Sponsor: Avenge Bio, Inc; MD Anderson T32 Training Grant; T32CA101642; MD Anderson CCSG Core Grant; P30CA016672.

5563 Poster Session

Circulating tumor DNA (ctDNA) monitoring in participants (pts) with ovarian cancer treated with neoadjuvant pembrolizumab (pembro) + chemotherapy (chemo) ± anti–immunoglobulin-like transcript 4 (ILT4) monoclonal antibody MK-4830.

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Background: ctDNA is a promising biomarker for predicting disease progression, survival, and surgical outcomes in patients with solid tumors. In a phase 1 study (NCT03564691), ILT4 inhibitor MK-4830 + pembro had a manageable safety profile and showed antitumor activity in pts with solid tumors. We present results from a global, randomized phase 2 study (NCT05446870) evaluating quantitative change in ctDNA in pts with high-grade serous ovarian cancer (HGSOC) who received neoadjuvant pembro + chemo ± MK-4830. **Methods:** Eligible pts were female, aged ≥18 y, with previously untreated histologically confirmed FIGO stage 3 or 4 HGSOC and an ECOG performance status of 0 or 1, and were candidates for interval debulking surgery. Pts were randomly assigned 1:1 to receive neoadjuvant MK-4830 800 mg + pembro 200 mg + chemo (paclitaxel 175 mg/m^2 and carboplatin AUC 5-6) (arm 1) or pembro + chemo (arm 2) IV Q3W for 3 cycles. Pts underwent interval debulking surgery followed by 3 cycles of adjuvant therapy with the neoadjuvant regimen; adjuvant bevacizumab IV Q3W was permitted. ctDNA was assessed at each cycle using the Signatera assay (Natera, Inc.). A constrained longitudinal data analysis model was used to estimate the posterior probability that the coefficient for treatment assignment was <0, evaluating whether the reduction in ctDNA from cycle 1 (C1) was larger in arm 1. The primary end point was change in ctDNA from C1 at C3 in pts with detectable ctDNA; safety was a secondary end point. **Results:** At data cutoff (Dec 20, 2023), 160 pts were enrolled; 159 pts received treatment (arm 1, n = 79; arm 2, n = 80). Median study follow-up was 8.3 months (range, 1.9-16.4) in arm 1 and 8.3 months (range, 2.1-16.3) in arm 2. Median age was 61.5 y in both arms. 64 pts (80.0%) in arm 1 and 68 pts (85.0%) in arm 2 had available ctDNA data at C1; 51 pts (63.8%) and 63 pts (78.8%), respectively, had available ctDNA data at C3. Median ratio of ctDNA C3 to C1 was 0.02 (range, 0-1.53) in arm 1 and 0.01 (range, 0-0.60) in arm 2. The posterior probability that the coefficient for treatment assignment was <0 in the model was 38.8%, indicating a low posterior certainty of larger ctDNA reduction in arm 1. AEs occurred in 75 pts (94.9%) in arm 1 and all pts (100%) in arm 2. TRAEs occurred in 74 pts (93.7%) in arm 1 and in 79 pts (98.8%) in arm 2; grade 3-5 events occurred in 37 pts (46.8%) and 44 pts (55.0%), respectively. TRAEs led to death in 2 pts in arm 1; no treatment-related deaths occurred in arm 2. **Conclusions:** In pts with HGSOC, reductions in ctDNA were similar between neoadjuvant/adjuvant MK-4830 + pembro + chemo vs pembro + chemo. Real-time tumor-informed ctDNA testing may be feasibly incorporated into future clinical trials as a surrogate outcome to evaluate response. The safety profile of MK-4830 + pembro + chemo was comparable to pembro + chemo. Clinical trial information: NCT05446870. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

5564 Poster Session

Preliminary analysis of disitamab vedotin combined therapy for HER2-expressing platinum-sensitive recurrent ovarian/peritoneal/fallopian tube cancer (Diversity study): A single-arm, multicenter phase II trial.

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Background: Platinum-sensitive recurrent epithelial ovarian/peritoneal/fallopian tube cancer (PSROC) patients often exhibit reduced responsiveness to chemotherapy following initial platinum-based regimens, necessitating the development of more effective treatment strategies. Disitamab vedotin (DV; RC48) is a novel humanized anti-HER2 antibody-drug conjugate (ADC) with greater specificity than conventional agents like paclitaxel. This study (NCT06420973) evaluates the efficacy and safety of DV-based combination therapy in patients with HER2-expressing PSROC. **Methods:** This single-arm, open-label, multicenter phase II study examines DV combination therapy in patients with HER2-expressing (IHC 1 to 3+) PSROC. Patients received DV (2.5 mg/kg) plus carboplatin (AUC 5), with or without bevacizumab (7.5–15 mg/kg), every 21 days for six cycles. Maintenance therapy included DV (up to eight cycles) with or without bevacizumab until disease progression. The primary endpoint is PFS. Secondary endpoints include ORR, DCR, OS and safety. An exploratory endpoint assesses quality of life using the EORTC QLQ-CIPN20 (excluding Item 20). **Results:** As of January 2025, 15 patients (median age 58 years, range 47-73) were enrolled, with 86.7% diagnosed with ovarian cancer and 93.3% having high-grade serous carcinoma. Genetic analysis identified 4 gBRCA1 mutations, 1 sBRCA2 mutation, 5 wild-type cases, and 5 with unknown status. HER2 expression was 73% for IHC 1+ and 27% for 2+. The median number of prior treatment lines was one, with a median follow-up of 3.2 months (range 1-6.8m). Efficacy was evaluated in 10 patients, while safety was assessed in all 15. The ORR was 70% (1 CR, 6 PR), with a DCR of 100%. The ORR for both BRCA mutations and wild-type was 66.7%. Among patients with HER2 IHC 1+, the ORR was 71.4%, while for 2+, it was 66.6%. Patients with PFI $>$12 months had a 75% ORR, compared to 50% for those PFI $<$12 months. Treatment-related adverse events (TRAEs) were reported in 80% of patients, with $\geq$ Grade 3 TRAEs at 26.7%, including neutropenia (n=1), thrombocytopenia (n=2), and diarrhea (n=1). No Grade 4 or 5 TRAEs were observed. The EORTC QLQ-CIPN20 score showed no significant impact on quality of life compared to baseline. As of January 23, 2024, one patient had disease progression. **Conclusions:** The preliminary findings indicate that DV combined therapy is effective and safe for the treatment of HER2-expressing PSROC, highlighting its potential as a valuable therapeutic option. Further research in this area is essential to validate these results. Clinical trial information: NCT06420973. Research Sponsor: Clinical Research Fund for Distinguished Young Scholars of Peking University Cancer Hospital; QNJJ2023003.

5565 Poster Session

IBI354, an anti-HER2 antibody-drug conjugate, in patients with locally advanced unresectable or metastatic ovarian cancers: Updated results from a phase I trial.

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Background: IBI354 is an antibody-drug conjugate consisting of trastuzumab (anti-HER2 antibody) conjugated to a topoisomerase I inhibitor. It has showed manageable safety and encouraging efficacy in patients (pts) with advanced gynecologic cancers (including ovarian cancers [OC], Shu et al, abstract No. 720MO at 2024 ESMO annual meeting). Here, we present the updated safety and efficacy in OC. **Methods:** Eligible OC pts with HER2 alteration (IHC 1+, 2+, 3+ and/or ISH+ and/or NGS confirmed mutation or amplification) who failed or were intolerant to standard treatment were enrolled from China and Australia. Pts received IBI354 at 2–12 mg/kg every three weeks (Q3W) or Q2W. Primary endpoint was safety. Secondary endpoints were objective response rate (ORR), disease control rate (DCR), duration of response (DoR), and progression-free survival (PFS) per RECIST v1.1. **Results:** As of November 12, 2024, 92 pts were enrolled (median age, 58.0 years; Asian, 95.7%; White, 4.3%; ECOG PS 1, 73.9%; IHC 1+, 65.2%; IHC 2+, 29.3%). The median follow-up time was 11.0 months (range: 8.0–19.0). Median treatment duration was 24.1 (range: 3.1–60.3) weeks with 21 (22.8%) pts still on treatment. Treatment-related adverse events (TRAEs) occurred in 79 (85.9%) pts with grade ≥ 3 TRAEs in 27 (29.3%) pts. The most common TRAEs were anemia (51.1%), white blood cell count decreased (45.7%), neutrophil count decreased (40.2%), and nausea (35.9%). Serious TRAEs occurred in 10 (10.9%) pts. Interstitial lung disease or pneumonitis was observed in 1 (1.1%) pt, which was grade 2 and not related to IBI354 considered by the investigator. TRAEs led to dose reduction in 2 (2.2%) pts. No TRAEs led to treatment discontinuation or death. For efficacy-evaluable pts (who had at least 1 post-baseline tumor assessment) dosed at 12 mg/kg Q3W (n = 40), confirmed ORR and DCR reached 55.0% (95% CI: 38.5–70.7) and 90.0% (95% CI: 76.3–97.2), respectively. In 22 pts with confirmed response in 12 mg/kg Q3W dose group, the median DoR was not reached with events occurred in 6 (27.3%) pts, and 9-month DoR rate of 58.1% (24.2–81.2). The median PFS was 7.1 months (95% CI: 5.2–not reached) with events occurred in 21 (51.2%) pts. The median overall survival (OS) was not reached with events occurred in 12 (29.3%) pts, and the 9 month OS rate was 70.7% (95% CI: 54.3–82.2). For the pts with HER2 IHC 1+ OC dosed at 12 mg/kg Q3W (accounting for 67.5% [27/40] of efficacy-evaluable pts at 12 mg/kg Q3W), ORR and DCR reached 55.6% (95% CI: 35.3–74.5) and 88.9% (70.8–97.6), respectively. **Conclusions:** IBI354 was well tolerated with a manageable safety profile and showed promising efficacy in pts with locally advanced unresectable or metastatic OC, especially in pts with HER2 lower expression. Clinical trial information: NCT05636215. Research Sponsor: None.

Successful induction of tumor-directed immune responses in high grade serious ovarian carcinoma patients after primary treatment using a whole tumor cell vaccine.

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Background: Improving disease free and overall survival in advanced high grade serous ovarian carcinoma (HGSOC) after primary treatment remains challenging. This phase 1 trial (NCT04739527) evaluated safety and immunogenicity of a whole tumor cell vaccine, vididencel, to prime or boost immune responses in HGSOC after primary treatment. Vididencel expresses tumor associated antigens (TAA) frequently upregulated in HGSOC. **Methods:** Patients with advanced HGSOC who completed primary treatment received 6 intradermal injections with vididencel: 4 biweekly doses of 25 million cells (week 0, 2, 4 and 6) followed by 2 boosters of 10 million cells (week 14 and 18). Peripheral blood mononuclear cells were obtained at week 0, 4, 10, 14, 18 and 22. Disease status was evaluated at week 22 using clinical assessment and CA125 levels. Primary endpoint was safety and the induction of immune responses, measured by IFNγ ELISPOT, to at least one TAA (i.e. WT-1, PRAME, NY-ESO, or MAGE-A3/4). Secondary endpoints were disease status at week 22 and survival. **Results:** Primary analysis at week 22 has been completed for all 17 patients. In total,16 received all 6 planned injections and 1 patient discontinued treatment after 4 injections due to disease progression. Vididencel showed in 12 out of 17 patients a vaccine-induced response (VIR) to at least one of the tested antigens and 7 of these patients showed a sustained immune responses to the same antigen (sVIR). Table 1 shows the distribution of induced immune responses. Five patients were also given maintenance treatment with PARP inhibitors and all these patients showed a VIR. Vididencel was well-tolerated, with no trAEs above grade 2. The most common trAEs were mild to moderate local injection site reactions, characterized by redness, swelling and inflammation. Two unrelated serious AEs occurred, both linked to disease progression. At week 22, 4 weeks after last vididencel treatment, 10 patients (59%) had stable disease, and 7 had progressive disease, with all patients still alive. Patients with a VIR or sVIR had a higher rate of SD than patients without a vaccine-induced immune response (67% and 71% versus 40%, respectively). Long-term follow of patients continues of which a swimmers plot will be shown. **Conclusions:** Vididencel is well tolerated and effective in eliciting or boosting a broad T-cell response in HGSOC patients after primary treatment. Short-term evaluation of clinical response at week 22 suggests better responses in patients developing a VIR or sVIR compared to those patients not having a detectable immune response to the vaccine. Clinical trial information: NCT04739527. Research Sponsor: Mendus AB.

Immune response outcome (N=17)		Responses to individual TAAs			
		WT1	PRAME	NY-ESO	MAGEA3/A4
Immune responders (N=12)	VIR (n=12)	6 of 12	3 of 12	4 of 12	7 of 12
	sVIR (n=7)	4 of 7	2 of 7	1 of 7	2 of 7
Non-responders (N=5)	No VIR (n=5)				

(s)VIR; (sustained) vaccine induced response.

5567 Poster Session

Optimizing an NGS low-pass–based method to detect genomic instability as a PARP inhibitor predictive biomarker in high-grade serous ovarian cancer.

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Background: In high-grade serous ovarian cancer (HGSOC) PARP inhibitors constitute a standard treatment in tumors harboring Genomic Instability (GI). This biomarker constitutes a valuable predictive tool for the use of PARP inhibitors. Available commercial solutions to determine the GI status, present some caveats that must be overcome. This study aims to set up an academic test in a cost-effective manner by applying open-source R libraries to establish GI status in Formalin-Fixed and Paraffin-embedded (FFPE) samples. **Methods:** The study was carried out in two stages, technical and analytical setup and clinical validation. Firstly, 16 FFPE samples, 8 tumoral tissue from gynecological malignancies, and 8 from healthy tissues were sequenced. This step aimed to establish favorable sequencing conditions followed by the tune-in of specific parameters for the analytical pipelines, QDNA, and Shallow-HRD (R v.4.3.11). Secondly, 44 FFPE samples from patients diagnosed with HGSOC and known GI score (GIS) were used for clinical validation. For this analysis, GIS determined by GIInger from Sophia Genetic was considered the gold standard. The series was constituted of 23 samples carrying genomic instability (GIS>=0) and 21 stable samples (GIS<0). Of note, intermediate libraries from targeted sequencing performed in clinical routine were used as input for sequencing. Individual libraries were then pooled and sequenced in a NextSeq 2000 (2x100 paired-end) (Illumina, San Diego, CA, USA) to achieve a 0.5x coverage. Recalibration of the method was performed using Maxstat algorithm implemented in R. All the analyses were performed in Python v3.8 or R v.4.3.11. **Results:** Best technical and analytical results were obtained for the QDNA pipeline without an X chromosome and bin size of 1 mb plus shallowHRD. By using this parameter, clinical validation comparing the GI results with GIS score obtained from the Sophia Genetics test was performed. In-house determination of GI resulted in 23 samples classified as unstable (score>=20) and 21 stable samples (score < 20). Re-calibration of the score using 20 as a new cut-off to dichotomize the variable, showed an optimum performance with a concordance of 86.4 % ($p < 6.2 -6$) with GIS classification. Thus, borderline samples called by shallowHRD pipeline (5/44) were re-classified as stable. Both continuous scores showed a correlation of 0.855 ($p < 1.5 -13$) and an Area Under the ROC curve of 0.906, presenting an excellent performance as a biomarker for genomic instability. **Conclusions:** We present a validated, routine-based and cost-effective test to determine GI in HGSOC, being easily transferrable to daily practice. Research Sponsor: Conselleria de Educación, Cultura, Universidades y Empleo. Generalitat Valenciana.; CIGE/2023/206

Real-world analysis of folate receptor alpha (FRα; FOLR1) expression in pan-tumor samples from over 6000 patients in the US.

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Background: FRα is overexpressed in several cancers, including ovarian and endometrial. The FRα-targeted antibody-drug conjugate mirvetuximab soravtasine-gynx (MIRV) showed survival benefit vs chemotherapy in patients with platinum-resistant ovarian cancer (PROC) with high FRα expression (Moore K, et al. *N Engl J Med*. 2023;389(23):2162-2174). Greater understanding of FRα expression and distribution in real-world (RW) settings may help enable FRα testing implementation for biomarker-guided treatment strategies. Here, we present analyses of FRα expression in RW patient tumor samples referred for FRα testing by immunohistochemistry (IHC). **Methods:** Uniquepatient tumor samples across different malignancies (N=6695) were acquired from RW healthcare settings in the US over a 12-month period. FRα expression was assessed by IHC using the VENTANA FOLR1 (FOLR1-2.1) RxDx Assay. Trained pathologists scored samples with ≥75% tumor cells with ≥2+ membrane staining as FRα positive. The clinicopathological features of each case, FRα prevalence, and impact of sample age were evaluated. **Results:** From the entire dataset (N=6695), 41% of samples were FRα positive, 54% were negative, and 5% were not evaluable. Of 2000 samples with known primary tumor origin: 1632 (82%) were primary or metastatic sites of disease from patients with ovarian cancer (39% FRα positive); 266 (13%) originated from distinct non-ovarian tumor types, including primary peritoneal, Müllerian, pelvic, and gynecological sites of unspecified origin (combined 33.1% FRα positive); the remaining 102 (5%) had unconfirmed tumor origin. Of 1678 samples with known histological subtype, FRα positive expression was observed in samples from serous (43.5% [646/1486]), mixed (37% [14/38]), and endometrioid (10% [5/48]) histology, whereas FRα positive expression was absent across all clear cell (0/91) and mucinous subtypes (0/15). FRα positive expression was detectable in unique patient samples across all sample ages, which ranged from <1 to >5 years. **Conclusions:** RWanalysis of 6695 patient tumor samples referred for FRα testing demonstrated FRα prevalence of 41%. Ovarian cancers represented most cases evaluated, and the 39% FRα positive rate was consistent with the FRα positive prevalence observed in MIRV clinical trials (35%). This RW analysis demonstrates that FRα is measurable in samples ranging from <1 to >5 years, suggesting prior samples may be utilized for FRα testing if a recent sample is unattainable. This is consistent with previous analyses from MIRV clinical trials where most patients with PROC were selected for enrollment based on high FRα expression from archival tumor specimens. Collectively, this large RW data set helps to characterize the RW prevalence of the clinically actionable biomarker FRα and supports using FRα testing for personalized ovarian cancer treatment plans. Research Sponsor: AbbVie.

5569 Poster Session

Association of HIPEC response in ovarian cancer with PI3K/RAS/Notch gene signatures: A whole transcriptomic analysis of U.S. and French HIPEC treated ovarian cancer patients.

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Background: Hyperthermic intraperitoneal chemotherapy (HIPEC) is associated with improved overall survival in Stage III epithelial ovarian cancer (EOC) patients. We set out to evaluate the gene signatures associated with HIPEC response in EOC patients. **Methods:** Ninety-one EOC patients who underwent HIPEC with pre-operative tumor samples at City of Hope (51) and CHU Lyon (40) were identified between 2014 and 2022. RNA isolation was performed from formalin-fixed paraffin-embedded samples, followed by Whole-transcriptome library construction. Following exclusion of non-high grade serous (HGS) samples, and quality control steps, twenty-four samples were excluded. Progression-free survival (PFS) was used to define HIPEC response. Cut-off PFS values were used to distinguish good vs poor responders in primary EOC patients (18 months, based on KGOG, CARCINO-HIPEC trials), and recurrent EOC patients (12 months, based on MSK, CHIPOR HIPEC trials). Differential Gene Expression Analysis comparing good and poor HIPEC responders identified significantly changed genes. Pathway analysis was conducted using gene set enrichment analysis (GSEA) against Hallmark. **Results:** A total of sixty HGS tumor samples with available survival data were analyzed. 63.3% were primary EOC, 36.7% recurrent EOC. Germline BRCA mutations affected 21.7% of patients. With a median follow up of 31.9 months, median PFS was 29.3 (95%CI: 15.3, 63.5) months in primary EOC patients and 26.0 (95%CI: 14.7, 37.1) months in recurrent patients. Median OS was not reached in either group. 60.0% had a recurrence. Thirty-eight patients were identified as good responders, with a median PFS of 37.1 mos. (95%CI: 26.4, NR); 18 patients were identified as poor responders, with median PFS of 11.4 months (95%CI: 7.5, 14.2). Differential gene expression analysis between good and poor responders revealed 29 significantly upregulated 35 downregulated genes in HIPEC responders. Top upregulated genes in HIPEC responders include MAPK signaling pathway genes (RIB2, ETV5, CAPN8, IGFR1), in addition to CCND1 and CEACAM1. In HIPEC responders, the top-ranking gene sets in the transcriptional signature included Notch, KRAS, and Wnt/beta-catenin signaling pathways. In poor HIPEC responders, the DNA damage repair associated pathways E2F targets and G2M checkpoint, were activated. Similar transcriptomic pathway signatures were observed in Non-recurrent versus Recurrent HIPEC patients: Non-recurrent tumors were enriched with Notch signaling, while Recurrent tumors were enriched with E2F target and G2M checkpoint pathways. **Conclusions:** Good HIPEC response is characterized by transcriptional signatures consistent with Type I EOC characteristics of PI3K/RAS/Notch signaling. Recurrence after HIPEC in HGS ovarian cancer is higher in patients with E2F/G2M transcriptional signatures. Research Sponsor: None.

5570 Poster Session

Immunotherapy with anti-PD-1 or PD-L1 in advanced ovarian cancer (OC): A meta-analysis of randomized trials.

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Background: Immunotherapy (IO) has shown promising results in several solid tumors, including gynaecological malignancies. While PARP inhibitors and bevacizumab had deeply improved outcomes in OC, prognosis remains poor, underscoring the need for innovative treatment strategies. Anti-PD-1 and PD-L1 monoclonal antibodies have been evaluated in randomized trials across both first-line and recurrent OC settings. This meta-analysis summarizes the available evidence to assess progression-free survival (PFS) benefits from IO-based strategies. **Methods:** Phase II and III randomized clinical trials (RCTs) evaluating IO-based strategies using PD1 or PDL1 inhibitors published between 2019 and 2024 were identified through PubMed, Embase, and the Cochrane Library, as well as conference proceedings. Eight trials with PFS as primary endpoint, conducted in first-line and recurrence settings, were included. Data on PFS by PD-L1 status were available in seven trials. Three trials included two experimental arms and were analysed separately. Hazard ratios (HRs), 95% confidence intervals (CIs), and PFS events were extracted for overall populations and subgroups. A random-effects model was employed for data analysis, with sensitivity analyses performed to explore outcome variability. **Results:** The meta-analysis included 8 trials comprising 6,205 patients. The addition of IO to chemotherapy or placebo showed no improvement in PFS (HR = 1.02, 95% CI 0.86-1.22). Subgroup analyses indicated no significant differences in PFS in first-line (HR = 0.99, 95% CI 0.78-1.26) or recurrence settings (HR= 1.07, 95% CI 0.80-1.44). In trials reporting PD-L1 status (47.5% PD-L1 positive population), IO-based therapies demonstrated a non-significant trend towards PFS improvement (HR = 0.94, 95% CI 0.77-1.13). Excluding IO-only arms yielded similar results (HR = 0.94, 95% CI 0.79-1.11). **Conclusions:** IO-based strategies did not provide a substantial PFS benefit in advanced OC, irrespective of disease setting or PD-L1 status. Identifying effective combination strategies and patient subgroups that may benefit from IO remains an open research question. Research Sponsor: None.

Harnessing EHR for goals of care: The role of electronic alerts for care optimization in gynecologic cancer patients at risk of death in 6 months.

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Background: This study employed the validated Surprise Question to evaluate the ability of an electronic health record (EHR) alert to predict 6-month mortality, prompt goals of care (GOC) documentation, and facilitate high-quality end of life (EOL) care for patients with gynecologic cancer. **Methods:** EHR coding identified patients in an outpatient academic gynecologic oncology practice seen more frequently than annually with scheduled imaging, CA125 values, or chemotherapy. Patients without a diagnosis of primary gynecologic cancer were excluded. An outpatient EHR alert posed the modified Surprise Question: "Would you be surprised if the patient passed away in the next 6 months?" Choices were "Yes" and "No" (both considered meaningful responses) and "Show me next time" (deferral response; excluded). "No" responders were instructed on-screen to document a GOC discussion and consider palliative care referral. We analyzed EHR alert data from August 1, 2021-December 31, 2022, and clinical events up to 22 months after this period. Continuous variables were compared using Wilcoxon rank-sum tests, categorical variables were compared with chi-square tests, and both Cox proportional hazards regression and log-binomial models were used to predict death/time to death. **Results:** Meaningful responses were elicited for 804 unique patients, of which 130 (16.2%) were "No" (not surprised). Among patients whose providers replied "No", 35.4% died within 6 months of that encounter, compared to 4.2% of "Yes" replies ($p<0.001$). Among patients with a documented GOC conversation, the median time from first "No" response to documented conversation was 0 days (IQR 0.0, 84), compared to 255 days (IQR 81, 501) for "Yes". Among patients who died, subjects in the "No" group were more likely to be enrolled in hospice at EOL than those in the "Yes" group (79.0% vs 63.5%, p=0.014). A "No" response to the Surprise Question had a higher RR for death at 6 and 12 months compared to age, race, or cancer type. **Conclusions:** For patients with gynecologic cancer, responses to a Surprise Question EHR alert effectively predict 6-month mortality and are associated with increases in both GOC discussions and hospice utilization. Research Sponsor: None.

Log-binomial predictors of death at 6 months (univariate model).

		Risk Ratio (RR)	95% CI of RR	p-value	% deaths
Age at 1st alert	<49	Reference		0.010	4%
	50-59	1.00	0.95-1.05		4%
	60-69	0.93	0.87-0.98		11%
	70+	0.93	0.88-0.98		11%
Race	Caucasian	Reference		0.063	8%
	Black/Other	0.95	0.91-1.00		12%
Cancer Type	Ovarian	Reference		0.16	8%
	Other	1.03	0.99-1.08		10%
Surprise Question Response	Yes	Reference		<.0001	4%
	No	1.48	1.31-1.69		35%

Safety and effectiveness of fuzuloparib in patients with ovarian cancer: A nationwide, multicenter, prospective real-world study.

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Background: Fuzuloparib, a poly (ADP-ribose) polymerase (PARP) inhibitor, is approved in China for the treatment of platinum-sensitive recurrent (PSR) ovarian cancer (OC) and for maintenance therapy in newly diagnosed advanced and PSR OC. This study aims to evaluate the safety and effectiveness of fuzuloparib in OC patients under real-world settings. **Methods:** This multicenter, prospective real-world study included patients from 27 centers across China between January 2022 and August 2024. Eligible patients were aged ≥18 years and suitable for fuzuloparib treatment (monotherapy or combination therapy). Patients also had histologically or cytologically confirmed epithelial OC, primary peritoneal or fallopian tube cancer. The outcomes observed in this study included the incidence of treatment-related adverse events (TRAEs), progression-free survival (PFS), and overall survival (OS). **Results:** A total of 260 patients who received fuzuloparib (171 on monotherapy, 66 on combination therapy, and 23 with unknown treatment type) were analyzed. Of these, 97 (37.3%) received first-line maintenance therapy, 112 (43.1%) received maintenance therapy for PSR disease, 23 (8.8%) received treatment for PSR disease, 20 (7.7%) received treatment for platinum-resistant recurrent disease, and 8 (3.1%) received other treatments. The median age was 57 years (interquartile range [IQR]: 51.0, 65.0). Among the patients, 215 (82.7%) had epithelial OC, 169 (65.0%) were diagnosed at stage III/IV. Of the 239 patients with available safety data, 149 (62.3%) reported at least one TRAE. The most common TRAEs were anemia (23.4%), thrombocytopenia (23.4%), leukopenia (18.8%), and lymphopenia (12.6%). Fifty-four patients (22.6%) reported grade 3 or higher TRAEs. The median follow-up time for the first-line maintenance therapy group was 11.4 months (IQR: 6.0, 17.4), with median PFS and OS not yet reached; the 1-year PFS rate was 90.7%, and the 1-year OS rate was 97.1%. In the PSR maintenance therapy group, the median follow-up time was 9.1 months (IQR: 4.2, 15.9), with median PFS of 17.3 months (95% confidence interval [CI]: 12.1-26.3) and median OS not yet reached; the 1-year PFS rate was 66.2%, and the 1-year OS rate was 92.0%. In the PSR treatment group, the median follow-up time was 12.7 months (IQR: 5.6, 19.9), with median PFS and OS not yet reached; the 1-year PFS rate was 77.8%, and the 1-year OS rate was 90.2%. In the platinum-resistant relapse treatment group, the median follow-up time was 8.9 months (IQR: 5.1, 13.2), with median PFS and OS not yet reached; the 1-year PFS rate was 59.1%, and the 1-year OS rate was 80.0%. **Conclusions:** This is the first large-scale real-world study assessing the safety and effectiveness of fuzuloparib. In the real-world setting, fuzuloparib shows favorable safety, with no new safety signals. The effectiveness outcomes align with trends observed in key clinical trials. Clinical trial information: NCT05206890. Research Sponsor: None.

EON: Phase II trial of etigilimab (MPH313) in combination with nivolumab in patients with recurrent platinum-resistant clear cell ovarian cancer.

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Background: A predictor of response to anti-PD1 therapy is the extent of CD8+ infiltration within the pretreated tumor. TIGIT has shown to suppress anti-tumor immune responses via increased CD4+ Tregs and disruption of CD226 co-stimulation. We hypothesized inhibition of TIGIT may reverse the immune suppressive tumor microenvironment thereby potentiating the efficacy of PD-1 blockade in ovarian cancer. We sought to explore toxicity and efficacy of the combination of TIGIT inhibitor, etigilimab, and PD-L1 inhibitor, nivolumab. **Methods:** Eligible patients (pts) had platinum-resistant recurrent clear cell ovarian cancer with no prior immunotherapy and unlimited prior lines. Measurable disease and adequate end organ function were required. Pts received etigilimab 1000mg IV and nivolumab 240mg IV every 2 weeks. Bayesian optimal phase 2 design was used to conduct the trial. Dual primary end points were toxicity assessment by CTCAE v5.0 and objective response per modified RECIST v1.1. Clinical benefit (CBR) was defined as objective response or stable disease (SD) for >/= 4 months. Progression-free survival was defined as time from first treatment to documented disease progression. NCT05715216. **Results:** 23 pts received at least one cycle of treatment. Median age was 54 years (range 38-73); 65.2% of pts were Non-Hispanic white, 17.4% Hispanic, 8.7% Black and 8.7% Asian. Median lines of prior therapy was 2 (range 0-8). No patient received prior PARP inhibitor. Grade 3 or 4 adverse events were observed in 47.8% of pts, the most common of which was abnormal liver function tests. Other common adverse events of any grade included nausea/vomiting (34.8%), fatigue (30.4%), and anemia (30.4%). Of 20 pts evaluable for response, objective response rate was 15.0% (95% CI 3.2-37.9%) with 1 complete response (CR) and 2 partial responses (PR). CBR was 30.0% (95% CI 11.9%-54.3%). Median duration of response was 8.6 months, with ongoing responses in 2 pts at 20.0 and 8.6 months. Median duration of clinical benefit was 7.5 months. Single-cell RNA seq analysis of tumor tissues from 9 pts (CR/PR=2, SD=4, PD=3) revealed immunologic changes in the tumor microenvironment after treatment. Notably, an increased frequency of plasma B cells (p=0.02) was associated with clinical response. **Conclusions:** The combination of etigilimab and nivolumab was well tolerated. Promising clinical response and duration of benefit was observed in a heavily pretreated population of pts with clear cell ovarian cancer. Our data highlight a potential role of B cells in clinical response. Further analysis on the association of benefit by molecular features is ongoing. Clinical trial information: NCT05715216. Research Sponsor: Mereo BioPharma Group PLC; U.S. National Institutes of Health; Focus Fund; U.S. National Institutes of Health; U.S. National Institutes of Health.

Potential of tumor-informed ctDNA as an early predictive indicator for relapse in advanced ovarian cancer.

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Background: Prediction of relapse following firstline treatment in patients (pts) with high-grade serous ovarian cancer (HGSOC) remains a major challenge despite recent advances. Reliable markers for assessment of recurrence risk are urgently needed to tailor treatment strategies with circulating tumor DNA (ctDNA) emerging as a promising candidate. **Methods:** In this prospective feasibility study, pts with advanced HGSOC who underwent primary surgical and systemic treatment at two large-volume centers for gynecologic oncology were evaluated between July 2021 and September 2024. Whole genome sequencing was used to develop a personalized multiplex digital polymerase chain reaction fingerprint assay by identifying structural variants, single nucleotide variants and indels in FFPE tumor tissue. Longitudinal blood samples were collected perioperatively (preop, postop day 2 and 10), during firstline chemotherapy (cycle 1, 3 and 6 [c6]) and follow up. CA-125 levels were tested accordingly. For statistical analyses, chi squared, log rank tests and Kaplan-Meier method for PFS were applied as appropriate. **Results:** As of 21st January, 2025, a total of 31 pts have available samples from preop through c6 with completed ctDNA data. In this cohort, 11 recurrences (35%) have been diagnosed at a median clinical follow-up of 16.8 months [mo] (range 5.7-38.4 mo), median progression-free survival (PFS) was 11.8 mo (range 5.7-22.9 mo). At c6, levels of CA-125 were $<$35 kU/L in 25 (81%) and $\geq$35 kU/L in 6 (19%) of the 31 pts. Clearance of ctDNA was noted for 19 out of 31 pts (61%). 16 of these 19 pts (84%) had previous complete cytoreduction. While rates for recurrence did not align with CA-125 levels $<$35 kU/L (63.6%) and $\geq$35 kU/L (36.4%, P=0.075) at c6, a significantly lower recurrence rate was observed for patients with ctDNA clearance at c6 (4 of 19, 21.1%) compared to 7 of 12 patients with persistent ctDNA (58.3%, P=0.034). In 21 patients with complete cytoreduction, five pts still had detectable ctDNA levels at c6. Three of these five pts had recurrence (60%), compared to two of 16 pts with ctDNA clearance (12.5%, P=0.023). Detection of residual ctDNA at c6 was strongly associated with an increased risk for recurrence in the overall cohort compared to pts with ctDNA clearance (HR: 5.78, 95%CI: 1.93 – 31.99, P=0.004). This effect appears to be more pronounced in pts with macroscopic complete cytoreduction, but was not seen in pts with residual tumor. **Conclusions:** Findings of this interim analysis underline the potential of tumor-informed ctDNA as a powerful tool for recurrence risk assessment in pts undergoing primary treatment for HGSOC. In contrast to CA-125, ctDNA evaluation at the time of completed firstline chemotherapy might serve as an early predictive marker for relapse. This information could help to develop patient-specific treatment strategies, especially in the subgroup of pts with complete macroscopic cytoreduction. Research Sponsor: None.

5575 Poster Session

AI-powered quantification of tumor-infiltrating lymphocytes from H&E stained images in ovarian cancer and its association with PARP inhibitor therapy outcomes.

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Background: Maintenance therapy with PARP inhibitors improves the prognosis of patients with advanced or recurrent ovarian cancer. However, a simple biomarker detectable at treatment initiation remains unclear. This study evaluated the relationship between prognosis and artificial intelligence (AI)-powered quantification of immune cells in tumor and stroma areas in hematoxylin and eosin (H&E) slides. **Methods:** We evaluated 28 ovarian cancer patients treated with PARP inhibitors in our institution from 2019 to 2021. We developed an AI model to detect the epithelium and lymphocytes, specifically T cells (CD3+) and B cells (CD20+), from H&E-stained slides. This model was trained using annotated datasets, which included 26,509 images of the epithelium and 12,273 images of lymphocytes. The tumor bed areas were precisely defined by pathologists. Subsequently, the AI model identified epithelial and lymphocyte regions within these predefined areas. Using a treatment duration of PARP inhibitor with 12 months or more as the criterion, we identified the most relevant immune cell type based on the AUCs of the ROC curve and determined cutoff values. Furthermore, tumor BRCA1/2 status was assessed by a custom-targeted NGS testing panel. A log-rank test with a p-value < 0.05, considered statistically significant, examined the relationship between prognosis and tumor characteristics. **Results:** A total of 61 H&E slides were analyzed by AI: 28 slides before first-line chemotherapy, 25 after first-line chemotherapy, and 8 were the recurrent sample. The highest AUC was the lymphocyte-to-tumor area ratio (tumor-infiltrating lymphocyte score in tumor area, tTIL score) before the initial treatment, with an AUC of 0.73. The cutoff value of the tTIL score was set to 0.000534 based on the Youden index, dividing patients into tTIL-low (n=14) and tTIL-high (n=14) groups. The median follow-up period of the censored cases was 62.5 months vs. 77.3 months (p = 0.71). There were no significant differences in age, histological subtype, initial treatment method, proportion of R0 surgery, or that of tumor BRCA1/2 pathogenic mutations between groups. PARP inhibitors were used as maintenance therapy for recurrent settings in 71.4% of cases in both groups. The 5-year overall survival (5-y OS) rate of tTIL-high was significantly better than that of tTIL-low (84.4% vs. 30.8%, p = 0.0068). The median duration of OS after initiation of PARP inhibitors was significantly longer in the tTIL-high group (23.8 months vs. not reached, p = 0.046), and especially in tumor BRCA1/2-negative cases, tTIL-high had a significantly better 5-y OS rate of 90% vs. 12.5% (p = 0.0015). **Conclusions:** AI-powered tTIL score may predict the prognosis of ovarian cancer patients treated with PARP inhibitors. Future efforts will focus on increasing sample size and optimizing the tTIL score cutoff to improve accuracy. Research Sponsor: None.

Genomic instability score (GIS) and benefit from olaparib (ola) and bevacizumab (bev) maintenance in high-grade ovarian cancer (HGOC): Phase III PAOLA-1 GINECO/ENGOT-ov25 trial exploratory analysis.

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Background: The PAOLA-1 trial showed that adding ola to bev as maintenance therapy improved overall survival (OS) of HGOC patients with *BRCA1/2* mutations (BRCAm) or homologous recombination (HR) deficiency (HRD) defined by the MyChoice HRD Plus assay with a GIS threshold of 42. This post hoc analysis of PAOLA-1 explored if alternative thresholds could better identify patients who benefit most from ola. **Methods:** New cutoffs were determined through OS analyses using Cox proportional hazards models with an interaction term for GIS. Tumors were categorized into HRP (GIS<42), HRDlow (42–60 for *BRCA1/2* wild-type [BRCAwt], 42–67 for BRCAm), and HRDhigh (>60 for BRCAwt, >67 for BRCAm). Genomic analyses included promoter methylation, BRCA loss of heterozygosity (LOH) and HR repair gene mutations. **Results:** Among 623 patients, 194 (31%) were BRCAm and 429 (69%) BRCAwt. Main clinical prognostic features were well-balanced across BRCAwt/HRDhigh, BRCAwt/HRDlow and BRCAwt/HRP as well as among BRCAm/HRDhigh, BRCAm/HRDlow and BRCAm/HRP. Ola+bev improved progression-free survival (PFS) and OS in BRCAwt/HRDhigh and BRCAm/HRDhigh (Table). Ola+bev improved PFS but not OS in BRCAwt/HRDlow and BRCAm/HRDlow. HRP tumors showed no PFS or OS benefit regardless of BRCA status. *BRCA1/RAD51C* promoters were methylated in 75% of BRCAwt/HRDhigh, 47% of HRDlow, and 3% of HRP. HRDlow tumors had fewer HR repair gene mutations than HRDhigh. Among HRP/BRCAm, 37% lacked BRCA LOH, suggesting functional BRCA. **Conclusions:** Our post-hoc subgroup analyses suggest that refined GIS thresholds identify three distinct populations of HGOC patients with varying survival benefits from ola+bev maintenance. Optimized GIS cutoffs may further improve patient stratification in future PARP inhibitors trials. Research Sponsor: None.

	BRCA WT				BRCA Mut			
	HRP	HRD low	HRD high	p	HRP	HRD low	HRD high	p
N	277	72	80		19	124	51	
BRCA mutation								0.36
BRCA1	-	-	-		11 (57.9%)	82 (66.1%)	38 (74.5%)	
BRCA2	-	-	-		8 (42.1%)	42 (33.9%)	13 (25.5%)	
No BRCA LOH	-	-	-		7 (36.8%)	1 (0.8%)	2 (4.0%)	p<0.001
HR gene methylation (NA=134)				p<0.001				
No	187 (96.9%)	26 (53.1%)	13 (24.5%)		-	-	-	
BRCA1	1 (0.5%)	15 (30.6%)	34 (64.2%)		-	-	-	
RAD51C	5 (2.6%)	8 (16.3%)	6 (11.3%)		-	-	-	
mPFS (95%CI), months								
Ola + bev	16.6 (15.2-18.2)	28.9 (20.3-NR)	38.9 (22.1-NR)		21.2 (13.9-NR)	51.4 (38.9-NR)	75.2 (NR-NR)	
Placebo + bev	16.2 (13.9-18.8)	16.4 (12.9-27.7)	17.0 (12.9-23.4)		20.3 (14.7-NR)	19.4 (16.6-24.0)	15.5 (8.7-NR)	
HR (95%CI)	1.00 (0.76-1.32)	0.51 (0.29-0.91)	0.42 (0.24-0.72)		0.80 (0.28-2.26)	0.39 (0.24-0.62)	0.17 (0.07-0.41)	
mOS (95%CI), months								
Ola + bev	36.8 (30.7-40.9)	54.0 (48.3-NR)	NR (54.1-NR)		47.0 (24.2-NR)	NR (NR-NR)	75.2 (NR-NR)	
Placebo + bev	40.4 (33.0-53.3)	52.4 (45.8-NR)	41.2 (34.0-NR)		43.1 (29.0-NR)	NR (59.8-NR)	55.2 (29.8-NR)	
HR (95%CI)	1.19 (0.87-1.62)	1.07 (0.55-2.07)	0.49 (0.26-0.94)		0.88 (0.28-2.79)	0.61 (0.32-1.17)	0.15 (0.05-0.50)	

Survival outcomes of advanced ovarian cancer treated with neoadjuvant chemotherapy versus primary cytoreductive surgery using a quality-assured decision-making approach.

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Background: Neoadjuvant chemotherapy (NACT) is recommended for advanced ovarian cancer patients with a low likelihood of achieving complete cytoreduction through primary cytoreductive surgery (PCS) or those with high perioperative risk profiles. The decision between NACT and PCS requires careful evaluation of the feasibility of achieving optimal cytoreduction, emphasizing an individualized approach. This study evaluates whether quality-assured decision-making regarding PCS, based on institutional protocols, improves survival outcomes. **Methods:** This retrospective study included 1,256 patients diagnosed with FIGO stage IIIB-IVB ovarian, fallopian tube, or primary peritoneal carcinoma who underwent either primary or interval cytoreductive surgery at the National Cancer Center Korea between January 2016 and December 2023. The institutional criteria approach determined NACT eligibility based on patient performance status and/or computed tomography findings indicative of suboptimal cytoreduction. The primary objective was overall survival (OS), while the secondary objective was progression-free survival (PFS). **Results:** Of 1,256 patients, 666 (53.0%) received NACT followed by ICS, while 590 (47.0%) underwent PCS. Median PFS was significantly longer in the PCS group than in the NACT group (28.6 vs 17 months; HR: 0.63, 95% CI: 0.55–0.73, $p < 0.001$). Median OS was also longer in the PCS group compared to the NACT group (92.8 vs 62.1 months; HR: 0.61, 95% CI: 0.51–0.74, $p < 0.001$). Five-year PFS and OS rates were 33.8% and 65.1% in the PCS group vs. 18.3% and 51.3% in the NACT group, respectively. Complete resection of macroscopic disease was achieved in 70.7% of patients overall, with comparable rates between the two groups ($p = 0.1$). **Conclusions:** PCS demonstrates superior OS and PFS compared to ICS following NACT in advanced ovarian cancer patients, underscoring its critical role within an individualized decision-making approach. Research Sponsor: None.

Summary of key outcomes.

Outcome	PCS (n = 590)	NACT + ICS (n = 666)	p-value	Hazard Ratio (HR, 95% CI)
Median PFS (months)	28.6 (24.2–31.7)	17.0 (16.1–18.6)	< 0.001	0.63 (0.55–0.73)
Median OS (months)	92.8 (89.1–NR)	62.1 (53.8–67.9)	< 0.001	0.61 (0.51–0.74)
5-year PFS rate (%)	33.8%	18.3%	-	-
5-year OS rate (%)	65.1%	51.3%	-	-
Complete Resection (%)	70.7%	70.7%	0.1	-

5578 Poster Session

Impact of rucaparib on circadian rhythms and adverse events in ovarian cancer: Insights from the MAMOC trial.

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Background: Ovarian cancer (OC) is a leading cause of gynaecologic cancer mortality, with most cases diagnosed at an advanced stage. Standard treatment involves cytoreductive surgery followed by chemotherapy. In high-grade OC, maintenance therapy, including PARP inhibitors (PARPi), plays a crucial role in delaying disease progression. PARP1, the primary target of these agents, interacts with the CLOCK-BMAL1 complex, which regulates circadian rhythms. This study investigates circadian disturbances in BRCA wild-type OC patients receiving rucaparib compared to placebo and evaluates their impact on patient-reported outcomes. **Methods:** This study is part of the Phase III, randomized, double-blind, placebo-controlled MAMOC trial (NCT04227522), which enrolled 42 patients with advanced high-grade OC after platinum-based chemotherapy and bevacizumab maintenance. Rucaparib was given to 28 patients, while 14 received placebo. Daily activity data and patient-reported outcomes, including quality of life (EORTC-QLQ-C30/OV28), Fatigue Symptom Inventory (FSI), and adverse event (AE/SAE) data, were collected for all patients. A subset of 15 patients (5 placebo, 10 rucaparib) underwent molecular circadian clock analysis using saliva samples collected pre-, during, and post-treatment to assess changes in the clock and cancer-related pathways via qPCR and NanoString technology. Mathematical modelling was used to determine 24-hour toxicity profiles. **Results:** Rucaparib treatment caused significant disruptions in circadian gene expression, notably a reduction in *BMAL1* expression, followed by an increase in *BMAL1* and *PER2* levels post-treatment. Dysregulation of *BMAL1* and *PER2* correlated with the frequency and severity of side effects, including fatigue. Circadian parameters such as amplitude, MESOR, and phase were predictive of patient-reported outcomes. In the rucaparib group, circadian parameters exhibited opposing associations with outcomes compared to placebo. Clock-associated genes, including *NFIL3* and *GSK3B*, showed altered expression patterns that normalized after treatment. Additionally, rucaparib induced phase shifts and amplitude changes in clock and cancer-related genes like *CRY2*, *RORC*, and *TP53*, which were associated with increased adverse effects, particularly fatigue and nausea. Mathematical modelling revealed variability in toxicity profiles based on individual circadian rhythms pointing to the relationship between clock disruption and side effect severity. **Conclusions:** Our findings highlight the role of circadian rhythm dysregulation in the toxicity of PARPi in OC. The study suggests that chronotherapy, aligning drug administration with patients circadian rhythms, may reduce side effects. Incorporating circadian biology into treatment strategies could thus contribute to optimize cancer therapies by enhancing efficacy while minimizing toxicity. Clinical trial information: NCT04227522. Research Sponsor: Clovis Oncology; MSH Medical School Hamburg; Charité/ BIH Digital Health Accelerator Program; Dr. Rolf Schwiete Stiftung.

Efficacy of third-line and later (3L+) therapies post poly (ADP-ribose) polymerase inhibitor (PARPi) exposure in recurrent platinum-sensitive ovarian cancer (PSOC): A pooled clinical trial database analysis.

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Background: Patients (pts) with PSOC often experience reduced efficacy and tolerability with each successive treatment (tx). While PARPi therapies have demonstrated clinical benefit in frontline and maintenance settings, most pts eventually experience progression of disease (PD) with limited tx options. Data establishing standard of care for PSOC was published prior to the PARPi era. This study evaluated the efficacy of tx in PSOC subsequent to PARPi exposure. **Methods:** Pooled pt-level data from <5 multinational clinical trials (CT) involving PARPi tx were sourced from the Medidata Clinical Cloud and included pts with PSOC diagnosis, ≥2 prior lines of platinum-based chemotherapy (PBC), most recent platinum-free interval (PFI) ≥6 months (mo), prior PARPi tx, initiation of tx subsequent to PARPi (defined as the index tx), and ECOG Performance Status (PS) ≤1 prior to the index tx. Index date was defined as the initiation of index tx. Outcomes included overall response rate (ORR), progression-free survival (PFS), and overall survival (OS). PFS was defined as the time from the index date to PD, death or start of new tx; pts with no PFS event were censored at the end of follow-up. PFS and OS were estimated using the Kaplan-Meier method and compared across subgroups with the log-rank test. Exploratory subgroup analyses of PFS and OS were conducted per factors identified in multivariable Cox models. **Results:** Among 130 pts (≥65 years, 36.9%; White, 87.7%; FIGO Stage III/IV, 89.2%; ECOG PS 0/1, 59.2%/40.8%; ≥3 prior lines of PBC, 23.8% [range, 2-5]; PFI ≥12 mo, 61.5%), the median duration of PARPi use was 13.24 mo (IQR, 9.22), and 96.9% experienced PD ≤106 days from PARPi discontinuation. Index tx included PBC (74.6%) and non-PBC (25.4%); 61.5% received combination tx. Median duration of index tx was 4.01 mo (95% CI, 3.71-4.93). ORR on index tx was 16.9% (95% CI, 10.9-24.5). Median PFS was 6.11 mo (95% CI, 5.06-7.39), with longer PFS in pts with PFI ≥12 mo vs 6 to <12 mo (7.39 mo [95% CI, 6.08-8.77] vs 4.44 mo [3.25-6.14]; *P*=0.002) and in pts with combination therapy vs monotherapy index tx (7.39 mo [95% CI, 6.21-8.61] vs 3.71 mo [95% CI, 3.12-5.75]; *P*=0.026). Median OS was 19.35 mo (95% CI, 17.77-22.08), with longer OS in pts with PFI ≥12 mo vs 6 to <12 mo (23.03 mo [95% CI, 19.29-33.81] vs 15.08 mo [95% CI, 11.89-19.68]; *P*<0.0001). PFS and OS were similar in PBC vs non-PBC as index tx. **Conclusions:** Median PFS with 3L+ tx for PSOC following PARPi exposure was 6.11 mo, establishing an efficacy benchmark for tx subsequent to PARPi exposure in this unique pt population and highlighting the need for more effective tx. Due to the lack of regular per-protocol imaging assessments after the start of non-trial tx, PFS values may be over-estimated. However, pooled CT data with long-term follow-up provide valuable insights not available from other sources. Research Sponsor: AbbVie.

5581 Poster Session

A multi-omics approach using lipids and proteins for early detection in individuals with signs and symptoms of ovarian cancer.

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Background: Late-stage ovarian cancer (OC) is diagnosed in 80% of patients, leading to a five-year survival rate below 30% and ranking OC as the fifth leading cause of cancer-related deaths in women. Non-specific abdominal symptoms overlap with benign disorders, delaying diagnosis. Testing symptomatic individuals can detect low disease burden, enabling high complete cytoreduction rates. However, current diagnostic tools lack sensitivity and specificity for early-stage OC, underscoring the critical need for novel biomarkers and approaches. **Methods:** We conducted a multi-omics analysis of serum from two independent, clinically annotated cohorts. Specimens were analyzed using UHPLC-MS untargeted lipidomics and a protein biomarker panel. Cohort #1 (N=544) from the University of Colorado Gynecologic Tissue and Fluid Bank and commercial vendors included patients diagnosed with OC (N=219: 80 early-stage I/II, 139 late-stage III/IV), and non-cancerous controls (N=325) for biomarker discovery. Cohort #2 (N=423) from Manchester University NHS Foundation Trust and commercial vendors included prospectively enrolled individuals with signs and symptoms of OC. Samples included patients diagnosed with OC (N=109 total: 52 stage I/II, 57 stage III/IV), and non-cancerous controls (N=314). Cohorts were processed independently. **Results:** Over 1000 features were identified in both cohorts. There was a significant overlap in common features confirming importance in indication for use population. The top features confirmed in both cohorts enabled machine learning-based modeling. Biomarker classes were modeled separately (lipids only, proteins only) and in combination (lipids and proteins), employing 20-fold cross validation. Models containing multi-omic features consistently exhibit the highest AUC compared to individual biomarker classes. AUC for the top-performing model applied to both cohorts was 95% (CI 94-96) for all controls vs. all OC, and 92% (CI 89-95) for all controls vs. early-stage OC. When compared with normal individuals, the AUC vs all OC across stages and sub-types was 97% (CI 96-98). **Conclusions:** Our top-performing models contain >50 multi-omic features common across two independent cohorts, comprised of 967 unique individuals. Combining LC-MS-based lipidomic profiling of serum with proteins represents a promising new approach as a clinical diagnostic for detecting OC in this complex patient population. Early detection in women with signs and symptoms of OC and faster triage to specialty care may lead to improved patient outcomes. Research Sponsor: None.

Early detection of ovarian cancer: An accurate high-throughput extracellular vesicle test.

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Background: The high mortality of Ovarian cancer (OC) has been attributed to late-stage diagnosis and the lack of an effective early detection strategy, particularly for asymptomatic women. In this study, we developed and validated a high-throughput OC detection test based on plasma extracellular vesicle (EV)-associated biomarkers. **Methods:** A case-control study was conducted to evaluate blood-borne EV-associated ovarian cancer biomarkers, including miRNAs, proteins, lncRNAs, miscRNAs, MtrRNAs, MttRNAs, rRNAs, scaRNAs, snRNAs, and tRNAs. Protein and RNA biomarkers were identified by mass spectrometry and RNA sequencing, respectively. Training (n=453) and independent test (n=471) sample sets were used to develop and validate a multivariate index assay (MIA). The MIA was further validated using a high-throughput, pathology laboratory compatible, EV isolation platform (EXO-NET) and two independent sample cohorts (n=97 and n=532). The classification accuracy, sensitivity and specificity of the MIA was compared to that of CA125 levels. **Results:** Discovery and Training phases - more than 100,000 EV-associated biomarkers were identified from 453 EV samples. The classification performance of these biomarkers was assessed using machine learning algorithms. EV-associated protein and miRNA biomarkers delivered the highest performing classifiers and, therefore, were used in subsequent MIA development and training. During the training phase, multivariate classification algorithms were validated using a 10-fold cross-validation method. The highest performing classifiers for EV-associated protein and miRNA, at specificity of 98%, achieved sensitivities of 90% and 82%, respectively. Validation phase: Locked classification algorithms (*i.e.* MIAs) were validated using two independent sample cohorts and reported classification accuracies of 92-98%, significantly outperforming CA-125 (CE = 62%, $p<0.001$). Automated high-throughput MIA – All stages OC: the best performing automated high-throughput MIA demonstrated an overall sensitivity of 92% (95% CI, 75–96%) and specificity of 93% (95% CI, 86–96%) for all stages of OC, Positive Predictive Value of 95% (CI, 93-96%) and Negative Predictive Value of 80% (CI, 76-89%) at 98% specificity (n=532). Stage I OC: Importantly, the MIA displayed a sensitivity of 90% (95% CI, 76–100%) and specificity of 96% (95% CI, 40%–99%) for stage I OC. While CA125 have an overall sensitivity for all stages of OC of 61% (95% CI, 53–69%), with a sensitivity of 44% for stage I (95% CI, 28–62%). **Conclusions:** In this study we report the development and validation of an accurate, automated high-throughput EV-based test for early detection of ovarian cancer. The test delivers significant improvements in sensitivity and specificity compared to CA-125, especially in detecting early-stage OC. Research Sponsor: Lion Medical Research Foundation; 2015001964; Ovarian Cancer Research Foundation; 2018001167; Medical Research Future Fund; MRF1199984 GA187319; National Health and Medical Research Council; 1195451; INOVIQ.

Hyperthermic intraperitoneal chemotherapy (HIPEC) for primary advanced-stage or recurrent ovarian cancer: A systematic review and meta-analysis of randomized controlled trials.

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Background: Ovarian cancer is the gynecologic malignancy with the highest mortality rate. Despite cytoreductive surgery (CRS) and adjuvant or neoadjuvant systemic therapy, the rate of peritoneal recurrence remains high. Hyperthermic intraperitoneal chemotherapy (HIPEC) has emerged as a potential treatment option, delivering high concentrations of heated chemotherapy directly to the tumor site, enhancing local cytotoxicity. **Methods:** We searched PubMed, Embase, and Cochrane for randomized clinical trials (RCTs) comparing CRS plus HIPEC versus CRS alone. Hazard ratios (HR), odds ratios (OR) and mean differences (MD) were pooled using Review Manager software version 5.4. Heterogeneity was assessed with I^2 statistics. The main outcomes were overall survival (OS), median OS, progression-free survival (PFS), median PFS, operative time in minutes, Grade 3 or higher adverse events, time from surgery to adjuvant chemotherapy and length of hospital stay (LOS) in days. Subgroup analysis was performed for primary and recurrent cancer outcomes. **Results:** A total of 1,259 patients from 8 RCTs were included, with 636 (50.52%) undergoing CRS with HIPEC. The median follow-up period ranged from 32 to 121.2 months. CRS plus HIPEC significantly improved OS (HR 0.76; 95% CI 0.62-0.93; p = 0.009; I^2 = 27%), with a significant benefit also observed in the subgroup analyses of primary ovarian cancer (HR 0.66; 95% CI 0.52-0.85; p = 0.001; I^2 = 0%). However, no significant difference was observed for recurrent ovarian cancer (HR 0.87; 95% CI 0.63-1.19; p = 0.38; I^2 = 39%). Median OS also significantly favored CRS plus HIPEC (MD 9.99; 95% CI 2.40-17.58; p = 0.01; I^2 = 0%). PFS was not significantly different between groups (HR 0.74; 95% CI 0.52-1.06; p = 0.10; I^2 = 76%). In subgroup analysis, PFS was significantly improved for primary ovarian cancer (HR 0.62; 95% CI 0.49-0.79; p = 0.0001; I^2 = 0%), but not for recurrent ovarian cancer (HR 0.80; 95% CI 0.41-1.56; p = 0.52; I^2 = 84%). Median PFS showed no statistical difference (MD 1.98; 95% CI -1.20-5.15; p = 0.22; I^2 = 29%). Time from surgery to adjuvant chemotherapy was not statistically different (MD -0.13; 95% CI -4.49-4.23; p = 0.95; I^2 = 0%). Operative time was significantly shorter in the control group (MD 127.75; 95% CI 89.61-165.89.; $p < 0.00001$; I^2 = 51%), as were LOS (MD 1.49; 95% CI 0.12-2.87; p = 0.03; I^2 = 0%) and Grade 3-5 adverse events (OR 1.50; 95% CI 1.05-2.16; p = 0.03; I^2 = 40%). **Conclusions:** In patients with ovarian cancer, HIPEC significantly improved OS, particularly in the subgroup of primary ovarian cancer. PFS was also significantly improved in this subgroup. However, these benefits were associated with higher rates of adverse events and longer LOS. Our analysis supports the use of HIPEC in the treatment of ovarian cancer, especially for patients with primary ovarian cancer. Research Sponsor: None.

Hyperthermic intraperitoneal chemotherapy in recurrent ovarian cancer: An updated systematic review and meta-analysis.

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Background: Ovarian cancer is the leading cause of mortality among gynecological malignancies in women. Disease recurrence remains a formidable challenge in the management of primary ovarian cancer. This systematic review and meta-analysis evaluate the impact of hyperthermic intraperitoneal chemotherapy (HIPEC) on overall survival (OS) and progression-free survival(PFS) in patients with recurrent ovarian cancer. **Methods:** A comprehensive literature search was conducted in PubMed, Embase, and Cochrane databases to identify randomized controlled trials (RCTs) published up to November 2024, comparing the outcomes of HIPEC combined with cytoreductive surgery (CRS) versus CRS alone in patients with recurrent ovarian cancer. A total of 459 articles were screened in accordance with the PRISMA guidelines. The primary endpoints analyzed were OS, PFS, and postoperative complications. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated using the inverse variance method for time-to-event outcomes, while the Mantel-Haenszel method was applied for binary outcomes to estimate relative risk (RR) and corresponding 95% CIs. Statistical heterogeneity was assessed using Cochrane's Q test and Higgins' I^2 statistic. Statistical significance was set at a p-value < 0.05. Data analysis was performed using R software version 4.4.2. **Results:** Following the screening process, four RCTs involving a total of 801 patients were included in the meta-analysis, and 398 patients (49.6%) received HIPEC. The pooled analysis demonstrated a non-significant improvement in OS for the HIPEC group (HR 0.8; 95% CI [0.55, 1.17]; p=0.159). Similarly, PFS did not significantly differ between the treatment and control groups (HR 1.04; 95% CI[0.46, 2.35];p=0.867). In terms of postoperative complications, patients who underwent HIPEC were at a significantly increased risk of developing anemia (RR 1.36; 95% CI[1.08, 1.72]; p=0.028) and sepsis (RR 2.11; 95% CI[1.44, 3.08];p=0.014). However, no significant differences were observed between the treatment and control groups regarding other postoperative complications, including urinary tract infection (RR 0.95;95% CI[0.19, 4.69];p=0.895), bowel obstruction (RR 0.77; 95% CI [0.25, 2.37]; p=0.426), pleural effusion (RR 1.49;95% CI[0.16, 14.16];p=0.525), and thrombosis (RR 1.99;95% CI[0.98, 4.07];p=0.053). **Conclusions:** The findings suggest that while HIPEC may offer a potential, albeit statistically non-significant, survival benefit in patients with recurrent ovarian cancer, it is associated with an increased risk of anemia and sepsis. Research Sponsor: None.

5585 Poster Session

Impact of body mass index, diabetes, and tumor mutational burden in ovarian, fallopian tube, and primary peritoneal carcinoma with BRCA1/2 alteration on poly(ADP-ribose) polymerase inhibitors.

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Background: Obesity and hyperinsulinemia are associated with increased fallopian tube (FT) epithelial DNA damage in women carrying germline BRCA1/2 mutations. Whether these states impact survival in patients with ovarian, FT, or primary peritoneal carcinoma (PPC) with BRCA1/2 mutations, particularly when treated with Poly (ADP-ribose) polymerase inhibitor (PARPi), remains unclear. Research on tumor mutational burden (TMB) in these malignancies and survival have yielded inconsistent results. **Methods:** Ovarian/FT/PPC patients with germline/somatic BRCA1/2 mutation who received ≥1 dose of PARPi therapy between 2015-2023 were included in this retrospective cohort. Clinical characteristics abstracted include age, ethnicity, histology, DM status, pre-treatment TMB (pTMB) on MSK-IMPACT, PARPi use. Progression-free survival (PFS) was estimated using Kaplan-Meier. Cox regression was used to evaluate associations with PFS. **Results:** 202 patients treated between March 2015 – Aug 2024 were included; median age was 60 (interquartile range 50.3-67.2), 117 (57.9%) were overweight/obese (body mass index [BMI] ≥ 25) and 21 (10%) had DM. 160 (79%) and 33 (16%) had ovarian and FT cancer respectively. 182 (90.1%) had high grade serous carcinoma. 80 (40%) had germline BRCA1, 48 (24%) had germline BRCA2, 50 (25%) had somatic BRCA1 and 28 (14%) had somatic BRCA2 mutations. 91 (58%) had pTMB ≤5 mutations/megabase [mut/Mb], 56 (36%) had pTMB >5 to <10 mut/Mb and 9 (6%) had pTMB ≥10 mut/Mb. Median pTMB was higher in overweight/obese than normal BMI (4.9 vs 4.3 mut/Mb, p=0.093). 118 (58%) received PARPi as first-line and 59 (29%) received PARPi as second-line maintenance. 190 (94%) received PARPi as monotherapy, 6 (3%) in combination with bevacizumab and 6 (3%) in combination with immunotherapy +/- bevacizumab on a clinical trial. 168 (83%) received olaparib, 24 (12%) received niraparib and 9 (4.5%) received rucaparib. In multivariable (MV) Cox regression analysis, somatic BRCA status (BRCA1 hazard ratio [HR]=2.22, 95% confidence interval [95% CI]: 0.55-8.98; BRCA2 HR=0.66, 95% CI: 0.12-3.77; p=0.022; reference was somatic BRCA wildtype) was independently associated with PFS, pTMB (>5 to <10 mut/Mb HR=0.62, 95% CI: 0.32-1.19; ≥10 mut/Mb HR=0.19 95% CI: 0.02-1.56; p=0.088) had borderline significance while BMI and DM status were not associated. A MV Cox model additionally including the interaction between BMI and DM illustrated worse PFS in overweight/obese DM patients with borderline significance (p=0.094). **Conclusions:** Higher pTMB trended toward longer PFS in ovarian/FT/PPC patients with BRCA1/2 mutations receiving maintenance PARPi and was more common in overweight/obese. Prospective trials should evaluate if TMB may predict for response to PARPi and whether obesity-mediated DNA damage alters treatment outcomes. Research Sponsor: None.

Survival outcomes for ovarian cancer patients in the post–poly ADP-ribose polymerase inhibitor (PARPi) era in the US.

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Background: PARPi introduction in clinical practice has led to major changes in the therapeutic landscape for ovarian cancer (OC)[1]. Olaparib is approved alone or in combination with bevacizumab for the first line maintenance therapy of BRCA-mutated or homologous repair deficient (HRD) OC. We hypothesize that the introduction of PARPi in routine clinical practice for maintenance therapy in OC has resulted in improvements in survival outcomes among OC patients (pts) treated in the real world. **Methods:** Pts with a diagnosis of stage III/IV epithelial OC age ≥18 years between 2000-2021 were obtained from the Surveillance, Epidemiology, and End Results (SEER) Database. A cutoff on 2017 was made based on the initial approval of PARPi for maintenance therapy. Statistical analyses were conducted with SPSS. Pts characteristics were reported in frequencies and compared with the Chi-squared test. The Kaplan-Meier method was used to estimate median OS. Cox Regression was used identify independent prognostic factors of survival. P-value ≤0.05 was considered statistically significant. **Results:** 59,913 pts were included with median age 63 years, 60.9% non-hispanic white, and 55.8% with serous histology. 44,873 pts were diagnosed in the pre-PARPi cohort and 15,040 in the post-PARPi cohort. 76.3% and 76.1% of pts received any chemotherapy and surgery, respectively. Similar distribution in analyzed variables was found when comparing among eras. The median OS for pre-PARPi pts was 37 months (95%CI: 36.4-37.6) and post-PARPi pts was 38 months (36.6-39.4), p=0.023. In multivariate analysis, pts diagnosed in the post-PARPi era had improved OS compared with pts in pre-PARPi era (HR=0.93, 95%CI:0.91-0.96, p<0.001). **Conclusions:** To the extent of our knowledge, this study is the first real world analysis of survival outcomes in OC pts after the introduction of PARPi at a population level in the US. The introduction of PARPi maintenance therapy has resulted in a modest improvement in OS in the overall OC population unselected for BRCA or HRD status. 1. Tew WP et al. J Clin Oncol. 2020 Oct 20;38(30):3468-93. Research Sponsor: None.

Oregovomab in combination with non-platinum chemotherapy for the treatment of PARP inhibitor– and platinum-resistant ovarian cancer: A two-cohort, single-arm phase 2 study (OPERA/KGOG3065/APGOT-OV6).

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Background: Oregovomab, an investigational murine monoclonal antibody against CA-125, has shown promising efficacy in a phase 2 study in patients with recurrent ovarian cancer. Herein, we report the primary results of OPERA/KGOG 3065/APGOT-OV6 on oregovomab in combination with non-platinum-based chemotherapy in patients with PARP inhibitor (PARPi)- and platinum-resistant epithelial ovarian cancer (EOC). **Methods:** This multicenter, investigator-initiated, two-cohort, single-arm phase 2 trial evaluated the efficacy and safety of oregovomab in combination with PLD or weekly paclitaxel in patients with PARPi- and platinum-resistant EOC. Patients who received one to three prior lines of chemotherapy will be assigned to Cohort 1 (oregovomab [C1,2,3,5,7 for five doses] + PLD q4w, n=28), whereas patients who received more than three prior lines of chemotherapy will be assigned to Cohort 2 (oregovomab [C1,2,3,5,7 for five doses] + weekly paclitaxel [D1,8,15 q4w], n=28). The primary endpoint of the study was objective response rate (ORR) based on RECIST version 1.1. The secondary endpoints are progression-free survival (PFS), overall survival (OS) and safety. For the exploratory endpoints, immunologic response was measured at pretreatment and at C2, 3, 5, 7, or EOT by assessing serum HAMA levels and performing flow cytometric analysis of PBMCs. This trial is registered with ClinicalTrials.gov (NCT05407584). **Results:** A total 56 patients (Cohort 1, n=28; Cohort 2, n=28) have been enrolled between July 12, 2022 and September 19, 2023. Median age was 59 years (range, 36–79). Fifty-two (92.9%) patients had high-grade serous adenocarcinoma. At the data cut-off, the median follow-up was 8.0 months for Cohort 1 and 6.5 months for Cohort 2. The ORR was 0.0% (95% CI: 0.0–12.3) in Cohort 1, and 28.6% (95% CI: 13.2–48.7) in Cohort 2. Eight patients (28.6%) in Cohort 2 achieved a partial response, while 12 (42.9%) patients in Cohort 1 and 3 (10.7%) patients in Cohort 2 had stable disease. Three patients withdrew from the study due to treatment-related adverse events (TRAEs). These included one case of neutropenia in Cohort 1 and cases of anemia and lymphedema in Cohort 2. No TRAEs leading to death were reported. The median PFS was 2.5 months (95% CI: 2.1–4.7) in Cohort 1, and 2.6 months (95% CI: 2.0–3.7) in Cohort 2. Serum HAMA levels significantly increased after C3 exclusively in Cohort 2, but no significant changes in peripheral T cells have been observed. **Conclusions:** Oregovomab plus weekly paclitaxel chemotherapy demonstrated encouraging activity and safety in heavily pre-treated PARPi- and platinum-resistant EOC. Clinical trial information: NCT05407584. Research Sponsor: Canariabio Inc.

5588 Poster Session

Platinum or non-platinum therapy in post-olaparib recurrent ovarian cancer: Analysis in matched cohorts.

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Background: Due to potential cross-resistance mechanisms efficacy of platinum agents may be dramatically reduced in patients with ovarian cancer which progressed during maintenance therapy with PARP-inhibitors. We conducted this study to examine whether administration of platinum compounds has clinical value in post-olaparib setting of treatment for epithelial ovarian cancer treatment. **Methods:** This was a single center retrospective study in matched cohorts. We selected ovarian cancer patients from N.N. Blokhin NMRCO ovarian cancer who were treated in 2014-2024 years for any FIGO stage high-grade serous or endometrioid advanced epithelial ovarian cancer and progressed during olaparib maintenance therapy. Patients were treated with standard platinum-based or non-platinum chemotherapy for recurrent advanced epithelial ovarian cancer. Cardinality matching was considered to ensure adequate balancing of the study arms. The primary endpoint of the study was progression-free survival (PFS) in patients treated with platinum-based and non-platinum chemotherapy. Overall survival was a secondary endpoint. **Results:** Cardinality matching with 1:2 ratio resulted in 126 matched patients for further analysis. Groups were well balanced without any significant differences in baseline characteristics. Median age in both treatment arms was 50 years with no differences in patients' age, risk groups, prevalence of BRCA-mutations, duration of olaparib therapy and platinum-free interval. With a median follow up of 7.4 mo. median PFS was 6.0 in the non-platinum chemotherapy arm and 6.5 mo. in the platinum-based therapy arm (HR 1.17; 95% CI 0.77-1.77; p=0.46). Estimated 1-year PFS was 13.1% and 8.3%, respectively. Median OS was 21.3 mo. and 23.1 mo. in platinum-based chemotherapy arm and non-platinum arm (HR 0.98; 95% CI 0.55-1.76; p=0.96). Subgroup analyses revealed no heterogeneity in therapy efficacy. **Conclusions:** Our study suggest no additional benefit from platinum-based chemotherapy in post-olaparib ovarian cancer, further prospective trials are warranted to find optimal therapeutic approaches for these patients. Research Sponsor: N.N. Blokhin NMRCO.

5589 Poster Session

A prospective, single-arm, phase 2 trial exploring the use of pamiparib combined with surufatinib as neoadjuvant therapy for advanced, unresectable ovarian cancer (PASSION).

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Background: Pamiparib is a selective PARP1/2 inhibitor, while surufatinib targets VEGFR1-3, FGFR1, and CSF-1R. We evaluated the efficacy and safety of combining pamiparib and surufatinib in neoadjuvant therapy (NAT) for advanced unresectable ovarian cancer (OC) in a broad, molecularly unselected population. **Methods:** This phase 2, single-arm study enrolled patients aged 18–70 with newly diagnosed OC in China. Participants received pamiparib (40 mg twice daily, 3 cycles) combined with surufatinib (250 mg twice daily, 2 cycles), followed by interval debulking surgery (IDS) and 4 cycles of platinum-based chemotherapy. Primary endpoint: complete resection (R0). Secondary endpoints: objective response rate (ORR), pathological complete response (pCR), progression-free survival (PFS), overall survival (OS), and safety. Tumor samples before and after treatment were analyzed by transcriptomics, proteomics, and single-cell transcriptomics. **Results:** Between Nov 2022 and Jan 2025, 32 patients were enrolled, 31 treated, and 1 withdrew. 26 patients completed NAT and underwent IDS, while 5 switched to other chemotherapy due to adverse events. Among resected patients (median age 56, 10 with stage IV), all showed objective responses. R0 was achieved in 24 (92.3%), R1 in 2 (7.7%). Median PFS and OS are not yet reached. Common grade 3/4 adverse events: leukopenia (32.2%), neutropenia (29%), and anemia (29%). No treatment-related deaths were recorded. Post-treatment, B and T cell proportions increased, associated with improved PFS and clinical outcomes. TLS formation was observed, and higher TLS density correlated with better prognosis and reduced tumor biomarkers. **Conclusion:** Pamiparib and surufatinib show promising efficacy and manageable toxicity in advanced OC, reshaping the tumor microenvironment and promoting immune infiltration. Clinical trial information: NCT05652283. Research Sponsor: None.

A comparative study of the real-world safety and effectiveness of metronomic cyclophosphamide and bevacizumab with or without pembrolizumab for recurrent ovarian cancer.

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Background: Metronomic cyclophosphamide and bevacizumab (CB) alone or in combination with pembrolizumab (CBP) are active regimens in heavily pretreated patients with recurrent ovarian cancer. However, it is unknown to what extent the addition of pembrolizumab augments the effectiveness or increases the toxicity compared to CB alone. **Methods:** We conducted a multi-institutional retrospective cohort study utilizing electronic medical records of patients treated for recurrent ovarian cancer in oncology practices affiliated with four New England hospitals from 2012 through 2024. We included patients who received either CB or CBP and abstracted baseline characteristics, outcomes, and adverse events. The overall response rate (ORR) was defined as the proportion of patients with a complete or partial response. Net benefit (NB) was defined as the proportion of patients with a response or stable disease based on clinician assessment. Kaplan Meier curves were used to summarize progression-free survival (PFS) and overall survival (OS). Cox regression models were used to calculate and estimate the relative hazard of death (OS) and death or progression (PFS). Multivariable models adjusted for age, number of prior lines of therapy, time since diagnosis, platinum sensitivity, BRCA status, and Charlson comorbidity index. **Results:** We identified 163 patients, of whom 126 (77.3%) received CB and 37 (22.7%) received CBP. The median age at enrollment was 65.4 in the CB arm and 62.9 in the CBP arm (p=0.21). Most patients were non-Hispanic White (85.9%), with high grade (96.6%) serous (87.1%), platinum-resistant (76.7%) ovarian cancer. There were no statistically significant differences in BRCA status (21.4% vs. 18.9%, p=0.04), the median number of prior lines (3 vs. 3, p=0.25), or the proportion of platinum-resistant patients (77.8 % vs. 73.0%, p=0.41) between the CB and CBP arms. The ORR was 19.8 vs 21.6 % (p=0.81), and NB was observed in 44.8% in the CB arm and 41.2% in the CBP arm (p=0.71). The median PFS was 5.2 versus 4.8 months in the CB and CBP groups (HR 1.02; CI 0.67 - 1.55, p=0.37). Median OS was 17.3 vs 15.2 months, respectively (HR 1.51; CI 0.93 – 2.46, p=0.96). Adjustment for potential confounders produced similar results for PFS (adjusted HR=1.25, CI 0.77 – 2.02, p=0.37) and OS (adjusted HR=1.56, 95% CI 0.91 – 2.70 p=0.16). Seventeen (45.9%) patients in the CBP arm developed an immune reaction during treatment, but hospitalization rates were similar in both groups (25.4% vs 21.6%, p = 0.64). **Conclusions:** The addition of pembrolizumab to metronomic cyclophosphamide and bevacizumab was not associated with an improved response rate, PFS, or OS among patients with heavily pretreated recurrent ovarian cancer. Research Sponsor: None.

Folate receptor alpha (FRα; FOLR1) expression and persistence in ovarian cancer in clinical trial samples and real-world patient cohort.

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Background: The FRα-directed antibody-drug conjugate mirvetuximab soravtansine-gynx (MIRV) provides survival benefit vs investigator's choice chemotherapy for FRα-high, platinum-resistant ovarian cancer (PROC). Understanding targetable FRα expression is important to inform patient care and guide trial development. FRα protein expression patterns, consistency over time, association with mRNA expression, and prognostic value in patients (pts) with ovarian cancer was evaluated. **Methods:** FRα protein expression was retrospectively established by immunohistochemistry (IHC) using the VENTANA FOLR1 (FOLR1-2.1) RxDx Assay (FOLR1 CDx) in high-grade serous ovarian cancer tumors from pts in the VELIA trial (NCT02470585) and a real-world (RW) cohort. RW tumors were tested at Caris Life Sciences and linked to health record data from the ConcertAI RWD360 product. FRα-high positivity was defined by a cutoff of ≥75% of viable tumor cells with ≥2+ membrane staining (used for MIRV treatment eligibility with approved FOLR1 CDx). RNA was measured using whole transcriptome RNAseq. IHC and mRNA concordance was determined using Receiver Operating Curve (ROC) analysis. **Results:** In the RW cohort (N=611), 40.9% were FRα-high. FRα-high prevalence was 40.3% and 40.5% in tumors with and without *BRCA1* mutations, respectively (mutation prevalence, 12.4%). FRα-high prevalence was 47.4% and 39.8% in tumors with and without *BRCA2* mutations, respectively (mutation prevalence, 8.8%). Thirty-six pts had 2 biopsies longitudinally collected with IHC results. Consistency of FRα IHC status across biopsies was 86%. FRα mRNA expression associated with IHC status (ROC area under the curve [AUC]=0.88; 95% CI, 0.84-0.91), with sensitivity and specificity of 83% using a cutoff maximizing Youden's Index. To understand the prognostic nature of pts with tumors with FRα-high expression, samples from the VELIA trial were used. FRα IHC was conducted on a subset of tumors, and 56/186 (30%) were FRα-high. FRα mRNA could robustly predict IHC status (ROC AUC=0.82; 95% CI, 0.75-0.88) with sensitivity of 85% and specificity of 72%. An mRNA cutoff best associated with FRα-high IHC was applied to an extended VELIA cohort in newly diagnosed pts with mRNA data available (N=709), and FRα mRNA was identified as a negative prognostic factor for progression free survival (Hazard Ratio=1.27; 95% CI, 1.05-1.5). **Conclusions:** FRα-high expression at both the protein and mRNA level was common and concordant in VELIA trial samples and RW patient samples. The expression status was consistent in longitudinally collected samples in most pts, suggesting that IHC on the diagnostic tumor sample may effectively establish FRα protein expression status over time. High FRα mRNA expression was a negative prognostic factor in VELIA despite positive association with homologous recombination deficiency and *BRCA* mutations. Research Sponsor: None.

5592 Poster Session

Distinguishing tumor vs. clonal hematopoiesis (CH)–derived *TP53* and *BRCA1/2* alterations in ovarian cancer liquid biopsies with a predictive algorithm to inform clinical decision-making.

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Background: CH results from mutations in hematopoietic stem cells and can occur in clinically relevant genes that are detected in liquid biopsy (LBx) of solid tumor patients. *TP53* and less frequently *BRCA1/2* can be detected in tumor and as CH potentially confounding interpretation of LBx results. Using an algorithmic method for CH prediction in a cohort of tubo-ovarian carcinoma (OC) LBx, we evaluated the prevalence of CH and non-CH alterations in *TP53* and *BRCA1/2* genes, CH frequency by circulating tumor DNA tumor fraction (ctDNA TF) and concordance in samples with paired tissue biopsies. **Methods:** Patients (pts) with a diagnosis of OC and LBx via FoundationOne Liquid CDx were included. ctDNA was quantified via TF. A machine learning model incorporating fragmentomics and other sequencing features was trained using LBx samples with equal-depth sequencing of plasma and white blood cells for short variant origin prediction (VOP) with output probabilities of origin (germline, tumor-somatic, or CH). Oncogenic short variants (i.e. mutations [mut]) with probability of being CH >0.5 were classified as CH and with probability <0.5 as tumor. Detection of CH and tumor *TP53*mut in paired tissue samples (FoundationOne CDx) was evaluated (n=355). **Results:** 1,405 pts met criteria for study inclusion. 498 (35%) had TF≥1%. Overall, *TP53*mut was detected in 74% (origin 30% tumor only, 23% CH only, and 21% both CH and tumor *TP53*mut), and 26% had no detected *TP53*mut Prevalence of VOP *TP53*mut groups varied by TF with TF<1% having more pts with no detected *TP53*mut (35% vs 9%) or only CH *TP53*mut (33% vs 4%) and fewer pts with only tumor *TP53*mut (18% vs 51%) or both CH and tumor *TP53*mut (13% vs 36%) than TF≥1%. The emerging drug target *TP53* Y220C was predicted to be CH in 42/68 (62%) LBx samples. Of the 333 individual *TP53*mut predicted to be CH on LBx, 310 (93%) were not detected in corresponding tissue. Of the 200 *TP53*mut predicted to be tumor on LBx, 176 (88%) were detected in paired tumor tissue. Overall, 9% of pts had at least one germline *BRCA1/2*mut, 4% had no germline *BRCA1/2*mut but had a tumor-somatic *BRCA1/2* alteration (51 with mut, 4 with truncating rearrangements or copy number loss), and 1% had only CH *BRCA1/2*. Of patients with non-germline *BRCA1/2*mut, 12/63 (19%) had only CH-derived *BRCA1/2*mut. **Conclusions:** >60% of OC LBx with *TP53*mut, including *TP53* Y220C, had evidence of CH contributing to cell free DNA. TF <1% was associated with higher rates of CH only *TP53*mut, but tumor-derived variants in *TP53* and other genes were still detected. The majority (93%) of TP53mut predicted to be CH were not detected in tissue biopsies of paired samples. While the majority of LBx with a *BRCA1/2*mut had germline or tumor-somatic muts, 6% of *BRCA1/2*mut LBx only harbored *BRCA1/2*mut predicted to be CH. Together, CH prediction and TF can be used to correctly contextualize LBx findings to support informed clinical decision making. Research Sponsor: Foundation Medicine Inc.

Neoadjuvant pamiparib in patients with newly diagnosed advanced ovarian cancer: A single-arm, prospective phase II trial.

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Background: While PARP inhibitors have shown robust efficacy as maintenance therapy in newly diagnosed ovarian cancer, their potential benefit in the neoadjuvant setting remains unclear. The Chemotherapy Response Score (CRS) serves as an important prognostic indicator following neoadjuvant chemotherapy. This study aims to investigate the efficacy and safety of combining pamiparib with neoadjuvant chemotherapy and bevacizumab in patients with newly diagnosed advanced ovarian cancer. **Methods:** In this single-arm, prospective phase II trial, eligible patients have newly diagnosed FIGO stage III–IV ovarian, fallopian tube, or primary peritoneal cancer; histologically confirmed high-grade serous or endometrioid adenocarcinoma; are ineligible for optimal primary debulking; have an ECOG performance status of 0–2; are aged ≥18 years; and have measurable lesions per RECIST 1.1. The treatment regimen comprises paclitaxel (175 mg/m^2, Day 1) and carboplatin (AUC 5, Day 2) every three weeks for up to six cycles. Bevacizumab (15 mg/kg, Day 1) is given every three weeks and discontinued six weeks before surgery. Pamiparib (40 mg twice daily) is administered for up to six cycles. Patients who tolerate therapy and become surgical candidates undergo interval debulking surgery, followed by consolidation and maintenance therapy at the investigator's discretion. The primary endpoint is the proportion of patients with CRS 3, assessed via postoperative pathology. Secondary endpoints include the pathological complete response (pCR) rate, the R0 resection rate, progression-free survival (PFS), and safety. The trial is ongoing. **Results:** Between March 2023 and January 2025, 29 patients (median age 61 years, range 44–79) were enrolled. FIGO stages were III in 19 patients (65.5%), IVA in 1 (3.4%), and IVB in 9 (31.0%). Of these, 28 had high-grade serous adenocarcinoma and 1 had endometrioid adenocarcinoma. Two patients withdrew consent after receiving one cycle of neoadjuvant therapy. Of the remaining 27, 17 received four cycles, 7 received three cycles, and 3 received two cycles. Interval debulking surgery was performed in 24 patients—all achieved R0 resection—while 2 patients declined surgery and 1 had the treatment regimen changed due to elevated CA125. Among the 24 surgical cases, CRS 3 was observed in 8 (34.8%), CRS 2 in 15 (65.2%), and CRS 1 in 1 (4.3%). No patient achieved pCR. Common adverse events included leukopenia (96.6%), neutropenia (96.6%), anemia (96.6%), and thrombocytopenia (72.4%), with grade 3–4 incidences of 58.6%, 72.4%, 27.6%, and 24.1%, respectively. No treatment-related deaths were reported. **Conclusions:** The preliminary results suggest that the addition of pamiparib to neoadjuvant chemotherapy plus bevacizumab offers promising efficacy and acceptable safety in newly diagnosed advanced ovarian cancer. Further data will be provided as the study progresses. Clinical trial information: 2200059119. Research Sponsor: None.

Characterization of copy number variations (CNV) patterns and pseudotime trajectories in high-grade serous ovarian cancer (HGSOC).

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Background: HGSOC is characterized by genomic instability, resulting in frequent CNVs. This study aimed to characterize CNV patterns and derive pseudotime trajectories in HGSOC. **Methods:** Patients with a diagnosis of HGSOC enrolled in the CGP program (NCT06020625) at Fondazione Policlinico Universitario A. Gemelli between March 2022 and December 2023 were analyzed using the TruSight Oncology 500 (TSO500) platform, covering CNVs across 523 genes. CNVs were classified as high- or low-level based on log2 segmented CN profiles. An absolute log2 value of 0.3 was used to define the fraction of altered genes. High-variability genes were identified using a variance threshold. The Leiden algorithm was applied to identify clusters based on modularity, and connectivity structures were mapped using the partition-based graph abstraction (PAGA) method. Pseudotime trajectories were modeled using diffusion-like random walks, with the root cluster chosen based on the fraction of altered genes. Non-negative matrix factorization (NMF) was used to identify gene-level CNV patterns. The number of altered genes per region was normalized to the total number of genes per chromosome arm. Chi-squared test was used to compare categorical variables. **Results:** A total of 597 HGSOC patients, 91% of whom were FIGO stage III-IV, were included. *TP53* mutations were identified in 96% of patients. *MYC* (13%) and *CCNE1* (9%) were the most frequently high-level amplified genes. 104 highly variable genes were included in the trajectory analysis. The Leiden algorithm identified 7 patient clusters, with a significant trend observed across clusters in the fraction of altered genes ($p<0.001$, Kendall's test for trend). Clusters 2 and 3 showed the lowest fraction of altered genes and were the most connected in the PAGA analysis. Using cluster 3 as the root, trajectory analysis revealed divergent branching patterns, with a significant Spearman correlation between pseudotime and the fraction of altered genes ($\rho=0.20$, $p<0.001$). Clusters also showed different percentages of homologous recombination (HR)-proficient patients ($p<0.001$) and mutations in *BRCA1* ($p=0.02$) and *BRCA2* ($p=0.006$). NMF identified 4 gene clusters based on CNV patterns, with distinct amplification and deletion profiles. Each cluster showed a different ratio of low/high-level CNVs. In the cluster characterized by high-level amplifications, *CCNE1* and *MYC* low/high-level ratios were 1.1 and 2.0, respectively. While specific chromosomal regions were enriched in the cluster characterized by low-level CNVs ($p<0.001$), clusters with high-level CNVs lacked specific regional associations. **Conclusions:** This study suggests that distinct patterns of CNVs in HGSOC are linked with genomic and clinical features. This application of CGP for CNV profiling could offer a cost-effective strategy to stratify HGSOC patients and guide personalized treatments. Clinical trial information: NCT06020625. Research Sponsor: None.

Analysis of serous carcinoma subgroup in FRUSICA-1: Fruquintinib plus sintilimab in treated advanced endometrial cancer (EMC) patients (pts) with pMMR status.

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Background: Serous carcinoma represents approximately 10% of all EMC, has the highest recurrence rate and is responsible for a disproportionate 40% of mortality in EMC. Additionally, the overall 5-year survival rate is only 33% for stage III-IV serous carcinoma. Fruquintinib (F, a highly selective VEGFR inhibitor) plus sintilimab (S, an anti-PD-1 monoclonal antibody) was evaluated in an open-label, single-arm phase 2 pivotal study (FRUSICA-1, NCT03903705), and demonstrated encouraging efficacy and favorable safety profile in treated advanced EMC pts with pMMR (proficient mismatch repair) status (Wu X, et al; 2024 ASCO). Here, we report the ad hoc updated analysis results of the serous carcinoma subgroup (data cutoff: May 15, 2024). **Methods:** Eligible pts had histologically confirmed, previously treated advanced EMC with pMMR status confirmed by central lab. They received F (5 mg QD, 2 weeks on/1 week off, orally) plus S (200 mg, IV, Q3W) in 21-day cycles until disease progression or unacceptable toxicity. Ad hoc analyses were conducted to evaluate the primary endpoint (ORR) and secondary endpoints (DCR, DoR, TTR, PFS, OS, and safety) of F+S in pts with endometrial serous carcinoma. **Results:** As of data cutoff date (May 15, 2024), 98 EMC pts with pMMR status were enrolled and received the combination treatment (ITT population), among them, 27 pts had serous carcinoma. In these 27 pts, median age was 63.1 years, 22 (81.5%) pts were in stage IV disease, 7 (25.9%) pts had received prior bevacizumab therapy, and 5 (18.5%) pts had received prior pelvic radiotherapy. IRC-assessed ORR was 37.0% (95%CI: 19.4%, 57.6%), DCR was 88.9% (95%CI: 70.8%, 97.7%). Median DoR and TTR was 17.9 (95%CI: 3.3, not estimable [NE]) months, and 2.4 (95% CI: 1.2, 4.0) months, respectively. With the median PFS and OS follow-up of 8.3 and 21.7 months, the median PFS and OS was 8.8 (95%CI: 6.9, 19.2) months and 19.0 (95%CI: 11.4, NE) months, respectively. These efficacy findings were similar with those observed in ITT population. Grade ≥3 treatment related adverse events (TRAE) occurred in 63.0% pts, and the most common ≥Grade 3 TRAEs included palmar-plantar erythrodysesthesia syndrome (22.2%) and hypertension (11.1%). **Conclusions:** F+S was tolerable and showed clinically meaningful efficacy in endometrial serous carcinoma, characterized by durable responses that were comparable across the ITT population. Clinical trial information: NCT03903705. Research Sponsor: HUTCHMED Limited.; Innovent Biologics, Inc.

A phase II trial of pembrolizumab plus olaparib for the treatment of patients with persistent/recurrent endometrial cancers.

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Background: Copy number-high (CNH) ECs are characterized by high levels of copy-number alterations and *TP53* mutations, and a subset may have a homologous recombination-deficiency (HRD) phenotype. The presence of an HRD-phenotype within CNH EC provides the rationale for using OLA in combination with PEM, as this exploits the mechanism of immune priming which creates further genomic instability and drives immune response. **Methods:** This is an investigator-initiated, single- arm, open-label, phase II trial evaluating the efficacy and safety of PEM + OLA in pts with persistent/recurrent *TP53*-mutant EC. Key eligibility criteria included age ≥18 years, measurable disease, £3 prior lines of therapy, all histologic types allowed with aberrant p53 IHC and/or mutant *TP53*. Carcinosarcomas were eligible if the epithelial component met the p53/*TP53* criteria. dMMR/MSI-H and *POLE* hotspot tumors were not eligible. All were PEM and OLA naïve and received OLA orally at 300mg every 12 hours and PEM 200mg every 3 weeks IV. Primary endpoint was objective response rate (ORR) by 24 weeks per RECIST 1.1. **Results:** At data cut off (December 12, 2024), 26 patients (pts) initiated therapy and 25 pts were evaluable for efficacy. Median age was 68 years (range:59-83). 13 pts (50%) had serous, 8 pts (31%) were mixed/high grade, and 4 pts (15%) had carcinosarcoma histology. 24 pts (92%) had 1 line of prior chemotherapy. 1 pt had a germline *BRCA2* and 1 pt had a somatic *BRCA1* mutation. 2 pts achieved complete response (CR), 6 pts achieved partial response (PR), resulting in an ORR of 32% (90% one-sided CI: 19.6-100%). Median duration of response was 10.5 months (80% CI:6.4-11.8). Median progression-free survival (PFS) was 4.8 months (80% CI: 3.6-5.9), and median overall survival (OS) was 21.2 months (80% CI: 9.4-NE). 50% (2/4) of carcinosarcoma pts achieved CR and PR, respectively. Most common ≥ grade 3 treatment related adverse events were anemia (12%), neutropenia (19%). 1 pt developed grade 3 pneumonitis, 2 pts developed grade 2 adrenal insufficiency. No new safety signals were identified. **Conclusions:** The combination of PEM + OLA has promising activity with durable responses observed in pts with persistent/recurrent *TP53*-mutant EC, including carcinosarcomas. Molecular subtype selection is critical in further investigation of this combination. Clinical trial information: NCT05156268. Research Sponsor: Merck; AstraZeneca.

Molecular testing in primary advanced or recurrent endometrial cancer: A cost-effectiveness analysis.

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Background: The Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) algorithm is a classification scheme for endometrial cancer (EC) based on sequential testing for DNA mismatch repair deficiency (dMMR), *POLE* exonuclease domain mutations, and p53 mutations. The cost-effectiveness of ProMisE vs no molecular testing to inform initial systemic treatment choice in patients with stage III/IV primary advanced/recurrent EC (pA/rEC) was assessed from payer and societal perspectives. **Methods:** A hybrid model comprising a decision tree for molecular classification (ProMisE vs no testing) followed by partitioned survival models (PSM; progression-free disease, progressed disease, and death) was developed. Lifetime costs and outcomes following first-line systemic treatments were estimated using this model. Patients in the no-testing arm were assigned to receive carboplatin-paclitaxel (CP), dostarlimab + CP, pembrolizumab + CP, or hormonal therapy (everolimus/letrozole). Patients in the ProMisE arm were assigned to the same treatments or bevacizumab + CP, according to their molecular profile. Survival functions were derived from published trial results. EQ-5D-5L utility values were sourced from the RUBY trial (NCT03981796). Costs were sourced from US-focused databases and publicly available literature. The base case presented a US third-party payer perspective. A scenario analysis presented a modified societal perspective. Model outcomes were total costs, total life-years (LYs), total quality-adjusted LYs (QALYs), and the incremental cost-effectiveness ratio (ICER) of ProMisE vs no testing. An annual discount rate of 3% per year was applied to future costs and outcomes. Uncertainty was evaluated using one-way (OWSA) and probabilistic sensitivity analyses (PSA). **Results:** From a third-party payer perspective, total LYs and total QALYs were 5.36 and 4.08, respectively, with ProMisE vs 3.83 and 2.89 with no testing. Total costs were $233,989 with ProMisE vs $155,305 with no testing. Thus, incremental LYs and QALYs were 1.53 and 1.19 greater with ProMisE vs no testing; incremental costs over a lifetime were $78,684 greater with ProMisE. Assuming a cost-effectiveness threshold of $150,000 per QALY gained, ProMisE was cost-effective with an ICER of $66,321 per QALY gained compared with no testing. In the OWSA, ProMisE remained cost-effective over all parameter ranges (±10%). In the PSA, ProMisE was below the threshold of $150,000/QALY for 97.7% of iterations. From a societal perspective, lifetime costs were lower (−$22,973) and QALYs greater with ProMisE vs no testing. **Conclusions:** ProMisE testing is cost-effective vs no testing when using a $150,000/QALY-gained threshold. Given the heterogeneity of molecular subtypes in stage III/IV pA/rEC, molecular testing enables personalized treatment that is clinically meaningful and high value from payer and societal perspectives. Research Sponsor: GSK.

E7386 study 102: Global dose-expansion cohort of E7386 + lenvatinib (LEN) in patients (pts) with advanced endometrial cancer (aEC) that progressed on platinum-based chemotherapy (chemo) and an anti-PD-(L)1 immunotherapy (IO).

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Background: There is a need for novel therapies for aEC that recurs after chemo and IO. LEN has antitumor activity in pts with aEC after platinum-based chemo [Vergote 2020] and is approved in combination with pembrolizumab for aEC following prior systemic therapy. E7386 is a novel oral anticancer agent that inhibits the interaction between β-catenin and CREB-binding protein. Study 102 evaluates E7386 + LEN in pts with solid tumors including aEC. A preliminary analysis of Study 102 (n=16) showed manageable safety and promising antitumor activity in aEC that progressed after platinum-based chemo and anti-PD-(L)1, including responses in pts with prior LEN. We report safety and antitumor activity for the complete dose expansion cohort (n=30) of pts with aEC. **Methods:** Pts with aEC that progressed after platinum-based chemo and IO received E7386 120 mg BID + LEN 14 mg QD (amended from 20 mg during enrollment). The primary endpoint was safety; secondary endpoints included ORR, duration of response (DOR), clinical benefit rate (CBR), and PFS by investigator per RECIST v1.1. **Results:** 30 pts were enrolled; 16 (53.3%) previously received LEN. By data cutoff (Oct 22, 2024), 9 (30.0%) pts had treatment ongoing. 29 (96.7%) Pts had treatment-related adverse events (TRAEs), most commonly vomiting (n=21, 70.0%). 12 (40.0%) Pts had grade 3 TRAEs, most commonly nausea/proteinuria/diarrhea/hypertension/anemia (n=2 each, 6.7%). No grade 4-5 AEs were observed. TRAEs led to study drug withdrawal of LEN and E7386 in 1 patient. Overall, 9 pts (3 with prior LEN) had a confirmed response (1 complete and 8 partial) for an ORR of 30.0%. In pts without prior LEN (n=14), the ORR was 42.9%. Additional data are in the Table. **Conclusions:** E7386 + LEN showed promising antitumor activity with a manageable safety profile in heavily pretreated pts with aEC following platinum-based chemo and IO. The dose-optimization phase of Study 102 for E7386 + LEN in pts with aEC is currently enrolling pts (NCT04008797). Clinical trial information: NCT04008797. Research Sponsor: None.

Age, median, yrs (range)	62.0 (36–76)
1 / 2 / 3 prior lines of therapy, n (%)	4 (13.3) / 16 (53.3) / 10 (33.3)
Endometrioid / serous / clear cell / other histology, n (%)	16 (53.3) / 3 (10.0) / 2 (6.7) / 9 (30.0)
Mismatch repair proficient / deficient / NA[a], n (%)[b]	16 (53.3) / 6 (20.0) / 8 (26.7)
***TP53* wild type/ mutation, n (%)[c]**	16 (53.3) / 14 (46.7)
Serious TRAEs, n (%)	7 (23.3)
ORR / CBR[d], % (95% CI)	30.0 (14.7–49.4) / 46.7 (28.3–65.7)
SD, n (%)	12 (40.0)
DOR, median, mos (95% CI)	8.0 (3.7–9.5)
PFS, median, mos (95% CI)	5.3 (3.0–8.9)

[a]Microsatellite instability-low (n=3); unknown (n=4); NA (n=1); [b]as reported by sites; [c]circulating tumor DNA analyses were conducted using plasma samples collected at baseline, and were annotated using OncoKB database to identify mutations in *TP53*; [d]complete response + partial response + stable disease ≥23 wks.
NA, not available.

Time to quality of life (QoL) improvement or deterioration in patients (pts) with primary advanced or recurrent endometrial cancer (pA/R EC) treated with dostarlimab plus chemotherapy in the ENGOT-EN6-NSGO/GOG-3031/RUBY trial.

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Background: In Part 1 of the phase 3 RUBY trial (NCT03981796) in pts with pA/rEC, dostarlimab + carboplatin-paclitaxel (DOST+CP) significantly improved progression-free survival and overall survival vs placebo (PBO)+CP. Patient-reported outcomes were a secondary endpoint. Here we present a post hoc analysis comparing timing of QoL improvement or deterioration by treatment. **Methods:** Pts were randomized 1:1 to receive DOST+CP or PBO+CP Q3W (6 cycles) followed by DOST or PBO monotherapy Q6W for ≤3 y. QoL was collected at each visit. Using data from the Sept 22, 2023 data cut (median follow-up 37.2 mo), analyses on time to first QoL improvement (TTI1) or deterioration (TTD1) were conducted for the EORTC QoL Questionnaire Core 30 (QLQ-C30) and Endometrial Cancer 24 (EN24) assessments using Cox regressions. Improvement or deterioration was classified ≥10-point change in the appropriate direction, per domain, from baseline. Results are reported for the primary study populations (overall and mismatch repair deficient/microsatellite instability-high [dMMR/MSI-H]). **Results:** A total of 494 pts were randomized, of which 118 were dMMR/MSI-H. For all QLQ-C30 and EN24 domains, TTI1 was similar between arms except pain in the overall population and role function in the dMMR/MSI-H population which reached nominal significance for earlier improvement in the DOST+CP arm (Table). The overall population had similar TTD1 in both arms, while time to deterioration was delayed in the DOST+CP arm for several domains (eg, global QoL, pain) in the dMMR/MSI-H population. **Conclusions:** With over 3 years of follow-up, DOST+CP was comparable to PBO+CP for TTI1 and TTD1 in the overall population of the RUBY trial and TTD1 was delayed in several QoL domains in the dMMR/MSI-H population. These results on patient experience of treatment further support the efficacy and safety data of dostarlimab for use in patients with pA/rEC. Clinical trial information: NCT03981796. Research Sponsor: GSK.

	Overall population			dMMR/MSI-H population		
	DOST+CP (N=245) n	PBO+CP (N=249) n	HR, *P* value	DOST+CP (N=53) n	PBO+CP (N=65) n	HR, *P* value
Time to first improvement						
Pain	154	131	1.37, *P*=0.008	32	37	1.20, *P*=0.442
Role function	111	97	1.28, *P*=0.076	32	26	1.67, *P*=0.048
Time to first deterioration						
Global QoL	194	222	0.85, *P*=0.109	33	57	0.61, *P*=0.027
Role function	203	219	0.97, *P*=0.796	36	57	0.58, *P*=0.015
Social function	200	219	0.97, *P*=0.763	33	57	0.60, *P*=0.020
Pain	202	218	0.86, *P*=0.119	37	55	0.63, *P*=0.031
Sexual interest	126	157	0.82, *P*=0.104	19	40	0.38, *P*=0.001
Sexual activity	114	143	0.81, *P*=0.102	15	34	0.42, *P*=0.005
Sexual enjoyment	105	140	0.77, *P*=0.044	13	31	0.56, *P*=0.092
Urological symptoms	173	201	0.83, *P*=0.073	30	52	0.50, *P*=0.003

n=number of patients with events.
CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; DOST, dostarlimab; MSI-H, microsatellite instability-high; PBO, placebo.

Time to subsequent therapy in patients (pts) with primary advanced or recurrent endometrial cancer (pA/rEC) receiving dostarlimab plus carboplatin-paclitaxel (DOST+CP) compared with pts receiving placebo plus CP (PBO+CP) in the ENGOT-EN6-NSGO/GOG-3031/RUBY trial.

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Background: In Part 1 of the phase 3 RUBY trial (NCT03981796), DOST+CP significantly improved progression-free survival (PFS) and overall survival (OS) in pts with pA/rEC, leading to approval for frontline treatment in the US and the EU. Time to first subsequent therapy (TFST) and second subsequent therapy (TSST) can provide further insights on the clinical benefit of a regimen as well as any clinical impact beyond first progression. **Methods:** Pts were randomized 1:1 to receive DOST+CP or PBO+CP Q3W (6 cycles) followed by DOST or PBO monotherapy Q6W for ≤3 years. Primary endpoints were PFS and OS in the overall population and PFS in the mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) population. Post hoc TFST and TSST analyses were performed at the second interim analysis (data cut, Sept 22, 2023) in the overall, dMMR/MSI-H, and mismatch repair proficient/microsatellite stable (MMRp/MSS) populations. TFST and TSST were defined as the time from randomization to the date of the first dose of first or second subsequent anticancer therapy after study drug, respectively, or death by any cause, whichever occurred first. **Results:** Of 494 pts randomized, 118 were dMMR/MSI-H and 376 were MMRp/MSS (Table). TFST and TSST were improved in all three populations. Median TFST was 5.1 and 2.5 mo longer in pts treated with DOST+CP vs PBO+CP in the overall and MMRp/MSS populations, respectively; median TFST was not reached (NR) in the DOST+CP arm of the dMMR/MSI-H population. Median TSST was extended by 11.4 and 8.1 mo in pts treated with DOST+CP vs PBO+CP in the overall and MMRp/MSS populations, respectively; median TSST was NR in the DOST+CP arm of the dMMR/MSI-H population. Hazard ratios favoring DOST+CP remained consistent between TFST and TSST in all populations evaluated. **Conclusions:** These results indicate prolonged TFST and sustained benefits through TSST with DOST+CP compared with PBO+CP across the overall, dMMR/MSI-H, and MMRp/MSS populations in the RUBY trial. Together with the statistically significant PFS and OS benefits, these findings support the frontline use of dostarlimab + CP as a standard of care in all pts with pA/rEC. Clinical trial information: NCT03981796. Research Sponsor: GSK.

	Overall		dMMR/MSI-H		MMRp/MSS	
	DOST+CP (n=245)	PBO+CP (n=249)	DOST+CP (n=53)	PBO+CP (n=65)	DOST+CP (n=192)	PBO+CP (n=184)
TFST, median (95% CI), mo	15.3 (12.3–20.1)	10.2 (9.1–10.9)	NR (19.8–NR)	10.5 (7.3–12.0)	12.7 (11.4–17.1)	10.2 (9.0–10.8)
HR (95% CI)	0.63 (0.51–0.78)		0.34 (0.20–0.57)		0.73 (0.58–0.92)	
TSST, median (95% CI), mo	31.3 (24.6–40.8)	19.9 (16.3–23.1)	NR (NR–NR)	24.0 (16.1–39.1)	26.8 (22.1–32.6)	18.7 (15.3–22.0)
HR (95% CI)	0.67 (0.53–0.85)		0.41 (0.23–0.74)		0.73 (0.57–0.94)	

NR, not reached; TFST, time to first subsequent treatment; TSST, time to second subsequent treatment.

5602 Poster Session

A phase II efficacy and safety study of HB0025 (a PD-L1/VEGF bispecific antibody) in combination with chemotherapy as first-line treatment for advanced or recurrent endometrial cancer.

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Background: HB0025, developed by Huaota, is a novel anti-PD-L1/VEGF bispecific antibody, with VEGFR1D2 linked at the N-terminal of anti- PD-L1 antibody. Carboplatin and paclitaxel (CP) alone or in combination with PD-(L)1 is a recommended regimen for first-line treatment of advanced endometrial carcinoma (EC) that the ORRs were 40%-68% regardless MMR status. This study assesses the efficacy and safety of HB0025 in combination with chemotherapy in EC patients. **Methods:** This open-label, multi-center phase II study of HB0025 with CP in primary advanced (stage III or IV) or first recurrent EC. Patients received 20mg/kg HB0025 every 3 weeks with CP for 4-6 cycles, followed by maintenance therapy with HB0025. The primary endpoint was objective response rate (ORR), assessed by RECIST v1.1. **Results:** As of Dec 25, 2024, 39 patients were enrolled. The median age was 59.0 years (range, 32.0-71.0). The median follow-up time was 3.3 months (range: 0.6-6.9). 31 patients had at least one post-baseline tumor assessment. The ORR and disease control rate (DCR) were 83.9% (26/31) and 100.0% (31/31), respectively. The ORR were 84.0% (21/25) in pMMR patients and 100.0% (4/4) in dMMR patients. Median duration of response (DOR) and progression-free survival (PFS) were not reached. Grade ≥3 treatment-related adverse events (TRAEs) occurred in 18 patients (46.2%), The most common grade ≥3 TRAEs (≥10%) included neutropenia (30.8%), leukopenia (15.4%), thrombocytopenia (10.3%). Any-grade immune-related adverse events (irAEs) only occurred in 2 patients (5.1%). Treatment-related serious adverse events (SAEs) were observed in 5.1% (2/39) of patients. No TRAE led to treatment discontinuation or death. Any-grade hemorrhage events occurred in 7 (17.9%) patients which were all grade 1 in severity. **Conclusions:** HB0025 in combination with chemotherapy demonstrated promising anti-tumor efficacy with good safety profile. Regardless MMR status, ORR with HB0025 plus CP improved significantly over histologically reported data. A multicentre, randomized, double-blind, controlled phase III trial will commence in 2025. Clinical trial information: NCT06758557. Research Sponsor: Shanghai Huaota Biopharmaceutical Co., Ltd.

Interim safety and antitumor activity data from a phase 1 study of INCB123667, a selective CDK2 inhibitor, in patients with metastatic recurrent endometrial cancer.

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Background: Cyclin E1 (CCNE1) overexpression or *CCNE1* amplification is a predictive indicator of poor prognosis in some endometrial cancers. Inhibition of cyclin-dependent kinase 2 (CDK2), the binding partner of CCNE1, is a potential therapeutic approach for cancers with increased CCNE1 activity. In an ongoing phase 1 study, INCB123667, a potent and selective CDK2 inhibitor, has shown acceptable safety and preliminary efficacy in patients (pts) with advanced solid tumors (NCT05238922). Here, we present interim safety and efficacy data from enrolled pts with metastatic recurrent endometrial cancer. **Methods:** Eligible pts had ECOG PS ≤1 and measurable disease (RECIST V1.1). Part 1A (dose escalation) enrolled pts with advanced/metastatic solid tumors; CCNE1 amplification (locally tested) was not mandatory. INCB123667 dosing started at 50 mg and escalated to 150 mg daily. In Part 1B (dose expansion), selected RDEs from Part 1A were expanded in 6 tumor-specific cohorts, including an ongoing cohort of pts with metastatic recurrent endometrial cancer with ≤3 prior lines of systemic treatment; pts were required to have locally tested *CCNE1* amplification or centrally confirmed CCNE1 overexpression. Blood samples were collected for ctDNA analysis. **Results:** As of Dec 19, 2024, 17/30 pts with metastatic recurrent endometrial cancer have been enrolled and received INCB123667: 3 in Part 1A (50 mg bid, n=2; 150 mg qd, n=1) and 14 in Part 1B (RDEs: 50 mg bid, n=9; 125 mg qd, n=5). Histologies included carcinosarcoma (n=5), high grade serous (n=6), endometroid (n=4), clear cell (n=1), and mixed serous and clear cell (n=1). Median number of prior systemic therapies was 3 (1-5), including 11 pts pretreated with anti-PD-1 based therapy. Median duration of treatment was 2.3 months (0.3-19.4) and 4 pts (23.5%) are still on treatment. Overall, 16 pts (94.1%) had treatment-emergent adverse events (TEAEs), predominantly anemia (n=8 [47.1%]), nausea (n=6 [35.3%]); thrombocytopenia, abdominal pain, and asthenia (n=5 [29.4%] each). Seven pts (41.2%) had grade 3-4 TEAEs, including neutropenia and thrombocytopenia (n=2 each). No pts discontinued due to TEAEs. Four out of 17 pts had a partial response and 3 had stable disease. Three responders had prior immunotherapy. Cyclin E1 overexpression was present in 3/4 responders, and 2/4 had *CCNE1* amplification and overexpression. Decreases in ctDNA were observed on treatment compared with baseline. **Conclusions:** In this interim analysis, single-agent INCB123667 at various doses has shown an acceptable safety profile in pretreated pts with metastatic recurrent endometrial cancer, including expected cytopenia. The encouraging antitumor activity including post-PD-1 based therapy failure supports future development of INCB123667 in advanced/metastatic endometrial cancer. Clinical trial information: NCT05238922. Research Sponsor: Incyte Corporation.

5604 Poster Session

Clinicopathological features and survival outcomes in women with endometrial neuroendocrine tumors.

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Background: Endometrial neuroendocrine tumors (ENET) are rare, representing about 0.8% of endometrial cancers. Due to their aggressive nature, they are often diagnosed at an advanced stage with no standardized treatment guidelines. This study provides data on the clinicopathological features and survival outcomes of ENETs. **Methods:** This IRB-approved retrospective cohort study evaluated patients with ENETs seen at MD Anderson Cancer Center between 1994 and 2024. All patients with a histology-confirmed diagnosis of ENET were included. Descriptive statistics was used to summarize patients' clinicopathologic features. Event-free survival (EFS) was defined as the time from 1st treatment to recurrence, progression, or death. Overall survival (OS) was defined as the time from start of 1st treatment to death. Kaplan-Meier was used to estimate OS and EFS, and Cox regression was used to estimate hazard ratios for prognostic factors. **Results:** A total of 97 patients were included. Median age at diagnosis was 60 years (range: 30–85). Median BMI was 30.3 kg/m2 (range: 17.1 - 76.7). 87% were white. FIGO stage at diagnosis was 31% stage I/II, 62% stage III/IV, and 5% unknown. 84% underwent primary surgery and 16% had neoadjuvant chemotherapy. For those who underwent surgery, 59% had chemotherapy and 39% had radiotherapy. 39% of patients were NED after completion of primary treatment, 38% progressed and 23% recurred. Median follow-up was 1.4 years (range 6 days to 15.7 years). Median EFS was 0.8 years (95% CI: 0.6–1.3). On multivariate analysis, patients treated with carboplatin/paclitaxel (C/P) (HR= 0.43, 95% CI: 0.24–0.79, p =0.006), or cisplatin/etoposide (C/E) (HR = 0.35, 95% CI: 0.20–0.62, p = 0.001) had a decreased risk of recurrence compared to no adjuvant therapy. Among Stage I/II patients treated with C/E had a decreased risk of recurrence compared to patients treated with C/P (HR= 0.16 (95% CI: 0.03–0.80), p=0.025). Median OS was 1.6 years (95% CI: 1.2–3.0). Multivariate analysis showed stage III/IV disease had almost 3 times the risk of death (p=0.0008). Treatment with C+P (HR =0.40, 95% CI: 0.22–0.74, p=0.003) or C+E had a HR= 0.35 (95% CI: 0.20–0.63), p= 0.0005, compared to patients receiving other or no chemotherapy. **Conclusions:** This study highlights the aggressive nature of ENETs, often diagnosed at advanced stage. Adjuvant therapy with cisplatin/etoposide was associated with reduced the risk of death compared to other treatments. Despite chemotherapy, median EFS was short, highlighting the need for improved treatment strategies. Research Sponsor: None.

5606 Poster Session

Quality of life and lifestyle changes during and after therapy in women with endometrial cancer: A global study of 1,066 patients (NOGGO, ENGOT, GCIG, ENGAGe-IMPROVE/EXPRESSION XI).

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Background: Endometrial cancer (EC) affects many women worldwide, yet the impact of the disease and its treatment on symptoms, lifestyle and quality of life is still poorly understood. This study aims to explore differences in symptoms, lifestyle and perceptions between patients undergoing active treatment and those undergoing follow-up care in order to better understand their needs. **Methods:** Patients diagnosed with EC were invited to complete an 80-item survey, available in both paper and online formats. General patient characteristics such as comorbidities, tumor stage and therapy as well as symptoms during and after treatment were recorded. Participants were categorized into two cohorts: those undergoing active treatment (cohort A) and those in follow-up monitoring (cohort B). **Results:** A total of 1,660 patients with EC from 17 countries participated between December 2021 and December 2024. The median age of the participants was 66 years [range: 20–94]. Of these, 581 (35%) were in cohort A, and 1,079 (65%) were in cohort B. No differences in common comorbidities were observed between cohorts. Anticoagulant use was higher in cohort A (22.7%) compared to cohort B (17.0%), while vitamin intake was more common in cohort B (32.4% vs. 25.8%). Quality of life was lower in cohort A, with 68.5% currently experiencing side effects compared to 45.8% in cohort B. Symptoms such as fatigue (39.6% vs. 15.1%), pain (23.6% vs. 10.8%), constipation (16.7% vs. 8.3%), loss of appetite (14.6% vs. 1.6%), and weight loss (11.5% vs. 2.1%) were more prevalent in cohort A. Physical activity levels increased after diagnosis for 49.7% in cohort B compared to 34.1% in cohort A. Smoking habits remained largely unchanged, with 15.3% (cohort A) and 14.0% (cohort B) reporting current smoking, and only 4.9% of all patients quitting after diagnosis, despite 19.2% acknowledging potential benefits. Interest in nutritional counseling was higher in cohort A (26.2% vs. 21.7%). Patients in cohort A perceived EC as a greater health threat compared to their other comorbidities (69.2% vs. 43.6%). **Conclusions:** Patients tend to recover from the physical and psychological burden of active treatment, showing improvements in physical activity levels and a reduction in symptoms. However, structured programs in follow-up care are essential to achieve long-term lifestyle changes, including enhanced physical activity and dietary habits. The observed interest in nutritional counselling during treatment presents an opportunity to develop targeted interventions. Despite encouraging increase in physical activity during follow-up, additional efforts are needed to maintain and reinforce these positive changes over time. Clinical trial information: DRKS00025954. Research Sponsor: GSK Research & Development Limited.

5607 Poster Session

The landscape of chromosomal instability in uterine leiomyosarcoma.

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Background: Uterine leiomyosarcoma (uLMS) has heterogeneous clinical presentations and outcomes. Although most uLMSs are associated with chromosomal instability, limited data exist on chromosomal instability patterns and their association with clinical outcomes. We sought to examine the chromosomal and genomic landscape of uLMSs and their association with survival outcomes. **Methods:** We identified 162 patients with uLMS who underwent matched tumor-normal next-generation sequencing at our institution between 2007 and 2024. Allele-specific copy number analysis was performed using the FACETS algorithm with genome-wide summary data as well as focal copy number data extracted and compared with clinical variables and survival outcomes. Appropriate statistical analyses were performed. **Results:** The median age at diagnosis was 55 years (range, 30-92). The uLMS in the cohort predominantly had conventional spindle cell morphology (n=122/162, 75%). At the time of diagnosis, 42% presented as FIGO stage I disease (68/162) followed by FIGO stage IV disease (60/162, 37%). ER expression data was available for 155 cases, with the majority of cases being ER positive (106/155, 68%). PR expression data was available for 145 cases, with most of the tumors expressing PR (87/145, 60%). The most common alterations in the cohort were *TP53* (117, 72%), *RB1* (78, 48%), *ATRX* (62, 38%), and *PTEN* (31, 19%). FACETS analysis showed that 15% of tumors (25/162) were hypoploid and 12% had whole-genome duplication (20/162). The median telomeric size was 50.1 Mb (interquartile range [IQR]: 40-59.3). The median number of telomeric allele imbalances was 6 (IQR: 3-9). The median fraction of genome with loss of heterozygosity was 0.28 (IQR: 0.14-10.5). Centromeric allele imbalance, whole-genome duplication, and fraction of copy number altered were associated with ER expression (adjusted P=0.025, 0.015, and 0.002, respectively). Multivariate survival analysis demonstrated that hypoploidy (hazard ratio: 3.3) and copy number alterations in *PIK3CD* (hazard ratio: 1.82) were associated with worse overall survival ($P<0.001$ for both). **Conclusions:** Although most uLMSs are caused by underlying chromosomal instability, the patterns in these tumors are variable, with some of the chromosomal instability configurations having prognostic implications. Further studies are needed to better understand the role of chromosomal instability in the stratification of the disease. Research Sponsor: None.

Post-hoc analysis evaluating selinexor maintenance therapy in patients with *TP53*wt endometrial cancer: Progression-free survival by clinical factors in the ENGOT-EN5/GOG-3055/SIENDO study.

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Background: At primary analysis of the phase 3 study of selinexor (SEL) maintenance treatment in patients (pts) with advanced/recurrent endometrial cancer (EC), improvement in median progression-free survival (PFS) for the intent-to-treat population was not clinically meaningful. However, a promising efficacy signal was seen in a pre-specified exploratory analysis of *TP53*wt EC. We present further exploratory PFS analyses of long-term follow-up data in *TP53*wt EC. **Methods:** ENGOT-EN5/GOG-3055/SIENDO (NCT03555422) was a double-blind randomized (2:1) study evaluating SEL vs placebo as maintenance treatment in pts with advanced/recurrent EC following response to prior systemic therapy. Post-hoc exploratory subgroup analyses include response to prior systemic chemotherapy, disease at time of prior systemic therapy, Eastern Cooperative Oncology Group (ECOG) performance status, histopathological subtype at initial diagnosis, and duration of last systemic therapy. Additional subgroups will be reported at the time of presentation. **Results:** Of 263 pts in the study, 113 (43.0%) had *TP53*wt EC (SEL, n = 77; placebo, n = 36). At data cut-off (April 1, 2024), PFS subgroup analyses generally showed benefit for SEL compared with placebo in the *TP53*wt subgroup regardless of clinical factor (table). Adverse events (AEs) were generally manageable and reversible. The most common AEs (overall/Grade ≥3) with SEL were nausea (89.5%/13.2%), vomiting (60.5%/2.6%), and diarrhea (44.7%/3.9%). Dual anti-emetics were not mandated. No meaningful differences in AEs were observed across subgroups. 17.1% of pts discontinued SEL due to AEs; 1 death occurred in the placebo group. **Conclusions:** A strong PFS signal was observed in the *TP53*wt subgroup across a range of key clinical factors at long-term follow-up. Efficacy and safety of SEL maintenance therapy were generally comparable across subgroups. A phase 3 trial is ongoing to further investigate SEL as maintenance therapy in pts with advanced/recurrent *TP53*wt EC (ENGOT-EN20/GOG-3083/Xport-EC-042, NCT05611931). Clinical trial information: NCT03555422. Research Sponsor: Karyopharm Therapeutics.

	Placebo, e/n (N = 36)	SEL, e/n (N = 77)	PFS, HR vs placebo (95% CI)
Response to prior therapy: PR	18/20	31/46	0.50 (0.27, 0.92)
CR	9/16	7/31	0.24 (0.09, 0.67)
Disease at time of prior therapy: Primary Advanced	12/17	18/34	0.58 (0.28, 1.21)
Recurrent	15/18	18/41	0.29 (0.14, 0.61)
ECOG: 0	16/22	20/43	0.24 (0.11, 0.53)
1 or 2	11/14	18/34	0.50 (0.20, 1.26)
Histopathological subtype: Endometrioid	22/29	33/65	0.45 (0.25, 0.79)
Non-endometroid	5/7	5/12	0.31 (0.07, 1.34)
Duration of last systemic therapy: 12 to <24 weeks	20/27	28/60	0.45 (0.25, 0.81)
≥24 weeks	7/9	10/17	0.66 (0.25, 1.74)

CI, confidence interval; CR, complete response; ECOG, Eastern Cooperative Oncology Group; e/n, patients with events/(patients with events + patients censored); HR, hazard ratio; PR, partial response.

The role of platinum-free interval in advanced endometrial cancer treatment: A real-world study of 843 patients.

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Background: Time between completion of last platinum-based chemotherapy (PBC) and recurrence is predictive of outcomes in recurrent ovarian cancer; however, its applicability to endometrial cancer (EC) remains uncertain. This retrospective real-world study assessed (1) platinum-free interval (PFI) duration between first-line (1L) PBC and second-line (2L) therapy for EC, (2) differences in patient (pt) and clinical characteristics by PFI, and (3) the association between PFI and outcomes. **Methods:** Using the US Flatiron Health electronic health record–derived deidentified database, we analyzed pts with advanced or recurrent EC who received 1L PBC between 1/1/2013 and 8/31/2022. PFI was defined as the time between completion of PBC and the start date of any 2L therapy. Overall survival (OS), time to treatment discontinuation (TTD), and time to next treatment (TTNT) were analyzed using Kaplan-Meier methods. The association between PFI and clinical outcomes was examined using Cox regression models. **Results:** Of 843 pts, 575 (68%), 147 (17%), and 121 (14%) had a PFI of <6, ≥6 to <12, and ≥12 months (mo), respectively. Pts with advanced disease, carcinosarcoma histology, or a history of surgery or radiation were more likely to have shorter PFI; those with a body mass index of ≥40 kg/m^2 or PD-L1 negative/not detected were more likely to have longer PFI ($P<.05$ for all). Pts with a PFI of <6, ≥6 to <12, or ≥12 mo had a median OS of 12.7, 17.9, or 30.5 mo and median TTNT of 9.8, 8.3, or 12.6 mo, respectively. Compared with pts with a ≥12-mo PFI, those with shorter PFI had a significantly higher risk of death, after adjusting for potential confounders (HR, 1.71 [95% CI, 1.27-2.29] for PFI of <6 mo; HR, 1.57 [95% CI, 1.12-2.20] for PFI of ≥6 to <12 mo). Median OS, TTD, and TTNT, and their association with PFI, are summarized in the Table. **Conclusions:** Our data suggest that platinum sensitivity is an applicable concept in advanced or recurrent EC and is associated with OS. These results may have implications for treatment selection and informing clinical trial designs in EC. Research Sponsor: GSK.

OS, TTD, and TTNT from the start of 2L treatment by PFI duration.

	Total (N=843)	PFI <6 mo (n=575)	PFI ≥6 to <12 mo (n=147)	PFI ≥12 mo (n=121)
OS, median (95% CI), mo	**14.9 (13.3-17.3)**	**12.7 (11.3-14.4)**	**17.9 (14.7-23.9)**	**30.5 (19.0-41.3)**
OS association with PFI, HR (95% CI)[a]		1.71 (1.27-2.29)[b]	1.57 (1.12-2.20)[b]	REF
TTD, median (95% CI), mo	**3.9 (3.6-4.2)**	**3.6 (3.2-3.9)**	**4.4 (3.7-5.2)**	**5.1 (4.2-6.5)**
TTD association with PFI, HR (95% CI)[a]		1.26 (1.02-1.56)[b]	1.09 (0.84-1.41)	REF
TTNT, median (95% CI), mo	**10.1 (9.0-11.1)**	**9.8 (8.5-11.3)**	**8.3 (6.9-10.3)**	**12.6 (10.3-15.9)**
TTNT association with PFI, HR (95% CI)[a]		1.20 (0.91-1.59)	1.44 (1.04-2.00)[b]	REF

[a]Cox regression models adjusted for prespecified potential confounders: PFI, race, age, ECOG performance status, histology, disease stage and grade at diagnosis, body mass index, MMR/MSI status, and receipt of 2L immunotherapy.
[b]$P<.05$ vs REF.

Adverse effects of immune checkpoint inhibitors in advanced endometrial cancer: A systematic review and meta-analysis.

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Background: Immune checkpoint inhibitors (ICIs) in combination with chemotherapy have become a standard first-line treatment for advanced endometrial cancer with increased response rate and progression free survival. While immune-related adverse effects (irAEs) are expected, it is interesting to know the rate of all treatment-related adverse effects (TRAEs). This meta-analysis evaluates the spectrum of adverse effects related to ICIs. **Methods:** Search of the PubMed, EMBASE and Cochrane Library for publications up to December 2024 yielded six randomized controlled trials (RCTs), namely RUBY, NRG-GY018, DUO-E, KEYNOTE-B21, AtTend, and MITO END-3 for this analysis. Uniformly, the experiment arms were ICIs plus paclitaxel and carboplatin, while the control arms were same chemotherapy agents, except the DUO-E trial included Olaparib in one of the experimental arms. The primary outcomes of this study were the pooled events of TRAEs and irAEs, analyzed using a random-effects model with RevMan 5.4. **Results:** A total of 3952 patients were included from 6 RCTs. The use of ICI was associated with irAEs, such as hypothyroidism, hyperthyroidism, rash and pneumonitis(Table). It was also associated with increased incidence of serious TRAEs (RR 1.64, 95%CI 1.09-2.48, p=0.02) and higher treatment discontinuation rates (RR 1.44, 95%CI 1.13-1.83, p=0.004). There was greater risk of hematologic toxicities, including anemia (RR:1.25, 95% CI 1.05-1.49), leukopenia (RR:1.40, 95% CI 1.10-1.77), and thrombocytopenia (RR:1.43, 95% CI 1.06-1.93) in ICI arm. ICI arm was at greater risk of hepatotoxicity (RR: 4.47, 95% CI 1.17-17.15), vomiting (RR: 1.43, 95% CI 1.19-1.73) and hypertension (RR:1.93, 95% CI 1.11-3.36). There were no significant differences in peripheral neuropathy (RR:0.96, 95%CI 0.89-1.04), fatigue (RR: 1.04, 95%CI 0.95-1.13), infusion related reactions (RR: 1.11, 95% CI 0.51-2.39), arthralgias (RR:0.58, 95% CI 0.21-1.57), or fatal TRAEs between the two treatment groups(RR:1.21,95% CI 0.69-2.12). **Conclusions:** Advanced endometrial cancer treatment with ICIs is linked to a diverse array of adverse effects. Patients in the ICI and chemotherapy arm demonstrated an increased risk of hematologic toxicity, hepatotoxicity, irAEs and higher treatment discontinuation rate compared to chemotherapy alone. However, no notable difference was observed in fatal TRAEs.
Research Sponsor: None.

	Events	Number of studies (n)	Number of patients included (N)	Risk Ratio, 95% Confidence Interval	P value
TRAEs	Any grade	6	3830	1.00 [0.99-1.00]	0.25
	Serious	5	2095	1.64 [1.09-2.48]	0.02
	Leading to discontinuation of treatment	4	2524	1.44 [1.13-1.83]	0.004
Immune mediated	Fatal	5	2095	1.21 [0.69-2.12]	0.51
	Any irAE	4	2524	2.30 [1.59-3.31]	<0.00001
	Rash	4	2159	2.96 [1.31-6.69]	0.009
	Hyperthyroidism	4	2802	3.32 [2.22-4.97]	<0.00001
	Hypothyroidism	6	3830	3.98 [2.87-5.52]	<0.00001
	Pneumonitis	4	2802	2.48 [1.18-5.18]	0.02

5611 Poster Session

The impact of prior neoadjuvant/adjuvant chemotherapy (NACT/ACT) on fruquintinib plus sintilimab outcomes in advanced endometrial cancer (EMC) patients with pMMR status: A subgroup analysis of FRUSICA-1.

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Background: FRUSICA-1 (NCT03903705) was an open-label, single-arm, pivotal phase 2 study to evaluate the efficacy and safety of fruquintinib (F, a highly selective VEGFR inhibitor) plus sintilimab (S, an anti-PD-1 monoclonal antibody) in previously treated advanced EMC patients (pts) with pMMR (proficient mismatch repair) status. The primary results of FRUSICA-1 have demonstrated encouraging efficacy (objective response rate [ORR]: 35.6%; median progression-free survival [PFS]: 9.5 mo; median overall survival [OS]: 21.3 mo) in the overall population (Wu X, et al; 2024 ASCO). In this updated exploratory analysis (data cutoff: May 15, 2024), we evaluated the association between prior NACT/ACT and clinical outcomes in this study. **Methods:** Pts who had histologically confirmed advanced EMC with pMMR status confirmed by central lab and had progression on 1 standard systemic therapy were eligible. They received F (5 mg QD, 2 weeks on/1 week off, orally) plus S (200 mg, IV, Q3W) in 21-day cycles until disease progression or unacceptable toxicity. The efficacy subgroup analysis was performed by prior NACT/ACT (Yes vs No). **Results:** As of May 15, 2024, a total of 98 EMC pts with pMMR status were enrolled and received the treatment with the median follow-up of 22.0 mo (95%CI: 20.5, 23.7). Based on pts with or without prior NACT/ACT (Yes vs No = 47 pts vs 51 pts), the baseline demographics and disease characteristics were well balanced. Independent Review Committee (IRC)-assessed ORR (34.0% vs 31.4%) and disease control rate (DCR, 85.1% vs 82.4%) were comparable, respectively. Median duration of response (DoR) in pts with NACT/ACT was 11.1 mo while not reached for pts without NACT/ACT. Median PFS were 7.1 mo (95%CI: 4.7, 13.8) vs 9.5 mo (95%CI: 5.5, not estimable), respectively with two 95%CIs highly overlapped. The 6-mo PFS rates were also comparable at 56.8% vs 59.7%. Median OS pending maturity, the 18-mo OS rates were nearly identical (58.7% vs 59.1%). **Conclusions:** In this updated exploratory analysis of pts with advanced EMC enrolled in FRUSICA-1 study treated with F plus S, encouraging outcomes were achieved in the overall population, including patients who had received prior NACT/ACT and those who had not, with durable and clinically meaningful responses. Clinical trial information: NCT03903705. Research Sponsor: HUTCHMED Limited; Innovent Biologics, Inc.

SHR-A1811 in patients (pts) with HER2-expressing advanced gynecological cancers (Gynecol C): A phase 2 study.

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Background: SHR-A1811 is a novel an antibody-drug conjugate consisting of a humanized HER2-directed monoclonal antibody, cleavable tetrapeptide-based linker, and DNA topoisomerase I inhibitor. We assessed SHR-A1811 in HER2-expressing advanced Gynecol C. **Methods:** Pts with ovarian cancer (OC) that had recurrence within 6 mo of last platinum-based therapy, and recurrent/metastatic endometrial cancer (EC) or cervical cancer (CC) that failed standard therapy were enrolled. Pts received SHR-A1811 at 4.8 or 6.4 mg/kg (Q3W, IV). The primary endpoint was ORR per RECIST v1.1. **Results:** As of Dec 25, 2024, 108 pts were enrolled (ECOG PS 1: 71.3%, prior VEGFR inhibitors: 53.7%, prior immunotherapies: 24.1%) including 46 pts with OC, 27 EC, and 35 CC. Rate of pts with HER2 IHC 3+ was 10.9%, 14.8%, and 31.4%; IHC 2+ was 54.3%, 70.4%, and 37.1%, respectively. The median follow-up was 8.1 mo (IQR, 4.7–10.7). For pts with OC, EC, and CC, ORR was 56.1%, 50.0%, and 63.6%, and PFS was 8.5 mo (95% CI, 5.7–NR), 5.6 mo (95% CI, 4.1–NR), and 10.7 mo (95% CI, 6.9–NR), respectively. In the 4.8 mg/kg cohort, for OC, EC, and CC, ORR was 56.8%, 52.0%, and 61.3%, and PFS was 8.5 mo (95% CI, 5.6–11.3), 7.2 mo (95% CI, 4.1–NR), and 10.7 mo (95% CI, 6.2–NR), respectively. Among OC, EC, and CC pts, ORR was 66.7% in 30 pts, 43.5% in 23 pts, and 66.7% in 24 pts with HER2 IHC 2+/3+, respectively. Additional antitumor activities are shown in Table. Treatment-related adverse events (TRAEs) of grade ≥3 occurred in 84 (77.8%) pts, with the most common being decreased neutrophil count (62.0%), decreased white blood cell count (48.1%), and anemia (28.7%). No TRAEs leading to discontinuation of treatment or deaths were reported. **Conclusions:** SHR-A1811 showed encouraging activity and manageable safety profile in pts with HER2-expressing advanced Gynecol C. Clinical trial information: NCT05896020. Research Sponsor: Jiangsu Hengrui Pharmaceuticals Co., Ltd.

Antitumor activity.

	4.8 or 6.4mg/kg				4.8 mg/kg			
	OC (N=46)	EC (N=27)	CC (N=35)	Total (N=108)	OC (N=42)	EC (N=26)	CC (N=33)	Total (N=101)
ORR[a]	23 (56.1)	13 (50.0)	21 (63.6)	57 (57.0)	21 (56.8)	13 (52.0)	19 (61.3)	53 (57.0)
DCR[a]	36 (87.8)	24 (92.3)	31 (93.9)	91 (91.0)	33 (89.2)	23 (92.0)	29 (93.5)	85 (91.4)
DOR, mo[b]	8.5 (5.8–NR)	7.0 (2.8–NR)	9.5 (5.7–NR)	8.5 (6.7–NR)	8.5 (5.8–NR)	7.0 (2.8–NR)	9.5 (4.2–NR)	8.5 (6.9–NR)
TTR, median (range), mo[b]	2.7 (1.1–4.4)	1.5 (1.1–5.3)	1.4 (1.2–5.4)	1.4 (1.1–5.4)	2.7 (1.1–4.4)	1.5 (1.1–5.3)	1.4 (1.2–5.4)	1.4 (1.1–5.4)
PFS, mo[c]	8.5 (5.7–NR)	5.6 (4.1–NR)	10.7 (6.9–NR)	8.3 (6.8–11.3)	8.5 (5.6–11.3)	7.2 (4.1–NR)	10.7 (6.2–NR)	8.5 (6.2–11.3)
6-mo OS rate, % (95% CI)[c]	89.5 (74.5–95.9)	85.4 (60.3–95.2)	93.6 (76.8–98.4)	90.2 (82.0–94.8)	91.2 (75.1–97.1)	84.6 (58.4–94.9)	93.2 (75.4–98.3)	90.5 (81.8–95.1)

Data are n (%), median (95% CI), or otherwise indicated.
[a]In pts with baseline and at least one post-baseline assessments; N was 41, 26, 33, 100, 37, 25, 31, and 93.
[b]In pts with confirmed CR or PR; N was 23, 13, 21, 57, 21, 13, 19, and 53.
[c]In full analysis set; N was 46, 27, 35, 108, 42, 26, 33, and 101.

5613 Poster Session

Evaluating the safety and efficacy of CRISPR/Cas9-modified tumor infiltrating lymphocytes (GT300) as monotherapy in advanced solid tumors.

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Background: Adoptive cell therapy using autologous tumor-infiltrating lymphocytes (TILs) has shown promising results in melanoma patients. However, its effectiveness in other solid tumors, especially "cold" tumors, is still being explored. GT300, a next-generation TIL product, is engineered using CRISPR/AaCas12bMax to disrupt two key immunoregulatory targets identified through genome-wide CRISPR screening. This modification aims to enhance TIL function and overcome the suppressive tumor microenvironment, potentially expanding its use to cold tumors like ovarian and colorectal cancer. Therefore, two studies were initiated to assess the preliminary safety and efficacy of GT300 in advanced solid tumors. **Methods:** The first-in-class study aims to enroll patients with advanced, treatment-refractory solid tumors, focusing on gynecological cancers. After determining the optimal biological dose (OBD), a monotherapy expansion phase will begin for patients with various solid tumors. Participants undergo nonmyeloablative (NMA) lymphodepletion and receive an infusion of the G300 TIL product, followed by IL-2 administration. **Results:** As of September 5, 2024, five patients have been enrolled in these two studies, with a median age of 55 years and a median of two prior therapy lines. After FC lymphodepleting chemotherapy, patients received GT300 infusions at doses of $\geq 1 \times 10^9$ viable cells. Four out of five patients subsequently received IL-2. Most adverse events (AEs) were Grade 1 or 2, with Grade 3/4 AEs including fever, rash, dental ulcer, anemia, and decreased platelet count. No DLTs were observed. The ORR was 60% (3/5 evaluable patients). Two patients (40%) achieved CR in cervical cancer and peritoneal papillary serous carcinoma, while one patient (20%) with ovarian cancer had a PR. Despite variations in TIL doses (3.2×10^9 to 1.90×10^{10} cells) and IL-2 regimens (up to 3.0×10^5 IU/kg), robust TIL proliferation was consistently observed post-infusion. Responders showed biphasic CD45+CD3+ T cell expansion, indicating sustained immune activation. An early increase in IFN-γ levels from days 3 to 10 strongly correlated with positive outcomes, suggesting its potential as an early efficacy biomarker. **Conclusions:** In patients with previously treated gynecological cancer, GT300, administered after FC lymphodepleting chemotherapy and followed by higher-dose IL-2, exhibited a manageable safety profile. GT300, a CRISPR/Cas9 dual knockout anti-exhaustion TIL product, showed favorable clinical outcomes with a 60% objective ORR, including 40% CR and 20% PR, with no DLTs observed. The infusion led to robust TIL expansion and IFN-γ secretion. These promising results indicate favorable long-term survival outcomes, durable responses, and no long-term safety concerns associated with GT300. Clinical trial information: NCT06145802, NCT06397963. Research Sponsor: None.

Feasibility of ChatGPT-4o in management of gynecologic oncologic patients in the emergency department.

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Background: Recent studies have highlighted the diagnostic and reasoning capabilities of ChatGPT in medicine. This study aims to evaluate the feasibility of using ChatGPT-4o to assist in managing emergency care for gynecologic oncologic patients, focusing on its potential to support physicians and generate patient education materials. **Methods:** We retrospectively reviewed real cases of gynecologic cancer patients who visited the emergency department of the National Cancer Center in Korea between 2005 and 2024 and identified 15 common cases for evaluation. For each case, four physicians (two gynecologic oncologists and two obstetrics and gynecology residents) assessed the cases based on nine criteria: relevance of differential diagnosis, relevance of suggested necessary examinations, speed in suggesting differential diagnoses and necessary examinations, relevance of examination interpretations, relevance of the final diagnosis, relevance of treatment plans, speed in suggesting the final diagnosis and treatment plans, relevance of prescribed orders, and speed of prescribing orders. Each criterion was scored on a scale of 0, 1, or 2, and total scores were calculated along with the total time taken to generate diagnoses, treatment plans, and actual order prescriptions. The same cases were then evaluated using ChatGPT-4o, with prompts specifically developed to enable consistent assessment. In addition to the nine criteria, ChatGPT-4o was also evaluated on the relevance and speed of patient education, with scores assigned on a scale of 0, 1, or 2. Furthermore, physicians provided feedback on their satisfaction with ChatGPT-4o's generated answers and patient education materials using the same scale. **Results:** ChatGPT-4o demonstrated a mean score of 17.1 (range, 14–18) across the 15 cases, outperforming physicians, who achieved a lower mean score of 13.4 (range, 5–17). The mean time taken by ChatGPT-4o to respond to all nine criteria was 108.4 (range, 69–142) seconds, significantly faster than physicians, who required an average of 391.4 (range, 126–786) seconds. For relevance of patient education, ChatGPT-4o achieved a mean score of 1.9 (range, 1–2) across the 15 cases, with response times consistently under 1 minute per cases. Physicians rated their satisfaction with ChatGPT-4o's generated diagnoses, treatment plans, and order recommendations at a mean score of 1.9 (range, 1–2). Similarly, their satisfaction with ChatGPT-4o's patient education materials was rated at a mean score of 1.8 (range, 1–2). **Conclusions:** ChatGPT-4o demonstrates feasibility as a promising supportive tool for managing emergency care in gynecologic oncologic patients, offering fast and relevant diagnoses, treatment plans, and patient education materials. Future research warrants developing practical applications and conducting prospective evaluations to optimize its integration in emergency departments. Research Sponsor: None.

5615 Poster Session

Clinical and demographic profiles and predictors of survival in epithelioid trophoblastic tumors: A population-based analysis.

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Background: Epithelioid trophoblastic tumor (ETT) is a rare form of gestational trophoblastic neoplasia. Existing studies on ETT have been limited by small sample sizes and a lack of robust socioeconomic and demographic analyses. This study aims to characterize the clinical and demographic profiles of ETT patients and evaluate survival outcomes. **Methods:** ETT cases diagnosed between 2000 and 2021 were extracted from the Surveillance, Epidemiology, and End Results (SEER) database. Survival outcomes were analyzed with Kaplan-Meier survival analysis, and the statistical significance of key variables was assessed using the log-rank test. Hazard ratios (HR) were calculated using Cox proportional hazards regression models. This data is compared to what is currently known based on the published literature. **Results:** A total of 100 patients with ETT were identified. The majority of cases (76%) were in patients aged 30 to 49 years. The cohort was predominantly white race (60%), with 72% identifying as Non-Spanish-Hispanic-Latino. Of patients with staging information (57%), 30% had localized disease. Socioeconomic analysis revealed that 60% of patients had a median household income below $80,000 annually, and 71% resided in metropolitan areas with populations exceeding one million. Black patients had risk of mortality compared to white patients [HR = 3.233; 95% CI: (1.021, 10.240), p = 0.046]. Patients with distant metastases or nodal involvement had significantly worse survival outcomes compared to those with localized disease [HR = 11.813; 95% CI: (1.379, 101.190); p = 0.024]. Among treatment modalities, 65% of patients underwent surgery, 33% received chemotherapy, and 3% received radiation therapy. Patients who received chemotherapy demonstrated a higher risk of mortality compared to those who did not [HR = 5.937; 95% CI: (1.788, 19.710); p = 0.004]. **Conclusions:** ETT patients exhibit significant survival differences based on race, distant disease at diagnosis, and chemotherapy use. These findings highlight the importance of addressing racial disparities, early diagnosis, and optimizing treatment strategies to improve outcomes for this rare malignancy. Further research is warranted to refine our understanding and guide clinical management. Research Sponsor: None.

Effects of surgery on the prognosis of patients with locally advanced vulva cancer: A retrospective study of the SEER database and a Chinese multicentre registry.

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Background: Vulva cancer is a rare gynecologic oncology, and lacks uniform recommendations in current guidelines, especially for locally advanced cases. This study seeks to explore prognostic factors and optimize treatment strategies for vulva cancer. **Methods:** This multi-center, cross-ethnic retrospective study collected patient data from 2003–2023 in the China Multi-center Registry and from 2004–2021 in the SEER database. Only pathologically confirmed cases of vulva cancer were included in the analysis. Patients lost to follow-up, under 20 years of age, were excluded. Survival outcomes were compared using Kaplan-Meier analysis, while prognostic factors were evaluated through the Cox proportional hazards model. Baseline characteristics between groups were balanced using inverse probability of treatment weighting (IPTW). The primary endpoint of the study was overall survival. **Results:** A total of 19,682 patients with vulva cancer were included in the study, comprising 604 patients in the Chinese cohort and 19,078 patients in the SEER cohort. Multivariate Cox regression models (China cohort: HR=0.46,95%CI:0.33-0.64, $P < 0.001$; SEER cohort: HR=0.43,95%CI:0.41–0.46, $P < 0.001$) indicated that surgery was associated with improved prognosis. In both cohorts of patients with locally advanced vulva cancer, surgery remained a protective prognostic factor (China cohort: HR =0.43,95%CI:0.27-0.69, $p < 0.001$; SEER cohort: HR=0.52 ,95%CI:0.47-0.57, $p < 0.001$). And the protective effect of surgery in patients with locally advanced disease remained significant after IPTW (China cohort: HR= 0.38 ,95%CI:0.24-0.63, $p < 0.001$; SEER cohort: HR=0.50 ,95%CI:0.44–0.56, $p < 0.001$). **Conclusions:** Although guidelines recommend non-surgical treatment as the preferred approach for patients with locally advanced vulva cancer, this large-scale, multicenter, cross-ethnic retrospective study demonstrates that surgery significantly improves prognosis and offers new insights for clinical practice. Research Sponsor: None.

Temporal and regional mortality trends due to pulmonary embolism in female patients with genital cancers in the United States from 1999 to 2020.

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Background: The involvement of pulmonary vessels by tumor emboli has been described from different primary sites of malignancy. Pulmonary embolism (PE) is a severe and potentially fatal complication in patients with female genital cancers, including ovarian, cervical, uterine, and vulvar malignancies. These cancers, along with associated treatments such as major abdominal surgery, chemotherapy, and hormone therapy, significantly increase the risk of venous thromboembolism (VTE), including PE. While previous studies detail the advancements in cancer detection and treatment, temporal and regional trends of PE-related mortality among female genital cancer patients remain poorly characterized. **Methods:** This retrospective study analyzes national mortality data from the CDC WONDER database to assess mortality trends from 1999 to 2020 across different demographic subgroups in the United States. Patients with a known history of genital cancer were identified and PE related mortality data was retrieved. Age-adjusted mortality rates (AAMRs) per 100,000 individuals were calculated further stratified based on sex, age (15-64 years and >64 years), race and census region. Rstudio was used to perform t-test and Mann Kendall test. **Results:** From 1999 to 2020, a total of 13,692 deaths were reported in female genital cancer associated pulmonary embolism in the US (AAPC: 0.421 (95% CI: 0.414-0.428)). The AAMR has risen from 0.363 in 1999 to 0.590 in 2020, indicating a worsening trend over the study period (τ: 0.680, $p<0.001$). AAMR varied greatly by region, with the Northeast having the highest AAMR (9.928). This was followed by the West (0.488), Midwest (0.43) and South (0.366). Black females had consistently higher AAMR than white females, with rates of 0.763 vs. 0.329 in 1999 and 0.976 vs. 0.523 in 2020, respectively. Females older than 65 years demonstrated a much higher total AAMR (1.506) compared to females between the ages of 15 and 65 (0.212) ($p<0.001$). Within the age group of 15-25 years, black females had higher AAMRs compared to white female ($p<0.001$). Black females of the age group >65 years demonstrated much higher mortality (total AAMR: 2.745) than white females of the same age group (1.419), and the highest AAMR overall ($P<0.001$). **Conclusions:** The analysis of AAMR for female genital cancer associated pulmonary embolism highlights a concerning disparity in this dangerous cancer related complication, particularly after 2015. This underscores the need for greater attention to be directed towards reproductive health and cancer related complications faced by black women and to address systematic inequalities in intervention and healthcare access. This can improve early detection and timely interventions in order to reduce mortality and improve outcomes for these patients. Research Sponsor: None.

TPS5618 **Poster Session**

TroFuse-020/GOG-3101/ENGOT-cx20: A phase 3, randomized, active-controlled, open-label, multicenter study comparing sacituzumab tirumotecan monotherapy vs treatment of physician's choice as second-line treatment for recurrent or metastatic cervical cancer.

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Background: Sacituzumab tirumotecan (sac-TMT; formerly MK-2870/SKB264) is an antibody–drug conjugate comprising a trophoblast cell-surface antigen 2 (TROP2)–antibody, a hydrolytically-cleavable linker, and the cytotoxic drug KL610023 (average drug/antibody ratio, 7.4). In an ongoing phase 1/2 study (MK-2870-001), sac-TMT monotherapy showed promising antitumor activity in participants with locally advanced unresectable/metastatic solid tumors that were refractory to standard therapies. This phase 3, randomized, open-label, multicenter study (NCT06459180) evaluates the efficacy and safety of sac-TMT monotherapy vs treatment of physician's choice (TPC) as second-line treatment in participants with recurrent/metastatic cervical cancer. **Methods:** Eligible participants are aged ≥18 years with progressive recurrent/metastatic cervical cancer, measurable per RECIST version 1.1 by the investigator, and had received 1 prior line of platinum doublet chemotherapy (±bevacizumab) and anti–PD-1/anti–PD-L1 therapy as a part of cervical cancer regimens. Participants must provide tissue from a core or excisional biopsy of a not previously irradiated tumor lesion. Approximately 666 participants will be randomly assigned 1:1 to receive either sac-TMT 4 mg/kg intravenously (IV) Q2W or TPC (pemetrexed 500 mg/m^2 IV Q3W; tisotumab vedotin 2 mg/kg IV Q3W; topotecan 1 or 1.25 mg/m^2 on days 1–5 of each 3-week treatment cycle; vinorelbine 30 mg/m^2 on days 1 and 8 of each 3-week treatment cycle; gemcitabine 1000 mg/m^2 on days 1 and 8 of each 3-week treatment cycle; or irinotecan 100 or 125 mg/m^2 on days 1, 8, 15, and 22 of each 6-week treatment cycle). Tumor imaging will be performed ≤28 days before treatment allocation/randomisation, then Q9W until week 54 and Q12W thereafter. The primary endpoint is OS; secondary endpoints include PFS assessed by blinded independent central review, objective response, duration of response, safety, time to deterioration, and patient-reported outcomes. Enrollment began in Q3 2024. Clinical trial information: NCT06459180. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

TPS5619 Poster Session

Randomized phase II study to evaluate treatment with induction therapy with nivolumab plus ipilimumab, followed by nivolumab with chemoradiotherapy versus standard of care with chemoradiotherapy for women with locally advanced cervical cancer.

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Background: Cervical cancer (CC) is one of the leading cause of death in developing countries, largely due to insufficient HPV vaccination coverage. The majority of patients are diagnosed with locally advanced disease. Current standard of care (SOC) for those patients is cisplatin-based chemoradiotherapy (P-XRT). Recent advances have shown improved overall survival (OS) with addition of pembrolizumab administered concurrently with P-XRT and as adjuvant therapy (Lorusso, Domenica et al., KN A18 - LANCET, 2024) as well as neoadjuvant chemotherapy with carboplatin and paclitaxel (McCormick et al, LANCET, 2024). In the metastatic setting, the phase I/II CheckMate 358 trial demonstrated high responses rates with the combination of nivolumab (N) and ipilimumab (I) (Oaknin Ana et al, LANCET, 2024). Currently, no trials have evaluated the use of immune checkpoint inhibitors as a neoadjuvant and concurrent strategy with P-XRT in locally advanced CC. Therefore, we hypothesized that induction N/I followed by nivolumab and P-XRT in locally advanced CC can improve clinical outcomes with a manageable toxicity profile. **Methods:** This is a phase II, randomized, clinical trial, including 116 patients with locally advanced cervical cancer (FIGO stages IIB-IVA). Treatment arms: Patients who are eligible for the study was randomized to one of the following treatment arms: - Experimental: Induction Nivolumab (N) 1mg/kg IV plus Ipilimumab (I) 3mg/kg IV every 3 weeks x 4 cycles followed by N 240mg every 2 weeks concurrently with P-XRT. - Control: P-XRT. Endpoints: Primary endpoint: 3-year Progression-Free Survival (PFS). Secondary endpoints: 3-year overall survival (OS), complete response rate (CRR), objective response rate (ORR), duration of response (DoR), health related quality of life (HRQoL) and toxicity profile. Statistics considerations: A total of 116 participants were randomized 1:1 (experimental arm Vs SOC), considering a dropout rate of 10%. A two-sided log-rank test at a 0.05 significance level provides 80% power to detect a difference between a 3-year PFS rate of 75% in the experimental arm versus 50% in the control arm. This calculation assumes a recruitment period of 24 months, and a total study duration of 60 months (up to 24 months of recruitment and 36-month follow-up after the end of treatment). Current Status: The study is ongoing, and the recruitment phase has been completed. The first patient was enrolled in September 2022, and the last patient in April 2024. All participants have finished the treatment phase and are currently in the follow-up phase. Final study results are expected by mid-2028 Clinical trial information: NCT05492123. Research Sponsor: BRAVA institute (BRAZIL).

TPS5620 **Poster Session**

A prospective, randomized control trial of concurrent paclitaxel and carboplatin along with radiotherapy versus concurrent cisplatin along with radiotherapy in carcinoma cervix patients at a tertiary care hospital of central India.

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Background: In India, cervical cancer accounted for 9.0% of all cancers and 18.3% (127,526) of new cases in 2022 as per GLOBOCAN. It is leading cause of cancer-related deaths in women in low and middle-income countries. Concurrent chemoradiotherapy (CCRT) with Cisplatin is standard for LACC but is often limited by nephrotoxicity & ototoxicity. Hence, the combination of paclitaxel and carboplatin has been explored for its potentially favorable toxicity profile and effectiveness. Thus comparative analysis of two concurrent chemoradiotherapy regimens examining their efficacy, toxicity profiles and suitability for patients. is assessed. The results can have significant implications for clinical practice, particularly in resource-limited settings where treatment- related toxicity and patient compliance are critical concerns. **Methods:** Simple randomization with open label study conducted to compare the efficacy and toxicity of concurrent radiotherapy with paclitaxel and carboplatin versus concurrent radiotherapy with cisplatin in patients with locally advanced cervical cancer. Conducted in Department of Radiation Oncology, GMC Nagpur from July 2024 to December 2026. Sample size 100 (50 each group assuming 10% dropout) Inclusion criteria: Age 18-70 years, histologically confirmed diagnosis, FIGO stage IB1 to IVA, ECOG 0-3, written informed consent, baseline audiometry. Exclusion criteria: Prior chemo-radiotherapy for cervical cancer, severe comorbid conditions, pregnant or breastfeeding women, and known hypersensitivity to study drugs. Intervention: Arm A: Concurrent Cisplatin with EBRT to pelvis with dose of 45-50 Gy/ 23-25 fractions followed by brachytherapy. Chemotherapy: Cisplatin 40 mg/m^2 IV weekly for up to 6 cycles. Arm B: Concurrent RT with Paclitaxel and Carboplatin. RT: Same as Arm A. Chemotherapy: Paclitaxel 50 mg/m^2 and carboplatin AUC 2 IV weekly for up to 6 cycles. Primary Outcomes: Locoregional control (RECIST criteria at 3,6,12 and 24 months post-treatment). Secondary Outcomes: Overall Survival, Progression-Free Survival, Disease-free survival, Toxicity, Quality of Life (EORTC QLQ-C30) questionnaire. Data Collection and Analysis: Baseline assessments-Medical history, physical examination, laboratory tests, imaging studies. During treatment- Weekly clinical assessments, laboratory tests and toxicity evaluations. Follow-up: Clinical assessments, Imaging studies and QoL at 0, 3, 6, 12 and 24 months post-treatment. Ethical Considerations: Ethical approval is obtained from relevant institutional review boards on 04/12/2024. Patients are under accrual. Research Sponsor: None.

TPS5621 Poster Session

ANA trial: Development of a diagnostic test and dynamic evaluation of ctDNA to optimize follow-up and tailor treatment in patients with HPV-related cervical and anal tumors.

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Background: Cervical and anal cancers treated with definitive radiotherapy (RT), with or without chemotherapy, frequently exhibit persistent disease or recurrence. Post-treatment imaging—the current gold standard for assessing response—faces limitations due to local inflammatory processes, necessitating repeated imaging and invasive biopsies, which increase complexity and costs. Circulating tumor DNA (ctDNA) has emerged as a promising biomarker for assessing recurrence or disease progression in HPV-associated cancers. This study proposes the development of a low-cost HPV ctDNA test. Additionally, it aims to evaluate ctDNA's accuracy compared to standard imaging and its role in guiding immunotherapy for patients at high risk of recurrence. **Methods:** ANA trial seeks to establish a novel, affordable diagnostic approach to optimize follow-up and treatment strategies for HPV-associated cancers, potentially improving outcomes while reducing costs. This is a prospective, single-center study with two components: 1. Non-interventional phase: Development and validation of a low-cost HPV ctDNA test. The test's accuracy will be compared with commercially available ctDNA tests and standard imaging in monitoring patients with HPV-associated cervical and anal cancers post-definitive RT or chemoradiotherapy. 2. Interventional phase (Phase II trial): A single-arm study evaluating the efficacy of early complementary immunotherapy in patients with persistent ctDNA positivity post-treatment. Eligibility criteria include patients with HPV-positive cervical or anal cancers undergoing definitive RT or chemoradiotherapy. The study will enroll 110 participants, stratified into two groups based on post-treatment ctDNA results: 68 ctDNA-negative patients for serial ctDNA monitoring and 16 ctDNA-positive patients for Phase II immunotherapy intervention. In this phase, patients will receive Pembrolizumab 200mg IV every 3 weeks for twelve months. Endpoints: The primary endpoint for the non-interventional phase is the sensitivity and specificity of the HPV ctDNA test compared to commercial ctDNA tests and imaging. Secondary outcome is cost-effectiveness of HPV ctDNA as a follow-up tool. For the interventional phase, the primary endpoint is the 6-month disease progression rate in ctDNA-positive patients receiving immunotherapy. Secondary outcomes include recurrence rates, and survival outcomes. Clinical trial information: NCT06640283. Research Sponsor: National Council for Scientific and Technological Development (CNPq); Process No. 444027/2023-8.

TPS5622 **Poster Session**

A phase II, single-arm, open-label clinical trial to evaluate the combination of cadonilimab injection and gut microbiota modulation in the treatment of persistent, recurrent, or metastatic cervical cancer following second-line therapy.

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Background: Current treatment options for cervical cancer include surgery, radiotherapy, and chemotherapy. For persistent, recurrent, or metastatic disease, systemic therapies such as targeted agents and immune checkpoint inhibitors (ICIs) play a crucial role. The NCCN 2023.V1 guidelines recommend PD-1/CTLA-4 bispecific antibody Cadonilimab as a second-line option for recurrent or metastatic cervical cancer. In April 2024, China's NMPA accepted an application for Cadonilimab plus platinum-based chemotherapy (± bevacizumab) as second-line treatment, based on the global phase III AK104-303 trial. Cadonilimab monotherapy demonstrated a 33.0% objective response rate (ORR) and a 12% complete response rate (CR) in platinum-resistant cervical cancer, with an ORR of 43.8% in PD-L1+ patients. Recent research highlights the gut microbiome as a key modulator of immunity and ICI responses across multiple cancers. Gut microbiota modulation may enhance antitumor immunity, improve ICI efficacy, and reduce immune-related adverse events. Fecal microbiota transplantation (FMT) has been shown to restore immune homeostasis by increasing short-chain fatty acid (SCFA) production, particularly butyrate, which strengthens the intestinal barrier and suppresses inflammation. Despite promising findings in other malignancies, no clinical studies have assessed the impact of gut microbiota modulation in advanced cervical cancer immunotherapy. Further investigations are needed to evaluate its therapeutic potential and underlying mechanisms, warranting clinical trials in this field. **Methods:** This study is a Phase II, single-center clinical trial conducted at Fujian Cancer Hospital. Patients will receive gut microbiota transplantation combined with intravenous (IV) administration of Cadonilimab. The recommended dosage of Cadonilimab is 10 mg/kg, with a treatment cycle of 21 days. On Day 1, patients will receive gut microbiota transplantation, followed by Cadonilimab administration on Day 3.Imaging assessments will be conducted every six weeks. The primary objective of the study is to evaluate the Objective Response Rate (ORR). Secondary objectives include Progression-Free Survival (PFS), Disease Control Rate (DCR), Duration of Response (DOR), Overall Survival (OS), PFS rate (≥6 months), and safety (assessed by CTCAE v5.0).Inclusion criteria: Patients with recurrent, metastatic, or persistent cervical cancer; histological types including squamous cell carcinoma, adenosquamous carcinoma, or adenocarcinoma, who are not candidates for curative surgery or radiotherapy. Trial status: The study is in the initiation phase, with plans to enroll 20 patients. As of this submission, patient enrollment has not yet begun. Research Sponsor: Joint Funds for the innovation of science and Technology, Fujian province; 2023Y9449.

TPS5623 Poster Session

A single-center, open-label, single-arm, phase I study with dose expansion cohort of sacituzumab govitecan in combination with cisplatin for patients with platinum sensitive recurrent ovarian and endometrial cancer.

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Background: Sacituzumab govitecan (SG) is an antibody-drug conjugate (ADC) composed of the irinotecan active metabolite SN-38 (govitecan) covalently linked to a humanized monoclonal antibody (hRS7) targeting trophoblastic cell-surface antigen-2 (Trop-2). Sacituzumab govitecan has demonstrated in vitro and in vivo activity against multiple solid tumors, including ovarian cancer and endometrial cancer. The Basket Trial, a phase I/II study of single agent sacituzumab govitecan in patients with epithelial cancers, showed clinical efficacy in endometrial cancer patients (n = 18) with an ORR of 22.2% (6.4-47.6) and median OS of 11.9 months (4.7 months – NR). Insufficient ovarian cancer patients were enrolled for response parameters to be met. The combination of platinum agents and topoisomerase inhibitors, such as irinotecan, has showed complementary effects in pre-clinical studies, however, the use in clinical practice has been limited by intolerable toxicity. Early trials have found that compared to irinotecan, a prodrug for SN-38, sacituzumab govitecan allows for improved targeted delivery of SN-38 to tumor tissue and increased therapeutic activity with relatively moderate toxicity. The tempering of the toxicity by this ADC may allow for the combination of cisplatin with sacituzumab govitecan to capitalize on the synergy between platinum agents and topoisomerase I inhibitors. The most common grade $\geq$ 3 adverse events that are seen with sacituzumab govitecan include leukopenia, neutropenia, and thrombocytopenia, thus the less myelosuppressive platinum agent cisplatin is the preferred platinum choice for this combination. **Methods:** Sacituzumab govitecan is being evaluated in combination with cisplatin in an open-label, non-randomized, dose de-escalation (phase 1) study with a planned dose expansion cohort in platinum sensitive, recurrent epithelial ovarian and endometrial cancer patients. Platinum sensitivity for both cancers is defined as cancer recurrence/progression occurring more than 6 months after the last dose of prior platinum therapy. The safety run in phase utilizes a 3+3 design with a de-escalated dose level if the starting dose of sacituzumab govitecan shows toxicity. The primary endpoint for the safety run-in is to determine the dose-limiting toxicity (DLT) and dose expansion cohort dose of sacituzumab govitecan when administered with a fixed schedule of cisplatin. The dose expansion cohort is designed to indicate proof of concept regarding the ORR, CBR, PFS, and safety of the combination regimen at the dose established in the safety run-in phase of the study. The study began enrolling patients October 2024 at our institution and is currently in phase 1 at the starting dose level of sacituzumab govitecan. Clinical trial information: NCT06040970. Research Sponsor: Gilead Sciences, Inc.

TPS5624 **Poster Session**

Rationale and study design of the KOV-HIPEC-04: 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). This trial aims to identify the survival benefit of HIPEC in stage III & IV ovarian cancer in the era of maintenance therapy of bevacizumab and/or PARP inhibitors. **Methods:** Ovarian cancer patients will be randomized at the time of interval cytoreductive surgery with achieving complete cytoreduction or cytoreduction with no more than 2.5mm size of residual disease to receive HIPEC (41.5 cisplatin 75mg/m^2, 90 minutes) or not (Control arm). After recovery from surgery, patients will receive postoperative platinum-based adjuvant chemotherapy followed by maintenance therapy with PARP inhibitor or bevacizumab. The primary objective of the trial is to evaluate OS in two groups. Secondary objectives are PFS, cancer-specific survival, time to first subsequent therapy (TFST), safety, CA-125 KELIM, 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 are finally studied. **Results:** The first patient was randomized on June 06, 2023. Until Jan. 26, 2025, 279 (53%) patients are randomized. There are no available results at the time of submission. **Conclusions:** The role of HIPEC during interval cytoreductive surgery will be discovered in stage III & IV ovarian cancer with this randomized trial (KOV-04, FOCUS) in the era of maintenance therapy of bevacizumab and/or PARP inhibitors for the first time. Clinical trial information: NCT05827523. Research Sponsor: National Cancer Center Korea (NCC2110790, NCC2110770).

TPS5625 **Poster Session**

A phase Ib, open-label trial of MOv18 IgE in patients with advanced ovarian cancer.

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Background: All antibodies currently approved for cancer therapy are monoclonal IgGs. MOv18 IgE is a first-in-class therapeutic IgE antibody to have entered the clinic, successfully completing a Phase I trial in patients with advanced solid tumours. MOv18 IgE targets folate receptor alpha (FRa), an antigen present on a variety of cancers including ovarian, endometrial, lung and triple negative breast cancer. In the first-in-human Phase I trial, MOv18 IgE was well tolerated (up to 12 mg), with urticaria the most frequent toxicity [Spicer, J., *et al. Nat Commun* 14, 4180 (2023)]. These results demonstrated the potential of MOv18 IgE as an anti-cancer therapy supporting further clinical development. MOv18 IgE's unique mechanism of action includes high affinity binding to its main cognate receptor, FcεR1, enabling immunosurveillance and potent myeloid cell driven tumour FRa killing. Additionally, IgE antibodies drive modulation of the tumour immune microenvironment to a more pro-inflammatory phenotype, increasing intra-tumoral levels of activated T cells and tumour killing macrophages. **Methods:** EPS101-10-02 is a two-part, Phase Ib, open-label, dose escalation and expansion trial in patients with PROC, whose disease has progressed after ≤4 prior regimens of anti-cancer therapy. Tumours must express FRa at ³5%, (1+, 2+ or 3+ membrane staining on at least 5% of tumour cells by IHC using the BN3.2 antibody), and patients must have a negative basophil activation test to stimulation with MOv18 IgE prior to Cycle 1, Day 1. Approximately 45 patients with measurable disease will be recruited. MOv18 will be given by IV infusion (starting dose 3 mg) on Days 1, 8 and 15 of a 21-day cycle. Treatment will continue until disease progression, unacceptable toxicity, withdrawal of consent or death. A range of translational endpoints will be evaluated. Primary objectives are to evaluate the safety and tolerability of MOv18 IgE and make a preliminary assessment of efficacy in PROC. Clinical trial information: NCT06547840. Research Sponsor: None.

TPS5626 Poster Session

SALVOVAR: A pragmatic randomized phase III trial comparing the salvage weekly dose-dense regimen to the standard 3-weekly regimen in patients with poor prognostic ovarian cancers (GINECO-OV130b; ENGOT-ov78).

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Background: The patients with an advanced epithelial ovarian cancer (EOC) treated with a neo-adjuvant platinum-based chemotherapy who are not amenable to a complete interval debulking surgery (IDS) due to a poorly chemosensitive disease (CA-125 KELIM score <1.0) have a particular poor prognosis (~20% overall survival at 5 years). Several studies suggested that these patients may have a benefit from a chemotherapy densification with the weekly dose-dense carboplatin-paclitaxel regimen. **Methods:** SALVOVAR trial (NCT06476184) is an academic pragmatic open-label multicentre international randomized phase III trial, including stage III-IV high-grade EOC patients who present 2 poor prognostic features after 3-4 cycles of standard neo-adjuvant chemotherapy with carboplatin-paclitaxel administered every 3 weeks: 1) an unfavorable standardized KELIM score <1.0; and 2) a disease considered to be not amenable to a complete IDS. The enrolled patients are randomly allocated (ratio 1:1) to an experimental arm (weekly dose-dense regimen: carboplatin AUC5 and paclitaxel 80 mg/m^2 on day1, day8, and day15, with 3 week cycles) or a control arm (continuation of the standard regimen given every 3 weeks) for 3 cycles. Bevacizumab will be added at investigator discretion. The stratification factors are: Planned administration of bevacizumab (yes, vs no); BRCA mutation (yes, vs no/unknown); and KELIM score strate (moderately unfavorable ≥0.7, vs very unfavorable <0.7). The objective is to show the superiority of the experimental arm with 2 co-primary endpoints: 1) percentage of patients achieving late complete cytoreductive surgery after chemotherapy densification (15% increase), and of overall survival (Hazard-ratio, 0.61). 250 patients will be randomized. The secondary endpoints include overall response rate, progression-free survival, percentage of patients receiving PARP inhibitor and safety. Social human sciences are planned with assessment of the patient/physician perceptions in the shared-decision-making; quality-of-life/patient-reported-outcomes; medico-economic investigation, along with surgical definition of standardized criteria for non-resectability, and inventory of BRCA/homologous-recombination assays used in real-life. The trial is activated in France and Japan. It will be open in United Kingdom, The Netherlands, Italy, Czech Republic, Slovenia, Hungary, Slovakia, and Israel. The recruitment started in July 2024. On January 15 2024, 62 patients had been pre-screened and 18 patients had been randomized. SALVOVAR trial is funded by a European Union HORIZON-MISS-CANCER-2022-01 research program, sponsored by ARCAGY-GINECO (France), and coordinated by Lyon University Hospital (HCL, France). Clinical trial information: NCT06476184. Research Sponsor: None.

TPS5627 Poster Session

A phase 3, open-label, randomized study of rinatabart sesutecan (Rina-S) vs investigator's choice (IC) of chemotherapy in patients with platinum-resistant ovarian cancer (PROC).

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Background: Ovarian cancer (OC) is the fifth leading cause of cancer-related death among women in the United States, with 12,730 estimated deaths in 2025. In patients (pts) with advanced OC, 70% experience recurrence and many develop platinum-resistant OC (PROC) after standard platinum-based treatment. Rinatabart sesutecan (Rina-S) is an antibody-drug conjugate targeting folate receptor alpha (FRα) with a novel hydrophilic protease-cleavable linker and exatecan, a topoisomerase I inhibitor. In cohort B1 of a phase 1/2 trial (NCT05579366), Rina-S 120 mg/m² every 3 weeks (Q3W) showed encouraging anti-tumor activity with a 50% objective response rate (ORR; 95% CI, 26-74), including 1 complete response, and was well tolerated in a heavily pretreated OC population, with >90% having PROC. Responses were observed regardless of FRα expression status. Here we report the design of an open-label, randomized, phase 3 study (NCT06619236) to investigate Rina-S vs IC chemotherapy in pts with PROC. **Methods:** This phase 3 study will enroll ~530 pts with platinum-resistant, high-grade serous or endometrioid epithelial OC, primary peritoneal cancer, or fallopian tube cancer regardless of FRα expression status (Table). Pts will be randomized 1:1 to receive Rina-S 120 mg/m² IV Q3W or IC chemotherapy (paclitaxel, topotecan, pegylated liposomal doxorubicin, or gemcitabine). Primary endpoint is progression-free survival. Secondary endpoints include overall survival, ORR, duration of response, CA-125 response, adverse events, and time to second disease progression. Additional endpoints include QTc changes and overall change from baseline and time to deterioration in Global Health Status/Quality of Life, and patient-reported outcomes. Follow-up visits will occur every 12 weeks for up to ~1 year after the treatment period. Clinical trial information: NCT06619236. Research Sponsor: Genmab A/S.

Key study criteria.

Inclusion Criteria	Exclusion Criteria
High-grade serous or endometrioid epithelial OC, primary peritoneal cancer, or fallopian tube cancer	Primary platinum-refractory disease, defined as OC that did not respond to a first-line platinum-containing regimen
Received 1 to 4 prior lines of therapy, including:	OC that progressed ≤91 days after last dose of a first-line platinum-containing regimen
Platinum chemotherapy	History of another malignancy ≤3 years or evidence of residual disease
Bevacizumab	Known active central nervous system metastases or carcinomatous meningitis
PARP inhibitor (if applicable)	
MIRV (if eligible)	
Platinum-resistant disease defined as:	
Pts who received ≥4 cycles of first-line platinum-based therapy who had a response and then progressed 91-183 days after last dose	
Pts who received 2 to 4 lines of platinum-based therapy and have progressed <183 days after last dose	

MIRV, mirvetuximab soravtansine; PARP, poly-ADP ribose polymerase.

TPS5628 **Poster Session**

Rationale and study design of the KOV-HIPEC-02R (RECOVER): A randomized, multicenter, open-label phase III trial of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in platinum-resistant recurrent ovarian cancer.

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Background: Hyperthermic intraperitoneal chemotherapy (HIPEC) administered during interval cytoreductive surgery following neoadjuvant chemotherapy has shown to increase progression-free survival (PFS) and overall survival (OS) rates, as indicated by the OV-HIPEC-01 and KOV-HIPEC-01 trials. A recent meta-analysis (Kim SI, Kim JH, et al., GO 2023) demonstrated a survival benefit associated with HIPEC, particularly after recent exposure of chemotherapy. Moreover, in ovarian cancer, HIPEC is suggested to be effective in overcoming chemotherapy resistance. **Methods:** This trial (KOV-02R, RECOVER) is a multicenter, open-label, 1:1 randomized, phase III trial that will enroll 140 patients with platinum-resistant recurrent epithelial ovarian cancer (NCT05316181). After cytoreductive surgery, patients undergo the HIPEC procedure at 41.5°C, with doxorubicin at 35mg/ m^2 and mitomycin at 15mg/m^2. Enrolled patients receive non-platinum compound systemic chemotherapy until disease progression. The primary objective is to evaluate progression-free survival between the HIPEC group and the control group. Secondary objectives include overall survival, cancer-specific survival, and safety and quality of life. Considering a 5-year enrollment period, 2-year follow-up, and a statistical power of 80%, 140 patients are needed, accounting for a 10% dropout rate. As of January 10, 2025, 115 patients (82.1%) have been randomized. Clinical trial information: NCT05316181. Research Sponsor: None.

TPS5630 **Poster Session**

SynKIR-CAR T cell advanced research (STAR)-101 phase 1 clinical trial for patients with advanced mesothelin-expressing ovarian cancer, mesothelioma, or cholangiocarcinoma.

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Background: Chimeric antigen receptor (CAR) T cells have transformed treatment of hematologic malignancy but have shown limited efficacy in solid tumors due to T cell exhaustion and lack of functional persistence. Second-generation CAR T cells targeting mesothelin via the SS1 scFv demonstrate safety and early tumor reduction but lack durable clinical benefit (1-3). SynKIR-110, a novel natural killer cell-signaling based CAR T therapy, employs a multichain signaling system designed to reduce exhaustion by activating T cells only upon tumor engagement. In vitro, SynKIR-110 matches CD3-based CAR T cells in cytokine production and tumor lysis, and in conventional CAR T-cell-resistant mesothelioma mouse xenograft models, SynKIR-110 eliminates tumors without observed toxicity (4). **Methods:** This first-in-human, Phase 1, multicenter, open-label, dose-escalation study evaluates the safety and feasibility of SynKIR-110 in patients with advanced mesothelin-expressing tumors, including ovarian cancer, cholangiocarcinoma, and mesothelioma. Participants receive non-myeloablative lymphodepletion with cyclophosphamide and fludarabine, followed by a single intravenous infusion of SynKIR-110. Up to six dose cohorts (3+3 design) will establish the maximum tolerated dose (MTD) or maximum feasible dose (MFD), with an expansion cohort at the recommended phase 2 dose to confirm safety and assess activity. Participants are followed for 12 months to evaluate best overall response, survival, drug persistence, immune function and potential correlation with pre-treatment tumor mesothelin levels, through exploratory analyses. Eligible patients must have recurrent or relapsed ovarian cancer, cholangiocarcinoma, or epithelial pleural or peritoneal mesothelioma after at least one prior systemic therapy. Additional eligibility criteria include measurable disease by iRECIST or mRECIST, ECOG performance status of 0-1, and adequate organ and bone marrow function. Cohort 1 completed without dose-limiting toxicities (DLTs). Enrollment in Cohort 2 initiated in 2025 and is ongoing. SynKIR-110 represents a promising approach to overcoming the limitations of CAR T cells in solid tumors. 1. Beatty GL et al. *Cancer Immunol Res*. 2014 Feb;2(2):112-20. PMID: 24579088. 2. Haas AR et al. *Mol Ther*. 2019 Nov 6;27(11):1919-1929. PMID: 31420241. 3. Beatty GL et al. *Gastroenterology*. 2018 Jul; 155(1):29-32. PMID: 29567081. 4. Wang E et al. *Cancer Immunol Res.* 2015 Jul;3(7):815-26. PMID: 25941351. Clinical trial information: NCT05568680. Research Sponsor: Verismo Therapeutics.

TPS5631 **Poster Session**

Evaluating zAvatar test-guided chemotherapy vs. standard of care in relapsed ovarian cancer and metastatic breast cancer: A multicenter randomized clinical trial (zAVATAR-FLUIDS).

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Background: Relapsed ovarian cancer and metastatic breast cancer (MBC) present significant challenges due to tumor heterogeneity and limited treatment efficacy. Despite numerous recent achievements in personalized medicine, we still lack real-time molecular biomarkers to guide therapeutic decision-making, often resulting in multiple lines of trial-and-error chemotherapy (CT), which ultimately exposes patients to unnecessary toxicities. The zAvatar test – a patient-derived zebrafish xenograft model – has shown to accurately predict tumor response to treatment, providing a real-time and non-invasive means of guiding personalized therapy in advanced cancers (Fior R, et al, 10.1038/s41467-024-49051-0). This trial evaluates the clinical utility of zAvatar as a predictive tool to optimize therapeutic decisions for patients with relapsed ovarian cancer or MBC, presenting with malignant pleural effusion or ascites. **Methods:** In this multicenter, open-label, randomized clinical trial, patients with relapsed ovarian cancer or metastatic HER2-negative breast cancer, ECOG performance status 0-2, measurable disease by RECIST 1.1 and 2 or more equally effective CT options, who need drainage of ascites or pleural effusion, are randomized (1:1) into two groups: the control group will receive CT based on physicians´ choice, while the experimental group will receive treatment guided by the zAvatar-test results. Both groups will have zAvatars generated from tumor cells isolated from ascitic or pleural effusion fluids. The trial will include 276 patients (138 per cancer type). The study aims at determining whether zAvatar-guided decisions lead to improved progression-free survival (PFS) compared to standard of care, as primary endpoint. Recruitment started in January 2025, with an anticipated recruitment period of 3 years (2025–2028). The first patient is expected to be randomized in February 2025 and undergo zAvatar-test evaluations in centralized lab. This trial paves the way for an innovative approach for personalized medicine by validating the zAvatar test's ability to tailor treatment options in advanced cancers, which shall in the future bring into practice a real-time, patient-specific decision-making functional test. Clinical trial identification: EU-CTR n. 2023-509598-22. Legal sponsor: Champalimaud Clinical Centre, Lisbon, Portugal. Funding: Liga Portuguesa Contra Cancro. Protocol FC2024-001. Clinical trial information: 2023-509598-22. Research Sponsor: Liga Portuguesa Contra Cancro.

TPS5632 Poster Session

Randomized study evaluating optimal dose, efficacy and safety of E7386 + lenvatinib versus treatment of physicians' choice in advanced/recurrent endometrial carcinoma previously treated with anti–PD-(L)1 immunotherapy.

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Background: E7386 is an inhibitor of protein-protein interaction between β-catenin and CREB binding protein (CBP). E7386 + lenvatinib has demonstrated manageable safety and promising antitumor activity in the dose-expansion cohort of Study 102 that included patients with advanced endometrial cancer previously treated with immunotherapy (Lee JY et al., *Ann Oncol* 2024). Considering these results, we are conducting a dose-optimization part of Study 102 (NCT04008797) in patients with advanced/recurrent endometrial carcinoma (aEC). **Methods:** Eligible patients (≥18 years) must have a confirmed diagnosis of aEC, and prior treatment with platinum-based chemotherapy and PD-(L)1-directed therapy. Up to 3 prior lines of therapy, regardless of setting, are allowed; prior hormonal therapy and radiation do not count as lines of therapy. Patients will be randomized (1:1:1:1) to E7386 120 mg BID + lenvatinib 14 mg QD (n=30); E7386 60 mg BID + lenvatinib 14 mg QD (n=30); lenvatinib 24 mg QD monotherapy (n=30); or treatment of physician's choice (TPC, doxorubicin 60 mg/m^2 Q3W or paclitaxel 80 mg/m^2 QW [3 weeks on/1 week off]; n=30 in total). Randomization will be stratified by region (Asia/North America/Rest of the World). The primary objective is to determine the optimal dose of E7386 + lenvatinib in aEC; additional objectives include: safety, assessing the contribution of E7386 to the overall treatment effect of E7386 + lenvatinib, and assessing the efficacy of E7386 + lenvatinib relative to TPC. Tumors will be assessed by investigators (per Response Evaluation Criteria in Solid Tumors [RECIST] version 1.1) every 8 weeks from the first dose. Adverse events will be monitored and graded according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. This multinational study is actively recruiting. Clinical trial information: NCT04008797. Research Sponsor: Eisai Inc.

TPS5633 Poster Session

Sapanisertib and serabelisib (PIKTOR) with paclitaxel and a diet substudy in patients with advanced/recurrent endometrial cancer (GOG-3111).

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Background: Patients with advanced/recurrent endometrial cancer have limited 2L+ treatment options. The PI3K/mTOR pathway regulates glucose homeostasis downstream of insulin/insulin receptor signaling and is mutated in >80% of endometrial cancer. Multi-node inhibition of this pathway with the combination of sapanisertib, an mTORC1/2 inhibitor, and serabelisib, a PI3Kα inhibitor, (PIKTOR) achieves more complete PI3K pathway blockade compared to single node inhibition in preclinical models. In a Phase 1b trial (NCT03154294) of triplet combination paclitaxel, serabelisib, and sapanisertib, the combination led to an overall response rate of 80% with 3 CR and 1 PR in 5 patients with advanced, treatment refractory endometrial cancer. This study evaluates whether PIKTOR with paclitaxel improves efficacy outcomes in participants with advanced/recurrent endometrial cancer with mutation(s) in the PI3K/AKT/mTOR pathway and who have failed prior systemic therapies. **Methods:** GOG-3111 is a Phase 2 (ClinicalTrials.gov ID NCT06463028), multi-center, open-label, single-arm trial evaluating the efficacy and safety of PIKTOR plus paclitaxel in participants with advanced/recurrent endometrial cancer. Approximately 40 participants will be enrolled in the main study and up to 50% of participants will have the option to receive triplet combination therapy with a diet. Eligible participants will have histologically confirmed diagnosis of advanced/recurrent endometrioid endometrial carcinoma and documented genetic mutation(s) in the PI3K/AKT/mTOR pathway by next generation tumor testing. Participants must have received >1 but no more than 3 prior systemic therapies for advanced/recurrent disease (ie, including platinum-based therapy and an immune checkpoint inhibitor either together or separately). Study interventions are 28-day cycles with: Paclitaxel: 80 mg/m2 IV weekly on Days 1, 8, and 15; PIKTOR (sapanisertib [1] 3mg and serabelisib [2] 100 mg) oral with food on Days 2-4, 9-11, 16-18, and 23-25. Radiographic imaging and RECIST v1.1 response assessment will be performed every 8 weeks starting at C1D1. The primary objective is to evaluate the objective response rate (ORR) and secondary objective is to evaluate efficacy via progression-free survival (PFS), PFS at 6 months, overall survival, clinical benefit rate, duration of response; and safety/tolerability of PIKTOR + paclitaxel. The substudy rationale is to evaluate the impact of diet on treatment tolerability and efficacy. Clinical trial information: NCT06463028. Research Sponsor: Faeth Therapeutics.

TPS5634 **Poster Session**

Debio 0123, a highly selective WEE1 inhibitor in adult patients with advanced solid tumors: A phase 1 dose escalation and expansion monotherapy study.

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Background: Debio 0123 is an oral, highly selective WEE1 inhibitor. WEE1 inhibition leads to S phase and G2/M cell cycle checkpoint bypass, allowing mitosis to occur without DNA repair, leading to mitotic catastrophe and cell death. This Phase 1 study (NCT05109975) is evaluating Debio 0123 monotherapy in patients with advanced solid tumors who have recurred or progressed following prior therapy and/or without available standard therapy. During the recently completed dose escalation, Debio 0123 was given once daily over a 21-day cycle and had a manageable safety profile with dose proportional pharmacokinetics. The recommended phase 2 dose is 260 mg (Papadopoulos, et al. ASCO2024,#2426). **Methods:** Following selection of RP2D, a 3-arm expansion phase is ongoing and currently enrolling patients, in both biomarker selected and unselected cohorts. Arm A includes patients with recurrent uterine serous carcinoma progressing after at least one prior line of platinum-based chemotherapy. Arm B includes patients with high-grade epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer that recurred to at least one prior line of platinum-based chemotherapy with high cyclin E1. Lastly, a biomarker-driven cohort (arm C) will enroll patients with specific locally advanced or metastatic solid tumors who have recurred or progressed following prior therapy and/or for whom no standard therapy is available. Additional key inclusion criteria are ECOG Performance Status 0-1, and measurable disease per RECIST 1.1. Debio 0123 will be administered once daily until disease progression, unacceptable toxicity, or withdrawal from the study. Primary endpoints are safety and tolerability and overall response rate (ORR) at recommended dose. Secondary endpoints include duration of response (DOR), progression-free survival (PFS), and overall survival (OS). Enrolment is ongoing in Spain, Switzerland and US. Clinical trial information: NCT05109975. Research Sponsor: None.

TPS5635 **Poster Session**

PENELOPE: A randomized phase II trial of first-line carboplatin and paclitaxel in combination with pembrolizumab, followed by maintenance pembrolizumab with or without nesuparib, in patients with newly diagnosed advanced or recurrent MMR-proficient endometrial cancer.

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Background: Clinical trials have demonstrated antitumor activity of the immune checkpoint inhibitors in endometrial cancer patients. Two landmark phase III RCTs, NRG-GY018 and RUBY, proved that the addition of pembrolizumab or dostarlimab to standard chemotherapy resulted in significantly longer progression-free survival (PFS) than with chemotherapy alone in patients with advanced or recurrent endometrial cancer. Meanwhile, both two trials consistently showed that the effective size of adding an immune checkpoint inhibitor to combination chemotherapy on PFS was smaller in MMR-proficient (pMMR) cohort, compared to those in MMR-deficient (MMRd) cohort. As poly(ADP-ribose) polymerase (PARP) inhibitors enhance the effects of immune checkpoint inhibitors when combined, improvement of PFS is expected by dual maintenance with pembrolizumab and a PARP inhibitor. Although the phase III DUO-E trial demonstrated elongated PFS from paclitaxel/carboplatin plus durvalumab followed by maintenance durvalumab with or without olaparib in patients with advanced or recurrent endometrial cancer, this trial is not designed to prove that addition of olaparib maintenance provides extra survival benefits. Nesuparib is a newly synthesized small-molecule chemical compound that inhibits both PARP-1&2 and tankyrase. The PENELOPE trial will investigate whether the addition of nesuparib to pembrolizumab maintenance after paclitaxel/carboplatin plus pembrolizumab treatment further improves PFS in patients with advanced or recurrent pMMR endometrial cancer. **Methods:** In this multicenter, open-label phase II clinical trial, patients with pMMR, stage III/IV or recurrent endometrial cancer, naïve to first-line chemotherapy, will be enrolled. Six patients will be enrolled in Stage 1 (safety run-in) and treated with TCP (paclitaxel/carboplatin + pembrolizumab 200 mg; q3w for six cycles) followed by maintenance treatment with P (pembrolizumab 400 mg; q6w up to 14 cycles) + N (nesuparib 150mg PO once a day; up to 14 months). The study will proceed to Stage 2 (dose expansion) if less than 33% of patients in Stage 1 experience a dose-limiting toxicity. Otherwise, additional patients will be enrolled in Stage 1 at lower dose level. In Stage 2, 80 patients will be randomized (1:1) to: arm A) TCP followed by maintenance treatment with P; arm B) TCP followed by maintenance treatment with P + N (150mg or 100mg PO once a day; up to 14 months). Patients will receive maintenance treatment until disease progression. Primary endpoint is investigator-assessed PFS (RECIST 1.1) of arm B vs. arm A, and key secondary endpoints are overall survival, overall response rate, disease control rate, duration of response, and safety. Enrollment began in Q4 2024. Clinical trial information: NCT06502743. Research Sponsor: Onconic Therapeutic INC.

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IMMUNORARE[5]: A national platform of 5 academic phase II trials coordinated by Lyon University Hospital to assess the safety and the efficacy of the immunotherapy with domvanalimab + zimberelimab combination in patients with advanced rare cancers—The Gestational Trophoblastic Tumors Cohort.

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Background: For patients with rare cancers, there is an unmet medical need to investigate innovative therapeutics beyond standard first-line treatment. These diseases are rarely evaluated in clinical trials. High-risk gestational trophoblastic tumors (GTT) are treated with polychemotherapy (especially EMA-CO) with high cure rate (~95%). However, patients resistant to polychemotherapy have a poor prognosis, and no validated regimen has been defined. Several case reports suggest that immune checkpoint inhibitors (ICIs) may be active, and a phase II trial with Camrelizumab + Apatinib showed a 50% cure rate. There is a strong rationale for concurrent blockade of the TIGIT and PD1 pathways in this disease. **Methods:** IMMUNORARE[5] (NCT NCT06790706) is a platform of 5 single-arm phase II trials testing the efficacy and tolerability of DOMVANALIMAB (anti-TIGIT) and ZIMBERELIMAB (anti PD-1) in 5 independent cohorts of rare cancers. The trial, sponsored by Lyon University Hospital, will be conducted in 15 French centers, in collaboration with the respective French national reference centers. The gestational trophoblastic tumor cohort, led in collaboration with the French Gestational Trophoblastic Disease Center, will enroll 27 patients with resistance or relapse after at least one line of polychemotherapy (e.g. EP low-dose, BEP, EMA-CO), assessable for biological response with serum hCG (human chorionic gonadotropin). Patients previously treated with immunotherapy are not eligible. Patients will receive intravenous DOMVANALIMAB and ZIMBERELIMAB, every three weeks, until hCG normalization followed by 5 consolidation cycles. The primary objective is the successful hCG normalization rate at 6 months. The secondary objectives are the resistance-free survival, overall survival and tolerance. The trial is designed with a two-stage Simon design, with the possibility of early termination for futility (5% one-sided alpha level, 80% power). The treatment will be considered interesting if the percentage of patients experiencing hCG normalization at 6-months is statistically higher than 35% (H0); 60% is expected (H1). Translational research projects will be developed to unravel the cellular and molecular mechanisms involved in treatment response. Moreover, data from the prospectively implemented database of the French Gestational Trophoblastic Disease Center will be analyzed to create a synthetic historical arm representative of the efficacy of the standard treatments in a similar patient population. Clinical trial information: NCT06790706. Research Sponsor: None.

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Stratification of vulvar squamous cell carcinoma (VSCC) by HPV and P53 status to guide excision: CCTG VU.2 STRIVE study (NCT06358469).

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Background: Early VSCC is treated surgically. The optimal approach to margin re-excision may depend on molecular subtype. HPV associated (HPV-A) VSCC has a good outcome and is radiosensitive; HPV independent (HPV-I) p53 abnormal(p53abn) VSSC has a worse outcome and is less radiosensitive. **Methods:** Prospective, international, multicentre, phase II platform study enrolling participants with VSCC stratified by HPV status: HPV- Associated (HPV-A) vs HPV-Independent (HPV-I). Criteria: Key eligibility: Primary diagnosis VSCC; surgically staged I-II (FIGO 2021), molecular/ tumour features known: HPV, margin assessment for tumour clearance, dVIN (differentiated-type vulvar intraepithelial neoplasia), p53. Key ineligibility: tumour HPV-I p53 wild-type, recurrent VSCC, stage III-IV, non squamous histotype, planned or previous RT or chemotherapy. Treatment arms: Cohort HPV-A: Margin negative for cancer but < 8mm (regardless of high grade squamous intra epithelial lesion): Active surveillance (AS). Cohort HPV-I p53abn margin: negative for cancer but <8 mm and/or positive for dVIN and/or positive p53abn: 2:1 randomization to re-excision versus AS. Primary objective: To estimate the 3-year local recurrence rate (LRR) for HPV-A and HPV-I VSCC surgically managed based on dVIN/p53 status, tumour margin clearance. Secondary objectives: recurrence free and disease specific survival, OS, economics, patient reported outcomes. Statistical design: Cohort HPV-A: n=120 enrolled over 3 years; the upper limit of a one-sided 95% CI for 3-year LRR would be 26% when the observed 3-year LRR=20%. Interim analyses (IAs) planned at 12, 24, 36 months after 1st enrollment and final analysis (FA) at 3 years after last enrollment. Cohort HPV-I: n=129, including 10% loss to follow-up, randomized over 3 years to re excision and surveillance arms in 2:1 ratio. 86 on re-excision arm would have at least 85% power with 95% confidence to exclude a 40% 3-year LRR in favour of a lower rate of 25%, while 43 on surveillance arm will enable an estimate of 3-year LRR at an accuracy that the half length of a two-sided 90% CI will be less than 13% when the observed rate is 40%. IA planned at 36 months after 39th patient enrolled to re-excision arm and FA at 3 years after last enrollment. Conduct to Date: This trial was activated Oct 1, 2024. Two enrollments as of Jan 19 2025. Supported by CCS grant #707213; CIHR #195984. Clinical trial information: NCT06358469. Research Sponsor: Canadian Cancer Society (CCS); 707213; Canadian Institutes of Health Research (CIHR); 195984.

TPS5638 **Poster Session**

Evaluation of indocyanine green (ICG) and handheld fluorescence imager in the management of early-stage gynecological cancer.

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Background: Current management in most early-stage cancers is complete lymphadenectomy for staging. Since surgery is the mainstay of treatment tailoring extent of surgery is vital. Only 15-20% of early-stage gynecologic cancers have lymph node metastases yet complete lymphadenectomy is recommended. Sentinel lymph (SLN)node evaluation is a bridge to avoid morbidity due to lymphadenectomy. Fluorescence imaging utilizing near-infrared (NIR) spectrum (700–900 nm) is a valuable tool for mapping lymphatics and lymph nodes and fluorescence imaging is available on robotic and laparoscopic platforms. However, open surgery is the preferred approach for most early-stage gynecological cancers except endometrial malignancy. This research plans to assess hand-held fluorescence imager using ICG dye for feasibility, ergonomics, accuracy and applicability in all gynecologic cancers. Indocyanine green (ICG) is a valuable agent for NIR lymphatic mapping and is used in routinely for sentinel node mapping of breast, skin and gastrointestinal carcinomas with superior safety profile. **Methods:** This exploratory study plans to recruit 30-50 women with early stage endometrial, cervical, ovarian, and vulvar malignancies for intraoperative evaluation of sentinel nodes using ICG and hand held fluorescence imager with SPY-PHI camera and pinpoint video processor(Stryker). Eligibility criteria include women aged 18 years and older, biopsy proven cases of endometrial, cervical & vulvar cancers. For women with suspected ovarian malignancy, sentinel node mapping will be done after laparotomy but SLN biopsy will be done once frozen section report is available. Indications for SLN biopsy are those with uterine confined malignancy (aggressive and non-aggressive endometrial histotypes), stage I cervical cancer with tumor size less than 4 cm, unifocal vulvar tumors less than 4 cm with negative groin nodes and women with stage I and II ovarian cancers and suspicious ovarian masses planned for hysterectomy and or salpingo-oophorectomy. 25 women of early-stage cancers have been enrolled. Fluorescence is detected by tracing fluorescent lymphatics to sentinel node prior to opening retroperitoneal spaces or incising skin in cases of vulvar cancer. Data is being captured and final analysis awaited. The distribution of cancer types till date are endometrial cancer n=12, cervical cancer n= 6, vulvar cancer n=1 and ovarian masses n=6. Sentinel lymph nodes were mapped in 23 out of 25 cases intra-operatively. Clinical trial information: CTRI/2023/03/051086. Research Sponsor: Indian Council of Medical Research; 9618.