# KEYNOTE-826: Final overall survival results from a randomized, double-blind, phase 3 study of pembrolizumab + chemotherapy vs placebo + chemotherapy for first-line treatment of persistent, recurrent, or metastatic cervical cancer.

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**Background:** The first interim analysis of KEYNOTE-826 (NCT03635567) showed that first-line pembrolizumab (pembro) + chemotherapy (chemo) provided statistically significant and clinically meaningful improvements in OS and PFS vs placebo (pbo) + chemo in patients (pts) with recurrent, persistent, or metastatic cervical cancer across all prespecified populations (PD-L1 combined positive score [CPS] ≥1, all-comer, and CPS ≥10). Here, we present the protocol-specified final OS analysis results of KEYNOTE-826. **Methods:** Eligible adults with persistent, recurrent, or metastatic cervical cancer not previously treated with systemic chemo (prior radiosensitizing chemo allowed) and not amenable to curative treatment (surgery or radiation) were randomized 1:1 to pembro 200 mg or placebo Q3W for up to 35 cycles + chemo (paclitaxel 175 mg/m$^2$ + cisplatin 50 mg/m$^2$ or carboplatin AUC 5), ± bev 15 mg/kg. Pts were stratified by metastatic status at diagnosis (yes/no), planned bev use (yes/no), and PD-L1 CPS (<1, 1 to <10, or ≥10). Dual primary end points were OS and PFS per RECIST v1.1 assessed by investigator review, each tested sequentially in the PD-L1 CPS ≥1, all-comer, and CPS ≥10 populations. **Results:** From Nov 2018 to Jan 2020, 617 patients were randomized (pembro + chemo, n = 308 [63.6% with bev]; pbo + chemo, n = 309 [62.5% with bev]); 548 (88.8%) pts had PD-L1 CPS ≥1 and 317 (51.4%) had CPS ≥10. At the Oct 3, 2022 data cutoff, median follow-up was 39.1 mo. Pembro + chemo significantly improved OS and PFS in the CPS ≥1, all-comer, and CPS ≥10 populations (Table). The pembro + chemo benefit was seen regardless of bev use. Grade ≥3 AE incidence was 82.4% in the pembro + chemo arm and 75.4% in the placebo + chemo arm. The most common grade ≥3 AEs were anemia (30.3% vs 27.8%), neutropenia (12.4% vs 9.7%), and hypertension (10.4% vs 11.7%). **Conclusions:** The addition of pembro to chemo ± bev significantly reduced the risk of death by 40% in the PD-L1 CPS ≥1 population, by 37% in the all-comer population, and by 42% in the CPS ≥10 population, and had a manageable safety profile. These data are consistent with the earlier results and provide further support for pembro + chemo ± bev as a new standard of care for first-line treatment of persistent, recurrent, or metastatic cervical cancer. Clinical trial information: NCT03635567. Research Sponsor: Merck & Co., Inc.

| | PD-L1 CPS ≥1 | | All-Comer | | PD-L1 CPS ≥10 | |
|---|---|---|---|---|---|---|
| **Pembro + Chemo n = 273** | Pbo + Chemo n = 275 | Pembro + Chemo n = 308 | Pbo + Chemo n = 309 | Pembro + Chemo n = 158 | Pbo + Chemo n = 159 | |
| **OS, median, mo** | 28.6 | 16.5 | 26.4 | 16.8 | 29.6 | 17.4 |
| **24-mo OS rate, %** | 53.5 | 39.4 | 52.1 | 38.7 | 54.4 | 42.5 |
| **OS, HR (95% CI)** | 0.60 (0.49-0.74); $P < 0.0001$ | | 0.63 (0.52-0.77); $P < 0.0001$ | | 0.58 (0.44-0.78); $P < 0.0001$ | |
| **PFS, median, mo** | 10.5 | 8.2 | 10.4 | 8.2 | 10.4 | 8.1 |
| **12-mo PFS rate, %** | 45.6 | 33.7 | 44.7 | 33.1 | 44.7 | 33.5 |
| **PFS, HR (95% CI)** | 0.58 (0.47-0.71); $P < 0.0001$ | | 0.61 (0.50-0.74); $P < 0.0001$ | | 0.52 (0.40-0.68); $P < 0.0001$ | |

# In situ immune impact of nivolumab + ipilimumab combination before standard chemoradiation therapy (RTCT) for FIGO IB3-IVA in patients (pts) with cervical squamous carcinoma: COLIBRI trial, a GINECO study.

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**Background:** We report the results of a window-of-opportunity phase 2 trial using neoadjuvant nivolumab + ipilimumab followed by standard chemoradiation therapy (RTCT) in cervical squamous cell carcinoma pts using the $CD8^+/FOXP3^+$ ratio as a surrogate marker of immune checkpoint blockade (ICB) *in situ* effect. Association with better clinical outcome after neoadjuvant chemotherapy and higher $CD8^+/FOXP3^+$ ratio was described in cervical cancer pts. However, immune modulation after ICB and correlation with treatment response needs to be characterized. **Methods:** The primary objective was to explore the changes in the ratio of $CD8^+/FOXP3^+$ in tumor biopsies performed before and after ICB (prior to standard RTCT) by multiplex-immunofluorescence (mIF) analyzing densities of CD8 effector T cells ($CD8^+$: $CD3^+CD8^+FOXP3^-$) and CD4 regulatory T cells ($FOXP3^+$: $CD3^+CD8^-FOXP3^+$). To normalize the distribution of the values, mIF data were log-transformed (log10). Targeted gene expression profiling of 2,549 genes using HTG technology allowed us to evaluate the 27-gene based 'HOT' score reported to be associated with immunologically active tumors (Foy J-P. *et al.*, 2022, Eur J Can). **Results:** Pts received 1 cycle of nivolumab 3 mg/kg (D1D15) + ipilimumab 1 mg/kg (D1) before starting RTCT + brachytherapy. After RTCT, pts could continue nivolumab in maintenance 480 mg total dose every 28 days for 6 months. Forty pts were treated (including 50% FIGO III-IV). There were no new or unexpected toxicity. Grade≥3 AEs related to ICB occurred in 3 pts. mIF data of the 28 evaluable pts revealed an increase of total $CD8^+$ cells (Wilcoxon, p=0.009), proliferating $CD8^+$ cells (p=0.002) and $CD8^+/FOXP3^+$ ratio (p=0.03) between baseline and before RTCT. In the 37 pts evaluable by HTG, a significant increase of expression of the *CD8A* gene (paired t-test, p=2.2e-05) and the 'HOT' score (paired t-test, p=3.1e-06) was observed after ICB. The Objective Response Rate on primary tumor before, after, at the end of treatment (EOT) is reported in table. Correlation between $CD8^+/FOXP3^+$ ratio, the 'HOT' score and response to treatment will be presented. **Conclusions:** These data indicate that neoadjuvant nivolumab + ipilimumab is safe and orchestrates *de novo* immune responses in cervical squamous cell carcinoma. The 82.5% CR rate on primary tumor 6 months post RTCT suggests favorable clinical outcomes. Clinical trial information: NCT04256213. Research Sponsor: Bristol-Myers Squibb.

**Primary tumor responses.**

| Primary tumor response (RECIST) | Before RTCT (After ICB induction) (%) | After RTCT (at 4W) (%) | EOT (at 24W) (%) |
|---|---|---|---|
| **Total cohort (N=40)** | | | |
| **CR** | 0 | 25 (62.5) | 33 (82.5) |
| **PR** | 6 (15.0) | 14 (35) | 4 (10.0) |
| **SD** | 32 (80.0) | 1 (2.5) | 0 |
| **PD** | 2 (5.0) | 0 | 2 (5.0) |
| **NE** | 0 | 0 | 1 (2.5)* |

CR, complete response; EOT, end of treatment; ICB, immune checkpoint blockade; NE, not evaluable; PD, progressive disease; PR, partial response; RTCT, radiochemotherapy; SD, stable disease; W, weeks. *no MRI done.

## Incorporation of triapine (T) with cisplatin chemoradiation (CRT) for locally advanced cervical and vaginal cancer: Results from NRG-GY006, a phase III randomized trial.

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**Background:** Definitive cisplatin-based chemoradiation (CRT) plus brachytherapy for locally advanced cervical cancer (FIGO IB3-IVA) results in sustained survival for 60-70% of patients. Recent studies integrating anti-PD-1 checkpoint immunotherapy (CALLA, NCT03830866) or consolidation chemotherapy (OUTBACK, ACTRN12610000732088) have not demonstrated a survival benefit over CRT. Intrinsic overexpression of ribonucleotide reductase may enhance DNA damage repair due to CRT. We report on the efficacy and tolerability of adding the ribonucleotide reductase inhibitor, triapine, to CRT. **Methods:** NRG GY006 is a randomized, open-label phase III clinical trial. Eligible patients had FIGO 2009 locally advanced cervical (stages IB2, II, IIIB or IVA without radiographic evidence of para-aortic nodal involvement) or stages II-IV vaginal cancer. Patients were randomly assigned to receive cisplatin (40 mg/m$^2$ weekly) with RT 45 Gy + lymph node boost alone (CRT) or CRT in combination with 15 total infusions of triapine (25 mg/m$^2$ IV) Mon/Wed/Fri (CRT + T). Both image guided IMRT or 3D RT were allowed but needed to be specified and pass a rigorous credentialing process. All RT plans had a pretreatment review with expert planning feedback to the sites. The primary endpoint was overall survival (OS); secondary endpoint was progression-free survival. Exploratory endpoints included rate of complete metabolic response on post treatment PET/CT imaging at 3 months and knowledge-based planning for image guided IMRT. The target sample was 450 with 127 OS events. The design was to provide 80% power to detect a 10% improvement in OS at 3 years over the control (or HR = 0.6) at 2.5% significance level including one interim futility analysis at 50% information time. **Results:** Between 1/15/16 and 9/22/22 448 eligible patients were randomized to CRT (n=224) or CRT+T (n=224). The database was locked on 10/18/22 with 69 deaths. Median age was 47 years (range 23-85 years). The majority had cervical cancer (93.3%) and squamous cell carcinoma (82%). 52% had FIGO stage II disease. Racial/ethnic distribution included non-Hispanic white (53.8%), Hispanic/Latina (22.5%), and black (15.2%). IMRT was used in (74.3%) and HDR brachytherapy (98.2%) of cases. No differences in Grade 3-5 toxicities were observed: CRT =52% and CRT +T= 49% with Two G5 toxicities (cardiac arrest and acidosis) in the CRT+T arm. 343 patients have completed all protocol directed therapy. With a median follow-up of 28 months (IQR 15-45 months), the median PFS and OS for both arms were not reached yet. HR for death was 1.018 (95% CI 0.634-1.635), the conditional power was 15% to detect a HR = 0.6 at 100% information time. **Conclusions:** The addition of triapine to CRT did not improve OS. Clinical trial information: NCT02466971. Research Sponsor: U.S. National Institutes of Health.

# Dostarlimab for primary advanced or recurrent (A/R) endometrial cancer (EC): Outcomes by blinded independent central review (BICR) of the RUBY trial (ENGOT-EN6-NSGO/GOG-3031/RUBY).

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**Background:** RUBY (NCT03981796) evaluated the efficacy and safety of the anti–programmed death 1 (PD-1) dostarlimab + standard of care (SOC) carboplatin paclitaxel (CP) versus CP alone in A/R EC. The primary endpoint of PFS by investigator assessment (INV) per RECIST v1.1 was significantly longer with dostarlimab+CP than placebo (PBO)+CP in the mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H; HR 0.28; 95% CI 0.162–0.495) and overall populations (HR 0.64, 95% CI 0.507–0.800). Here we present secondary efficacy endpoints by BICR. **Methods:** RUBY is a phase 3, global, randomized, double-blind, multicenter, PBO-controlled study. Patients (pts) with primary advanced stage III or IV or first recurrent EC were randomized 1:1 to receive dostarlimab 500 mg, or PBO, plus carboplatin AUC 5 and paclitaxel 175 mg/m$^2$ Q3W (6 cycles), followed by dostarlimab 1000 mg, or PBO, monotherapy Q6W for up to 3 y. Secondary endpoints by BICR assessment per RECIST v1.1 were PFS, ORR, DOR, and DCR in the overall and dMMR/MSI-H populations. **Results:** 494 pts were randomized (245:dostarlimab+CP; 249:PBO+CP); 47.8% had recurrent disease, 18.6% and 33.6% had primary stage III and IV disease, respectively. PFS by BICR was longer with dostarlimab+CP than PBO+CP in the dMMR/MSI-H (HR 0.29; 95% CI 0.158–0.543) and overall populations (HR 0.66; 95% CI 0.517–0.853; Table). Consistent benefits were seen with dostarlimab+CP for ORR, DCR, and DOR by BICR in the dMMR/MSI-H and overall populations (Table). Safety was previously reported. **Conclusions:** Dostarlimab+CP showed clinically meaningful improvement in BICR-assessed PFS in the dMMR/MSI-H and overall populations compared with CP alone. The HRs for PFS per BICR and per INV were consistent, which supports the reliability of PFS by INV in EC trials. Benefits were seen in all BICR-assessed endpoints, which were consistent with INV. Dostarlimab+CP represents a new SOC for pts with primary A/R EC. Clinical trial information: NCT03981796. Research Sponsor: GSK.

| | dMMR/MSI-H | | Overall | |
|---|---|---|---|---|
| | Dostarlimab +CP N=53 | PBO+CP N=65 | Dostarlimab +CP N=245 | PBO+CP N=249 |
| **PFS by INV, HR (95% CI)** | 0.28 (0.162–0.495) *P*<0.0001 | | 0.64 (0.507–0.800) *P*<0.0001 | |
| **PFS by BICR, HR (95% CI)** | 0.29 (0.158–0.543) | | 0.66 (0.517–0.853) | |
| **Probability of PFS by BICR at 24 mo, % (95% CI)** | 66.3 (50.8–77.9) | 26.0 (13.5–40.5) | 42.5 (35.2–49.6) | 25.4 (18.9–32.4) |
| **ORR by BICR, % (95% CI; n/N)[a] CR, % (n)** | 77.1 | 63.3 | 68.2 | 59.4 |
| **PR, % (n)** | (62.7–88.0; 37/48) | (49.9–75.4; 38/60) | (61.6–74.2; 152/223) | (52.7–65.8; 136/229) |
| | 22.9 (11) | 13.3 (8) | 20.6 (46) | 14.8 (34) |
| | 54.2 (26) | 50.0 (30) | 47.5 (106) | 44.5 (102) |
| **DCR, % (95% CI; n/N)[a]** | 91.7 (80.0–97.7; 44/48) | 91.7 (81.6–97.2; 55/60) | 88.3 (83.4–92.2; 197/223) | 86.9 (81.8–91.0; 199/229) |
| **mDOR (95% CI), mo[a]** | NE (13.1–NE) | 6.9 (5.5–10.1) | 12.9 (8.2–NE) | 6.7 (5.7–8.3) |

[a]Assessed in pts with evaluable disease at baseline.
CR, complete response; PR, partial response; NE, not estimable. *no MRI done.

# Patient-reported outcomes (PROs) in primary advanced or recurrent endometrial cancer (pA/rEC) for patients (pts) treated with dostarlimab plus carboplatin/paclitaxel (CP) as compared to CP in the ENGOT-EN6/GOG3031/RUBY trial.

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**Background:** In RUBY, a phase 3, global, randomized, double-blind, placebo (PBO)-controlled trial, dostarlimab+carboplatin/paclitaxel demonstrated significant and clinically meaningful improvement in PFS compared with PBO+CP in pts with pA/rEC. PROs are reported here. **Methods:** 494 pts with pA/rEC were randomized 1:1 to dostarlimab (D)+CP or PBO+CP Q3W for 6 cycles followed by D or PBO monotherapy Q6W ≤3 yrs or to disease progression. EORTC QLQ-C30 and EN24 were prespecified secondary endpoints. PROs were administered on Day 1 of each treatment (tx) cycle (C), end of tx (EOT), and at safety and survival follow-ups and reported here for C7, the end of chemotherapy (chemo) and C13, and the end of 1 yr of study. Change (chg) from baseline (BL) to C7/C13 was calculated for all scales assessed. Mixed model for repeated measures analysis was conducted to generate least-squares means (LSM), adjusting for correlations across multiple time point assessments within a pt and controlling for the BL value for the global, pain, fatigue, and physical function (PF) scores. **Results:** PRO outcomes were similar for D+CP and PBO+CP through the chemo period (C7). The table shows selected scores at C7 and C13 for mean (SD) and chg from BL. Further, no differences across the 3 yr period between the 2 arms were reported; LSM (standard error) for global QoL was 0.5 (1.42; *P*=0.72), PF was −0.7 (1.39; *P*=0.63), fatigue was 0.2 (1.75; *P*=0.91) and pain was −1.0 (1.99; *P*=0.62). Mean chg from BL to EOT showed improvement in back/pelvic pain for D+CP and deterioration in global QoL/GHS, social functioning, body image, and chg in taste for pts on PBO+CP. **Conclusions:** Dostarlimab + CP significantly improved PFS while maintaining HRQoL, further supporting its use as a standard of care in pA/rEC. Clinical trial information: NCT03981796. Research Sponsor: GSK.

| Domain: | D + CP BL Mean (SD) | D + CP BL to C7 Mean chg (SD) | D + CP BL to C13 Mean chg (SD) | PBO + CP BL Mean (SD) | PBO + CP BL to C7 Mean chg (SD) | PBO + CP BL to C13 Mean chg (SD) |
|---|---|---|---|---|---|---|
| Global QoL/GHS | 67.7 (21.63) | −1.8 (22.79) | 3.3 (23.51) | 69.7 (21.15) | −2.3 (23.10) | −0.9 (19.25) |
| Physical Function | 77.7 (20.83) | −6.9 (22.82) | 2.4 (20.64) | 76.2 (21.92) | −6.8 (21.09) | −0.1 (18.22) |
| Role Function | 73.9 (28.77) | −6.9 (34.88) | 4.6 (33.46) | 77.5 (28.89) | −8.4 (32.94) | −0.2 (28.17) |
| Emotional Function | 76.2 (18.40) | 2.0 (18.75) | 5.4 (20.16) | 78.6 (19.41) | 2.5 (22.64) | 4.0 (19.85) |
| Cognitive Function | 87.4 (16.96) | −4.8 (19.78) | −3.2 (16.95) | 88.7 (16.86) | −6.8 (21.70) | −4.6 (21.73) |
| Social Function | 79.7 (24.70) | −3.8 (31.55) | 3.8 (25.90) | 83.0 (23.75) | −4.5 (27.08) | 1.8 (21.93) |
| Pain* | −2.4 (19.40) | −3.6 (30.85) | −2.4 (34.02) | 25.2 (27.68) | 1.1 (26.34) | 2.1 (22.52) |
| Fatigue* | 31.1 (22.57) | 10.3 (26.67) | −1.2 (22.73) | 30.2 (23.84) | 9.0 (26.78) | −2.4 (19.40) |
| EN24 back/pelvic pain* | 29.0 (28.81) | −10.1 (31.89) | −5.6 (35.72) | 28.6 (31.25) | −6.3 (30.62) | −3.0 (25.90) |

*Lower scores indicate reduced symptom severity.

**5505** **Oral Abstract Session**

## Randomized controlled phase III trial of weekly paclitaxel ± ofranergene obadenovec (VB-111) for platinum-resistant ovarian cancer (OVAL Study/GOG 3018).

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**Background:** Ofranergene obadenovec (ofra-vec, VB-111) is a nonreplicating adenoviral vector with a murine pro-endothelin 1 (PPE-1-3X) promoter and pro-apoptotic Fas-tumor necrosis factor receptor 1 (TNFR1) chimeric transgene thought to have a dual mechanism of action: vascular disruption and immune activation. **Methods:** This is a randomized, placebo-controlled, double-blind, multi-center randomized phase III trial (ClinicalTrials.gov identifier: NCT03398655) of ofranergene obadenovec combined with paclitaxel vs paclitaxel with placebo for the treatment of patients with recurrent platinum resistant ovarian cancer (PROC). Patients were randomly assigned 1:1 to receive IV VB-111 $1x10^{13}$ viral particles (VPs) every 8 weeks with weekly IV paclitaxel 80 mg/m2 or placebo with paclitaxel until disease progression. The dual primary endpoints were overall survival (OS) and progression free survival (PFS) as assessed by Blinded Independent Central Review (BICR). **Results:** Between December 2017 and March 2022, 409 patients were randomized at 86 clinical sites in US, Israel, Spain, Poland and Japan. The median PFS was 5.29 months in the VB-111 arm and 5.36 months in the control arm; hazard ratio (HR) 1.03 (CI: 0.83-1.29, p = 0.7823), and median OS with was 13.37 months vs. 13.14 months HR 0.97 (CI: 0.75–1.27 p = 0.8440). Objective response rates (ORR) were similar in both arms: RECIST 1.1 ORR was 28.9% with VB-111 vs. 29.6% with control (CA-125 ORR 41.1% vs 49.4%). In both treatment arms response to CA-125 was a substantial prognostic factor for both PFS and OS. In the VB-111 arm, the HR in CA-125 responders compared to non-responders was for PFS HR 0.2428 (CI: 0.1642-0.3588), and for OS HR 0.3343 (CI: 0.2134-0.5238). Safety profile was consistent with the known safety profile of ofra-vec and was characterized by common transient flu like symptoms such as fever and chills. **Conclusions:** The addition of ofranergene obadenovec to paclitaxel did not improve PFS or OS. Clinical trial information: NCT03398655. Research Sponsor: VBL Therapeutics.

**LBA5506** **Oral Abstract Session**

# Durvalumab with paclitaxel/carboplatin (PC) and bevacizumab (bev), followed by maintenance durvalumab, bev, and olaparib in patients (pts) with newly diagnosed advanced ovarian cancer (AOC) without a tumor BRCA1/2 mutation (non-tBRCAm): Results from the randomized, placebo (pbo)-controlled phase III DUO-O trial.

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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, 2023, issue of the *Journal of Clinical Oncology*.**

# Luveltamab tazevibulin (STRO-002), an anti-folate receptor alpha (FolRα) antibody drug conjugate (ADC), safety and efficacy in a broad distribution of FolRα expression in patients with recurrent epithelial ovarian cancer (OC): Update of STRO-002-GM1 phase 1 dose expansion cohort.

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**Background:** Luveltamab tazevibulin (luvelta) is a novel FolRα-targeting ADC with a stable cleavable linker and a 3-aminophenyl hemiasterlin warhead (DAR of 4) that induces cytotoxic and immunologic cell death. Using site-specific conjugation technology, luvelta is designed to target a broad range of FolRα expressing OC. STRO-002-GM1 is a global phase 1 study evaluating luvelta in patients with relapsed OC. We provide updated data from the initial ovarian expansion cohort. **Methods:** The study enrolled advanced OC pts who had progressive platinum resistant (PROC) after 1-3 prior lines or platinum sensitive disease after 2-3 prior lines of platinum chemotherapy. Pts were randomized 1:1 to received luveltamab at 4.3 or 5.2 mg/kg given IV every 3 weeks until disease progression. Prophylactic corticosteroid eyedrops were not required/administered. FolRα expression was not required for study entry but was analyzed retrospectively in archival tissue using the FOLR1 IHC assay (Ventana Medical Systems). The scoring paradigm assessed percentage of cells with any intensity expression (TPS). TPS >25% was selected for further analysis. **Results:** 44 pts were enrolled (23 pts at 4.3 mg/kg and 21 pts at 5.2 mg/kg). For pts with a TPS >25% (n=35), the median prior lines of therapy was 2.5 (range 1-3), 69% had prior bevacizumab treatment, and 83% prior PARP inhibitor treatment. Investigator assessed efficacy data for pts with a TPS >25% are presented in the table. The most common grade ≥ 3 treatment emergent adverse events (TEAEs) included neutropenia (70.5%), arthralgia (18.2%), and anemia (13.6%). G3/4 neutropenia had a higher incidence at 5.2 mg/kg than 4.3 mg/kg (76% vs 65%); most notable for G4 neutropenia (52% vs 22%). 1 pt at each dose level had febrile neutropenia. TEAEs led to dose delay in 80% of pts with a higher incidence at 5.2 mg/kg (95% vs. 65%). TEAEs led to dose reduction in 61% of pts with a higher incidence at 5.2 mg/kg (76% vs. 48%). 1 pt had a G5 sepsis with G4 neutropenia. Neutropenia, arthralgia and anemia were managed with standard medical treatment and dose reductions. **Conclusions:** These dose expansion data confirm activity of luvelta at starting doses ranging from 4.3-5.2 mg/kg in recurrent OC with FolRα expression as low as TPS>25% and supports further clinical study in this population. The global phase 2/3 REFRaME registration study will evaluate luvelta in PROC pts with TPS >25%. Clinical trial information: NCT03748186. Research Sponsor: Sutro Biopharma, Inc.

**Efficacy data for subjects with FolRα TPS>25%.**

| Population | Endpoint | All | 4.3 mg/kg | 5.2 mg/kg |
|---|---|---|---|---|
| **RECIST Evaluable** | | N=32 pts | N=16 pts | N=16 pts |
| | **ORR (95% CI)** | 37.5% (21.1, 56.3) | 31.3% (11.0, 58.7) | 43.8% (19.8, 70.1) |
| | **mDOR (95% CI)** | 5.5m (2.5, 11.0) | 13m (4.5, NE) | 5.4m (2.4, 6.1) |
| **Enrolled** | | N=35 pts | N=19 pts | N=16 pts |
| | **mPFS (95% CI)** | 6.1m (4.1, 7.0) | 6.1m (4.0, 8.3) | 6.6m (2.9, 7.6) |

# Final survival analysis of the phase III OVHIPEC-1 trial of hyperthermic intraperitoneal chemotherapy in ovarian cancer after ten year follow-up.

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**Background:** The randomized, phase 3 OVHIPEC-1 trial (NCT00426257) investigated the addition of hyperthermic intraperitoneal chemotherapy (HIPEC) to interval cytoreductive surgery in patients with stage III epithelial ovarian cancer who were ineligible for primary cytoreduction. OVHIPEC-1 previously demonstrated improved recurrence-free and overall survival after 4.7 years of follow-up. Here, we report the final survival outcomes after ten years of follow-up. In addition, we report new data on the subsequent anti-cancer treatments given after disease progression. **Methods:** Patients were randomized to receive interval cytoreductive surgery with or without HIPEC, after receiving three cycles of neo-adjuvant carboplatin and paclitaxel. Randomization was performed at the time of surgery when either complete (no visible disease) or optimal cytoreduction (residual tumor measuring $<$10mm in diameter) was anticipated. All patients received an additional three cycles of adjuvant systemic chemotherapy. We analyzed survival according to the intention-to-treat principle using stratified log-rank tests and Kaplan-Meier methods. Subsequent lines of therapy were compared between arms. **Results:** At a median follow-up of 10.1 years, 114 of 123 patients (92.7%) who underwent surgery alone and 109 of 122 patients (89.3%) who had surgery-plus-HIPEC experienced recurrence, progression, or death from any cause. Median recurrence-free survival was 10.7 months in the surgery group compared to 14.3 months in the surgery-plus-HIPEC group (HR, 0.63; 95% confidence interval [CI], 0.48-0.83; stratified P$<$0.001). One hundred and eight patients (87.8%) in the surgery group have died as compared to 100 patients (82.0%) in the surgery-plus-HIPEC group. Median overall survival was 33.3 versus 44.9 months (HR, 0.70; 95% CI, 0.53-0.92; stratified P=0.011), respectively. Subsequent anti-cancer therapies, including chemotherapy (platinum and non-platinum based), secondary surgery, poly (ADP-ribose) polymerase (PARP) inhibitors and bevacizumab, were received by 104 patients (84.6%) in the surgery group and 100 patients (82.0%) in the surgery-plus-HIPEC group. The median number of subsequent systemic treatment lines was 2 (IQR 1-3) in both arms. **Conclusions:** This study provides the first long-term survival analysis of HIPEC in ovarian cancer and confirms the benefit of HIPEC in patients with primary stage III epithelial ovarian cancer undergoing interval cytoreductive surgery. No imbalance in subsequent therapy after disease recurrence was found that could explain the improved overall survival after HIPEC. Clinical trial information: NCT00426257. Research Sponsor: Dutch Cancer Society (NKI 2006-4176).

# Hyperthermic intraperitoneal chemotherapy in platinum-sensitive relapsed epithelial ovarian cancer: The CHIPOR randomized phase III trial.

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**Background:** Standard treatment for patients with first platinum-sensitive relapse of epithelial ovarian cancer (EOC) is based on surgery and second-line systemic chemotherapy (CT). The role of hyperthermic intra-peritoneal chemotherapy (HIPEC) remains uncertain. **Methods:** The CHIPOR multicentric randomized phase III trial (NCT01376752), conducted in 31 institutions, enrolled patients with a first platinum-sensitive relapse (platinum-free interval of ≥6 months) of EOC. Patients were treated with 6 cycles of platinum and taxane based CT ± bevacizumab, and those amenable to a complete cytoreductive surgery at the end of CT were enrolled and randomly assigned to receive HIPEC (cisplatin 75 mg/m² at 41°C for 60 min) or not. Randomization was performed during complete cytoreductive surgery, stratified by center, surgical outcome (no residual disease vs residual <0.25 cm), chemotherapy-free interval before relapse, and PARP inhibitor use (yes vs no). The primary endpoint was overall survival (OS). The target sample size was 404 evaluable patients, providing 80% power at 5% alpha after 268 deaths. Secondary endpoints included progression-free survival (PFS), peritoneal PFS, patient-reported outcomes, safety, and postoperative morbidity and mortality (≤60 days after surgery). **Results:** Between May 11, 2011, and May 14, 2021, 415 patients were randomized. Baseline characteristics were balanced between treatment arms. At the data cutoff (Jan 8, 2023), with a median follow-up of 6.2 years, 268 patients (65%) had died. Efficacy results are summarized below. **Conclusions:** HIPEC significantly improves OS and peritoneal PFS of women with first platinum-sensitive relapse of EOC treated with second-line platinum-based CT followed by secondary complete cytoreductive surgery. Ongoing analyses, including patient reported outcome, BRCA status, bevacizumab exposure, and subsequent therapy, will be presented. Clinical trial information: NCT01376752. Research Sponsor: The trial was supported by R&D UNICANCER, by a Clinical Research Hospital Program grant from the French Ministry of Health/Institut National du Cancer and by French national Ligue against cancer.

| Endpoint | | HIPEC (n=207) | No HIPEC (n=208) |
|---|---|---|---|
| **OS** | **Events, n (%)** | 126 (61) | 142 (68) |
| | Median, months (95% CI) | 54.3 (41.9–61.7) | 45.8 (39.9–54.2) |
| | HR (95% CI)* | 0.69 (0.50–0.94), p=0.020 | |
| **Global PFS** | **Events, n (%)** | 180 (87) | 184 (88) |
| | Median, months (95% CI) | 10.2 (9.3–12.1) | 9.8 (8.8–11.9) |
| | HR (95% CI)* | 0.82 (0.64–1.06) | |
| **Peritoneal PFS** | **Events, n (%)** | 151 (73) | 157 (75) |
| | Median, months (95% CI) | 13.1 (10.7–16.3) | 12.2 (9.8–13.1) |
| | HR (95% CI)* | 0.71 (0.54–0.94) | |
| **Postoperative adverse events, n (%)** | **Grade 3/4** | 32 (15) | 22 (11) |
| | Grade 3/4 renal toxicity | 8 (4) | 1 (<1) |
| | Grade 5 | 0 | 3 (1) |
| **Gastrointestinal stoma, n (%)** | | 20 (10) | 10 (5) |

*Stratified on stratification factors. HR = hazard ratio.

**LBA5511** **Clinical Science Symposium**

# An international randomized phase III trial comparing radical hysterectomy and pelvic node dissection (RH) vs simple hysterectomy and pelvic node dissection (SH) in patients with low-risk early-stage cervical cancer (LRESCC): A Gynecologic Cancer Intergroup study led by the Canadian Cancer Trials Group (CCTG CX.5-SHAPE).

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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, 2023, issue of the *Journal of Clinical Oncology*.**

# Randomized phase 2 study of gemcitabine with or without ATR inhibitor berzosertib in platinum-resistant ovarian cancer: Final overall survival (OS) and biomarker analyses.

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**Background:** The multicenter, open-label, randomized phase 2 NCI-9944 study (NCT02595892) demonstrated that addition of ATR inhibitor (ATRi) berzosertib to gemcitabine increased progression-free survival (PFS) compared to gemcitabine alone (HR = 0.57, one-sided log-rank p = 0.044, which met the one-sided significance level of 0.1 used for sample size calculation). Final overall survival (OS) and corresponding biomarker analyses are reported here. **Methods:** Patients (pts) with platinum-resistant high-grade serous ovarian cancer and unlimited previous lines of cytotoxic therapy in the platinum-sensitive setting but no more than one line of cytotoxic therapy in the platinum-resistant setting, were randomized 1:1 to gemcitabine/berzosertib versus gemcitabine alone. Randomization was stratified based on platinum free interval (PFI), PFI$\leq$3 months versus $>$ 3 months. Crossover from gemcitabine to gemcitabine/berzosertib was allowed upon disease progression by RECIST 1.1. OS was a secondary endpoint while preplanned exploratory correlative studies included assessment of DNA repair pathways and replication stress (RS) alterations by targeted gene sequencing and/or immunohistochemistry (IHC). **Results:** Seventy pts were randomly assigned to treatment with gemcitabine/berzosertib (34 pts) or gemcitabine alone (36 pts); 15 pts crossed over from gemcitabine to gemcitabine/berzosertib. At the final OS analysis (92.9% maturity), median follow-up was 53.2 weeks in the gemcitabine/berzosertib and 43 weeks in the gemcitabine alone groups. Median OS in the intent-to-treat (ITT) population was 59.4 weeks in the gemcitabine/berzosertib group versus 43.0 weeks in the gemcitabine alone group (HR 0.79, 90% CI 0.52-1.2, one-sided p = 0.18). However, when patients who crossed over to gemcitabine/berzosertib were excluded from analysis, a significant OS benefit was observed with gemcitabine/berzosertib (HR 0.60, 90%CI 0.37$-$0.97); HR was 0.26 (90% CI 0.1$-$0.7) in pts with PFI$\leq$3 months and 0.89 (90%CI 0.50$-$1.59) in pts with PFI $>$ 3 months. Furthermore, significant OS benefit was observed in pts with RS-low tumors (HR 0.39, 90%CI 0.17$-$0.91, defined as tumors harboring no genomic RS alterations related to loss of RB pathway regulation and/or oncogene-induced RS) but not in pts with RS-high tumors (HR 0.74, 90%CI 0.35$-$1.56). Additional targeted gene sequencing and IHC analyses as well as analyses adjusting for patient crossover will be reported at the meeting. **Conclusions:** In the ITT population, gemcitabine/berzosertib did not significantly improve OS versus gemcitabine alone. Pts with PFI$\leq$3 months and pts with RS-low tumors may derive a survival advantage from addition of berzosertib to gemcitabine in the platinum-resistant setting. Clinical trial information: NCT02595892. Research Sponsor: U.S. National Institutes of Health.

# Correlation of cyclin E1 expression and clinical outcomes in a phase 1b dose-escalation study of azenosertib (ZN-c3), a WEE1 inhibitor, in combination with chemotherapy (CT) in patients (pts) with platinum-resistant or refractory (R/R) epithelial ovarian, peritoneal, or fallopian tube cancer (EOC).

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**Background:** Azenosertib (ZN-c3) is a novel, selective, and orally bioavailable WEE1 inhibitor demonstrating single-agent antitumor activity. Azenosertib may inhibit CT-induced DNA damage repair and provide benefit in pts with platinum R/R EOC. Cyclin E1 amplification/overexpression is present in ≥35% of metastatic ovarian cancer. High expression/amplification of Cyclin E1 is a poor prognostic marker and predictive of lack of response to platinum-based CT. Ovarian models overexpressing Cyclin E1 have exquisite sensitivity to azenosertib *in vitro* and *in vivo*; forced Cyclin E1 overexpression sensitizes cell lines with low endogenous Cyclin E1 to azenosertib. **Methods:** This open-label, multicenter study (NCT04516447) assessed azenosertib + paclitaxel (PAC), carboplatin (Carbo), gemcitabine (GEM), or pegylated liposomal doxorubicin (PLD) in pts with metastatic high-grade serous EOC after ≤2 lines of CT including platinum CT. Primary endpoint is safety and identification of RP2D of each combination. Secondary endpoints include clinical activity. Azenosertib was given continuously or intermittently QD in 21 or 28D cycles until PD or unacceptable toxicity. **Results:** 103 pts were enrolled; at data cut-off, 94 were efficacy evaluable. 26.6% had a partial response (PR) and median progression free survival (PFS) = 9.03 mo (95%CI: 5.52-11.01). Azenosertib + PAC demonstrated the highest ORR [9/18 (50%)], followed by Carbo [9/27 (33.3%)]; ORR for azenosertib + PLD or + GEM was 14.3% (5/35, 2/14 respectively). 80 pts had available Cyclin E1 expression data by IHC; higher Cyclin E1 (H-score >50) correlated with higher ORR and longer PFS (ORR = 31.3% vs 7.7%; PFS = 10.35 vs 3.25 mo, HR=0.3; Table). Frequent Grade ≥3 TEAEs (%) were neutropenia (44.4), thrombocytopenia (30.3), anemia (12.1), leukopenia (11.1), fatigue (10.1), diarrhea (6.1), nausea (5.1), and vomiting (5.1). **Conclusions:** Azenosertib + CT is well tolerated and has encouraging clinical activity, with durable responses in pts with platinum R/R EOC. Pts with Cyclin E1 overexpressing tumors, a subgroup with suboptimal benefits from CT, demonstrated significant improvements in ORR and PFS vs pts with tumors having low expression. These data support a planned trial of azenosertib + CT vs CT alone in Cyclin E1 overexpressing platinum R/R EOC. Clinical trial information: NCT04516447. Research Sponsor: Zentalis Pharmaceuticals.

| | Azenosertib + PAC (n=18) | Azenosertib + Carbo (n=27) | Azenosertib + GEM (n=14) | Azenosertib + PLD (n=35) | Total (N=94) |
|---|---|---|---|---|---|
| ORR, % | 50.0 | 33.3 | 14.3 | 14.3 | 26.6 |
| Pts with IHC Available (N) | 15 | 23 | 13 | 29 | 80 |
| ORR by Cyclin E1 (n/N; %) | | | | | |
| High | 8/15; 53.3 | 7/18; 38.9 | 2/11; 18.2 | 4/23; 17.4 | 21/67; 31.3 |
| Low | 0/0; 0 | 0/5; 0 | 0/2; 0 | 1/6; 16.7 | 1/13; 7.7 |
| mPFS, mo | 7.36 | 4.24 | NE | 9.03 | 9.03 |
| mPFS by Cyclin E1, mo | | | | | |
| High | 7.36 | 10.35 | NE | 11.01 | 10.35 |
| Low | NE | 2.14 | NE | 3.75 | 3.25 |
| HR | NE | 0.1 | NE | 0.4 | 0.3 |

# A phase II trial of palbociclib combined to letrozole after progression on second-line chemotherapy for women with ER/PR-positive high-grade serous or endometrioid ovarian, fallopian tube, or peritoneal cancer: LACOG 1018.

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**Background:** Treatment options for patients with high-grade ovarian serous (HGSC) or endometrioid carcinoma (HGEC) who progress after receiving chemotherapy for recurrence are limited. **Methods:** LACOG 1018, a phase II, single-arm, multicenter trial evaluated the efficacy of letrozole 2.5mg/day po continuously plus palbociclib 125mg/day po for 21 days in 28-day cycles in patients with histologically proven ovarian HGSC or HGEC, fallopian tube or peritoneal cancer who had progressed on prior chemotherapy for locoregional recurrence or metastatic disease (at least one platinum-based regimen). Patients had centrally confirmed ER and/or PR positivity ($>$ 10% by immunohistochemistry) and ECOG PS 0-2. The primary endpoint was progression-free survival (PFS) at 12 weeks by RECIST 1.1. Secondary endpoints were overall survival (OS), overall response rate (ORR), clinical benefit rate (CBR) and safety. Tumor evaluations were performed every 6 weeks until week 24. Sample size was calculated as 31 patients for the primary endpoint (90% power to detect a two-sided significance level of 5%, 45% PFS at 12 weeks) and 39 patients for secondary endpoints considering 10% drop-out. NCT03936270. **Results:** A total of 41 eligible patients were included in five Brazilian centers between Feb2020-Jan2022 (table). The PFS-week12 rate was 63.4% (95%CI 46.8 – 76.1). At the time of analysis (cut-off date Jan 18th, 2023) median follow-up was 18.1 months (95%CI 12.9 – 24.3), and 37 PFS events had occurred. Median PFS was 4.2 months (95%CI 2.7 – 5.5) and median OS was 13.4 months (95% CI 10.4 – 20.1). The ORR was 7.7% (N=3 PR) and the CBR was 71.8%. Treatment-related adverse event rates of any grade and grade 3-4 were 95.1 % and 51.2 %, respectively. Grade 3-4 neutropenia was reported in 17 (41.5%) patients, and febrile neutropenia in 1 (2.4%). Only one patient (2.4 %) discontinued the treatment due to toxicity. At the cut-off date, three patients remained on treatment. **Conclusions:** Palbociclib combined to letrozole demonstrated a significant efficacy in terms of PFS rate at 12 weeks (63.4%) and CBR (71.8%), with no new safety concerns in women with recurrent advanced and metastatic hormone receptor-positive ovarian cancer. These results warrant further investigation of palbociclib plus letrozole in high-grade ovarian cancer. Clinical trial information: NCT03936270. Research Sponsor: Pfizer.

| Characteristic | N (%) |
|---|---|
| Age, median (range) - years | 60.8 (42.6-82.8) |
| ECOG 0-1 | 40 (97.6%) |
| Previous line of systemic chemotherapy | |
| 2 | 23 (56.1%) |
| 3 | 15 (36.6%) |
| 4 | 3 (7.3%) |
| Platinum-resistant | 13 (31.7%) |
| Ca125 ≥ UNL | 33 (84.6%) |
| BRCA mutated | 4 (9.7%) |

**5515** **Poster Discussion Session**

# Initial efficacy and safety results from ENGOT-ov60/GOG-3052/RAMP 201: A phase 2 study of avutometinib (VS-6766) ± defactinib in recurrent low-grade serous ovarian cancer (LGSOC).

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**Background:** LGSOC is a RAS/MAPK pathway driven cancer that constitutes ≤10% of ovarian cancer. There are no FDA approved treatments specifically for LGSOC. Avutometinib is a novel small molecule RAF/MEK clamp. Focal adhesion kinase (FAK) activation is a resistance mechanism to RAF/MEK inhibition, and defactinib, a small molecule inhibitor of FAK, has shown synergistic antitumor activity with avutometinib in preclinical models. The combination of avutometinib and defactinib has demonstrated a high rate of confirmed and durable responses (overall response rate [ORR] = 46%) in recurrent LGSOC (Banerjee S, ESMO 2021). **Methods:** A registration-directed phase 2, adaptive, multicenter, randomized study was initiated to evaluate avutometinib ± defactinib in patients with *KRAS* mutant (mt) and *KRAS* wild-type (wt) recurrent LGSOC to identify the optimal regimen based on confirmed ORR by blinded independent central review (Part A) and determine the efficacy of the optimal regimen (Part B) (NCT04625270). Pts were randomized to avutometinib 4 mg orally (PO), twice weekly, 3 weeks on, 1 week off (mono) or avutometinib 3.2 mg PO twice weekly + defactinib 200 mg PO BID 3 weeks on, 1 week off (combo). Key inclusion criteria include histologically confirmed recurrent LGSOC, known *KRAS* status and prior systemic therapy with platinum chemotherapy. Unlimited additional prior lines, including prior MEK inhibitor, were permitted. Here we present efficacy results from Part A (evaluable patients, N=59) and safety data from all pts enrolled (N=121). **Results:** In Part A, the median number of prior systemic regimens was 3 for mono, and 4 for combo. In evaluable patients, a confirmed ORR of 7% (2/30) was observed for mono (13% *KRAS* mt, 0% *KRAS* wt), and an ORR of 28% (8/29) was observed for combo (27% *KRAS* mt, 29% *KRAS* wt). Two of 4 patients previously treated with a MEK inhibitor showed a confirmed partial response (PR) on the combination arm. A high disease control rate (PR or SD ≥ 8 weeks) was observed for both mono (90%) and combo (93%). The majority of treatment related adverse events (AEs, any grade) for combo (N=57) were mild to moderate. The most common Grade ≥3 AEs for combo were blood CPK increase (15.8%), fatigue (5.3%), diarrhea (3.5%), dermatitis acneiform (1.8%), and rash (1.8%). A similar AE profile was observed for mono (N=64). Most AEs were manageable/reversible. On the combo arm, 90.6% (±20%) of planned doses were given and 9% (n=5) of pts discontinued due to AEs [asymptomatic elevated blood CPK (n=3) and fatigue (n=2)]. **Conclusions:** The interim data support avutometinib + defactinib as an active go-forward regimen in heavily-pretreated recurrent LGSOC, regardless of *KRAS* status. No new safety signals were observed, and most AEs were mild to moderate. Enrollment continues in Part B for the combination of avutometinib and defactinib. Clinical trial information: NCT04625270. Research Sponsor: Verastem Oncology.

**5516** **Oral Abstract Session**

## Camrelizumab plus apatinib in patients with advanced or recurrent endometrial cancer after failure of at least one prior systemic therapy: A single-arm phase II trial.

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**Background:** The first stage results of a Simon's two-stage single-arm phase II trial showed promising antitumor activity and manageable safety of camrelizumab (a humanized anti-PD-1 monoclonal antibody) plus apatinib (a highly selective VEGFR2 inhibitor) in patients with advanced or recurrent endometrial cancer after failure of prior systemic therapy. Here, we report the primary results of this trial. **Methods:** This open-label, single-arm, phase II trial used a minimax Simon's two-stage design. Patients with advanced or recurrent endometrial cancer that had progressed after at least one prior systemic therapy were treated with camrelizumab (200 mg, intravenously, every two weeks) and apatinib (250 mg, orally, daily) on a four-week cycle until disease progression or intolerable toxicity. The primary endpoint was the objective response rate per Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1. Other assessed endpoints were disease control rate, time to response, duration of response, time to treatment failure, progression-free survival, overall survival, and treatment-related adverse events. **Results:** Between January 20, 2020 and October 14, 2022, 36 patients (median age: 60 [range: 29, 76] years; 17 [47.2%] had Eastern Cooperative Oncology Group [ECOG] performance status 1; 15 [41.7%] had received at least two prior systemic therapies) were enrolled. At the date of data cutoff (December 31, 2022), the median follow-up time was 13.9 (interquartile range: 5.8-23.2) months. All 36 patients were evaluable for efficacy, the confirmed objective response rate was 44.4% (95% CI: 27.9%, 61.9%) and the conformed disease control rate was 88.9% (95% CI: 73.9%, 96.9%), with two complete response, 14 partial response, and 16 stable disease. The median progression-free survival was 6.4 (95% CI: 5.2, 13.0) months. The treatment-related adverse events of grade 3 or greater occurred in 19 (52.8%) patients, with increased gamma-glutamyltransferase (8 [22.2%]), hyperglycemia (4 [11.1%]), hypertension (4 [11.1%]) and increased direct bilirubin (4 [11.1%]) being most common. Reactive cutaneous capillary endothelial proliferation occurred in 6 (16.7%) patients and all were grade 1 or 2. No treatment-related death occurred. **Conclusions:** Camrelizumab plus apatinib show promising antitumor activity and manageable toxicity in patients with advanced or recurrent endometrial cancer after failure of prior systemic therapy and warrant further investigation. Clinical trial information: ChiCTR2000031932. Research Sponsor: National Natural Science Foundation of China (No. 82002758).

**5517** **Poster Discussion Session**

## A phase II basket trial of dual anti–CTLA-4 and anti–PD-1 blockade in rare tumors (DART) SWOG S1609: The vulvar cancers.

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**Background:** Dual checkpoint inhibition with Anti-PD-1 and anti-CTLA4 checkpoint inhibitors have proven to be effective in several malignancies but their potential role in various rare solid cancers is yet to be established. The efficacy of immunotherapy in vulvar cancer patients has not been explored. This study presents the first results of ipilimumab and nivolumab in vulvar cancers (cohort 35) of the SWOG S1609 Dual Anti-CTLA-4 & Anti-PD-1 blockade in Rare Tumors (DART) trial. **Methods:** DART is a prospective, open-label, multicenter/multi-cohort phase 2 clinical trial of ipilimumab (1mg/kg intravenously every 6 weeks) plus nivolumab (240mg intravenously every 2 weeks). The primary endpoint was objective response rate (ORR) (RECIST v1.1) (confirmed complete (CR) and partial responses (PR)); progression-free survival (PFS), overall survival (OS), stable disease (SD) $>$ 6 months, and toxicity are secondary endpoints. **Results:** Sixteen evaluable patients (median age, 55.5 years) were analyzed. 14 cases were of squamous cell carcinoma histology and 2 were of poorly differentiated carcinoma. ORR was 18.8% (3/16, 25% when including one unconfirmed PR). There was 1 CR (SCC; PFS of 465 days) and 2 PR (both SCC; one with 57% regression with PFS of 1022 days, another with 53% regression with PFS of 501 days). Of note, there was one SCC patient with unconfirmed PR that showed 69% regression with PFS of 209 days. Overall clinical benefit rate (CBR; no progression $>$ 6months) was 31.3% (5/16). The median PFS was 2.2 months, 6-month PFS 33%, 1-year PFS 20%. The median OS was 7.6 months, 6-month OS 62%, 1-year OS 44%. The most common adverse events were diarrhea, fatigue, pruritus, anorexia, and nausea (25%, n = 4 each). Grade 3-4 adverse events occurred in 25% of patients (n = 4). There was 1 grade 3-4 adverse event (6.7%) that led to discontinuation, and 1 (6.7%) grade 5 death adverse event. **Conclusions:** Ipilimumab plus nivolumab in vulvar cancers resulted in an ORR of 18.8% and CBR of 31.3%, with durable responses seen. Correlative studies to determine response and resistance markers are ongoing. Expanded prospective studies exploring the role of immunotherapy in vulvar cancers are warranted. Clinical trial information: NCT02834013. Research Sponsor: U.S. National Institutes of Health; Bristol-Myers Squibb.

**5519** **Poster Discussion Session**

# Efficacy and final safety analysis of pre- and co-administration of nivolumab (Nivo) with concurrent chemoradiation (CCRT) followed by Nivo maintenance therapy in patients (pts) with locally advanced cervical carcinoma (LACvCa): Results from the phase I trial, GOTIC-018.

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**Background:** LACvCa is associated with a poor prognosis, and CCRT is the standard treatment for LACvCa pts. Anti-PD1 monoclonal antibodies are associated with increased survival in recurrent or persistent CVCa pts; thus, Nivo may enhance antitumor immune responses. We previously reported that the addition of pre- and co-administration of Nivo was safe and feasible in the acute phase in pts with LACvCa who were treated with CCRT (GOTIC-018; JMA-IIA00425). Herein, we report the efficacy and final safety of GOTIC-018. **Methods:** The GOTIC-018 study was a multicenter, multi-cohort phase I study of Nivo plus CCRT in pts with LACvCa. The treatment plan in cohort A was co-administration of Nivo (240 mg/body once every 2 weeks) with CCRT followed by Nivo maintenance therapy for 52 weeks. The treatment plan in cohort B was pre-CCRT (two doses of Nivo before CCRT) followed by co-administration of Nivo with CCRT followed by Nivo maintenance therapy. Efficacy was evaluated using the RECIST v1.1. Tumor biopsies were obtained before treatment in each cohort and after two doses of Nivo in cohort B. **Results:** 30 pts (15 in each cohort) were enrolled between May 2019 and June 2021. There were one stage IVA, 11 stage IIIB, 16 stage II, and two stage IB2 tumors based on FIGO 2008. 28 squamous cell and 2 adenocarcinomas were included. 27 of the 30 tumors were positive for high-risk HPV, 14 were positive for PD-L1 TPS, and all tumors were microsatellite stable. The median follow-up was 15.2 months. The median number of Nivo cycles was 30 and 32 for cohorts A and B, respectively. 26 pts completed the study protocol, two discontinued Nivo due to AEs, and two withdrew their consent during the maintenance phase. Ten and eight pts in cohorts A and B, respectively, required Nivo interruption. The best overall response rates were 100% and 93.3% in cohorts A and B, respectively. A total of 73.3% of the pts achieved a complete response in each cohort. The 12-months progression-free survival rate was 100% of the evaluable 29 pts for each cohort. The most common grade $\geq$ 3 AEs were neutropenia (60.0 and 26.7% in cohorts A and B, respectively), followed by diarrhea (13.3 and 26.7%, respectively), and anemia (13.3 and 16.7%, respectively). Grade $\geq$ 3 irAEs were observed in two (13.3%) and one (6.7%) pts in cohorts A and B, respectively. The most common grade $\geq$ 3 irAEs were increased serum lipase levels in two pts. In addition, 6 of the 12 tumors that were PD-L1 TPS negative turned positive after two doses of Nivo in cohort B. **Conclusions:** The addition of pre- and co-administration of Nivo followed by Nivo maintenance therapy appears safe and shows encouraging efficacy in pts with LACvCa treated with CCRT. Pre-CCRT administration of Nivo may affect the tumor microenvironment. Clinical trial information: JMA-IIA00425. Research Sponsor: Ono.

## Neoadjuvant camrelizumab plus chemotherapy for locally advanced cervical cancer (NACI study): A prospective, single-arm, phase II trial.

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**Background:** First-line treatments for locally advanced cervical cancer (LACC) have limited efficacy and neoadjuvant chemotherapy (NACT) is an emerging approach, however, two-thirds of patients (pts) respond to it and pts without response benefit little. PD-1 inhibitors have shown promising role in recurrent or metastatic cervical cancer. This study aims to evaluate the efficacy and safety of preoperative PD-1 inhibitor camrelizumab combined neoadjuvant therapy for LACC. **Methods:** The study is designed as a multicenter, open-label, single-arm, prospective phase II study. Pts are enrolled if they had previously untreated LACC (2018 FIGO staged IB3, IIA2 and IIB/IIIC1r (tumor size $>$ 4cm). Eligible pts will receive neoadjuvant chemo-immunotherapy (NACIT), defined as one cycle of cisplatin (75-80 mg/m2, iv) plus nab-paclitaxel (260 mg/m2, iv) NACT and subsequent two cycles of camrelizumab (200mg, iv) combined NACT. Either surgery or concurrent chemoradiotherapy are conducted according to the response as per the Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1. The primary endpoint was objective response rate (ORR), and the secondary endpoints were pathological complete remission (pCR) rate, rate of postoperative adjuvant treatment, event-free survival, overall survival and safety. **Results:** From Dec 1, 2020 to Feb 1, 2023, 83 pts were enrolled, and 78 pts were evaluated for response. The ORR was 100% (95%CI, 95.38 to 100), with 14 (17.95%) complete response (CR) and 64 (82.05%) partial response. Regarding the pathological findings of 76 pts who underwent radical surgery, 30 (39.47% (95%CI, 28.44 to 51.35)) pts achieved pCR, while 17 (22.37%) needed postoperative adjuvant treatment as indicated in NCCN guideline, of who 14 had positive pelvic nodes, positive surgical margin, and/or positive parametrium and the other three met Sedlis criteria. RECIST CR was significantly associated with pCR ($P = 0.016$). Pre-treatment PD-L1 expression (Combined Positive Score) was a predictive biomarker for RECIST CR ($P = 0.036$) but not for pCR ($P = 0.078$) in these evaluated patients. Grade 3 or 4 treatment-related adverse events occurred in 35 (44.87%) pts during NACIT; the most common were lymphocytopia (25.64%), neutropenia (12.82%) and leucopenia (8.97%). **Conclusions:** NACIT for LACC demonstrated extremely high ORR and pCR rate with manageable toxicity profile, and greatly reduced the need of postoperative adjuvant therapy. Clinical trial information: NCT04516616. Research Sponsor: Jiangsu Hengrui Medicine, Lianyungang, China; Chinese Clinical Medical Research Center for Obstetrical and Gynecological Diseases.

# Toxicity profile and discordance between patients/physicians regarding niraparib maintenance in recurrent ovarian cancer (ROC) patients: Lessons from the NIQOLE real-life study—GINECO study.

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**Background:** Niraparib (NI) maintenance is a standard of care in platinum-sensitive ROC. Based on pivotal randomized trials, toxicity profile appears manageable through adapted drug dosing. However, data on tolerance and feasibility for unselected patients (pts) are missing, especially regarding pts' reported adverse events (AE). **Methods:** NIQOLE study is a real-life longitudinal multicenter, phase IV study in ROC pts treated with NI maintenance. NI starting dose was adapted to pts' weight and platelet count. The primary endpoint was to describe physicians' reported AE (NCI-CTC-AE, grading from 0 to 5) leading to treatment modifications (TM), defined by dose reduction or treatment interruption/discontinuation from baseline to month 3 and delay of first TM. Secondary endpoints included duration of treatment and pts' reported AE. Progression rates were exploratory endpoints. Owing to a digital device, pts provided remoted weekly AE (NCI PRO-CTC-AE, grading from 0 to 3) which were accessible to investigators. Concordance between the main symptomatic AEs reported by pts and those reported by physicians was analyzed. **Results:** 139 pts were treated: median age 70 [44-88], high-grade serous histology 91%, BRCA mutation 5%, first relapse 72%, prior bevacizumab 71%. The median delay from platinum-based regimen and NI was 49 days [15-109]. NI starting dose was 200 mg in 80% of pts and the median treatment duration was 5.6 months [0.2-21]. Progression rates at 3 and 6 months were 19 and 45%, respectively. At 3 months, 60% (n=84%) of pts had at least one TM, of whom 47% (n=66) were treatment-related AEs: dose reduction in 17/66 (26%), interruption in 53/66 (80%) and discontinuation in 11/66 (17%). The first AE inducing TM occurred at 22 days (median) [2 -91]. Thrombocytopenia was the main AE leading to TM (70% of cases). 24% of AEs were grade 3-4. Remoted PRO-CTC-AEs were acknowledged by physicians in 59% of cases of whom 31% led to adaptation of pts' care. During the 3 months, 98% of pts reported symptomatic AEs (including nausea, constipation, fatigue, dry mouth and insomnia), of which 66% were grade 3. There was a very poor correlation (<0.20) between symptomatic AEs reported by the pts vs by the physicians (table). **Conclusions:** In real life, despite initial individual dosing, NI maintenance requires frequent TM during the first 3 months of treatment. There is a strong discrepancy between symptomatic AEs regularly captured by pts and those reported by physicians during clinics. Next generation of clinical trials should integrate pts' perspective to better assess toxicity and manage treatment course. Clinical trial information: NCT03752216. Research Sponsor: GSK.

| Main symptomatic Aes | Patients (%) | | Physicians (%) | |
|---|---|---|---|---|
| | All | Severe* | All | Severe** |
| Fatigue | 93 | 32 | 43 | 2 |
| Nausea | 73 | 12 | 26 | 0 |
| Constipation | 86 | 40 | 26 | 2 |
| Dry Mouth | 78 | 22 | 9 | 0 |
| Insomnia | 90 | 22 | 12 | 0 |

*Grade 3 according to PRO-CTC-AE, ** Grade 3 and 4 according to CTC-AE.

**5522** **Poster Discussion Session**

## The Normal Risk Ovarian Screening Study (NROSS): Twenty-one year update.

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**Background:** The Normal Risk Ovarian Screening Study (NROSS) tested a two-stage screening strategy in post-menopausal women at conventional hereditary risk where significantly rising CA125 prompted transvaginal sonography (TVS) and abnormal TVS prompted surgery to detect ovarian cancer. **Methods:** A total of 7,856 healthy postmenopausal women were screened annually for a total of 50,596 women-years in a single arm study (NCT00539162). Serum CA125 was analyzed with the Risk of Ovarian Cancer Algorithm (ROCA) each year. If risk was normal ( $<$ 1:2000), women returned in a year. If risk was elevated ( $>$ 1:500), TVS was undertaken immediately and if risk was intermediate, CA125 was repeated in 3 months, risk recalculated, and the participant re-triaged. An average of 2% of participants were referred to TVS annually. **Results:** Thirty-four patients were referred for operations detecting 15 ovarian cancers and 2 borderline tumors with 12 in early stage (I-II). In addition, 7 endometrial cancers were detected with 6 in early stage. Thus, the positive predictive value (PPV) of the NROSS trial was 50% (17/34) for detecting ovarian cancer and 74% (25/34) for any cancer, far exceeding the minimum acceptable study endpoint of 10% PPV. As 4 ovarian cancers and 2 borderline tumors were diagnosed within a year of each participant's last normal risk, the sensitivity for detecting ovarian and borderline cancer was 74% (17/23) and 70% of ROCA-detected cases (12/17) were in stage I-II. NROSS screening reduced incidence of late stage (III-IV) disease by 34% compared to the United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) control arm and by 30% compared to US SEER values. Results of our NROSS trial contrast dramatically with those of the recently reported UKCTOCS that showed only a modest 14% early-stage shift, underlying a lack of reduction in mortality. Across multiple randomized trials of mammography, those trials that demonstrated at least a 20% late-stage incidence reduction had a significant mortality reduction, whereas those with less of a stage shift did not. **Conclusions:** An elevated ROCA, characterized by a significantly rising CA125, prompted referral of 2% of participants to TVS each year and required only 2 operations to detect each case of ovarian cancer, indicating that CA125 used in this way is adequately specific for effective screening. While the NROSS trial was not powered to detect reduced mortality, the high specificity, PPV and marked stage shift support further development of this strategy. Clinical trial information: NCT00539162. Research Sponsor: U.S. National Institutes of Health; Cancer Prevention Research Institute of Texas; UT MD Anderson Moon shot; Concord (MA) Detect Ovarian Cancer Early Fund.

**5523** **Poster Discussion Session**

## The effects of the Covid-19 pandemic on practice patterns and outcomes in patients diagnosed with gynecologic malignancies in the United States.

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**Background:** The Covid-19 pandemic caused historic disruptions in the United States healthcare system due to many factors, including a lack of medical equipment and pharmaceutical availability, over-capacitated hospital censuses, and limited essential workers. The short- and long-term effects on patients diagnosed with gynecologic malignancies during this time have yet to be delineated. **Methods:** The National Cancer Database (NCDB) was queried for patients diagnosed with ovarian, uterine, and cervical malignancies from 2019 (pre-covid) to 2020 (covid). Descriptive statistics of practice patterns and outcomes were performed and compared using IBM SPSS Statistics (version 29.0). **Results:** Within the NCDB, 10,261 patients were diagnosed with ovarian cancer in 2019 compared to 8,501 in 2020. A significantly higher proportion of ovarian cancer patients were diagnosed with stage IV disease at diagnosis in 2020 (32.7%) compared to 2019 (30.9%), $p = 0.007$. Patients were less likely to undergo primary debulking surgery during covid (37.7%) compared to pre-covid (40.5%), $p < 0.001$. There was no significant difference in time from diagnosis to initiation of treatment (median: 9 vs. 9 days), nor was there a difference in the proportion of patients undergoing cytoreductive surgery to no gross residual disease (54.3 vs. 54.3%). 42,828 patients were diagnosed with uterine cancer in 2019 compared to 37,431 in 2020. A significantly higher proportion of uterine cancer patients were diagnosed with stage IV disease at diagnosis in 2020 (8.7%) compared to 2019 (8.2%), $p = 0.016$. The median time from diagnosis to initiation of treatment was 28 days in 2020 compared to 30 days in 2019, $p < 0.001$. The proportion of uterine cancer patients receiving primary radiation was higher during covid (1.7% vs. 0.5%), $p < 0.001$. Additionally, the proportion of uterine cancer patients receiving primary hormonal management was also higher during covid (2.5% vs. 2.1%, $p < 0.001$). 9,289 patients were diagnosed with cervical cancer in 2019 compared to 7,661 in 2020. A significantly higher proportion of cervical cancer patients were diagnosed with stage IV disease at diagnosis in 2020 (16.6%) compared to 2019 (14.9%), $p = 0.0021$. The median time from diagnosis to initiation of treatment was 31 days in 2020 compared to 32 days in 2019, $p = 0.005$. **Conclusions:** We identified significant variations in practice patterns and outcomes in patients diagnosed with gynecologic malignancies in the United States in 2020 (covid) compared to immediately before covid (2019). Notably, we found a significantly higher proportion of patients presenting with advanced disease stages in all queried ovarian, uterine, and cervical cancer patients. Long-term follow-up and survival outcomes are currently pending. Research Sponsor: None.

**5524** **Poster Session**

## Active bone marrow-sparing to reduce the incidence of grade 3+ acute hematologic toxicity in patients with locally advanced cervical cancer who receive chemo-radiotherapy: A single-center prospective randomized controlled trial.

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**Background:** Acute haematologic toxicity is the most common side effect of chemoradiotherapy in patients with locally advanced cervical cancer .We aim to test the efficacy of single-photon emission computed tomography-defined active bone marrow-sparing volumetric-modulated arc therapy in reducing grade 3+ acute hematologic toxicity (HT) in locally advanced cervical cancer patients treated with chemoradiotherapy. **Methods:** This was a prospective, single-center, open label, randomized clinical trial that enrolled locally advanced cervical cancer patients. Participants were randomized to the $^{99m}$Tc sulfur colloid SPECT-defined ABMS VMAT (ABMS group) or control group, who received weekly cisplatin concurrently with volumetric-modulated arc therapy followed by high-dose-rate intracavitary brachytherapy. The ABMS group additionally received SPECT-defined ABM dose constraints. The primary endpoint was the incidence of grade 3+ acute hematologic toxicity.Secondary objectives included acute gastrointestinal toxicity, planning Target Volume (PTV) coverage, dosimetric parameters of organs at risk (OARs), progression-free survival (PFS), overall survival (OS). **Results:** A total of 192 FIGO stage IB-IIIB patients were randomized treated (96 each in the ABMS control groups). The median follow-up was 24.0 months. The incidence of grade 3+ acute hematologic toxicity in the ABMS group was significantly lower than that in the control group (32.3% vs 53.1%, $p<0.01$). The number of patients completing five cycles of cisplatin was 88.5% in the ABMS group and 75% in the control group, and the difference was significant (p=0.02). There were no significant differences in the mean dose to 95%, 97% and 99%of the PTV between the ABMS group (45.1 Gy, 44.6 Gy, and 43.3 Gy, respectively) and the control group (45.4 Gy, 44.8 Gy, and 43.6 Gy). There were no differences in dosimetric parameters of OARs ,acute gastrointestinal toxicity, 2-year PFS or 2-year OS between the two groups. Patients in the control group had nonsignificantly worse 2-year distant metastasis than patients in the ABMS group (17.8% vs. 11.1%, p=0.19). **Conclusions:** ABMS VMAT significantly reduced grade 3+ acute HT and improved chemotherapy delivery compared with the control treatment. We found weak evidence of the effect of ABMS VMAT on distant metastasis. Clinical trial information: ChiCTR-IOR-16010214. Research Sponsor: This study was supported by the Sichuan Medical Association youth innovation project (NO. Q16082.NO.Q21022) and the health commission of YIbin City (NO.2019yw029).

**5525** **Poster Session**

## Neoplastic and blood-based biomarkers of response in patients with advanced endometrial cancer: Results from NRG GY012.

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**Background:** NRG GY012 is a randomized, 3-arm phase II study, comparing olaparib (O) and the combination of cediranib and olaparib (CO) to the reference arm cediranib (C) for metastatic pretreated, endometrial cancer (EC). The trial found a trend towards benefit for CO and no benefit for O compared to C. Archival tumor and prospective blood samples were collected for biomarker analysis. **Methods:** Targeted next-generation sequencing (BROCA-GO) was used to detect pathogenic variants (PV) and loss of heterozygosity (LOH) in DNA from paired blood and archival cancers. The LOH cut-off was identified at 11% for HRD based on testing ovarian cancers with known HRD. Plasma samples collected at baseline, cycle 2 day 1, and end-of-treatment were analyzed via multiplex ELISA for 25 angiogenic and inflammatory circulating protein biomarkers (Angiome); IL6 was of specific interest. Prognostic associations with PFS and OS were analyzed using proportional hazards models (PhM) stratified by histology and adjusted for treatment assignment. Predictive associations (PFS and OS) were analyzed using PhM stratified by histology and including main effects for both treatment assignment and biomarker group plus an interaction term. **Results:** In 97 patients (pts) with evaluable tumor, BROCA-GO identified 370 somatic PV; *TP53* (61%) was the most commonly mutated gene. PV in homologous recombination repair (HRR) genes were identified in 5 cases (5%). Somatic PVs were identified in *BRCA2*, *RAD51B* and *PALB2*. 1 pt had a germline *BRCA1* PV. 2 cases had somatic PV that might restore HRR: 1 case with a somatic BRCA2 PV had somatic PVs in *CHD4* and *TP53BP1*; the *TP53BP1* frameshift PV was present only in the recurrent and not primary cancer. LOH was available for 45 cases. LOH high occurred in 16 (35.6%) cases and was exclusive to EC with *TP53* mutations (p=0.0003). LOH was not associated with outcome in any of the arms. For the circulating biomarker analysis (N=96), median IL-6 was 4pg/ml. IL-6 levels $>$4pg/ml were associated with increased risk of progression (HR: 1.59; 95% CI: (1.04-2.42); p-value=0.032). In predictive analyses, pts with IL-6 $>$ 4 pg/ml receiving C or C+O had increased PFS (3.8 mo vs 1.9 mo) and OS (11.9 mo vs 5.7 mo) compared to pts receiving O, the interaction p value did not reach statistical significance. **Conclusions:** LOH high status was not associated with outcome to O. There were too few cases with HRR PVs to determine their relationship to PARPi response. The restriction of LOH high to cancers with *TP53* mutation may suggest that genomic LOH in ECs correlates better with aneuploidy than with HRR function indicating that at least some biomarkers of PARPi response vary between tumor types. IL-6 levels were prognostic of PFS but were not predictive of either OS or PFS for pts receiving C compared to pts receiving O in this small study. Further analysis of the complete Angiome and integration with the BROCA-GO dataset are ongoing. Clinical trial information: NCT03660826. Research Sponsor: U.S. National Institutes of Health.

**5526** **Poster Session**

## Molecular tumor profiling and therapy selection in advanced gynecological cancers: A retrospective cohort analysis from the Australian Molecular Screening and Therapeutics (MoST) Program.

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**Background:** Gynecological (gyne) cancers are highly diverse with distinct sites of origin and histological subtypes that can limit development of evidence-based therapies. Comprehensive genomic profiling (CGP) has an increasing role in characterizing clinically relevant molecular subsets and in identifying actionable biomarkers with potential to guide therapy selection. **Methods:** MoST (ACTRN12616000908437) is an Australia-wide precision oncology program for adult patients (pts) with advanced cancers and limited treatment options. Tumor specimens are analysed by CGP and genomic results tiered by the level of evidence supporting matched therapies (https://topograph.info). Pts are followed for subsequent treatment and survival. Here, we present data for the MoST gyne cancer cohort. **Results:** Between Sept 2016 and Oct 2022, 533 gyne tumors were sequenced, with included pts having a minimum 4 months (mo) follow-up. Key histotypes included: ovarian serous (n=162) and non-serous (n=46) epithelial tumors; uterine carcinomas (n=99) and sarcomas (n=108); cervical carcinomas (n=51); germ cell and sex-cord stromal tumors (n=18); carcinosarcomas (n=33); and vulva/vaginal tumors (n=16). The median number of reported variants was 3 (IQR 2-5) and tumor mutational burden 3.1 mut/Mb (IQR 1.3—5.5, Range 0—284); 9 (2%) tumors were microsatellite unstable; and 22 (4%) had high level loss-of-heterozygosity (confirmed on validated genome-wide assays). The most common pathways involved in this pan-gyne cohort were: p53 (n=287, 54%), PI3K/AKT (n=227, 43%), cell cycle (n=182, 34%), and mitogen-activated protein kinase (n=91, 17%). Pathogenic mutations in *BRCA1/2* were identified in 29 tumors (5%; 18 in ovarian serous cancers), whereas 81 tumors (15%) had alterations in other homologous recombination genes, most commonly uterine sarcomas (n=32, 30%). Actionable genomic biomarkers matched to a clinically active treatment (TOPOGRAPH tier 1-3) were identified in 207 (39%) tumors. In 19 pts (3.5%) who received Tier 1-3 matched therapy after CGP, a trend towards longer survival was observed (median OS 22.3 mo, 95% CI 17.3 to not reached) compared to those receiving unmatched therapy (n=65, median OS 14.9 mo, 10.2 to 22.1, p=0.052) following CGP. No OS difference was seen in pts who received matched investigational therapy (Tier 3B/4, n=31, median OS 17.0 mo, 8.1 to NR) versus only unmatched therapy (n=118, median OS 14.0 mo, 11.3 to 22.5; HR 0.97, 0.57 to 1.64; p=0.91). **Conclusions:** CGP identified actionable genomic results in nearly half of advanced gyne cancers, with enrichment in particular histotypes that supports testing above current standard of care. Trends in prolonged OS with subsequent matched therapies may be better realized with earlier testing and improved drug/clinical trial access. Research Sponsor: Australian Government.

**5527** **Poster Session**

## Association of HRD ovarian cancer by RAD51 with hot immune microenvironment: Translational analyses of MITO 16A/MaNGO-OV2 trial.

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**Background:** Homologous recombination repair (HRR)-deficient Ovarian Cancer (OvC) is sensitive to PARP inhibitors and platinum salts. Genomic HRR-deficiency (HRD) tests (i.e. Myriad MyChoice) are currently used to guide treatment selection in the maintenance setting. However, they are showing a limited predictive value, they are expensive and static, i.e. unable to capture the restoration of the HRR functionality, as a mechanism of drug resistance. **Methods:** We performed the functional and dynamic RAD51 test on 164 patients with high-grade serious OvC, enrolled in the MITO16A/MANGO OV2 trial and treated with first-line therapy containing carboplatin, paclitaxel, and bevacizumab. The RAD51 assay included the immunofluorescence of gH2AX (as a marker of Double Strand Breaks DNA damage), BRCA1 and RAD51 nuclear foci. Stromal Tumor Infiltrating Lymphocytes (TIL) by Immunohistochemistry, and gene expression profile were performed on the same samples. **Results:** RAD51 assay was informative on 70% (115/164) of the samples. On evaluable samples, median gH2AX score was 57%. BRCA1 foci by immunofluorescence were detected on 55% (49/112) of the samples; 45% (63/112) of the tumors did not show BRCA1 foci likely due to germline or somatic BRCA1 mutations, or BRCA1 promoter hypermethylation. RAD51 identified 69% (79/115) of all tumors as HRD, with a median RAD51 score of 8.8%. HRD tumors presented a statistically significantly higher TIL content than HRR-proficient ones ($p = 0.03$). **Conclusions:** Our preliminary results confirmed the feasibility of the RAD51 functional assay on primary untreated OvC. The association between HRD by RAD51 and TIL content encouraged to investigate the efficacy, in clinical trials, of the combination of PARPi and immune-checkpoint inhibitors on selected patients (i.e. HRD by RAD51 and TIL high). Gene expression profile and comparison of the HRD status by RAD51 and genomic HRD (both Myriad MyChoice and academic) and correlations with clinical outcomes will be available for the meeting. Research Sponsor: Associazione Italiano Ricerca sul Cancro (AIRC).

**5528** **Poster Discussion Session**

## Advanced cervical cancer therapy: Comparison of contemporary expert and healthcare professional recommendations from an online treatment decision tool.

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**Background:** Practice patterns for the management of advanced cervical cancer are rapidly evolving given the emergence of novel treatment options. We developed an online Interactive Decision Support Tool (IDST) for advanced cervical cancer to provide expert guidance to healthcare professionals (HCPs). **Methods:** With input from 5 experts, an IDST was developed for patient scenarios with newly diagnosed (ND) and recurrent/second-line (2L) advanced cervical cancer. The IDST included expert insights on 352 scenarios based on criteria such as adenopathy, disseminated disease status, previous therapy, and actionable biomarkers (PD-L1, MMR/MSI, TMB). Users were asked to enter specific patient criteria and their intended management approach. The IDST then showed the 5 expert recommendations for that specific scenario and HCPs were asked to indicate whether the recommendations changed their intended treatment plan. Expert recommendations vs user-selected therapy for different scenarios were analyzed. We present self-reported practice patterns in this disease setting and the impact of expert recommendations on treatment choice. **Results:** At this interim analysis, 141 unique learners used the IDST, entering 232 unique patient scenarios. Data from the IDST also showed areas of consensus and controversy in treating patients with advanced cervical cancer. For locally advanced, ND, no adenopathy and no metastases, all experts recommended pelvic chemoradiation with or without brachytherapy vs only 61% of HCPs; 16% and 3% of those entering cases for the locally advanced ND setting indicated expert recommendation changed their treatment choice and that barriers impeded the recommendations, respectively. For advanced ND, with adenopathy, metastatic, PD-L1–positive cervical cancers, all experts vs 50% of HCPs chose an immunotherapy-containing platinum-based chemotherapy regimen with/without bevacizumab; 9% of those indicated barriers to implementing expert recommendations. In 2L recurrent disease, all experts chose either single-agent immunotherapy (if PD-L1 positive) or tisotumab vedotin (if PD-L1 negative) vs 45% and 40% of HCPs, respectively; 19% of those selecting 2L therapy in the recurrent setting said the expert recommendations had changed their intended choice. **Conclusions:** Analysis from this IDST indicates differences in practice patterns between experts and HCPs for various case scenarios of advanced cervical cancer. Online decision support tools may increase the number of HCPs making optimal treatment decisions for advanced cervical cancer, particularly when new data, indications, and guideline updates must be considered. Updated and detailed analyses from the IDST will be presented. Research Sponsor: Clinical Care Options.

**5529** **Poster Session**

# SHR-1701 in combination with platinum-based chemotherapy and BP102 (a bevacizumab biosimilar) for persistent, recurrent, or metastatic cervical cancer: Data from a phase 1b/3 study.

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**Background:** Platinum-based chemotherapy (chemo) ± bevacizumab is the standard first-line therapy for cervical cancer, regardless of PD-L1 expression. SHR-1701 is a novel bifunctional fusion protein targeting PD-L1 and TGF-βRII, and shows promising efficacy and controllable safety in pretreated patients (pts) with cervical cancer. This ongoing phase 1b/3 study aims to assess the addition of SHR-1701 to standard first-line therapy. **Methods:** In the phase 1b part, eligible pts had persistent, recurrent, or metastatic squamous-cell carcinoma, adenocarcinoma, or adenosquamous cell carcinoma of the cervix not previously treated with systemic chemo for recurrence or metastasis and not amenable to curative treatment. Prior chemo-radiotherapy was permitted for recurrence, if mono-chemo was used as sensitizer. Pts were given SHR-1701 (30 mg/kg), paclitaxel (175 mg/m$^2$), cisplatin (50 mg/m$^2$) / carboplatin (AUC 5), and BP102 (15 mg/kg) every 3 weeks. The primary endpoints were safety and ORR. **Results:** From Feb 26 to Aug 12, 2022, 31 pts were enrolled. Median age was 55 years (range, 27-71). 24 (77.4%) had squamous-cell carcinoma, and 7 (22.6%) had adenocarcinoma. 20 (64.5%) had metastatic disease, 7 (22.6%) had recurrent cervical cancer, and 4 (12.9%) had persistent cervical cancer. Grade ≥3 treatment-related adverse events (TRAEs) were reported in 25 (80.6%) pts, with the most common being decreased neutrophil count (n=16, 51.6%), decreased white blood cell count (n=12, 38.7%), and anemia (n=8, 25.8%). TRAEs led to discontinuation of any study agent in 8 (25.8%) pts; of note, only 2 (6.5%) pts discontinued SHR-1701 due to TRAEs (grade 3 infusion reaction and grade 3 immune-mediated rash). No treatment-related deaths occurred. Efficacy outcomes are summarized in Table. ORR was 77.4%, with 4 CRs and 20 PRs; responses were ongoing in all 24 responders. DCR was 93.5%. Shrinkage in target lesions was observed in 30 (96.8%) pts. PFS rate at 6 months reached 93.5%. **Conclusions:** SHR-1701 plus platinum-based doublet chemo and BP102 provided a manageable safety profile and potent antitumor activity in pts with persistent, recurrent, or metastatic cervical cancer, supporting the subsequent randomized, double-blind, placebo-controlled phase 3 part. Clinical trial information: NCT05179239. Research Sponsor: Jiangsu Hengrui Pharmaceuticals Co., Ltd.

**Efficacy outcomes.**

| | All pts (n=31) |
|---|---|
| **Best overall response, n (%)** | |
| **CR** | 4 (12.9%) |
| **PR** | 20 (64.5%) |
| **SD** | 5 (15.1%) |
| **PD** | 2 (6.5%) |
| **ORR, % (95% CI)** | 77.4% (58.9-90.4) |
| **DCR, % (95% CI)** | 93.5% (78.6-99.2) |
| **6-month PFS rate, % (95% CI)** | 93.5% (76.6-98.3) |

CR, Complete response; PR, partial response; SD, stable disease; PD; progressive disease; ORR, objective response rate; DCR, disease control rate; PFS, progression-free survival; pts, patients.

**5530** **Poster Session**

## Efficacy and safety of combining PD-1 blockage and human papillomavirus vaccine for patients with relapsed/refractory advanced cervical cancer.

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**Background:** The prognosis for patients with relapsed/refractory advanced cervical cancer is dismal with a 5-year survival rate of 17%. Limited treatment options were available including platin based therapy, antiangiogenic therapy and immune therapy. Immune checkpoint blockage with anti-programmed cell death 1 (PD-1) antibodies had an overall response rate of 17% among a minority of patients. Recently a phase II study showed human papillomavirus (HPV) 16 vaccination amplified PD-1 antibodies in incurable HPV16 positive cancer with an ORR of 33%. But the study enrolled majority were oropharyngeal cancer patients (92%). Here, we designed and conducted phase II clinical trial to assess the efficacy and safety of combining anti-PD-1 antibody and HPV vaccination for patients with relapsed/refract cervical cancer. **Methods:** In this single-arm, single-center phase II clinical trial, patients with relapsed/refract cervical cancer were registered (NCT04096911) and enrolled from Dec, 2019 to Dec, 2022 in Department of Oncology, Northern Jiangsu People's Hospital, Yangzhou, China. All patients received prior radiation therapy and had at least one or more lines of therapies. Duration of follow up for censored patients was 36 months. The recombinant human papillomavirus quadrivalent vaccine (0.5ml) was given subcutaneously on day 0, third month, and $6^{th}$ month. Anti-PD-1 antibody, 200mg was given intravenously every 3 weeks starting on day 1 for up to 2 years. **Results:** As of Dec 21, 2022, thirteen patients were enrolled in the trial. The median age was 55 years (range, 52 to 83 years). The overall response rate was 69.2%. Disease control rate was 84.9%. Median duration of response was 7.07 months (95%CI, 1.94 to 15.8 month). Six patients achieved complete response. Median overall survival was 13.96 month. No grade 3 and 4 toxicity occurred. **Conclusions:** Our study was the first clinical trial using HPV vaccine as therapeutic agent in advance cervical cancer treatment. Up to date, immunotherapy along in cervical cancer had limited response rate less than 20% and the combination therapies was less than 40%. In our study, the overall response of 69.2%, disease control rate of 84.9% and median overall survival of 13.96 months were significantly higher compared with anti-PD-1 antibody alone or any current available regiment combinations in relapsed/refract advance cervical cancer patients. We also found synergistic effect of T cell and B cell plays an important role in our study. It appears neoantigen associated with tumor was easier to initiate immune response in cervical cancer patients. This is the first time to show employing combined immune therapeutic agents only is a novel effective clinical strategy in relapsed/refract advance cervical cancer. Clinical trial information: NCT04096911. Research Sponsor: None.

**5531** **Poster Session**

## The efficacy and safety of tislelizumab plus bevacizumab and chemotherapy as first line therapy in patients with persistent, recurrent, or metastatic cervical cancer: A multicenter, phase II study.

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**Background:** Patients (pts) with persistent, recurrent, or metastatic cervical cancer are at high risk of progression after first line standard treatment with platinum-doublet chemotherapy ± bevacizumab. The addition of programmed death-1 (PD-1) inhibitor to this standard treatment has shown improved survival profiles in pts with PD-L1 positive. This study aims to investigate the efficacy and safety of PD-1 inhibitor (tislelizumab) plus bevacizumab and platinum-doublet chemotherapy as the first line therapy in pts regardless of the PD-L1 expression status. **Methods:** Pts with persistent, recurrent, or metastatic cervical cancer were enrolled and received tislelizumab 200 mg + bevacizumab 7.5 mg/kg + cisplatin 50 mg/m$^2$ or carboplatin AUC5 + paclitaxel 175 mg/m$^2$ IV D1 Q3W. This study comprised two parts: safety run-in (Part 1) and cohort expansion (Part 2). In Part 1, a total of 6 pts were enrolled and underwent safety assessment during the first treatment cycle (21 days). If no more than 2 of 6 pts were observed with dose-limiting toxicity (DLT), pts will be allowed to continue treatment and additional 43 pts will be enrolled (Part 2). The primary endpoint was progression-free survival. A one-sample log-rank test with a total sample size of 49 pts with one sided alpha of 5%, achieved 85% power to detect a difference in PFS between the investigated treatment and historical control. The secondary endpoints were objective response rate (ORR), disease control rate (DCR), duration of response (DOR) and safety and tolerability. **Results:** We report the preliminary results of this study. No DLT was observed among the first 6 pts in Part 1 stage and the study proceeded to the Part 2. Until Oct 28, 2022, a total of 24 pts were enrolled with the median age of 56.0 years. 6 (25.0%) pts were diagnosed with stage IV disease at the study entry and 21 (87.5%) were with squamous cell carcinoma. At the data cutoff time of Nov 30, 2022, among the 19 efficacy evaluable pts, the unconfirmed ORR was 73.7% (14/19, 95% CI: 48.8%-90.8%), and the DCR was 100% (19/19, 95% CI: 82.3%-100.0%). With the median follow up time of 3.8 months, DOR was not reached. The incidence of treatment related adverse events (TRAEs) of any grade was 79.2% (19/24), and grade ≥3 TRAEs occurred in 45.8% (11/24) pts. Most common TRAEs (≥20%) of any grade were anemia (58.3%, 14/24), decreased platelet count (37.5%, 9/24), alopecia (29.2%, 7/24), decreased white blood cell count (25.0%, 6/24), and weight decreased (20.8%, 5/24). Immune related adverse events were all grade 1-2 (16.7%, 4/24). Severe adverse events were reported in 4 (16.7%) pts. **Conclusions:** Tislelizumab plus bevacizumab and chemotherapy showed preliminary promising efficacy and was well-tolerated as the first line therapy in pts with persistent, recurrent, or metastatic cervical cancer. Clinical trial information: NCT05247619. Research Sponsor: BeiGene (Beijing) Co., Ltd.

# A confirmatory trial of modified radical hysterectomy for patients with FIGO stage IB1 cervical cancer with tumor diameter preoperatively estimated at 2 cm or less: Japan Clinical Oncology Group study, JCOG1101.

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**Background:** The standard surgery for Stage IB1 uterine cervical cancer is radical hysterectomy (RH, Piver class III hysterectomy). However, RH is highly invasive, and there is a need to establish less invasive techniques. We conducted a single-arm confirmatory trial (JCOG1101) to evaluate the efficacy and safety of modified radical hysterectomy (MRH) in patients with tumor diameter ≤ 2 cm Stage IB1 cervical cancer (jRCT: jRCTs031180167). **Methods:** From January 2013 to August 2017, 240 patients were enrolled from 40 institutions in Japan. Eligibility criteria included: (1) FIGO 2008 Stage IB1 cervical cancer; (2) histologically proven squamous cell carcinoma, adenocarcinoma (mucinous or endometrioid) or adenosquamous carcinoma; (3) tumor diameter ≤ 2 cm (measured by MRI or conization specimen); and (4) neither distant LN metastasis nor distant metastasis in CT. In case that the cancer could be microinvasive, conization was required to exclude Stage IA cases. The protocol surgery involved cutting the anterior layer of the vesicouterine ligament of the uterus and dissecting regional lymph nodes. Only laparotomy was permitted: laparoscopy and robotic surgery were not allowed. Postoperative irradiation was administered in cases where pelvic LN or parametrial invasion was positive, depth in the cervical wall invasion was ≥ 2/3, or surgical margin was < 1 cm by pathological findings. The primary endpoint was 5-year overall survival (OS). We set the expected 5-year OS of MRH at 95.8% (5-year OS of RH in JCOG0806A, retrospective observational study) and the threshold 5-year OS at 90.8%. **Results:** Among 225 eligible patients, 193 (85.8%) were pT1b1 (UICC 7th), and 184 (81.8%) had pathological maximal tumor diameter ≤ 2 cm. Parametrial involvement, lymph node metastasis, ≥ 2/3 stromal invasion and < 1 cm surgical margin were observed in 3 (1.3%), 16 (7.1%), 30 (13.3%) and 11 (4.9%) patients, respectively. Thirty-nine patients (17.3%) underwent adjuvant (chemo)radiation. Median follow-up was 77.7 months. Five patients (2.2%) died, and 5-year OS was 98.2% (90% CI: 96.0-99.2, > 90.8%). Thirteen patients (5.8%) relapsed (8 local recurrence and 5 distant recurrence), and 5-year relapse-free survival was 94.7% (95% CI: 90.8-96.9%). Self-urination was observed in all patients, and residual urine disappearance up to 56 days after urethral catheter removal was observed in 213 patients (94.7%). Median time to disappearance of residual urine after urethral catheter removal was 1 day. There was no treatment-related death. Grade 3/4 non-hematological adverse events were observed in 17 patients (7.6%), including 8 infection and 4 hemorrhage. **Conclusions:** In this study, MRH was as effective as RH and less invasive. MRH can be considered a standard surgery for tumor diameter ≤ 2 cm Stage IB1 uterine cervical cancer. Clinical trial information: UMIN000009726, jRCTs031180167. Research Sponsor: Labour and Welfare of Japan, Japan Agency for Medical Research and Development (AMED); The National Cancer Center of Japan Research and Development Funds.

**5533** **Poster Session**

# Patient-reported outcomes during pelvic radiation therapy: A secondary analysis on sexual function from NRG-RTOG 1203.

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**Background:** NRG-RTOG 1203 reported that intensity-modulated radiation therapy (IMRT) reduced patient-reported GI and GU toxicities in cervical/endometrial cancer patients receiving adjuvant RT, as compared to standard whole field pelvic RT (WPRT). We conducted a secondary analysis of patient-reported sexual function (PR-SF) to compare this endpoint among treatment groups and identify factors associated with sexual dysfunction. **Methods:** Patients on NRG-RTOG 1203 were randomly assigned to WPRT vs. IMRT and completed the PRO-CTCAE for GI toxicity and the cervical cancer FACT-Cx at baseline, week 5 of RT, and at 4-6 weeks, 1-year, and 3-years post-RT. Patient responses to FACT-Cx sexual function questions were analyzed. The between arm frequency and severity of responses were tested using chi-square. PR-SF was compared with PRO-CTCAE GI toxicity using chi-square. A repeated measures logistic regression model was used to determine the impact of clinical/treatment factors on sexual function by dichotomizing the responses. **Results:** Of the 279 patients included for primary analysis, 236 (85%) completed PR-SF questions; 125 (53%) in the WPRT arm and 111 (47%) IMRT. There were no significant differences in PR-SF between treatment groups ($p>0.05$). PR-SF improved for both groups post-RT, except responses to "my vagina feels too narrow or short" worsened (Table). Women without abdominal pain interference at 4-6 weeks post-RT were less likely to fear sex (74.2% vs. 25.8%, $P=0.03$) and more likely to like their body appearance at 1 year (95.7% vs. 4.3%, $P<0.01$) compared to women with interference. Women liked the appearance of their body less during RT vs. at baseline (OR 1.95, 95% CI 1.04-3.64, $P=0.04$). Women were less interested in sex during RT in both arms (WPRT: OR 3.61, 95% CI 1.40-9.34; IMRT: OR 3.96, 95% CI 1.02-15.34) and at 4-6 weeks post-RT for IMRT (OR 3.16, 95% CI 1.14-8.72) vs. at baseline. **Conclusions:** PR-SF was similar between treatment groups. PR-SF during and post-RT was not significantly reduced compared to baseline with the exception of patients with abdominal pain interference, who had significantly worse PR-SF at 4-6 weeks and 1-year post-RT. Clinical trial information: NCT01672892. Research Sponsor: U.S. National Institutes of Health.

**Longitudinal change in the percent of women reporting "very much" or "quite a bit".**

| | Baseline | During RT | 4-6 Weeks Post-RT | 1-Year Post-RT | 3-Years Post-RT |
|---|---|---|---|---|---|
| "I am bothered by discharge/ bleeding from my vagina" | (n=201) 3.1% | (n=203) 1.5% | (n=201) 0.5% | (n=179) 1.1% | (n=49) 0% |
| "I am afraid to have sex" | (n=192) 14.9% | (n=184) 19% | (n=192) 12.5% | (n=174) 12.6% | (n=48) 6.3% |
| "My vagina feels too narrow/short" | (n=190) 6% | (n=183) 8.2% | (n=190) 8.9% | (n=171) 11.1% | (n=47) 10.6% |
| "I feel sexually attractive" | (n=190) 25.2% | (n=189) 21.7% | (n=190) 18.9% | (n=173) 24.9% | (n=47) 23.4% |
| "I am interested in sex" | (n=192) 24.3% | (n=192) 14.1% | (n=192) 20.8% | (172) 22.1% | (n=47) 19.1% |
| "I like the appearance of my body" | (n=198) 29.9% | (n=197) 22.8% | (n=198) 26.8% | (178) 27.0% | (n=48) 29.2% |

**5534** **Poster Session**

## The value of progression-free survival at three years as a primary endpoint for studies on radiotherapy in patients with locally advanced cervical cancer: Individual patient data from Chinese National Cancer Center and validation from 27 global randomized trials.

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**Background:** A traditional endpoint for locally advanced cervical cancer (LACC) clinical trials is overall survival with five years of follow-up (5-year OS). The use of a shorter-term endpoint could significantly speed the translation of research findings into practice. The primary hypothesis was that PFS with three years of follow-up (PFS36) is an appropriate primary endpoint to replace 5-year OS. **Methods:** The primary hypothesis was developed from our individual data, was further investigated using phase III randomized controlled trials (RCTs), and then externally validated by phase II trials and retrospective studies up to 2022. Correlation analysis at the treatment-arm level was performed between 2-, 3-, 4-, and 5-year PFS rates and 5-year OS. Correlation analysis was performed using the Pearson correlation coefficient r in weighted linear regression, with weight equal to patient size. The MEDLINE, Embase, and PubMed databases, together with the Cochrane Central Register of Controlled Trials, were searched from January 1, 1999, to February 2, 2023. Articles eligible for inclusion contained complete survival data. **Results:** A total of 613 patients with histologically confirmed, FIGO 2009 stage IB–IVA cervical cancer who underwent radiotherapy at our institute from January 2010 to December 2013 were eligible. Individual patient data were pooled to explore the correlation between PFS and the OS trend. The recurrence rates for years 1 through 5 were 12.9%, 7.3%, 3%, 2.3%, and 1.8%, respectively. The median recurrence time was 13 months and the median time from recurrence to death was 12.2 months. Within all the recurrence, 47.3% of recurrences occurred during the first year, 71.4% in the first two years, and 85% in the first three years. Patients who did not achieve PFS36 had a 5-year OS rate of 30.3%. In contrast, a 5-year OS rate of 98.2% was observed in patients who achieved PFS36. Further data were extracted from 27 randomized phase III trials on LACC. The trials included 57 arms, with a pooled sample size of 7,692 patients. In trial-level surrogacy, PFS36 ($r^2$, 0.778) was associated with 5-year OS. Sensitivity analysis demonstrated reasonable overall consistency. The correlation between PFS36 and OS was externally validated using independent phase II trials and retrospective data. In total, 23 studies representing 5,174 patients were included. PFS ($r^2$, 0.719) was found to be associated with 5-year OS. **Conclusions:** A significant correlation was found between PFS36 and 5-year OS in clinical trials on patients with locally advanced cervical cancer. This correlation was found both within patients and across trials. These results suggest that PFS36 is an appropriate endpoint for LACC trials of radiotherapy-based regimens. Research Sponsor: None.

**5535** **Poster Session**

# A multicenter, open-label, single-arm, phase II trial to evaluate the efficacy and safety of geptanolimab (GB226) in the treatment of patients (pts) with programmed cell death ligand 1 (PD-L1)–positive recurrent or metastatic cervical cancer, for whom prior platinum-containing chemotherapy has failed.

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**Background:** Geptanolimab (GB226) is a novel anti-programmed cell death 1 (PD-1) antibody, exhibiting good tolerance and promising efficacy in pts with advanced/recurrent solid tumor/lymphoma in previous phase I/II studies. This study is a two-part, multicenter, single-arm phase II study of GB226 in pts with recurrent or metastatic cervical cancer recruited from 28 clinical sites in China. In Part 1, we observed encouraging antitumor activity of GB226 with 11 PRs in 46 PD-L1 positive (combined positive score, CPS≥1) pts. Here we report the efficacy and safety results from Part 2 of this trial. **Methods:** In part 2, PD-L1 positive (CPS≥1) pts with recurrent or metastatic cervical cancer who had received one or more lines of platinum-containing chemotherapy were enrolled and treated with GB226 (intravenous infusion, 3 mg/kg) once every 2 weeks until disease progression or intolerable toxicity. The primary endpoint was objective response rate (ORR) assessed by Independent Review Committee (IRC) per RECIST 1.1. Secondary endpoints included duration of response (DOR), progression-free survival (PFS), overall survival (OS) and safety. **Results:** In Part 2, 123 pts were enrolled. As of July 28, 2022, after a median follow-up of 16.69 months (95%CI: 11.07, NR), 100 pts who met the study population criteria were eventually included in the full analysis set (FAS). 46% (46/100) of pts had received ≥2 lines of prior systemic therapy and 90% (90/100) had squamous cell carcinoma. The ORR was 18.0% (18/100; 95%CI: 11.03%, 26.95%) assessed by IRC, including 5 pts with CR (5.0%) and 13 pats with PR (13.0%); Median DOR was not reached (95%CI: 7.16, NR), median PFS was 1.91 months (95%CI: 1.87, 3.55), and median OS was 16.69 months (95%CI: 11.07, NR). Clinical benefit was observed across most patient subgroups, with a trend of higher ORR in pts with squamous cell carcinoma, no previous bevacizumab use and higher CPS. Among 123 safety-evaluable pts, 97 (78.9%) pts experienced a treatment-related adverse event (TRAE). The most common TRAE (≥10%) were hypothyroidism (24.4%), anemia (21.1%) and hyperthyroidism (13.8%), most of which were grade 1 and 2. Treatment-related grade 3/4 adverse events occurred in 25 (20.3%) and 2 (1.6%) pts, respectively. No grade 5 TRAEs occurred. 7 (5.7%) pts discontinued treatment due to a TRAE. The most common immune-related adverse events (irAE, ≥5%) were hypothyroidism 27 (22.0%) and hyperthyroidism 16 (13.0%). **Conclusions:** GB226 demonstrated durable antitumor activity and manageable safety profile in pts with recurrent or metastatic cervical cancer. Clinical trial information: NCT03808857. Research Sponsor: Genor Biopharma Co., Ltd.

**5536** **Poster Session**

## Final results of a phase II trial of prolgolimab with platinum-based therapy and bevacizumab in patients with advanced cervical cancer.

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**Background:** Here we present the final results of single-arm phase II CAESURA (NCT03912402) study of prolgolimab (anti-PD-1 antibody) with platinum doublet and bevacizumab in subjects with advanced cervical cancer (CC). **Methods:** 58 patients (pts) with metastatic or recurrent/persistent CC with measurable disease received prolgolimab (3 mg/kg) Q3W together with paclitaxel, platinum drug (cis- or carboplatin) and bevacizumab for 6 cycles and then therapy with prolgolimab and bevacizumab until disease progression or toxicity. Objective response rate (ORR) was assessed by central radiology review per RECIST 1.1 (primary endpoint) and iRECIST criteria. CT scans were performed after 9 and 18 weeks of treatment and in case of suspicion on disease progression. **Results:** Distant metastases at screening had 42 pts, 16 had recurrent or persistent CC. The median age of pts was 48 [38; 58] years old. Squamous cell carcinoma was diagnosed in 50 of 58 subjects. PD-L1 CPS $\geq$ 1 (22C3) was found in 45 pts, CPS $<$ 1 in 6 cases. ORR per RECIST 1.1 was 63.8% (37 of 58 pts) and included 2 complete, 35 partial responses. ORR per iRECIST was 70.7% (41 of 58 pts) with 2 complete and 39 partial responses. At the cut-off date (12 months) PFS (secondary endpoint) per RECIST 1.1 criteria counted 8.5 (95% CI 5.7; 10.9) months, per iRECIST criteria it reached 13.1 (95% CI 8.1; 13.6) months. Median overall survival was not reached. Any grade adverse events (AEs) occurred in 98% (57/58) of pts, of them in 69% (40/58) they were related to study treatment, including 12 cases of severe events (gr. 3 or higher). Immune-related AEs (irAEs) occurred in 38% (22/58) of pts. The most common irAEs were gr. 1–2 endocrine disorders (26%), including thyroid disorders and one case of gr. 2 adrenal insufficiency. Other important irAEs included 2 cases of enterocolitis (gr. 3 and 4), 1 case of dermatitis (gr. 3), several cases of gr. 2–3 transaminase elevation (9%). In 15 pts at least one component of study treatment was discontinued due to AE, of them 4 events were related to study treatment (including immune-related enterocolitis and adrenal insufficiency). **Conclusions:** Prolgolimab in combination with chemotherapy and bevacizumab demonstrated promising efficacy, known and acceptable safety profile in pts with advanced CC. Phase III placebo-controlled trial evaluating prolgolimab with chemotherapy and bevacizumab (NCT03912415) as first-line therapy option in subjects with CC is ongoing. Clinical trial information: NCT03912402. Research Sponsor: BIOCAD.

**5537** **Poster Session**

## Development of cervical cancer patient reported clinical outcome assessment scale (CC-PRO137): A dedicated tool for multidimensional evaluation of treatment outcomes.

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**Background:** Worldwide, cervical cancer ranks fourth among female malignant tumors in terms of both incidence and mortality. In addition, there is an increasing trend of cervical cancer incidence among younger women. Since the uterus is located at the center of vascular-neural traffic of the pelvic floor, cervical cancer surgery may damage the function of multiple systems such as urinary, digestive, neurological, endocrine, and pelvic floor muscles, and further lead to short- and long-term effects in the psychological domain including sexual status, anxiety, and depression. Therefore, we developed the current scale, Cervical Cancer Patient Reported Clinical Outcome Assessment Scale (CC-PRO137), aimed to construct a functional patient self-report system scale to conveniently and accurately quantify the quality of life of cervical cancer patients from multiple dimensions. **Methods:** Items included in the scale were proposed by gynecologic oncologist, and were evaluated and modified by experts in various specialties. This scale (CC-PRO137) includes 3 domains and 13 modules, including physiological systems, psychological related symptoms, social life status. A total of 304 participants were tested within 6 and 12 months postoperatively. Subgroup analyses were carried out for different time period, stages, surgical methods and adjuvant treatment plans. **Results:** The reliability analysis showed that the Cronbach's $\alpha$ in each module of the physiological domain was between 0.602-0.929, the composite reliability was between 0.226-0.946, and the test-retest reliability was between 0.660-0.829; the Cronbach's $\alpha$ of the psychological domain were between 0.700-0.940, the composite reliability was between 0.584-0.950, and the test-retest reliability was between 0.697-0.807; the Cronbach's $\alpha$ of the social domain was between 0.836-0.861, the composite reliability was between 0.777-0.886, the test-retest reliability was between 0.732-0.792, and the reliability of each module was optimal. The content validity adopted the expert judgment. Convergent validity (CV) analysis showed that the average variance extraction of each module in the physiological domain was between 0.382-0.706, in the psychological domain was between 0.433-0.801, and in the social domain was 0.440-0.616. The convergent validity of each module was acceptable. **Conclusions:** Our results showed the effectiveness of CC-PRO137 as a comprehensive assessment tool for cervical cancer patients' quality of life, suggesting that the scale can accurately measure subtle changes postoperatively. CC-PRO137 can be a useful tool to quantitatively assess cervical cancer patients. Research Sponsor: Shanghai Shenkang Hospital Development Center's Shenkang Promotion of Clinical Skills and Clinical Innovationin Municipal Hospitals Three-Year Action Plan (2020−2023) Major Clinical Research Project (Grant No. SHDC2020CR1048B); the General Program of National Natural Science Foundation of China (Grant No.82271654), the Public Welfare Project "JiShiQiYi" of Beijing Health Alliance Charitable Foundation (Grant No.KM-JSQY-002), the "ZaiDing-Le" Foundation from Beijing Kanghua Foundation for the Development of Traditional Chinese and Western Medicine (Grant No. KH-2020-LJJ-008).

**5538** **Poster Session**

# A peptide-based human papillomavirus therapeutic vaccine, PepCan, or *Candida* adjuvant alone in treatment of cervical intraepithelial neoplasia 2/3 (CIN2/3).

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**Background:** A non-surgical alternative for treating CIN2/3 would be desirable for women of child-bearing age due to a risk of cervical incompetency in subsequent pregnancies following surgical treatments. PepCan consists of four current good manufacturing-grade HPV 16 E6 peptides and a *Candida* skin testing reagent (Candin, Nielsen Biosciences), because of *Candida*'s ability to regress common warts in humans, and to promote T cell proliferation and interleukin-12 secretion *in vitro*. **Methods:** In this single-center, randomized, double-blind Phase II study (NCT02481414), women with biopsy-confirmed CIN2/3 were treated with PepCan or *Candida* (1:1). Four intradermal injections were given 3 weeks apart which were followed with two visits 6 months apart. Histological responses (primary endpoint) were assessed using quadrant biopsies, and those whose lesions regressed to no CIN were considered to be responders. Regression rate of each treatment group was compared to that of a historical placebo group following the same treatment schedule. A sample size of 35 per arm had 93% power to test the null hypothesis that $\pi = 0.29$ (historical control placebo rate) and detect a difference of 0.31 with a two-sided type I error of 5%. Adverse events (AEs) were assessed using Common Terminology Criteria for Adverse Events Version 4. **Results:** Of 99 subjects screened, 81 (81.8%) qualified for vaccination, and 80 received at least one vaccination. No dose-limiting toxicity was observed. With the intention-to-treat analysis, PepCan showed 30.8% efficacy (12 of 39, $p$=0.16) while *Candida* demonstrated 47.6% efficacy (20 of 42, $p$=0.0004). Likewise, with the per-protocol analysis, PepCan showed 45.8% efficacy (11 of 24, $p$=0.06) and *Candida* showed 62.1% efficacy (18 of 29, $p$=0.0002). There was no difference between efficacy of PepCan and *Candida*. **Conclusions:** PepCan and *Candida* treatments are safe. Only *Candida* was effective in inducing histological regression in the intention-to-treat and per-protocol analyses. *Candida* could become a new treatment for CIN2/3 by eliciting general immune stimulation similar to checkpoint inhibitors. Clinical trial information: NCT02481414. Research Sponsor: U.S. National Institutes of Health; University.

**Comparisons of histological responses between each treatment and a historical placebo group.**

| | PepCan | *Candida* | Historical Placebo* |
|---|---|---|---|
| **Intention-to-treat** | | | |
| **No. patients** | 12/39 | 20/42 | 34/149 |
| **Percentage of patients** | 30.8<br>90% CI (18.8, 45.0) | 47.6<br>90% CI (34.2, 61.3) | 22.8 |
| **P value~** | 0.16 | 0.0004 | |
| **Per-protocol** | | | |
| **No. patients** | 11/24 | 18/29 | 34/117 |
| **Percentage of patients** | 45.8<br>90% CI (28.2, 64.2) | 62.1<br>90% CI (54.4, 88.1) | 29.1 |
| **P value~** | 0.06 | 0.0002 | |

*Myeskens et al., J Natl Cancer Inst, 1994; ~binomial test.

**5539** **Poster Session**

## Surgical resection based on ontogenetic cancer field theory for cervical cancer: 10-year updated results of the MMR study.

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**Background:** Previously published findings from our center suggest that carcinoma of the cervix propagates within ontogenetic cancer fields, tissue compartments defined by staged morphogenesis. In the MMR study we aimed to determine whether surgical treatment that accounts for stage-associated, ontogenetic cancer fields and their associated lymphoid tissues results in locoregional tumor control without the need for adjuvant radiotherapy. **Methods:** The Leipzig School Mesometrial Resection Study (MMR study) is an ongoing, prospective, single-center, observational cohort study including patients with primary cervical cancer. All study participants undergo either total or extended mesometrial resection (TMMR or EMMR) and therapeutic lymph node dissection. Because this treatment strategy enables surgical removal of all locoregional at-risk tissues, no adjuvant radiotherapy is necessary, even in the presence of established risk factors. The trial is registered at the German Clinical Trials Register, number DRKS00015171. For this updated analysis, we identified patients in our institutional study database with primary cervical cancer staged IB1 – IIA2 according to the 2009 International Federation of Gynecology and Obstetrics staging system. Using the Kaplan-Meier estimator, we calculated recurrence free and overall survival. **Results:** Between October 16, 1999, and December 16, 2020, 420 patients were treated per protocol and followed up for a median of 136 months (IQR 77-190). The median age was 42 years (IQR 36-51). 329 patients (78.3%) had stage IB1, 58 (13.8%) stage IB2, 24 (5.7%) stage IIA1 and 9 (2.1%) stage IIA2 disease. Patients had either squamous cell (n = 297, 70.7%), adenocarcinoma (n = 104, 24.8%), adenosquamous (n = 18, 4.3%) or other (n = 1, 0.24%) histology. The nodal status was pN0 in 349 (83.1%) patients and pN1 in 71 (16.9%) of the cases. Clinically occult parametrial involvement was present in 47 (11.2%) patients. 10-year overall survival was 90.2% (95% confidence interval [CI] 87.1-93.4) and recurrence-free survival was 90.6% (95% CI 87.8-93.6). Stratified for lymph node status 10-year overall survival was 91.7% (95% confidence interval [CI] 88.5-95) for pN0 and 83.2% (95% confidence interval [CI] 74.6-92.9) for pN1. Recurrence-free survival was 93.8% (95% CI 91.2-96.5) for pN0 and 75.4% (95% CI 65.9-86.3) for pN1. **Conclusions:** Despite dispense of adjuvant radiotherapy, patients treated with total or extended mesometrial resection with therapeutic lymph node dissection have excellent survival outcomes. Additional multicenter studies are needed to further investigate and confirm our results. Clinical trial information: DRKS00015171. Research Sponsor: None.

**5541** **Poster Session**

## Association between serum folate and vitamin B12 and cervical high-risk human papillomavirus (HPV) infection.

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**Background:** Serum concentration of folate (vitamin B9) and vitamin B12 were inversely associated with cervical intraepithelial neoplasia and cervical cancer in some studies. The association between folate and vitamin B12, and human papillomavirus (HPV) infection has not been well elucidated. We evaluated whether low serum level of folate and vitamin B12 was associated with high-risk HPV (hrHPV) infection. **Methods:** The study population was 6,452 women, aged 18-59 years old, enrolled in the National Health and Nutrition Examination Survey (NHANES), from 2003 to 2016, in the United States. In this cross-sectional study, odds ratios (ORs) of hrHPV were calculated, by quintiles of low folate and vitamin B12 combined, using logistic regression models. **Results:** The mean age (standard deviation) of the women was 36.98 (12.19) years. Women in the lowest quintile had less than 20.6 nmol/L of folate and less than 248 pmol/L of vitamin B12. Some of the women, 23% (1,509/6,452), were hrHPV positive. In age-adjusted models, low folate and vitamin B12 was significantly associated with hrHPV infection. The ORs and 95% confidence intervals (CI) was (OR: 0.704, 95% CI: 0.509 - 0.975, $p = 0.034$) for the second, (OR: 0.671, 95% CI: 0.479 - 0.940, $p = 0.020$) third, (OR: 0.534, 95% CI: 0.370 - 0.770, $p = 0.0008$) fourth and (OR: 0.476, 95% CI: 0.33 - 0.679, $p < 0.0001$) fifth quintiles, compared to women in the lowest quintile. The association remained statistically significant after the models were further adjusted for smoking status and income level; women in the highest quintile were less likely to have hrHPV infection compared to those in the lowest quintile (OR: 0.541, 95% CI: 0.343 - 0.855, $p = 0.008$). **Conclusions:** This study supports an association between low serum levels of folate and vitamin B12, and hrHPV infection, among women in the United States. Research Sponsor: American Cancer Society Research Scholar Grant RSG-22-079-01-CSCT.

**5542** **Poster Session**

## Efficacy and safety of camrelizumab in combination with radiation and chemotherapy for recurrent or metastatic cervical cancer.

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**Background:** Cisplatin-based concurrent chemoradiation regimens have been suggested to be beneficial in recurrent or metastatic cervical cancer. Immunotherapy has also shown good therapeutic efficacy in recurrent or metastatic cervical cancer. Among them, Pembrolizumab in combination with chemotherapy has been used for first-line treatment of advanced PD-L1-positive cervical cancer. Meanwhile, Camrelizumab has shown good anti-tumor activity and manageable toxicity in patients with locally advanced cervical cancer. The primary objective of this study is to evaluate the efficacy and safety of Camrelizumab in combination with concurrent chemoradiation in patients with recurrent or metastatic cervical cancer. **Methods:** Patients diagnosed with recurrent or metastatic cervical cancer received Camrelizumab combined with concurrent chemoradiotherapy, radiotherapy:External beam radiotherapy (EBRT) 1.8-2.15 Gy/f, a total of 28 fractions; Brachytherapy: high-risk CTV using image guidance 28 Gy in 4 fractions (18 Gy in 3 fractions for posthysterectomy recurrent patients); chemotherapy regimen used TP regimen (paclitaxel: 175 mg/m$^2$, cisplatin: 75 mg/m$^2$, Q3W 6 cycles); Camrelizumab 200 mg Q3W 6 cycles. The primary endpoint of this trial was objective response rate (ORR), and secondary endpoints were progression-free survival (PFS), overall survival (OS), disease control rate (DCR), and incidence of adverse reactions. **Results:** From September 16, 2020 to September 30, 2022, a total of 29 patients were recruited. 27 of these patients completed 6 cycles of planned treatment. 27 patients had a median age of 53 years (33-73 years), ECOG PS 0 (n = 8), ECOG PS 1 (n = 14), ECOG PS 2 (n = 1). The ORR rate was 96.30% (26/27), including 17 patients with CR, 9 patients with PR, and 1 patient with SD Treatment-related AEs were mainly lymphocyte count decreased, anemia, and white blood cell count decreased, with overall safety manageable and no treatment-related deaths. **Conclusions:** Camrelizumab combined with concurrent chemoradiation in patients with recurrent or metastatic cervical cancer has good efficacy, low side effects and acceptable toxicity. Clinical trial information: NCT04884906. Research Sponsor: None.

**5543** **Poster Session**

# The spectrum of homologous recombination deficiency in cervical cancer: Is it also a cervical issue?

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**Background:** Tumors deficient in homologous recombination DNA damage repair (HR-DDR) demonstrate sensitivity to therapeutic agents targeting the HR-DDR pathway, such as poly-ADP ribose phosphate (PARP) inhibitors. The landscape of homologous recombination deficiency (HRD) is not well-characterized for cervical cancer; thus, we sought to analyze the prevalence of somatic pathogenic gene variants (PGVs) in HRD genes in cervical cancers. **Methods:** The American Association for Cancer Research's (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE) database version 13.0 was queried for all cervical cancer tumors via cBioPortal (http://genie.cbioportal.org). This is a publicly available, multi-institutional database of next-generation sequencing (NGS) genomic profiles of multiple tumors. PGV frequencies of 27 genes involved in HR-DDR were descriptively reported for cervical cancer tumors, with histologic stratification: *ATM, ARID1A, ATRX, BRCA1, BRCA2, BARD1, BRIP1, BLM, BAP1, CHEK1, CHEK2, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCL, MRE11, NBN, PALB2, RAD50, RAD51, RAD51B, RAD51C, RAD51D, WRN*. **Results:** A total of 857 cervical tumors from 817 patients were included for analysis. At least one somatic PGV in an HRD gene was found in 16.5% of all tumors (141/857). When stratified by histological subtypes with at least 25 tumors sequenced, highest frequencies of $\geq$1 PGV in HRD genes were observed in mucinous cervical cancer (13/66, 19.7%), cervical adenocarcinoma (48/262, 18.3%), squamous cell cervical cancer (53/349, 15.2%), adenosquamous cervical cancer (6/43, 14.0%) and neuroendocrine cervical cancers (5/42, 11.9%). Substantial rates of PGVs in HRD genes were also observed in histological subtypes with fewer than 25 sequenced tumors. Across all tumors, HRD genes with the highest frequencies of PGVs were *ARID1A* (9%), *BAP1* (3%), *ATM* (1.6%) and *BRCA1* (1.6%). **Conclusions:** NGS data demonstrate a substantial rate of somatic PGVs in HRD genes in cervical cancers, including among HPV related subtypes. These data suggest the need to expand routine functional HRD status assessment to cervical cancers in order to further characterize the landscape of HRD in these tumors. Furthermore, genetically driven clinical trials are warranted to evaluate the efficacy of HRD-targeted therapies such as PARP inhibitors, ataxia telangiectasia, and Rad-3 related kinase (ATR) inhibitors. Research Sponsor: None.

| Tumor Histology (n = tumors sequenced for ≥1 HRD gene) | Frequency of tumors with ≥1 HRD PGV | HRD gene with highest PGV frequency* |
|---|---|---|
| **Squamous Cell (349)** | 15.2% | *BAP1*, 6.5% |
| **Adenocarcinoma (262)** | 18.3% | *ARID1A*, 11.2% |
| **Mucinous (66)** | 19.7% | *ARID1A*, 11.6% |
| **Adenosquamous (43)** | 14.0% | *ARID1A*, 8.8% |
| **Neuroendocrine (42)** | 11.9% | *ARID1A*, 16.1% |
| **Serous (22)** | 13.6% | *ARID1A*, 8.8% |
| **Endometrioid (21)** | 9.5% | *ARID1A*, 12.5% |
| **Clear Cell (19)** | 42.1% | *ARID1A*, 37.5% |
| **Mesonephric (10)** | 20.0% | *ARID1A*, 8.0%, *NBN*, 8.0% |
| **Rhabdomyosarcoma 3** | 33.3% | *CHEK2*, 50.0% |

**5544** **Poster Session**

## Phase 1 dose escalation study of SL-172154 (SIRPα-Fc-CD40L) in platinum-resistant ovarian cancer.

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**Background:** SIRPα-Fc-CD40L is a hexameric, bi-functional fusion protein consisting of SIRPα linked to CD40L via an inert Fc linker. This molecule competitively inhibits CD47 to enhance tumor cell phagocytosis and activates CD40 to increase antigen processing and cross-presentation by antigen presenting cells (APCs) to CD8 T cells, thus bridging innate and adaptive immunity. **Methods:** This first-in-human, Phase 1 dose escalation study evaluated SL-172154 in patients (pts) with advanced platinum resistant ovarian, fallopian tube and primary peritoneal cancers (PROC). SL-172154 was administered intravenously across 5 dose levels (0.1, 0.3, 1.0, 3.0, 10mg/kg). Dose escalation followed a modified toxicity probability interval 2 design. Objectives included evaluation of safety, dose-limiting toxicity (DLT), recommended phase 2 dose, pharmacokinetic and pharmacodynamic (PD) parameters, and antitumor activity per RECIST 1.1. **Results:** As of 3 Jan 2023, 27 pts (median age 66 years [range 33-85]; median of 4 prior systemic therapies [range 2-9]) with ovarian (70%), fallopian tube (15%) or primary peritoneal (15%) cancer were dosed. Treatment-emergent AEs (>15%) regardless of grade (G) included infusion related reaction (IRR) (67%), fatigue (44%), nausea (33%), back pain (26%), constipation, diarrhea (both 22%), decreased appetite and pruritus (both 19%). There was one DLT of G3 ALT increased at 10mg/kg requiring dose interruption for resolution. A maximum tolerated dose was not reached. G3/4 treatment-related AEs (>1pt) were AST increased (G3) and lymphopenia (G4), each in 2 pts (7%); all were fully resolved with no dose modifications. There were no fatal AEs, no AEs that led to drug discontinuation and no events of cytokine release syndrome. The frequency of IRR events increased with increasing dose, and slowing the rate of infusion was utilized for mitigation. SL-172154 Cmax and AUC increased with dose with greater than proportional exposure noted at 3 and 10mg/kg potentially due to target saturation. These findings were supported by dose-dependent target engagement of CD47 and CD40 on CD4 T cells and B cells respectively, approaching 100% by 3 mg/kg. Rapid dose-dependent egress of CD40+ B cells was maximal at ≥3mg/kg. SL-172154 induced dose-dependent responses in IL-12, CXCL-8, CXCL-10, IL-10, CCL2, CCL20, and CCL22, which also approached a plateau at ≥3mg/kg. Analysis of peripheral and tumor immunophenotypes and anti-drug antibodies in response to SL-172154 is ongoing and will be presented. Best response was stable disease in 6/27 response evaluable (22%) pts. **Conclusions:** SL-172154 is well tolerated in heavily pretreated PROC pts. IRRs were readily manageable. Maximal CD47 and CD40 target engagement and CD40-dependent PD effects were observed with ≥3mg/kg SL-172154. 3mg/kg is a safe, tolerable, and pharmacologically active dose for evaluation in combination studies in pts with PROC. Clinical trial information: NCT04406623. Research Sponsor: Shattuck labs.

**5545** **Poster Session**

## Correlating expression of NaPi2b and FRa in high grade serous ovarian cancer (HGSOC).

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**Background:** Biomarker driven therapies are increasingly being used for gynecologic cancers, with mirvetuximab soravtansine, a Folate Receptor alpha (FRa) targeting antibody drug conjugate (ADC) being a recent FDA approved agent for patients with FRa positive PROC. Uptifitamab rilsodotin (UpRi) is a late-stage, first in class NaPi2b-targeting ADC with a novel scaffold-linker-payload that enables high drug to antibody ratio and a controlled bystander effect. Approximately 29% of HGSOC patients have FRa positive tumors (Roche VENTANA FOLR1 (FOLR-2.1) RxDx Assay. USPI 2022); ~59% have NaPi2b positive tumors (Okeke et al, USCAP 2022). With the high unmet medical need in PROC and the evolving landscape of available treatments, understanding biomarker expression and correlation between FRa and NaPi2b is critical. Here we evaluate NaPi2b and FRa RNA expression correlation in HGSOC. **Methods:** Tumor samples (N=84) from the Ph1b UpRi expansion (EXP) cohort were analyzed via Nanostring (770 immune-focus genes from IO 360 panel + 30 customized ADC-related genes) to evaluate the association between NaPi2b and FRa expression. The cutoff for NaPi2b RNA positive or negative was based on approximately 60% of HGSOC patients having NaPi2b positive tumors (top 60% of samples based on expression deemed NaPi2b positive; bottom 40% NaPi2b negative) and FRa RNA cutoff assumed that ~30% of samples were FRa positive. To correlate the NaPi2b expression level between RNA and IHC, the N=84 samples with known expression levels via IHC were analyzed via Nanostring. **Results:** When evaluating NaPi2b and FRa RNA expression correlation, 21% (N=18) of samples had both NaPi2b positive and FRa positive expression. 38% (N=32) samples were NaPi2b positive and FRa negative. No statistically significant association was observed (Chi-squared test, p=0.129). NaPi2b RNA and IHC expression was evaluated; a statistically significant association was observed (Kappa statistic, p=0.001). Results are in the Table below. **Conclusions:** Based on this analysis of a limited sample size, there does not appear to be an association between FRa and NaPi2b expression, with the majority of NaPi2b positive samples not being FRa positive. Additionally, general NaPi2b prevalence and the correlation of expression between RNA and IHC suggest that NaPi2b may be a rational biomarker to integrate in RNA tumor panel testing. This research underscores the importance of early, comprehensive testing of all relevant biomarkers to guide therapy selection, and suggests that additional research is needed to evaluate the potential association between FRa and NaPi2b expression via IHC. Research Sponsor: Mersana Therapeutics.

| N (% of total) | | NaPi2b RNA | |
|---|---|---|---|
| | | Positive (upper 60%) | Negative (lower 40%) |
| **FRa RNA** | Positive (upper 30%) | 18 (21.4%) | 7 (8.3%) |
| | Negative (lower 70%) | 32 (38.1%) | 27 (31.2%) |
| **N (% of total)** | | **NaPi2b RNA** | |
| | | Positive (upper 60%) | Negative (lower 40%) |
| **NaPi2b IHC** | Positive (TPS $>$ 75) | 38 (45.2%) | 14 (16.7%) |
| | Negative (TPS $<$ 75) | 12 (14.3%) | 20 (23.8%) |

## Systematic high-throughput combination drug screen to enhance poly (ADP-ribose) polymerase (PARP) inhibitor efficacy in ovarian cancer.

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**Background:** PARP inhibitors currently offer the greatest benefit to patients with loss-of-function *BRCA1* or *2* mutations or other causes of homologous recombination deficiency (HRD). We hypothesized that combination therapy, possibly by augmenting or inducing an HRD phenotype, would enhance the efficacy of PARP inhibition in epithelial ovarian cancer. **Methods:** We performed a high-throughput screen of an informer set containing FDA-approved drugs, clinical candidates, and small-molecule probes to identify synergistic partners with olaparib in representative HRD and non-HRD human epithelial ovarian cancer cells. Single agent activity was described by area under the curve of the Hafner growth rate index (AUC_GRI) and synergy was ranked by cumulative difference from Bliss ($\Delta_{Bliss}$). Analysis of the drug screen was performed using algorithms developed by the Gulf Coast Consortia's Combinatorial Drug Discovery Program at the Texas A&M Institute of Bioscience and Technology. MTT assays were then independently performed to verify and characterize synergy between CT7439, an agent selected following the drug screen, and olaparib. MTT data were analyzed using the SynergyFinder Plus web application. **Results:** In an initial single agent screen, we identified 62 compounds with a mean AUC_GRI $<0.75$, indicating inhibitory activity. Prioritizing more potent agents and those of mechanistic interest, we selected 40 hits to validate and advance to a combination screen. Diverse mechanisms of action were represented among the hits, including many small molecule inhibitors of various cell cycle pathways. Following a combination screen with olaparib, the compounds selected for final validation were: AZD 7762 (CHK1/2 inhibitor), dinaciclib (pan-CDK inhibitor), onalespib (HSP90 inhibitor), and SN-38 (topoisomerase 1 inhibitor). The $\Delta_{Bliss}$ for these agents are presented in the table. Due to mechanistic rationale and concern for overlapping toxicities among the other candidates, we focused further study on CDK inhibitors. In MTT assays, we identified robust synergy between olaparib and CT7439, a next-generation oral CDK12/13 inhibitor, with a mean Bliss synergy score of 1.31 and scores as high as 22.03 at certain concentrations in the non-HRD model OVCAR-5. These findings were recapitulated in the HRD cell lines OVCAR-4 (mean Bliss synergy score 1.56) and OVCAR-8 (mean Bliss synergy score 5.69). Results from an *in vivo* model will be presented as well. **Conclusions:** Pairing a PARP inhibitor and CDK inhibitor, a strategy identified by a high-throughput drug screen and known to impair homologous recombination, resulted in robust synergy in both HRD and non-HRD ovarian cancer models. Clinical translation of this combination may enhance the efficacy of PARP inhibitors in patients with ovarian cancer. Research Sponsor: MD Anderson Ovarian Cancer Moon Shot; CPRIT Grant #RP200668.

| Compound | Mean $\Delta_{Bliss}$ |
|---|---|
| **AZD 7762** | 6.62 |
| **Dinaciclib** | 1.93 |
| **Onalespib** | 1.83 |
| **SN-38** | 6.70 |

**5547** **Poster Session**

## The impact of adjuvant platinum-based chemotherapy in early adult granulosa cell tumor of the ovaries: A meta-analysis of comparative studies.

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**Background:** Adult granulosa cell tumors (AGCT) are the most common type of malignant ovarian sex chord stromal tumors but only comprise 2 to 5 percent of all malignant ovarian neoplasms. Most granulosa cell tumors have an indolent growth pattern, and prognosis depends on the disease stage at diagnosis and the presence of residual disease after surgery. Though these tumors have metastatic potential, their tendency for late relapses is well documented. Despite the lack of supporting data, the National Cancer Centers Network recommends platinum-based adjuvant chemotherapy (AC) for Stage I with intermediate and high-risk features. Most studies have failed to show any benefit of AC with disease-free or overall survival. However, several of these studies were small, and some had short median follow-ups. Others included advanced stages and the juvenile variant of the disease. Therefore, we conducted this meta-analysis to evaluate the impact of AC on disease recurrence in a stage I enriched AGCT. **Methods:** A review of the medical literature was conducted using online databases. Inclusion criteria consisted of English language, diagnosis of AGCT, studies with a preponderance of stage I, comparative studies of AC versus none, and studies that reported recurrence rates. Studies that had a preponderance of advanced stages or juvenile variants were excluded. A meta-analysis using the fixed effects and random effects models was conducted. **Results:** Seven retrospective comparative studies with a total of 500 patients were included. The average median age was 47 years, and the average median follow-up was 58 months. Approximately 79% of the sample were stage I, and 79% of stage I were IC. Most AC regimens used were BEP and EP, though it varied among the regions. Platinum-based AC in early-stage AGCT failed to impact recurrence rates compared to clinical observation (HR=1.39, 95%CI 0.86-2.25, $I^2$=48%, p=0.18). **Conclusions:** This is the first meta-analysis to show that adding platinum-based adjuvant chemotherapy to surgery does not improve the recurrence rate in early AGCT. Therefore, in the absence of evidence supporting any benefit of AC in this disease, recommendations to use AC should be re-evaluated, especially since the risk of platinum-based AC with or without Bleomycin is well-documented and carry potentially serious side effects. Research Sponsor: None.

# Nivolumab plus ipilimumab (N+I) in patients (pts) with ovarian cancer (OC) with *BRCA1/2* mutation (mut): Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) study.

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**Background:** TAPUR is a phase II basket study evaluating antitumor activity of commercially available targeted agents in pts with advanced cancers with genomic alterations. Results in a cohort of pts with OC with *BRCA1/2* mut treated with N+I are reported. **Methods:** Eligible pts had advanced OC, measurable disease, ECOG performance status (PS) 0-2, adequate organ function, and no standard treatment (tx) options. Genomic testing was done in CLIA-certified, CAP-accredited labs. PD-L1 status was not routinely reported. Pts received I at 3 mg/kg every 3 wks for 4 doses with N at 1 mg/kg IV every 3 weeks (wks) for 4 doses. N alone was then continued at 240 mg every 2 wks or 480 mg every 4 wks until disease progression. Primary endpoint was disease control (DC) per investigator defined as complete or partial (PR) response per RECIST v. 1.1, or stable disease of at least 16+ wks duration (SD16+). CA-125 levels were not routinely reported. Simon 2-stage design tested the null DC rate of 15% vs. 35% (power = 0.85; $\alpha = 0.10$). If $\geq$2 of 10 pts in stage 1 have DC, 18 more pts are enrolled; otherwise, the cohort is closed. If $\geq$7 of 28 pts have DC, the null DC rate is rejected. P-value calculated based on 2-stage design. Secondary endpoints were progression-free survival (PFS), overall survival (OS), and safety. **Results:** 33 pts with OC and *BRCA1* (n=20), *BRCA2* (n=10), or both mut (n=3) were enrolled from Sept 2017 to Oct 2019. 6 pts were not evaluable for efficacy analysis; 1 pt was found to be ineligible after enrolling, 5 pts discontinued tx before the post-baseline tumor evaluation due to an adverse or serious adverse event (SAE). Table shows demographics and efficacy outcomes. 6 pts with PR were observed for an OR rate of 22% (95% CI: 9% to 42%) and a DC rate of 27% (90% CI: 13% to 36%); the null hypothesis of a 15% DC rate was not rejected (p=0.17). 3 pts with PR had *BRCA1* mut only, 2 pts had *BRCA2* mut only and 1 pt had both *BRCA1* and *BRCA2* mut. Of the 6 pts with PR, 4 had microsatellite (MS) stable (MSS) tumors and MS status was not reported in 2. Of the 4 with MSS, 3 had a tumor mutational burden (TMB) $\leq$ 10 mutations per megabase and 1 had TMB of 11. 11 pts had at least 1 tx-related SAE, including acute kidney injury, ALT/AST increase, colitis, dehydration, diarrhea, E. coli, electrolyte disorder, fever, nausea/vomiting and pneumonitis. **Conclusions:** N+I did not meet prespecified criteria to declare a signal of activity in pts with OC and *BRCA1/2* mut. However, given 22% of pts had PR (2 with $>$1 year duration) in this heavily pretreated cohort, additional study may be warranted to further evaluate efficacy. Clinical trial information: NCT02693535. Research Sponsor: Bristol Myers Squibb; AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly and Company, Genentech, Merck, Pfizer, Seagen.

| Demographics (N=33) and efficacy outcomes (n=27). | | |
|---|---|---|
| **Median (Med) age, years (range)** | | **59 (47-86)** |
| **ECOG PS, %** | 0 | 25 (76) |
| | 1 | 7 (21) |
| | 2 | 1 (3) |
| **Prior systemic regimens, %** | 0-2 | 3 (9) |
| | ≥3 | 30 (91) |
| **DC rate, % (OR and SD16+) (90% CI)** | | 27 (13, 36) |
| **OR rate, % (95% CI)** | | 22 (9, 42) |
| **Med PFS, wks (95% CI)** | | 8.1 (8.0, 8.3) |
| **Med OS, wks (95% CI)** | | 45 (20, 133) |

**5549** **Poster Session**

## Utility of surgically documented minimal residual disease as a therapeutic target and early surrogate of frontline treatment outcomes in ovarian cancer.

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**Background:** Cure rates for patients with advanced stage ovarian cancer have not changed over the last four decades likely due to inability to eradicate residual cancer cells after frontline therapy. Identifying clinically undetectable minimal residual disease (MRD) after frontline therapy by second look laparoscopy (SLL) has potential to a) uncover mechanisms of chemoresistance, b) identify MRD-specific therapeutic targets, and c) allow for earlier intervention with investigational therapies. The objective of this study is to describe the initial safety and feasibility of SLL and illustrate clinical pathologic correlates. **Methods:** This IRB-approved observational, single-center study includes patients with epithelial high-grade ovarian cancer with complete CA-125 and radiologic response after frontline treatment who underwent SLL from 4/2017-12/2022. Patients were subsequently offered standard of care or investigational maintenance therapy options based on homologous recombination deficiency (HRD) and MRD status. Summary statistics described the study population, chi-square tests compared categorical variables, and progression free survival (PFS) based on MRD status was estimated using Kaplan-Meier method and compared using log rank test. **Results:** 64 patients underwent SLL with a median of 8 biopsies (range 1-16). The majority of patients had stage III-IV disease (89%), and high-grade serous histology (89%). Approximately half (52%) of patients underwent neoadjuvant chemotherapy (NACT) with interval tumor reductive surgery (TRS). MRD was present in 28 patients (44%), and the presence of MRD was associated with a worse PFS (HR 3.1, 95% CI 1.5-6.3; 9.2 vs 24.6 months; P=0.002). MRD was more frequent among NACT recipients compared to those who underwent primary TRS (61% vs 26%, P=0.005), those with HRD negative tumors (63% vs 22%, P=0.003), and those with R1 versus R0 resections (71% vs 35%, P=0.012). Of patients with MRD, 20 patients (71%) received bevacizumab until progression as part of a clinical trial (NCT02884648), 3 (11%) received bevacizumab off trial, 4 (14%) received a PARP inhibitor (all HRD positive) and 1 received other therapy. There was one (1.6%) intraoperative complication requiring conversion to laparotomy. **Conclusions:** SLL is feasible, overall safe, and detected MRD in 44% of ovarian cancer patients who were in radiologic and CA-125 remission after frontline therapy. MRD rates were higher in patients who received NACT and HRD negative patients, and PFS was significantly longer in patients without residual disease. MRD rate by SLL may have utility as an early surrogate for efficacy in trials evaluating novel frontline investigational therapies. Knowledge of MRD status in this patient population enables interventional, observational, and translational investigations, as well as personalized prognostic counseling. Research Sponsor: MD Anderson Cancer Center Support Grant; Break Through Cancer.

# Efficacy of subsequent therapies in patients (pts) with advanced ovarian cancer (AOC) in the phase III PAOLA-1/ENGOT-ov25 trial according to whether disease progression occurred during or after the end of olaparib (ola) maintenance.

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**Background:** In the PAOLA-1/ENGOT-ov25 trial (NCT02477644), maintenance ola (a PARP inhibitor) + bevacizumab (bev) led to prolonged progression-free and overall survival vs placebo (pbo) + bev in AOC pts, specifically those with homologous recombination-deficient (HRD+) tumors (Ray-Coquard *et al*. ESMO 2022, LBA29). Here, we explore the efficacy of subsequent chemotherapy (CT) in pts after progression on first-line (1L) treatment in PAOLA-1. **Methods:** The efficacy of subsequent CT was explored by analyzing the median time from first subsequent therapy (FST) to second subsequent therapy (SST). Efficacy was compared by FST type, HRD status, and timing of progression (during/after ola). A multivariate Cox model was used in ola + bev pts to identify prognostic factors influencing time from FST to SST, including HRD status, platinum-free interval (PFI), clinical risk based on disease stage and surgical status, timing of progression, and response to 1L CT. All *P* values are exploratory. **Results:** In total, 544/806 (67.5%) pts progressed and received subsequent CT: 338/537 (62.9%) ola + bev pts and 206/269 (76.6%) pbo + bev pts. In the overall population and in the subgroup who received platinum-based combination therapy (PBC), time from FST to SST was shortest in pts who progressed during ola (Table). Pts who progressed after ola had similar outcomes to pbo + bev pts (Table). Efficacy was broadly consistent regardless of HRD status (Table). The multivariate analysis confirmed that progression after (vs during) ola prolonged time from FST to SST (hazard ratio [HR] 0.65, 95% confidence interval [CI] 0.50–0.84; *P*=0.0011) independently of other known prognostic factors, such as PFI ≥12 vs <12 months (HR 0.38, 95% CI 0.29–0.51; *P*<0.0001) or lower vs higher clinical risk (0.58, 0.42–0.81; *P*=0.0015). **Conclusions:** In this *post hoc* exploratory analysis of PAOLA-1, the efficacy of subsequent CT at relapse appeared dependent on whether progression occurred during or after the end of ola treatment. Efficacy was reduced when relapse occurred during ola but was comparable between pts who progressed after ola vs pbo + bev pts. Clinical trial information: NCT02477644. Research Sponsor: This work was supported by ARCAGY Research, AstraZeneca, Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, and F. Hoffmann-La Roche.

**Time from FST to SST.**

| FST | Progression during ola | Progression after ola | Pbo + bev |
|---|---|---|---|
| **Any CT** | **6.1 (4.9–7.3)** *n=192** | **11.4 (10.2–13.2)** *n=145** | **11.9 (10.8–12.9)** *n=206* |
| **HRD+** | 7.2 (5.5–8.6) *n=55* | 12.7 (10.2–15.5) *n=66* | 13.9 (11.4–17.0) *n=100* |
| **HRD–** | 6.0 (4.4–7.7) *n=98* | 10.6 (9.7–15.4) *n=53* | 10.8 (9.5–12.5) *n=66* |
| **PBC** | **7.3 (5.7–8.4)** *n=157* | **12.0 (10.3–14.8)** *n=132* | **12.9 (11.8–14.1)** *n=162* |
| **HRD+** | 7.3 (6.3–9.6) *n=46* | 12.7 (10.2–15.5) *n=64* | 14.3 (12.4–19.0) *n=85* |
| **HRD–** | 6.6 (4.6–8.6) *n=81* | 12.9 (10.3–17.2) *n=46* | 11.8 (10.6–13.2) *n=47* |

*1/338 pts not treated. Kaplan–Meier estimates; median months with 95% CIs. HRD+ defined as tumor *BRCA* mutation and/or genomic instability score ≥42 (Myriad MyChoice HRD Plus assay)

**5551** **Poster Session**

# Real-world data from a multi-center study: Insights to the efficacy and safety in patients with ovarian cancer (OC) received niraparib as first-line (1st-L) maintenance therapy (MT).

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**Background:** Niraparib has significantly extended PFS as 1st-L MT OC in PRIMA/PRIME. Due to the more complex in treatment and status of the patients (pts) in clinal practice, more real-world data is needed to verify the efficacy and safety of Niraparib. Meanwhile, exploring the link between clinical characters and PFS, may to establish a clinical model to predict Niraparib benefits. **Methods:** This is a retrospective multicentric study recruiting OC pts received Niraparib as 1st-L MT from fourteen hospitals throughout China from Jan. 2019 to Dec. 2021. The database lock-time was on Dec. 31st, 2022. The pts' basic characters, especially biomarkers, KELIM scores, etc. were recorded. Survival analyses were conducted using the Kaplan-Meier method and log-rank test, and 95% CI were calculated. The primary endpoint was PFS, and secondary endpoints included time to treatment discontinuation (TTD), time to first subsequent therapy (TFST) and safety. The exploratory endpoint was to establish a clinical prediction model of Niraparib benefits. **Results:** 199 pts' data were analyzed. The median(m) follow-up at the time of the data cutoff was 14.93 months (mos) (12.17, 39.47). Baseline characteristics were shown in Table. MPFS was not reached (NR) (29.80 to not be estimated, NE), with maturity 29.64%, and PFS rate at 6, 12, 18, 24mos was 89.4%, 79.5%, 68.3%, 64.5% respectively, showing the efficacy of Niraparib. MPFS (95% CI) in subgroups were as follows: BRCAwt 23.83mos (23.83 to NE); HRD negative 15.63mos (12.6 to NE); KELIM < 1 NR (15.33 to NE); BRCA1/2m, HRD positive and KEILM≥1 subgroups were all NR yet, due to the no longer enough follow-up time and low data maturity. Multivariate analysis found that pts with <65 years, BRCA1/2m, HRD positive, KELIM > 1, and R0 after primary cytoreductive surgery were likely to have longer PFS. The rate of grade ≥3 thrombocytopenia was 19.1%. Treatment discontinuation occurred in 11 (5.5%) pts due to TEAEs. The clinical prediction model for probability of progression was established from 149 pts (training dataset): Score = 0.612 $Age_{>65}$ + 0.3889 $BMI_{\leq 23.90}$ + 0.097 $FIGO_{IV}$ + 0.191$Chronic_{N}$ +1.398 $Surgery\ result_{R1/R2}$ +2.552 $BRCA_{wt}$. The probability of disease progression received Niraparib in 6, 12 and 18m can be obtained by mapping the score to the nomogram. **Conclusions:** The efficacy and safety of Niraparib in this study are consistent with the results in PRIME. The clinical predictive model established in this database needs more data to be matured and verified. Research Sponsor: Beijing Science & Technology Innovation Fund (KC2021-JX-0186-143).

Some baseline characteristics.

| Characteristics | Number | % |
|---|---|---|
| Age (years), medium (range) | 57.00 (51.00, 63.50) | |
| BMI, medium (range) | 23.05 (21.09, 25.12) | |
| BRCA mutational status | | |
| BRCAm | 40 | 20.1 |
| BRCAwt | 131 | 65.8 |
| Unknown | 28 | 14.1 |
| HRD status | | |
| Positive | 66 | 33.2 |
| Negative | 52 | 26.1 |
| Unknown | 81 | 40.7 |
| KELIM score | | |
| >1 | 55 | 27.6 |
| ≤1 | 23 | 11.6 |
| Unknown | 121 | 60.8 |

**5552** **Poster Session**

## Venous thromboembolism prophylaxis during neoadjuvant chemotherapy for patients with ovarian cancer.

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**Background:** The primary objective was to assess the rate of venous thromboembolism (VTE) in patients with ovarian cancer who received neoadjuvant chemotherapy (NACT) following a quality improvement (QI) intervention of routine pharmacologic VTE prophylaxis compared to patients that did not receive prophylaxis. **Methods:** This is a retrospective cohort study of patients with pathologically confirmed ovarian cancer that received NACT between January 2009 to December 2021 from a single institution. Patients were excluded if VTE was diagnosed prior to initiating NACT. Routine pharmacologic VTE prophylaxis during NACT started in January 2017 following a QI initiative. VTE events were diagnosed by doppler scan of extremities or computed tomography of the chest ordered for symptomatic patients or diagnosed incidentally on routine treatment imaging. Patient factors and perioperative variates of interest were investigated for their association with VTE events through univariate and multivariate models. **Results:** A total of 290 patients with ovarian cancer received NACT and were included, with 106 of 290 patients (36.5%) receiving pharmacologic prophylaxis during NACT. Rate of VTE prophylaxis prior to the QI intervention was 3.68% (n=5) compared to 65.58% (n=101) after. The rate of VTE during NACT was 11.41% (n=21) without prophylaxis and 2.83% (n=3) with prophylaxis (p=0.013) (Table). The rate of any VTE event from the start of NACT through adjuvant chemotherapy was 20.11% (n=37) without prophylaxis and 4.72% (n=5) with prophylaxis ($p<0.01$). There was no difference in adverse bleeding events in those that received prophylaxis to those that did not (0% vs 1.32%, p=0.239). On univariate analysis, VTE prophylaxis was associated with a decreased risk of VTE during NACT (OR 0.23; 95% CI: 0.06-0.78) and any VTE during primary treatment (OR 0.19; 95% CI 0.07-0.52). On multivariate analysis, VTE prophylaxis remained significantly associated with reduced VTE rates during NACT and during primary treatment (p=0.02 and p=0.001, respectively). **Conclusions:** Routine administration of pharmacologic VTE prophylaxis during NACT for patients with ovarian cancer is associated with reduced risk of VTE during NACT and throughout primary treatment and is not associated with adverse bleeding events. Research Sponsor: None.

**VTE events with and without VTE prophylaxis during NACT.**

| Characteristics | No VTE Prophylaxis N=184 (63.4%) | VTE Prophylaxis N=106 (36.5%) | p-value |
|---|---|---|---|
| **Total VTE Events** | 37 (20.11%) | 5 (4.72%) | **<0.01** |
| **NACT VTE** | 21 (11.41%) | 3 (2.83%) | **0.013** |
| **VTE within 30 days of surgery** | 7 (3.80%) | 1 (0.94%) | 0.265 |
| **Adjuvant Chemotherapy VTE** | 11 (5.98%) | 1 (0.94%) | 0.062 |

NACT: neoadjuvant chemotherapy; VTE: venous thromboembolism.

**5553** **Poster Session**

## Circulating tumor DNA (ctDNA) as a marker of residual disease and recurrence in resected stage I-IV epithelial ovarian cancer (EOC).

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**Background:** The management of EOC remains challenging, with a high risk of relapse despite surgery, chemotherapy and maintenance therapy. Detection of ctDNA after surgery and adjuvant chemotherapy (CT) may identify patients (pts) at highest risk of recurrence suitable for treatment escalation. Our primary aim was to investigate the use of ctDNA as a marker of residual disease following both surgery and adjuvant CT that might predict later recurrence. **Methods:** In this multi-centre observational study, we collected blood samples post-op and 6-8 weeks post-CT completion from pts with debulked stage I-IV EOC planned for adjuvant CT. Pre-cycle 1 CT and pre-op blood was also collected from some pts who received neoadjuvant CT. We used a tumor-informed approach for ctDNA analysis with whole exome sequencing of tumor tissue followed by detection of up to 50 variants in the plasma with the SaferSeqS assay. The primary outcome was recurrence-free survival (RFS), calculated using the Cox proportional-hazards model. **Results:** 81 pts who had post-op ctDNA results were included. 84% had high grade serous histology and 23% had BRCA mutations. Median number of tumor-informed variants analyzed in the plasma was 44 (range 3-60). Overall, post-operative ctDNA was detected in 63 of 81 (78%) of pts, 18 of 26 (69%) in Stage I-II and 45 of 55 (82%) in Stage III-IV. Pts who were ctDNA negative post-surgery had longer RFS versus who were ctDNA positive (HR 3.28, 95% CI 1.39 to 7.72, p = 0.007). Estimated RFS at 2 years was 78% among pts who were ctDNA negative post-surgery and 44% among the ctDNA positive group. Pts with BRCA mutations were less likely to have positive post op ctDNA (OR 0.12, 95% CI 0.036 to 0.39, $p < 0.001$). For post-CT ctDNA, estimated RFS at 2 years was 74% in the ctDNA negative pts versus 43% in the ctDNA positive group but this was not statistically significant (HR 1.64, 95% CI 0.84 to 3.18, p = 0.15). Pts with zero residual disease were more likely to be ctDNA negative post-surgery (OR 12.36, 95% CI 1.54 to 99.4, p = 0.018). Post-op ctDNA outperformed post-op CA-125 in predicting recurrence; pts with elevated CA-125 post-surgery had shorter RFS compared to those with normal CA-125 post-surgery (HR 1.99, 95% CI 1.15 to 3.42, p = 0.013). Of 18 pts who had neoadjuvant CT, pre-treatment ctDNA was detected in 17 (94%). Only two pts had clearance of ctDNA post neoadjuvant CT and both had zero residual disease at surgery. For the pts that maintained positive ctDNA results post-op, 7/15 (47%) pts had zero residual disease. **Conclusions:** ctDNA detection after ovarian cancer cytoreduction identifies pts at very high risk of recurrence. Pts with BRCA mutations were more likely to have negative ctDNA post-op. The role of ctDNA in guiding neoadjuvant and adjuvant therapy to improve outcomes, warrants further investigation. Clinical trial information: ACTRN12617001119381. Research Sponsor: Marcus Foundation; Epworth Medical Foundation Grant.

**5554** **Poster Session**

## Safety and efficacy of PIPAC in patients with ovarian cancer with peritoneal metastases: A first-in-US phase I study.

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**Background:** Epithelial ovarian cancer (EOC) is characterized by chemoresistant recurrences primarily confined to the intraperitoneal cavity, frequently leading to malignant small bowel obstructions. Intraperitoneal (IP) chemotherapy has been incorporated in EOC, but only in the first-line setting. Pressurized intraperitoneal aerosolized chemotherapy (PIPAC) is a novel IP drug delivery method that optimizes tissue penetration depth and drug distribution, to treat recurrent peritoneal malignancies. Recent trials outside the U.S. demonstrated partial to stable response following PIPAC in recurrent EOC. To date, no clinical trials have been completed investigating the role of PIPAC in EOC in the United States. **Methods:** We performed a multicenter prospective phase I trial using IP cisplatin 10.5 mg/m2 and doxorubicin 2.1 mg/m2 via PIPAC at 6-week intervals. Patients were eligible if they had recurrent disease with peritoneal metastasis; extraperitoneal metastasis was allowed. The primary endpoint was dose-limiting toxicity (DLT). Secondary endpoints included progression free survival, PCI scoring, RECIST measurements, and quality of life (QoL). The patients with gastric and uterine cancers' toxicity data were used but given inherent prognostic differences the treatment efficacy for these patients were not used in this analysis. Adverse event (AE) monitoring was graded using CTCAE spanning 18 weeks. Following completion of treatment ($^3$2 PIPACs) patients were followed up every 12 weeks. QoL was measured using patient-reported assessments at 0, 6, 12, and 18 weeks. Baseline demographics were summarized. Mean change in PCI was calculated between cycle (C) 1 and 2, and cycle 2 and 3. Toxicities attributed to the surgery or PIPAC were reported with highest grade for each patient. **Results:** Nine heavily pretreated, recurrent patients were enrolled in the trial: 7 with platinum-resistant recurrent EOC, 1 with uterine cancer, and 1 with gastric cancer. PIPAC completion rate was 71.4%. Median age of participants was 65 years. Median prior lines of chemotherapy were 4 (range 2 - 10). No surgical complications occurred in the cohort. Two patients came off study: one for G3 abdominal pain and the other for G3 anorexia. For the EOC cohort, the median PCI reduction was -1.4% (C1 to C2) and -2.8% (C1 to C3). One low-grade serous EOC patient demonstrated a partial response based on RECIST criteria and received 6 cycles. Two EOC patients showed an initial response based on PCI reduction, but progressed following Cycle 2. Overall, QoL was stable. **Conclusions:** PIPAC with cisplatin/doxorubicin in platinum-resistant ovarian cancer is well tolerated. Intraperitoneal responses were seen in a subset of low-grade serous ovarian cancer patients, which may warrant further study. Heavily pretreated, platinum-resistant high-grade EOC patients derived limited intraperitoneal control from PIPAC monotherapy. Clinical trial information: NCT04329494. Research Sponsor: Internal Funding.

**5555** **Poster Session**

## Analyses of tumor microenvironment affecting the survival in patients with ovarian cancer receiving intraperitoneal chemotherapy: Translational research from the phase 3 trial of intraperitoneal therapy for ovarian cancer with carboplatin (TRiPocc).

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**Background:** The iPocc trial is a randomized, global phase (P) 3 study of intraperitoneal (IP) versus intravenous (IV) carboplatin with dose-dense paclitaxel chemotherapy in epithelial ovarian cancer (EOC) patients that demonstrated an improved progression-free survival (PFS) but not overall survival (OS) in the former. IP chemotherapy induces an antitumor immune response and increases survival in a murine xenograft model. This study aimed to assess whether immunological background affected the clinical outcomes of patients receiving IP chemotherapy. **Methods:** Fresh frozen tumor samples at the time of primary surgery were obtained from 116 patients who joined the iPocc P3 trial for microarray analysis. Cell-type deconvolution was performed using MCP counter. Single sample Gene Set Enrichment Analysis was performed to evaluate the tumor immune microenvironment. Clinical data were obtained from the iPocc P3 trial. We stratified 116 patients according to the high or low values of each factor determined by the median values. The Kaplan-Meier method and log-rank test were used to analyze PFS and OS. **Results:** A total of 116 patients were assigned to either the IP (n=59) or IV (n=57) group. The most common histologic type was serous (58.6%), followed by endometrioid (17.2%) and clear cell (12.1%). The patients who received IP therapy had longer OS than those who received IV therapy in the group with a high infiltration of T cells, NK cells, or cytotoxic lymphocytes in the MCP counter (median OS: not reached (NR) vs 75.0 months, P=0.041, NR vs. 75.0 months, P=0.042, NR vs 65.2 months, P=0.031), but not in the group with a low infiltration. Similarly, the IP therapy improved OS in the patients with high expression of immune-related genes such as *CD8A*, *FOXP3* or *PDCD1* (median OS; NR vs 65.2 months, P=0.035, NR vs 65.2 months P=0.030, NR vs 53.1 months, P=0.016), but not in the patients with low expression of those genes. In addition, a multifaceted evaluation was conducted because of the limitations of evaluating the interaction between cancer and immunity using a single factor. When the patients were divided into two groups, “Immune Hot” and “Immune Cold” based on the hierarchical clustering analysis with 4 parameters representing “Innate immunity,” “T cells,” “Interferon gamma response” and “Inhibitory molecules,” the IP therapy increased both PFS and OS compared to the IV therapy in the “Immune Hot” group (median PFS; 35.5 vs 23.4 months, P=0.024, median OS; NR vs 75.0 months, P=0.040), but not in the “Immune Cold” group. **Conclusions:** IP therapy may improve the survivals in EOC patients with a high immunological background. Further studies are warranted to validate this hypothesis and to clarify the impact of IP therapy on the tumor immune microenvironment. Clinical trial information: NCT01506856 / GOTIC-001/ JGOG3019. Research Sponsor: None.

**5556** **Poster Session**

## Pegylated liposomal doxorubicin and carboplatin versus paclitaxel and carboplatin as first-line treatment for Chinese patients with ovarian cancer: A multi-center, randomized, open-label trial.

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**Background:** Paclitaxel combined with carboplatin is a standard first-line chemotherapy regimen for ovarian cancer. This study was designed to evaluate the efficacy and safety of pegylated liposomal doxorubicin (PLD) plus carboplatin (CD) compared with paclitaxel plus carboplatin (CP) as first-line treatment for epithelial ovarian cancer (EOC). **Methods:** Patients with stage IC to IV EOC, fallopian tube cancer, or primary peritoneal cancer were eligible for enrolment in this open-label, randomized controlled trial at 20 centers in China. Patients were randomly assigned 1:1 to CD group (carboplatin area under the curve [AUC] 5 plus PLD 30 mg/m$^2$) or CP group (carboplatin AUC 5 plus paclitaxel 175 mg/m$^2$) every 3 weeks for 3-6 cycles. The primary end point was progression free survival (PFS); secondary end points were overall survival (OS), objective response rate (ORR), disease control rate (DCR) and safety. **Results:** Between March, 2019 to December, 2021, 395 patients were enrolled, of whom 391 patients were analyzed (195 assigned to CD, 196 to CP). Baseline characteristics were balanced between the two treatment groups. The median follow-up was 21.6 months for the CD group and 22.5 months for the CP group. There was no significant difference in PFS between the two arms (P=0.516); the median PFS was 28.1 months and 30.1 months in the CD and CP arms, respectively. OS data were immature at data cutoff, with a total of 26 deaths in the two treatment groups. In patients with at least one measurable lesion at baseline, ORR was 65.5% in the CD arm and 66.2% in the CP arm (P= 0.941); DCR was 74.1% and 73.8% in the CD and CP arms, respectively (P= 0.971). Among patients who were evaluable by GCIG CA125 criteria, CA125 response was obtained in 86.0% and 88.5% of patients in the CD and CP arms, respectively (P=0.560). More frequent grade 1 to 3 alopecia (32.1% vs 12.3%) and neurotoxicity (20.4% vs 0%) were observed in the CP arm; more hand-foot syndrome (grade 1 to 3, 10.8% vs 2.6%), and oral mucositis (grade 1-3, 12.8% vs 5.1%) in the CD arm. **Conclusions:** The efficacy of CD regimen is comparable to that of CP, with less alopecia and neurotoxicity. CD may be an alternative first-line treatment for EOC. However, survival data are not yet mature, and longer follow-up is needed. Clinical trial information: NCT03794778. Research Sponsor: CSPC Ouyi Pharmaceutical Group Co., Ltd.

**5557** **Poster Session**

## The role of innate immune system in modulating CHK1 inhibitor (CHK1i) response in BRCA wild-type (BRCAwt), platinum-resistant high-grade serous ovarian cancer (PR-HGSOC): Exploratory analysis from a phase II study of CHK1i prexasertib.

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**Background:** Immune checkpoint blockade, *e.g.,* anti-PD-1/PD-L1, demonstrated limited efficacy in HGSOC despite high levels of tumor-infiltrating lymphocytes, suggesting the innate, rather than adaptive, immune system may play a prominent role in anticancer response. Preclinical studies suggest CHK1i modulates the innate immune milieu. We previously showed clinical activity of prexasertib in BRCAwt, PR-HGSOC patients (pts). Here, we investigated the association of innate immunogenic features with CHK1i response. **Methods:** Prexasertib was given at 105 mg/m$^2$ IV every 14 days in a 28-day cycle. Baseline (BL) fresh core biopsies were collected from pts enrolled in the biopsy (Bi) cohort for RNA sequencing. Computational immunogenomic analysis (CIBERSORT) was used for immune cell fractions quantification. Blood samples (BS) were obtained at BL and cycle 1 day 15 (C1D15) from pts enrolled in both Bi and non-Bi (nBi) cohorts for multiparametric flow cytometry (FC) analysis to evaluate dynamic changes in immune cell subsets. Mann-Whitney and Wilcoxon tests were used to compare unpaired and paired data, respectively. **Results:** 49 BRCAwt, PR-HGSOC pts were enrolled in the Bi cohort (n=25) and nBi cohort (n=24). 39 were evaluable per RECIST v1.1. 18/39 pts (46.2%) had a clinical benefit (CB), defined as progression-free survival$\geq$6 months. Transcriptomic profiles of BL biopsies (n=15) met the quality control and assurance (Gene Similarity Index, Principal Component Analysis) for further *in silico* analysis. CIBERSORT analysis did not exhibit any differences in the immune cell fractions between CB and non-CB (NCB) groups at BL. FC analysis on paired BS (BL and C1D15) showed an increase of immunosuppressive monocytic myeloid-derived suppressor cells (M-MDSCs, $p<0.001$) and classical monocytes (CM, $p=0.003$) in the NCB group (18 paired BS). In the CB group (19 paired BS), CD141+ and CD1c+ dendritic cells (DCs) express higher rates of CD83, a marker of maturity and functionality ($p<0.001$ and $p<0.001$, respectively), despite no increase in the absolute number of DCs. At C1D15, a higher rate of M-MDSCs (median 7.8% vs. 5.52%; p=0.03) and CM (median 40.7% vs. 31.7%; p=0.03) were found in the NCB group (n=18) compared to the CB group (n=19); also, CM showed lower expression of HLA-DR in the NCB group (median 19.25% vs. 27.8%; p=0.02). **Conclusions:** Collectively, our data suggest the possible involvement of innate immunity in modulating CHK1i response. Increasing peripheral immunosuppressive cells and lower immunocompetence of the innate immune system may contribute to CHK1i resistance, whereas the functionality of DCs may be involved in the response. Enhancing innate immunity may represent a strategy to increase CHK1i response in this hard-to-treat population. Clinical trial information: NCT02203513. Research Sponsor: U.S. National Institutes of Health.

**5558** **Poster Session**

## DNA methylation patterns between tissue and blood samples in ovarian cancer.

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**Background:** Altered DNA methylation pattern, with functional consequences in the activity of key carcinogenic pathways, has been shown to be involved in the carcinogenesis of ovarian cancer. Tumor DNA is released into the blood via apoptosis or necrosis. Therefore, cell-free DNA (cfDNA) methylation alteration can also be detected in blood, which has shown promising performance in ovarian cancer early detection and prognostication. However, the difference of DNA methylation patterns between the tissue and blood samples of ovarian cancer is still unclear. **Methods:** PERCEIVE-I study (NCT04903665) is a prospective study aimed at the early detection of gynecological malignancies. Blood and paired tissue samples from this study were collected at the Fudan University Shanghai Cancer Center. Blood samples from age-matched non-cancer controls were also collected. All the blood and paired tissue samples were sequenced by a target methylation panel covering ~490,000 CpG sites. Finally, The ovarian cancer methylation patterns were analyzed based on 11 paired cancer-adjacent tissue samples and 170 blood samples (cancer, n=48; non-cancer control, n=122). **Results:** In total, 7,225 differentially methylated blocks (DMBs) were identified by comparing cancer and adjacent tissues, with 5,093 hypomethylated and 2,132 hypermethylated. By contrast, there were 5,853 hypomethylated and 8,685 hypermethylated DMBs in cancer blood samples compared with non-cancer controls. Among the 7,225 DMBs in tissues, 3,962 (54.8%) blocks were also observed to be altered in blood samples, including 2,354 hypomethylated blocks and 1,114 hypermethylated blocks. GO analysis revealed that these hypomethylated blocks were mainly associated with functions such as regulation of synaptic membrane and DNA-binding transcription activator activity, while the hypermethylated blocks were mainly enriched in the pattern specification process, transcription factor complex, and the DNA-binding transcription activator activity. The alteration of the above 3,962 DMBs in tissue were highly correlated with the alteration in blood (correlation coefficient of 0.71, 0.50, 0.73 and 0.73 for stage I-IV, respectively). Furthermore, in patients carrying germline *BRCA1/2* mutations (n=11), most of the above DMBs were not significantly different from those without germline *BRCA1/2* mutations (n=37). **Conclusions:** In this study, we demonstrated that blood DNA methylation alteration was highly consistent with tissue DNA methylation alteration in ovarian cancer, indicating the sustained release of DNA methylation signals from the primary cancer sites. These results suggest that cfDNA methylation can be used as reliable biomarkers for the early detection of ovarian cancer. Clinical trial information: NCT04903665. Research Sponsor: None.

# *BRCA1* and *RAD51* methylation impact on outcome in patients with advanced ovarian cancer: A PAOLA-1 ancillary study.

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**Background:** The PAOLA-1/ENGOT-ov25 trial showed that adding olaparib (ola) to maintenance bevacizumab (bev) after first-line therapy led to a progression-free and overall survival benefit in advanced ovarian high-grade carcinoma (AOC) patients with homologous recombination deficiency (HRD) (Myriad MyChoice$^{R}$ Genomic Instability Score) or *BRCA1/2* mutations *(BRCAmut).* Here, we address the impact of *BRCA1* and *RAD51C* epimutations to improve our understanding of GIS beyond *BRCAmut.* **Methods:** *BRCA1 and RAD51C* methylation analysis was assessed and quantified in pre-treatment biopsies (66%), after neoadjuvant chemotherapy (NACT) (20%) or unknown (14%) from bisulfite converted DNAs using fluorescent methylation specific PCR and methylation specific droplet digital PCR (ddPCR). Methylation status was correlated to clinical data, BRCA1/2 mutations, GIS and HRD scores, PFS (PFS1, PFS2) and OS. R (r-project.org) was used for statistical analysis. **Results:** Among the 537 patients randomized to maintenance ola + bev and 269 to placebo (pbo) + bev, 348 and 171 were available for methylation analysis. Their baseline molecular and clinical characteristics were well balanced with those of the entire cohort. Promoter methylation was identified in 67 (12.9%) samples for *BRCA1* and 25 (4.8%) for *RAD51C* (4 were methylated on both genes). Methylation and *BRCAmut* were mutually exclusive except for 3 samples. Mean GIS scores were 62.5 [59.6-65.5]; 59.4 [57.2-61.5]; 54.2 [50.5-57.8]; 23.4 [21.6-25.2] for *BRCA1* or *RAD51C* methylated (*met-tumors), BRCAmut*, *non-mut/non-met* HRD+ (*b-/m-HRD+*) and HRP (proficient) tumors respectively. Among *met-tumors* 92% (66/72) were GIS positive (>42). The mean GIS score of *Met*-tumors were significantly higher than that of b-/m- HRD+ samples (p=0,009). Benefit of adding ola maintenance to bev was in a similar between patients with *met* AOC and those with *b-/m- HRD+* tumors (*table*). **Conclusions:** Methylated BRCA1/RAD51 tumors are HRD+ and provide to ovarian cancer patients a similar clinical benefit of ola+bev as patients with *b-/m- HRD+* tumors. Methylation assessment represents a rapid and cost effective tool; which coupled with *BRCA1-2* somatic testing allows the identification of the majority (81%) of HRD+ AOC. Clinical trial information: NCT02477644. Research Sponsor: Fondation ARC pour la recherche sur le cancer.

| | BRCAmut | | met | | b-/m- HRD+ | | HRP | |
|---|---|---|---|---|---|---|---|---|
| | Olaparib | placebo | Olaparib | placebo | Olaparib | placebo | Olaparib | placebo |
| N | 106 | 50 | 59 | 26 | 31 | 20 | 152 | 75 |
| Median PFS1 | 66.3 [42.6-75.2] | 22.0 [16.6-26.3] | 29.8 [22.0-42.1] | 17.4 [11.1-27.7] | 57.1 [18.7-NR] | 16.6 [11.8-24.9] | 16.7 [15.3-18.8] | 15.1 [14.0-18.7] |
| HR | 0.42 [0.27-0.66] | | 0.49 [0.29-0.84] | | 0.34 [0.17-0.67] | | 0.9 [0.73-1.34] | |
| Median OS | NR | 66.8 [55.6-NR] | 64.3 [53.3-NR] | 65.4 [32.3-NR] | NR [38.5-NR] | 54.4 [39.9-NR] | 36.6 [30.5-44.9] | 42.1 [28.7-54.2] |
| 5-years survival | 75% | 54% | 56% | 52% | 54% | 44% | 28% | 35% |
| HR | 0.52 [0.30-0.92] | | 0.76 [0.42-1.50] | | 0.78 [0.35-1.76] | | 1.2 [0.86-1.71] | |

(NR: Not reached)

**5560** **Poster Session**

## Randomized phase 2 trial of personal dendritic cell (DC)-autologous tumor antigen (ATA) vaccines in newly diagnosed advanced ovary cancer.

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**Background:** Advanced ovarian cancer has a high recurrence rate and poor overall survival (OS). The addition of DC-ATA AV-OVA-1, a personal vaccine consisting of autologous DC pulsed with ATA, was investigated to pursue improving OS. **Methods:** A multi-center, 2:1 double-blind randomized phase 2 trial was designed for patients with newly diagnosed stage 3 or 4 epithelial ovary cancer to determine feasibility of manufacturing study product, and to compare safety and efficacy between DC-ATA and autologous monocytes (MC). Primary endpoint was OS from randomization. Following completion of debulking surgery and chemotherapy, about 6 to 7 months after initial tumor collection, patients were screened and eligible for randomization if a short-term cell line was established from resected tumor, sufficient numbers of MC were collected by leukapheresis, and ECOG status was 0 or 1. Intent was to enroll 99 patients stratified by whether they had residual cancer. MC were differentiated into DC by incubating with IL-4 and GM-CSF. DC-ATA was produced by incubating DC with an ATA lysate prepared from irradiated self-renewing tumor cells. Just prior to each treatment, DC-ATA or MC was admixed in 500 mg GM-CSF and injected s.c. at weeks 1, 2, 3, 8, 12, 16, 20 and 24 (up to 8 doses). Interferon-gamma elispot assays were performed on cryopreserved mononuclear cells obtained from heparinized blood collected prior to each of the first 3 injections. Patients were monitored for adverse events (AE), immune response, OS, and progression-free survival (PFS). Analysis was planned after 44 deaths. **Results:** During the SARS-CoV-2 pandemic the sponsor terminated accrual and long-term follow up. 70/72 tumors yielded a successful cell line. 20/70 patients did not proceed with leukapheresis. Sufficient MC were collected from 47/50 patients. 45 patients were randomized: 29 to DC-ATA, 16 to MC. Study arms did not differ in patient age, cancer stage, use of neoadjuvant therapy, ECOG status, or residual cancer. Injections were well-tolerated. No patient stopped therapy because of toxicity. Mean number of injections were 7.7 and 7.3. Study arms did not differ in type, proportion or severity of AE, which typically were mild to moderate, short-lived, and self-limited. Number of interferon-gamma elispots were unchanged after MC (p=0.256), but more than doubled after DC-ATA (p-0.0012). The 45 patients were followed for 1 to 31 months from randomization. Median PFS (24 events) was 16.9 months (95% CI 9.2 to 18.7); median OS was not reached (8 deaths). 1-yr OS was 91% (95% CI 78.9, 96.9), 2-yr was 80% (95% CI (49.7, 93.7). There was no difference between study arms in PFS (p=0.837) or OS (p=0.790). **Conclusions:** Manufacturing DC-ATA was feasible and treatment well-tolerated. There were no differences in AE, PFS or OS between study arms, but survival analyses were severely underpowered. An enhanced immune response was detected after DC-ATA. Clinical trial information: NCT02033616. Research Sponsor: AIVITA Biomedical Inc.

**5561** **Poster Session**

## Cell-free DNA in plasma and ascites as a biomarker of bevacizumab response: A translational sub-study of the REZOLVE (ANZGOG-1101) clinical trial.

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**Background:** The REZOLVE clinical trial investigated the effect of administering bevacizumab via the intraperitoneal route to reduce re-accumulation of ascites in patients with ovarian cancer who were not suitable for further chemotherapy. Plasma and ascites were collected throughout for translational research. Ascites contains cell-free DNA (cfDNA), a large proportion of which is tumour derived (ctDNA). There is increasing interest in cfDNA in plasma, yet little is known of it in ascites. Objectives: To compare cfDNA in ascites and plasma in terms of total concentration, tumour proportion and endothelial-cell derived (ec-cfDNA) proportion and investigate their association with clinical outcomes (paracentesis-free interval, overall survival) and CA125 level. **Methods:** Longitudinal plasma and ascites samples were collected from 20/24 participants and stored at -70°C for up to 8.5 years. cfDNA was extracted from 0.3-1 mL fluid using conventional protocols. Standard and methylation-specific PCR was used to measure total cfDNA, ctDNA and ec-cfDNA. Values were correlated with time to paracentesis pre- and post-bevacizumab treatment (the primary trial outcome) as well as overall survival, using log-rank tests. Relationships with clinical CA125 levels were tested by Pearson's correlation coefficient. Comparisons between plasma and ascites used non-parametric analyses. **Results:** cfDNA was detected in all samples, with higher yield in ascites (average 669 ng/mL) than plasma (average 75 ng/mL, $p<0.0001$). ctDNA was detected in 30/32 (94%) ascites samples and 37/56 (68%) plasma samples. ctDNA was detected in plasma and/or ascites from each patient at at least 1 time point. ctDNA proportion was higher in ascites than plasma ($p<0.0001$) and ec-cfDNA proportion was higher in plasma than ascites ($p=0.002$). High ctDNA (>75%) in ascites at baseline was associated with significantly shorter paracentesis-free interval (median interval 47.5 versus 84 days, hazard ratio (HR) 2.21, 95% confidence interval (CI) 0.85 to 5.73, $p=0.039$). ctDNA presence in plasma at baseline was unfavourable for survival (median survival 56 versus 242 days, HR 3.21, 95% CI 1.15 to 9.00, $p=0.008$). A significant positive correlation was observed between ctDNA proportion in plasma and CA125 level measured within 7 days ($p=0.0006$). No difference in total cfDNA, ctDNA nor ec-cfDNA was observed between participants who were bevacizumab responders and non-responders in the trial. **Conclusions:** Sufficient cfDNA was obtained from plasma and ascites to perform qPCR for three biomarkers. Ascites was found to contain proportionately more ctDNA, while plasma contained more ec-cfDNA. The early evidence presented here supports the potential value of cfDNA biomarkers in plasma and ascites, however incorporation of their collection in future clinical trials will allow further investigation. Research Sponsor: Philanthropic.

# Efficacy and safety of niraparib maintenance therapy in patients with newly diagnosed advanced ovarian cancer who had measurable residual disease: A post-hoc subgroup analysis of the PRIME study.

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**Background:** Niraparib maintenance therapy significantly prolonged progression-free survival (PFS) versus placebo in patients with newly diagnosed advanced ovarian cancer (aOC), but its antitumor activity remains unclear in those with measurable residual disease (MRD) after first-line platinum-based chemotherapy (1LCT). This study aims to report the efficacy, including antitumor activity, and safety of niraparib maintenance therapy in patients with MRD after 1LCT from the phase 3 PRIME trial (NCT03709316). **Methods:** In PRIME, adults with newly diagnosed aOC who had received cytoreductive surgery and responded to 1LCT were randomized 2:1 to receive niraparib or placebo with stratification by receipt of neoadjuvant chemotherapy, response to 1LCT, status of germline *BRCA* mutations, and tumor homologous recombination deficiency status. Tumor assessment was conducted at baseline and every 12 weeks thereafter by blinded independent central review (BICR) according to RECIST, version 1.1. Between 29 June 2018 and 11 November 2019, 384 patients were randomized (255 niraparib, 129 placebo). The data cut-off date was 30 September 2021. This *post-hoc* analysis reports BICR-assessed objective response rate (ORR) and PFS in patients with MRD at baseline. An initial response was confirmed ≥4 weeks later. **Results:** In total, 73 (19.0%) patients (47 niraparib, 26 placebo) had MRD at baseline. Baseline characteristics were well balanced between the two MRD groups. Complete and partial responses, both confirmed, were observed in 12 (25.5%) and 15 (31.9%) niraparib-treated patients and 3 (11.5%) and 5 (19.2%) placebo-treated patients, respectively, leading to a confirmed ORR of 57.4% with niraparib and 30.8% with placebo (odds ratio, 3.20; 95% confidence interval [CI], 1.11–9.11). ORRs by biomarker status are provided in the table. Median PFS (95% CI) was 22.3 (8.7–not estimable) months with niraparib versus 8.3 (5.6–11.0) months with placebo (hazard ratio, 0.36; 95% CI, 0.19–0.71). Treatment-emergent adverse events (TEAEs) of grade ≥3 occurred in 28 (59.6%) niraparib-treated patients and 7 (26.9%) placebo-treated patients. TEAEs led to treatment discontinuation in three (6.4%) niraparib-treated patients and one (3.8%) placebo-treated patient. **Conclusions:** In patients with newly diagnosed aOC who had MRD after 1LCT, niraparib maintenance therapy tended to induce additional antitumor activity and led to a clinically meaningful increase in PFS versus placebo. Clinical trial information: NCT03709316. Research Sponsor: This study was funded by Zai Lab (Shanghai) Co., Ltd and partially supported by the National Major Scientific and Technological Special Project for Significant New Drugs Development in 2020, China [grant number 2020ZX09101-014.

**ORRs by biomarker status.**

| ORR, % (CR/PR/N) | Niraparib | Placebo |
|---|---|---|
| **Germline *BRCA* mutations** | | |
| **Yes** | 69.2 (2/7/13) | 37.5 (0/3/8) |
| **No** | 52.9 (10/8/34) | 27.8 (3/2/18) |
| **Homologous recombination status** | | |
| **Deficient** | 61.3 (10/9/31) | 29.4 (2/3/17) |
| **Proficient** | 50.0 (2/6/16) | 33.3 (1/2/9) |

CR, complete response; ORR, objective response rate; PR, partial response.

**5563** **Poster Session**

## Ex vivo tumor testing platform for predicting clinical response to platinum-based therapy in patients with high grade serous ovarian cancer.

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**Background:** Precision medicine for cancer patients has brought effective novel therapy options over the past decades. However, treatment for high-grade serous ovarian cancer (HGSOC) is still based on platinum-containing therapy. Around 30% (Morgan 2020) of primary disease patients do not respond to this treatment, and non-response rates in residual disease are higher still. We present an ex vivo 3D tumor testing platform that predicts patient-specific response to standard of care therapy using the CA125 half-life, the primary ovarian cancer marker (Charkhchi, 2020). **Methods:** Patients with HGSOC, eligible for platinum-based neoadjuvant chemotherapy (NACT), were included in the study between 2019 and 2022 in the Netherlands (IRB P18.032). Clinical data was collected including CA125 levels at baseline and after 2-4 courses of NACT. Tumor clusters enriched from ascites were embedded in hydrogel and exposed to first-line (carboplatin, paclitaxel) and second-line therapies (doxorubicin, gemcitabine, topotecan and olaparib). Screening plates were imaged in a high content screening 3D platform. Morphological features were extracted after image analysis and fitted as dose-response (Hill-) curves. A Bayesian linear regression model was trained on the AUCs of carboplatin and paclitaxel to predict the CA125 half-life. The result was classified according to clinical standards: insensitive (IN, progressive and stable disease), moderate response (MR), or strong response (SR). In addition, for each second-line treatment the top 25% strongest responding samples were classified as *sensitive* while the bottom 25% were classified as *resistant* samples. **Results:** The model was trained using 30 patients. The correlation coefficient between the predicted and actual CA125 half-life is 0.739 ($R2 = 0.55$). This results in a classification accuracy of 87% (insensitive: 100% ($n = 2$), MR: 80% ($n = 14$), SR: 80% ($n = 14$)). The percentage of samples, per response class, responding to at least one of the alternative chemotherapies is as follows: SR: 58% (8/14), MR: 29% (4/14) and IN 50% (1/2). For olaparib the equivalent results are SR: 36% (5/14), MR: 21% (3/14) and IN: 0% (0/2). When sufficient tumor content is received, the assay has a technical success rate of 89%. Results are delivered in two weeks. **Conclusions:** The presented platform for *ex vivo* tumor testing predicts clinical response to platinum-based NACT in HGSOC patients. The same platform measured patient specific patterns of relative sensitivity to other chemotherapies. The platform enables better stratification of responders vs non-responders, and can support informed treatment decisions for first-line and second-line therapies. The value of integration of this predictive tool in the clinical routine will be assessed in an ongoing prospective trial for patients with suboptimal response and recurrent disease. Clinical trial information: P18.032. Research Sponsor: VitroScan BV; Subsidy: EUREKA Eurostars.

**5564** **Poster Session**

## Phase 2 trial of TRC102 (methoxyamine HCl) with temozolomide (TMZ) in patients with granulosa cell ovarian cancer.

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**Background:** TRC102 is a novel small molecule that binds to reactive aldehyde created in apurinic/apyrimidinic (AP) sites, inhibiting base excision repair (BER), which is implicated as a pathway of resistance to alkylating agents. In preclinical studies, TRC102 demonstrated synergistic anti-tumor activity when TRC102 was combined with the alkylating agent temozolomide (TMZ) and the phase 1 trial of this combination reported 4 patients with partial response, two of which were of granulosa cell ovarian cancer (GCOC) histology. Here we report the phase 2 results of the combination TRC102 and TMZ in the GCOC cohort (NCT01851369). **Methods:** We conducted an open-label, single center Simon 2-stage trial including patients (pts) with GCOC who received $\geq$ one line of therapy in the metastatic setting. TRC102 was dosed at 125 mg (100 mg for BSA $<$ 1.6) and TMZ was dosed at 150 mg/m$^2$ orally on day (D) 1-5 in 28-day cycle (C). Restaging CT scans every 2 Cs were evaluated by RECIST v1.1. Mandatory paired biopsies (C1D1 pretreatment and C1D4 3-4 hours after drug administration) and optional blood samples for circulating tumor cells (CTC) were collected at set time points for pharmacodynamic analyses. **Results:** Nine pts with GCOC (7 adult, 2 juvenile histology) were enrolled as of 12/23/2022. Median age was 53 years (range 21-79) and median prior lines of therapy was 6 (range 3-9). Most common grade (G) 1 and G2 treatment-related adverse events (trAE) were fatigue, myelosuppression, nausea, and vomiting. One pt had G3 trAE of vomiting. No toxicity-related treatment discontinuations and no treatment-related deaths were reported. The median PFS for the 8 evaluable pts was 3.7 months. One pt exited the study after one C per pt's choice with no restaging available. Four pts had stable disease (SD) as their best response. Of those who had SD, one pt completed 26 Cs prior to progression, one pt completed 11 Cs as of data cut-off but continues on study, two pts completed 6 Cs (one pt went off study for PD and one by pt choice). MGMT analysis was performed for 3 pts, including the pt still on study after 11 Cs with SD. MGMT immunohistochemistry (IHC) of pretreatment biopsies were positive for protein expression, consistent with unmethylated MGMT status. No significant induction in the levels of the DNA damage response markers $\gamma$H2AX, pNbs1, and RAD51 was detected in 5 evaluable post-treatment biopsy samples as compared to the pre-treatment timepoint. **Conclusions:** TRC102 combined with TMZ was well-tolerated and demonstrated durable disease control in 4 pts, which is promising in this heavily pretreated GCOC cohort. MGMT analysis suggests that unmethylated MGMT status and protein expression does not preclude response to TRC102/TMZ combination therapy. Analysis of CTCs and biopsy samples are ongoing to further elucidate possible biomarkers of response. Funded by NCI Contract No. HHSN261201500003I. Clinical trial information: NCT01851369. Research Sponsor: U.S. National Institutes of Health.

**5565** **Poster Session**

## Germline variants in non-*BRCA1/2* homologous recombination-related genes and ovarian cancer: Analysis of tumor phenotype and survival.

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**Background:** *BRCA1/2*-associated ovarian cancer (OC) exhibits homologous recombination (HR)-deficiency (HRD) and a better prognosis than *BRCA1/2*-wildtype (WT) OC. However, it is unclear if patients with germline pathogenic variants (gPV) in other HR-related genes have a similar tumor phenotype. We sought to define OC molecular features from patients with gPV in other HR genes and analyze survival compared to patients with *BRCA1/2* and WT OC. **Methods:** We identified patients with OC treated at our institution who underwent tumor-normal sequencing using MSK-IMPACT targeting 341-505 cancer-related genes with germline analysis of ≥76 genes from 7/2015-12/2020. Biallelic inactivation was inferred via assessments of loss of heterozygosity (LOH) at gPV in non-*BRCA1/2* HR-related genes (*ATM, BARD1, BRIP1, FANCA, FANCC, NBN, PALB2, RAD50, RAD51B, RAD51C,* and *RAD51D).* Clinical characteristics were compared to patients with *BRCA1/2*-associated and WT OC using non-parametric tests. Progression-free (PFS) and overall-survival (OS) were calculated from date of pathologic diagnosis using the Kaplan-Meier method. Left truncation at date of MSK-IMPACT consent was applied. Whole-exome sequencing (WES) was performed in a subset of OCs. **Results:** Of 882 patients with OC, 56 (6.3%) had gPV in non-*BRCA1/2* HR-related genes compared to 95 (10.8%) patients with *BRCA1*-associated OC (58 germline, 37 somatic) and 59 (6.7%) patients with *BRCA2*-associated OC (40 germline, 19 somatic). Patients with a deleterious genetic alteration were diagnosed with OC at younger age and more likely to have high-grade serous histology compared to the WT group ($p < 0.01$). High rates of biallelic alterations were observed amongst gPV in *BRIP1* (11/13), *PALB2* (3/4), *RAD51B* (3/4), *RAD51C* (3/4), and *RAD51D* (8/10), and WES was performed in a subset ($n = 27$) of tumors from these patients with adequate tumor purity (>30%). We observed a higher tumor mutational burden (TMB), median 2.5 (1.1-6.0) vs. 1.2 (0.6-2.6) mut/Mb, and enrichment of HRD mutational signatures in tumors associated with *PALB2* and *RAD51B/C/D* compared with *BRIP1* ($p < 0.01$), although markers of telomeric-allelic imbalance (TAI), large-scale state transitions (LST) and fraction of genome altered (FGA) were similar. PFS and OS varied by gene group with best survival in *BRCA1/2*-associated OC, even after adjustment for clinical covariates in multivariable models ($p < 0.01$). Although we observed heterogeneity in PFS and OS for those with gPV in other HR-related genes by biallelic status and HRD phenotype, none had significantly better survival than those with WT OC. **Conclusions:** OCs associated with gPV in non-*BRCA1/2* HR-related genes represent a heterogenous group. OCs in those with gPV in *PALB2* and *RAD51B/C/D* preferentially harbored biallelic alterations and displayed an HRD phenotype. Research Sponsor: U.S. National Institutes of Health; MSKCC.

# Anastomotic leakage following bowel resection in radical cytoreductive surgery for ovarian cancer: A subgroup analysis of the prospective AGO-OVAR.OP3/LION.

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**Background:** Anastomotic leakage (AL) is an important and severe complication following bowel resection in cytoreductive surgery (CRS) for ovarian cancer (OC). Identifying patients (pts) at risk for AL could improve clinical management and reduce frequency and severity of complications. **Methods:** AGO-OVAR.OP3/LION intraoperatively randomized 647 pts with advanced OC (FIGO IIB-IV) following complete cytoreduction with unsuspicious lymph nodes to either undergo systematic pelvic and paraaortic lymphadenectomy (LNE) or not. All pts who underwent bowel resection were included in this analysis. Potential prognostic impact of AL was analyzed by Kaplan-Meier method and log-rank tests regarding progression-free (PFS) and overall survival (OS). Risk factors for AL in a subset of clinicopathological parameters were evaluated by calculating odds ratio (OR) with 95% confidence interval (CI) in univariate and multivariate logistic regression models. A stepwise variable selection algorithm using the Akaike Information Criteria (AIC) for identification of the final logistic regression model was applied. *P* values presented were two-tailed, and $P<0.05$ was considered as statistically significant. **Results:** Among all 647 randomized pts, AL was noted in 24 (3.7 %) pts. The AL rate of the 336 pts with bowel surgery during CRS (median age 61.3 years; 316 large bowel, 94 small bowel resections) was 7.1% (24/336 pts). Pts following stoma formation had an AL rate of 5.5% (3/55 pts) compared to 7.5% (21/281 pts) in pts without stoma. Median PFS was 18 months in pts with AL versus 19 months in the no-AL-group (hazard ratio (HR) 0.86; 95% CI 0.5 to 1.4, $P=0.53$), median OS was 31 months in the AL group and 58 months in the no-AL-group (HR 0.69; 95% CI 0.4 to 1.2, $P=0.17$). The clinicopathological characteristics “volume of blood loss” (OR 1.05 per 100cc; 95% CI 1.01-1.10) and “LNE vs non-LNE” (OR 4.10; 95% CI 1.60-12.62) were identified as factors potentially predictive for AL in univariate analysis, and both factors (volume of blood loss [OR 1.04 per 100cc, 95% CI 1.0001-1.09], LNE vs non-LNE [OR 3.67, 95% CI 1.41-11.39]) remained a significant independent factor in multivariate analysis. **Conclusions:** Considering the high surgical complexity in this large prospective surgical trial, the overall rate of AL following bowel surgery was relatively low and had no significant impact on PFS or OS. While protective stoma formation was not identified as protective factor in this cohort, volume of blood loss and LNE procedure were clinical parameters associated with higher risk of AL. Being potential surrogates for extensive surgery, these factors should be considered in perioperative management in pts with advanced OC. Further specific factors predicting AL were not identified. Clinical trial information: NCT00712218. Research Sponsor: Deutsche Forschungsgemeinschaft; Austrian Science Fund.

**5567** **Poster Session**

## Proactive assessment of patient reported outcomes in patients with ovarian cancer.

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**Background:** Patient reported outcome (PRO) measures are key instruments to provide an evaluation of health outcomes from the patient's perspective. Assessment of PROs may help identify the nature, severity, and time course of symptoms of concern in patients with ovarian cancer. The ability to access this information in real-time, including changes over time, could improve patient safety and decision-making. **Methods:** This systematic review evaluated the proactive or real-time assessment of PROs in patients with ovarian cancer undergoing systemic therapy. Medline, Embase, and Cochrane databases were searched (up to February 2022), and prospective ovarian cancer studies (experimental or observational) that incorporated PROs (including quality of life) were included. Conference abstracts were excluded. Primary objective was to assess the frequency of studies incorporating proactive use of PROs. A secondary objective was to describe PRO reporting. Descriptive statistics were used. **Results:** 3,071 articles were screened, with 117 included in the final analysis. Studies were published between 1990-2022 and contained 35,735 patients (median 140 patients per study; inter-quartile range 58-415). Median time from patient enrollment initiation to study publication was 7 years (range 1-15). Most studies were experimental/clinical trials (n=93, 79%), followed by observational (n=23, 20%) and not reported (n=1; Table). Among experimental studies, 56% (52/93) were phase III, 35.5% (33/93) phase II, 6.5% (6/93) phase I or I/II trials and it was not reported in two. Therapeutic strategies were assessed in 98% (91/93) of experimental studies, being the most frequent one chemotherapy (n=53, 58%), followed by antiangiogenics and PARP inhibitors (n=8, 9%, each). Types of observational studies were descriptive 43.5% (10/23), cohort 26% (6/23), cross-sectional 22% (5/23), or other 9% (2/23). PROs were the primary objective in 7.5% (7/93) and 83% (19/23) of experimental and observational studies respectively. The table describes PRO reporting standards per type of study. PROs were assessed in real-time in 0.8% (1/117) of studies. **Conclusions:** Completion of PRO and quality of life questionnaires involve time and effort for patients with ovarian cancer. PRO questionnaire responses were only assessed in real-time in $<1\%$ of analyzed studies. Efforts should be made to incorporate proactive assessment of PROs to optimize patient care and safety. Research Sponsor: None.

**Summary of PRO reporting information provided in the study publication.**

| | Observational or not reported n=24 % (n) | Experimental n=93 % (n) | Overall n=117 % (n) |
|---|---|---|---|
| **Questionnaire type** | 100% (24) | 97% (90) | 97% (114) |
| **Questionnaire number/ frequency** | 96% (23) | 85% (79) | 87% (102) |
| **Missing data** | 46% (11) | 69% (64) | 64% (75) |
| **Collection method (e.g. paper, electronic)** | 21% (5) | 5% (5) | 8.5% (10) |
| **Minimally important difference** | 12.5% (3) | 20% (19) | 19% (22) |
| **Real-time assessment** | 0% | 1% (1) | 0.8% (1) |

**5568** **Poster Session**

## The effect of maintenance hormone therapy on overall survival in advanced-stage low-grade serous ovarian carcinoma: A risk-set matched retrospective study.

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**Background:** Low-grade serous ovarian carcinoma (LGSOC) is a rare malignancy often treated similarly to high-grade serous ovarian carcinoma (HGSOC) despite differences in clinical behavior and carcinogenesis. Observational studies suggest that, among patient with advanced-stage LGSOC, maintenance hormonal therapy (HT) following primary treatment is associated with improved progression free survival. We conducted a multi-institutional observational study to investigate whether HT is associated with an overall survival advantage in this setting. **Methods:** We included patients with histologically confirmed stage III or IV LGSOC diagnosed between Jan 1, 2004, and Dec 31, 2019, treated in Commission on Cancer accredited cancer programs in the US. Patients who received HT within 6 months of diagnosis were matched to controls who did not initiate HT during this timeframe. The primary outcome was risk of death from any cause, within five-years of initiation of HT or observation. For each treated patient, we employed risk-set propensity score matching to identify a control in a manner that avoided the introduction of immortal-time-bias, and balanced groups with respect to year of diagnosis, upfront treatment strategy, age, stage, race/ethnicity, comorbidity index, insurance status, zip-code median income, and cancer program type. **Results:** There were 296 patients who initiated HT within 6 months of diagnosis, and 2,805 potential controls. Patients who received HT were more often treated in academic medical centers (55% vs 44%), diagnosed later in the study period (62% vs 23% diagnosed in 2018-2019), and received upfront chemotherapy less frequently (55% vs 83%). After risk set and propensity score matching, we identified 204 patients treated with HT and 204 untreated controls, who were otherwise similar with respect to measured covariates. In the matched cohort, maintenance HT was associated with a reduction in the risk of death (hazard ratio 0.61; 95% CI 0.37-0.99), corresponding to a 60-month survival of 71% compared with 61%, and an improvement in 5-year life expectancy of 3.6 months (95% CI 0.004-7.2). **Conclusions:** Maintenance hormone therapy following primary management of LGSOC is associated with an overall survival benefit compared with observation. Research Sponsor: None.

**5569** **Poster Session**

## CD47 expression in ovarian cancer: Dynamic correlation with lymphocyte and macrophage features as well as thrombospondin-1 (TSP-1) under neoadjuvant chemotherapy.

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**Background:** To date, the results of immunotherapy strategies to treat ovarian cancer (OC) have been unfulfilling. A more comprehensive knowledge of the intricate immune tumor microenvironment (iTME) as well as the effects of chemotherapy on immune features may reveal novel immune targets. CD47 is overexpressed in OC and correlates with shorter survival and immune evasion via interaction with circulating ligands such as TSP-1. Little is known about how the CD47 receptor or its ligand TSP-1 changes under chemotherapy or their association with other features of iTME. In the randomized CHIVA trial, we therefore investigated CD47 expression in OC patients at diagnosis and after neoadjuvant chemotherapy (NACT) and assessed its relationship to other iTME features, including circulating level of thrombospondin-1 (TSP-1). **Methods:** Tumour samples were collected from 105 patients from the CHIVA trial, a GINECO-GINEGEPS study. CD47 expression was assessed by IHC in paired samples before and after NACT and scored by H-score: staining intensity (0, +1, +2, +3) x % cells positive (0-300). At baseline, we defined a $CD47^{high}$ (highest quartile, score above 240) and $CD47^{low}$ population (lowest quartile, score under 150). $CD4^+$, $CD8^+$, $CD68^+$, $CD163^+$, $FoxP3^+$ cells were assessed by IF and scored as number of positive cells. The Pearson correlation coefficient (r) was used to determine the linear correlation between CD47 expression and other immune markers. Circulating TSP-1 was quantified by ELISA on paired plasma samples pre- and post-NACT. **Results:** While $CD47^{high}$ does not correlate with CD4 and CD8 expression at baseline, a correlation with CD8 (r=0.59, p=0.02) and a trend with CD4 (r=0.49, p=0.05) is observed after NACT. These linear correlations do not exist in the $CD47^{low}$ population. In addition, NACT induces a 2-fold decrease in $FoxP3^+$ cells, but only within the $CD47^{high}$ group (p=0.028). Thus, both the $CD4^+/FoxP3^+$ (p=0.001) and $CD8^+/FoxP3^+$ (p=0.005) ratios were increased by 2-fold under NACT, exclusively in OC patients with $CD47^{high}$ expression. Interestingly, these correlations appear to be T-cell specific as no correlation exist when considering CD68 and CD163 before or after NACT, neither for $CD47^{high}$ nor $CD47^{low}$. In parallel, we determined that the plasma level of TSP-1, a preferential CD47 agonist, was very high (>1500 ng/mL) in OC patients and decreased by about 2-fold after NACT. Interestingly, a pattern emerges in which the highest level of circulating TSP-1 is associated with the $CD47^{low}$population. **Conclusions:** Our data suggest that OC patients with the highest CD47 expression profile at baseline have greatest lymphocyte influx post-NACT and may be most likely to benefit from post-operative immunotherapy. Whether blocking the immune-suppressive CD47:TSP1 interaction in this subset would provide an alternative strategy merits investigation. Clinical trial information: NCT01583322. Research Sponsor: French National Cancer Institute (INCa).

**5570** **Poster Session**

## Trends in ovarian cancer incidence and incidence-based mortality: A 15-year population-based analysis.

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**Background:** The predicted incidence and incidence-based mortality (IBM) of ovarian cancer (OC) in 2023 is lower than prior years. OC encompasses a range of heterogeneous cancers with subtypes categorized on histology and site of origin. Given differences in survival and treatment paradigms, we aim to characterize trends in OC incidence and IBM based on histology and site of origin to determine what factors are responsible for the decline. **Methods:** Patients with OC from 2000-2019 were identified from the US Surveillance, Epidemiology, and End Results 17 registry database. Using ICD-O-3 codes, patients with epithelial, stromal, and germ cell cancers of the ovary, fallopian tube, and peritoneum were included. Incidence and IBM were reported as age-adjusted rates and stratified by cancer subtype. Using Joinpoint 4.9.1.0, we characterized piecewise log-linear time trends to identify inflection points in the rates' annual percentage change (APC). **Results:** The incidence of epithelial OC decreased significantly from 2004-2019 (APC -1.24%). When stratified by disease stage, this trend was seen in distant disease (APC -2.11%) and unknown/unstaged disease (APC -3.40%); however, there was a significant increase in incidence of local disease (APC +0.83%). There was no significant change in the incidence of germ cell and stromal OC from 2004-2019 in all stages. (APC -0.30% and +0.33%). Among all OC subtypes, there was a significant decline in incidence from 2000-2019 (APC -1.57%) with a sharper decline from 2015-2019 (APC -3.41%). Among all cancer subtypes, the incidence trended down from 2000-2019, with a significant decline from 2015-2019 (APC -2.37%). Similar trends are observed in IBM. Among all stages of epithelial OC, there was a significant decrease in IBM from 2006-2019 (APC -2.02%). When stratified by disease stage, there was a decline in IBM in local disease (APC -7.19%, 2014-2019) and distant disease (APC -2.44%, 2010-2019). There were no changes in IBM of germ cell and stromal OC from 2004-2019 (APC +0.78% and -0.20%). Among all cancers, IBM significantly decreased from 2006-2019 (APC -2.28%). When stratified by disease stage, there was no change among local disease and an increase in regional disease from 2006-2019 with the increase from 2006-2010 (APC +14.35%) compared to 2010-2019 (APC +1.45%). Conversely, there was a significant decrease in IBM for distant disease (APC -2.51% from 2010-2019) and unknown/unstaged disease (APC -3.27% from 2006-2019). **Conclusions:** There has been an overall decline in incidence and IBM of OC over a 15-year period, primarily driven by the epithelial histology. Over the past 20 years, OC has been increasingly diagnosed at earlier stages with a corresponding improvement in survival. While stage migration and improved survival may contribute to these trends, they do not entirely explain them. As new treatments become available, the incidence and IBM of OC may further decline. Research Sponsor: None.

**5571** **Poster Session**

## Mechanisms of resistance to bispecific T-cell engager therapy for ovarian cancer.

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**Background:** Patients with recurrent ovarian cancer (OC) invariably develop multidrug resistance and have poor prognoses. Bispecific T-cell engager (BiTE) immunotherapy represents an innovative therapeutic modality where cytotoxic T-cells are activated and recruited to tumor cells using a predefined tumor-associated antigen. Clinical trials evaluating BiTEs in OC are currently in progress with promising results, and exploration of potential mechanisms of resistance to BiTEs could provide meaningful insight into disease biology and combination strategies. **Methods:** After obtaining informed consent, experiments were performed on patient samples collected under an IRB-approved tissue-banking protocol. Samples were collected before patients started clinical trials and at disease progression. Serum, peripheral blood mononuclear cells (PBMCs), and malignant ascites were collected when available for translational analysis. Immune cell subsets were evaluated for activation and exhaustion via flow cytometry, and tumor cells were subjected to western blot analysis and IHC. Ex vivo cytotoxicity assays were performed using BITEs, patient tumor samples, OC cell lines (immortalized), and patient-derived and healthy donor PBMCs. Patient serum samples were analyzed by multiplex ELISA to determine cytokine and chemokine signatures. **Results:** Serum and PBMC samples from 10 patients and ascites from 2 patients were used for these analyses. Cells derived from patient ascites after progression on BiTEs were primarily comprised of tumor cells and myeloid-derived suppressor cells (MDSCs). These tumor cells had lost expression of the target antigen recognized by the BITE and upregulated markers as N-cadherin and vimentin with concordant downregulation of E-cadherin consistent with epithelial to mesenchymal transition (EMT). Ascites immune subset analysis showed a predominance of CD11B+, CD163+, and PD-L1+ cells. Compared to PBMCs from healthy donors, patient PBMCs showed higher frequencies of CD4+ TIM3+ LAG3+ cells consistent with T-cell dysfunction. Compared with healthy donors, serum from patients revealed higher levels of myeloid recruiting and activating chemokines and cytokines (CCL3, CXCR3, CXCL10, and IL18) and low immunostimulatory cytokines (IL-7 and IFN-$\alpha$). Coculture of patient tumor cells with BiTEs and T-cells ex vivo showed diminished cytotoxicity, consistent with the loss of target antigen expression. Patient PBMCs retained cytotoxicity against OC cell lines ex vivo, suggesting preserved cytotoxic capacity. Finally, T-cells cocultured in the presence of patient serum displayed suppressed cytotoxicity against OC cell lines. **Conclusions:** Resistance to BiTE therapy is multifactorial, primarily involving tumor-associated antigen loss, EMT, and an immunosuppressive tumor microenvironment. Combination treatment approaches to mitigate these factors might increase response rates. Research Sponsor: Nile Albright Research Foundation; Julie Fund, Mary Margaret Darling Flatley Foundation, Worden Fund.

# Patterns of ovarian cancer care in an elderly population in Australia: A prospective cohort study from the National Gynaecology Oncology Registry (NGOR).

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**Background:** Elderly women with ovarian cancer are often undertreated in comparison to best practice. The National Gynae-Oncology Registry (NGOR) is Australia's first country-wide clinical quality registry (CQR) measuring compliance with optimal care defined by a set of clinical quality indicators (CQIs). **Objectives:** To assess compliance with a predefined set of CQIs for elderly women with newly diagnosed ovarian cancer aged $>75$ compared to non-elderly women aged $<75$ years of age from the NGOR sites. **Methods:** All women with newly diagnosed ovarian cancer from May 2017 – July 2022 were eligible for inclusion. Data were collected from medical records and relevant hospital linked databases by expert data managers. **Results:** A total of 1590 women were eligible for inclusion from 21 hospitals across 5 Australian states. The CQI data were subsequently aggregated and are summarised in the table. The proportion of elderly women receiving first-line chemotherapy with a platinum and taxane doublet was significantly lower compared to non-elderly (60% vs 89%, $p < 0.001$). The proportion of women with sub-optimally debulked or Stage IV cancer who received first-line chemotherapy with a platinum/taxane doublet and bevacizumab was significantly lower in elderly women compared to non-elderly (10% vs 30%, $p < 0.001$) . Enrolment in clinical trials or translational research was significantly lower in elderly women compared to non-elderly (13% vs 21%, p=0.002). The remaining CQIs showed no significant differences between the age groups. **Conclusions:** In this cohort, most measures of best practice were not significantly different between elderly and non-elderly women, with the exception of elderly women receiving less first line doublet chemotherapy, less doublet chemotherapy with bevacizumab in sub-optimally debulked or Stage IV cancer, and less likely to be enrolled in clinical trials or translational research. While these 3 CQIs represent a minority of the overall list of CQIs, such lack of compliance may result in significant differences in quality of life and overall survival for elderly women with ovarian cancer. Subsequent investigation is therefore warranted to confirm and explain these findings. Research Sponsor: MRFF.

**Clinical Quality Indicators by age group.**

| CQI | Women aged < 75 (n = 1307) | Women aged >75 (n = 283) | p-value |
|---|---|---|---|
| Presented at a multi-disciplinary team meeting | 98 % | 98 % | 0.7 |
| Histological or cytological diagnosis confirmed prior to receiving first-line neoadjuvant chemotherapy. | 88 % | 91% | 0.3 |
| Primary surgery (no macroscopic residual disease) | 57 % | 50% | 0.4 |
| Interval surgery (no macroscopic residual disease) | 46% | 40% | 0.4 |
| 1st line chemotherapy with a platinum/taxane doublet | 89% | 60% | **<0.001** |
| 1st line chemotherapy with a platinum/taxane doublet and bevacizumab in sub-optimally debulked or Stage IV cancer | 30% | 10% | **<0.001** |
| Enrolled in clinical trial/translational research | 21% | 13% | **0.002** |

**5573** **Poster Session**

## Impact of cytoreductive surgery on survival outcomes for recurrent adult-type granulosa cell tumors of the ovary.

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**Background:** Adult-type granulosa cell tumor of the ovary (aGCT) is a rare tumor that often relapses and the optimal management strategy is not known. Cytoreductive surgery (CRS) offers an attractive option for disease confined to the abdomen/pelvis. However, few studies have evaluated the role of CRS compared to systemic therapy alone. Thus, the study objective was to determine the impact of secondary, tertiary, and quaternary CRS on survival outcomes for patients with relapsed aGCT. **Methods:** This was an IRB-approved retrospective cohort study that evaluated all patients with relapsed aGCT who were enrolled in the Rare Gynecologic Malignancy Registry at MD Anderson. Study inclusion criteria were patients who had histology-proven aGCT, were above 18 years of age, had at least one documented relapse, and had received treatment or treatment planning at MD Anderson. Progression-free survival (PFS) endpoints were the outcomes of interest and were defined as follows: PFS2 was defined from first recurrence to subsequent progression or death (PFS2), PFS3 was defined as second relapse/progression to third relapse/progression or death, and PFS4 was similarly defined. PFS2, PFS3, and PFS4 were estimated with methods of Kaplan and Meier and were modeled via cox proportional hazards regression. Analyses were performed among those with resectable disease at time of disease progression. **Results:** Among the 369 aGCT patients identified from January 1970 to October 2022, 162 met the study inclusion criteria for analysis. The mean age of diagnosis was 44.4 years old and the majority were initially diagnosed with stage 1 disease (72.8%). The median follow-up time for all patients was 5.86 years (range 0.09 – 34.27). At the first relapse, there were 151 patients who had resectable disease with 128 who underwent secondary CRS. PFS2 was significantly improved among those who underwent CRS compared to those who did not (HR 0.50, 95% CI 0.30 – 0.81; p = 0.005) with the median PFS2 difference being 18.24 months (p = 0.006). At the second relapse/progression, there were 120 patients with resectable disease with 52 who underwent tertiary CRS. PFS3 was significantly improved among those who underwent CRS compared to those who did not (HR 0.57, 95% CI 0.39 – 0.84; p = 0.004) with the median PFS3 difference being 6 months (p = 0.01). At the third relapse/progression, there were 96 patients with resectable disease with 46 who underwent quaternary CRS. There was a trend towards improved PFS3 among those who underwent CRS compared to those who did not (HR 0.69, 95% CI 0.45 – 1.06; p = 0.09). The use of systemic or hormonal therapy did not confer additional PFS benefit among those who underwent CRS. **Conclusions:** For relapsed, resectable aGCT, CRS may offer a beneficial impact on PFS. Future studies should evaluate the role of CRS on survival outcomes. Research Sponsor: None.

**5574** **Poster Session**

## A phase 1 study of the SYK inhibitor fostamatinib and weekly paclitaxel for recurrent platinum-resistant ovarian cancer.

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**Background:** Response to chemotherapy in patients (pts) with recurrent platinum-resistant ovarian cancer (PROC) is generally $< 15\%$. Spleen tyrosine kinase (SYK) is overexpressed in PROC and is a key mediator of paclitaxel resistance in ovarian cancer cells. Fostamatinib (Fos), an orally available inhibitor of SYK, is currently FDA approved for the treatment of idiopathic thrombocytopenic purpura. The active form of Fos (R406) was shown to synergistically enhance taxane-mediated cytotoxicity in preclinical ovarian cancer models. This phase 1 study aimed to identify the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D) of Fos when combined with standard weekly paclitaxel (wPac) for pts with PROC. **Methods:** Pts with PROC, defined as progression $\leq$6 months of last platinum, were eligible. A modified toxicity probability interval (mTPI) dose escalation design was used to determine the MTD/RP2D and response was assessed using RECISTv1.1 criteria. All pts received paclitaxel (wPac) 80mg/m$^2$ intravenously on Days 1, 8, and 15, of a 28-day cycle. Fos was administered orally twice a day (BID) on a continuous schedule. Three dose levels (DL) were planned: DL1 - 100mg, DL2 - 150mg, and DL3 - 200mg. MTD was determined based on cycle 1 dose-limiting toxicities (DLTs) and responses were assessed every 2 cycles. A dose expansion cohort to further assess adverse events (AEs) and tolerability was performed. **Results:** 27 eligible pts, median age 62 years (range 35-79 years) with high-grade serous (n = 18), clear cell (n = 4), carcinosarcoma (n = 3), or other (n = 2) histology were treated at 3 centers. Twelve pts were treated in the dose escalation cohort (DL1 = 6, DL2 = 3, DL3 = 3). Common AEs at least possibly attributed to Fos, wPac, or both included diarrhea (70%), fatigue (52%), anemia (44%), neutropenia (33%), nausea (33%), hypertension (30%), and dysgeusia (30%). Treatment-emergent grade 3-4 AEs were neutropenia (37%), anemia (26%), and thromboembolic event (22%). During DL1, updated toxicity management guidelines not consistent with the original protocol were released and 2 of the 3 pts treated prior to the amendment were not considered evaluable for DLT. Thus 3 more pts were enrolled to DL1 after the amendment. Of the 10 pts evaluable for DLT in dose escalation, no DLTs were reported on any of the 3 DLs (DL1 = 4, DL2 = 3, DL3 = 3). DL3 was selected for dose expansion. One of 15 pts in the dose expansion cohort had a DLT (neutropenia) and one patient had a grade 5 infection. Of 18 pts treated at DL3, 7 (39%) had partial or complete response (95% CI: 17.3, 64.3%). Overall, 27 patients received a median of 3 cycles (range 0-10). Analysis of pharmacokinetic and correlative molecular studies of target expression are ongoing. **Conclusions:** The RP2D of Fos will be 200 mg orally BID when combined with wPac. AE profile of the combination was as expected and the combination demonstrated promising efficacy in pts with recurrent PROC. Clinical trial information: NCT03246074. Research Sponsor: U.S. National Institutes of Health; Alleghany Health Network; Johns Hopkins.

**5575** **Poster Session**

## Anlotinib combined with carboplatin/paclitaxel and maintenance anlotinib as front-line treatment for newly diagnosed advanced ovarian cancer: A phase II, single-arm, multi-center study (ALTER-GO-010).

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**Background:** Several studies have shown that antiangiogenic drug combined with chemotherapy as first-line treatment, followed by antiangiogenic drug maintenance therapy significantly improve outcomes for patients with ovarian cancer. Anlotinib, a highly effective VEGFRs, FGFRs, PDGFRs and c-kit multi-target tyrosine kinase inhibitor, has been approved for multiple tumor types in China. The aim of this single arm, multicentric, phase II study is to investigate the efficacy and safety of using anlotinib combined with carboplatin/paclitaxel as front-line treatment for advanced ovarian cancer patients. **Methods:** Eligible patients with FIGO stage III–IV primary epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer and ECOG PS 0-1 undergo primary cytoreductive surgery or interval debulking surgery, will receive 6-8 cycles of chemotherapy (paclitaxel 175 mg/m2 + carboplatin area under the curve [AUC] 5 q3w) and anlotinib (12 mg po qd, days 1-14, 21 days per cycle, anlotinib will be omitted from the first treatment cycle to prevent delayed wound healing). After chemotherapy finished, anlotinib continues as maintenance monotherapy until disease progression, unacceptable toxicity, or death. Patients with prior anti-angiogenic therapy or major surgical procedure within 28 days before starting anlotinib therapy will be excluded. The primary endpoint is progression free survival (PFS). Key secondary endpoints include overall response rate, disease control rate per RECIST1.1, overall survival, safety. **Results:** From 9 Sep 2021 to 30 Jan 2023, 30 pts were enrolled, including 96.7% (29/30) high-grade serous carcinoma (HGSC) and 3.33% (1/30) endometrioid carcinoma (EC). The median age was 56 years old, with 96.7% (29/30) patients in FIGO stage III and 3.33% (1/30) in stage IV Median follow-up was 5.36 (95% CI: 3.68, - 7.98) months. PFS rates at 6 months and 9 months were both 100%. Twenty-nine patients (96.7%) experienced adverse events (AE) of any level. The most common AEs include white blood cell decreased, neutrophil count decreased, anemia, platelet count decreased, lymphocyte count decreased and hypertension. There was no treatment-related death during the study. **Conclusions:** Preliminary results of anlotinib combined with carboplatin/paclitaxel have shown favorable efficacy and tolerated safety profile in newly diagnosed advanced ovarian cancer patients. Clinical trial information: NCT04807166. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

**5576** **Poster Session**

## Understanding differences in the rates of BRCA/HRD testing and treatment in 1st line maintenance in patients with ovarian cancer treated by gynecologic oncologists compared to other providers: A quality initiative by Integra Connect (IC) PrecisionQ.

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**Background:** The role of PARPi in the treatment of advanced ovarian cancer (aOC) has expanded in recent years. In this context, South Carolina Oncology Associates (SCOA) partnered with Integra Connect (IC) on a quality initiative (QI) to evaluate the rate of *BRCA* and HRD testing in newly diagnosed OC patients and the use of maintenance therapy in the 1st line (1L) setting in aOC. Patients with aOC at SCOA are typically managed by gynecologic oncologists. **Methods:** Using the IC Precision Q real-world database of over 1 million cancer patients across 275 sites of care, we assessed newly diagnosed OC patients evaluated via medical chart curation from 1/1/2020 to 6/30/2022 for BRCA and HRD testing at SCOA (N = 81) and other oncology practices (N = 1,045). We also studied the use of maintenance therapy in patients with stage II-IV OC who completed platinum-based chemotherapy from 1/1/2020 to 6/30/2022 at SCOA (N = 75) and other oncology practices (N =899). SCOA was compared to other oncology practices in terms of provider specialty treating the patient, rates of HRD and *BRCA* testing, and use of 1L maintenance treatment in patients with or without BRCA or HRD mutations. Descriptive analyses were used. Proportions were compared using a two tailed two sample z-test. **Results:** Among newly diagnosed patients at SCOA, 95% of patients with OC were primarily managed by a gynecologic oncologist compared to 5% at other practices. The rate of *BRCA* testing at SCOA was 81% (66 of 81) compared to 75% (788 of 1045) and HRD testing was 60% (49 of 81) compared to 39% (403 of 1045) at other oncology practices in the IC database. The difference in HRD testing was significant ($p < 0.01$). The use of 1L maintenance regardless of biomarker status was 64% (48 of 75) at SCOA compared to 50% (449 of 899) at other practices. The difference in 1L maintenance use was significant ($p<0.05$). PARPi were used at SCOA for maintenance therapy in 82% (38 of 46) of patients compared to 74% (314 of 427) at other practices. The use of maintenance in *BRCA* or HRD positive patients was 84% (21 of 25) at SCOA compared to 75% (151 of 201) for other practices. **Conclusions:** In this real-world study, treatment by gynecologic oncologists was associated with higher rates of *BRCA* and HRD testing and higher use of 1L maintenance treatment in patients with aOC compared to other practices. These findings underscore the importance of gynecologic oncologists in the management of aOC to ensure optimal testing and adherence to treatment guidelines. Research Sponsor: None.

**5577** **Poster Session**

## First-in-human, phase I study of CBP-1008, a bi-specific ligand drug conjugate, in patients with advanced solid tumors.

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**Background:** Folate receptor α (FRα) and vanilloid subfamily member 6 of transient receptor potential channels (TRPV6) are overexpressed in many solid tumors including ovarian cancer hence could be promising therapeutic targets. CBP-1008 is a first-in-class bi-specific ligand drug conjugate targeting FRα and TRPV6 carrying monomethyl auristatin E (MMAE) as payload. **Methods:** CBP-1008 was administered by intravenous infusion. Phase Ia study included a dose-escalation period initiated by accelerated titration (0.015, 0.03mg/kg d1,15; q28d) and then switched to 3+3 scheme (0.12, 0.15, 0.17, 0.18mg/kg d1,15; q28d) and a dose expansion period. Phase Ib clinical expansion study included 3 cohorts, platinum-resistant ovarian cancer (PROC), metastatic triple negative breast cancer (TNBC) and other solid tumors. The primary objective was to assess the safety and preliminary efficacy. **Results:** As of September 30, 2022, 178 patients received at least one dose of study drug were enrolled (phase Ia: n=35; phase Ib: n=143) and received median 3 prior regimens. Included tumor species were PROC (n=101), TNBC (n=25), ER+/Her2+ breast cancer (BC) (n=17), colorectal cancer (n=6), pancreatic cancer (n=12) and others (n=17). In phase Ia study, DLTs were observed in 3 patients (0.12, 0.15, 0.18mg/kg, n=1 each), including grade 4 hypophosphatemia, neutropenia, febrile neutropenia, and grade 3 hyperglycemia, alanine aminotransferase (ALT) elevation. MTD was not yet reached. Majority of adverse events were mild to moderate. Grade 3/4 treatment-emerging adverse events (TEAEs) occurred in ≥ 3% subjects were neutropenia (n=85), decreased leukocyte count (n=49), anaemia (n=10), AST elevation (n=7), ALT elevation (n=7). Drug-related death was observed in 1 patient. A total of 82 PROC patients at dose of 0.15mg/kg or above were evaluable for efficacy assessment. There were 21 patients achieved partial response (PR) and 30 patients achieved stable disease (SD). The objective response rate (ORR) and the disease control rate (DCR) were 25.6% and 62.2%, respectively. The median progression-free survival (mPFS) was 3.7 months (95% CI: 2.7-5.1). In 34 PROC patients with FRα expression ≥25% and ≤3 prior treatment regimens, ORR was 32.4% and mPFS was still 3.7 months (95% CI: 3.3-7.3). Given the small sample size, efficacy data of breast cancer and other solid tumors will be analyzed after recruiting more patients. **Conclusions:** The current result showed that CBP-1008 has manageable safety profile. Antitumor activity was observed in PROC patients at dose of 0.15mg/kg or above, especially in PROC patients with FRα expression ≥25% and ≤3 prior treatment regimens. Jifang Gong, Jian zhang and Ning Li contributed equally to this work. Xichun Hu , Lin Shen and Lingying Wu are the corresponding authors. Clinical trial information: NCT04740398. Research Sponsor: Coherent Biopharma (Suzhou) Co., Ltd.

**5578** **Poster Session**

## Response to subsequent platinum-based chemotherapy post PARP inhibitor in recurrent epithelial ovarian cancer.

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**Background:** Maintenance therapy with PARP inhibitors (PARPi) can increase progression free survival (PFS) for recurrent or metastatic platinum-sensitive epithelial ovarian cancer (EOC). Little is known about disease trajectory following treatment with these agents, though some evidence suggests a decreased response to subsequent platinum-based chemotherapy. This retrospective cohort study assessed real-world response rates to platinum-based chemotherapy for recurrent high grade EOC following treatment with a PARPi. **Methods:** All patients prescribed a PARPi as maintenance therapy for recurrent or metastatic EOC at the Ottawa Regional Cancer Center (ORCC) from September 2017 to May 2022 were included. PFS following penultimate therapy (line of therapy preceding PARPi initiation) as well as the PFS following subsequent platinum-based chemotherapy in patients with disease progression more than 6 months after penultimate therapy were calculated. Incidence of platinum resistance in patients with disease progression following PARPi therapy was determined. **Results:** 91 patients were included in the analysis including 54 patients on niraparib and 36 patients on olaparib. Follow-up after initiation of PARPi ranged from 4.6 months to 62.0 months with a median of 16.3 months. 54 (59.3%) of patients experienced disease progression after initiation of PARPi therapy, including 10 (11.0%) who progressed within 6 months of their penultimate therapy. Of the 44 patients who experienced disease progression more than 6 months following penultimate therapy, 32 (72.7%) were rechallenged with platinum-based chemotherapy. Of these, 16 (50.0%) experienced further disease progression with 14 (43.8%) progressing within 6 months of their platinum rechallenge. Median PFS following platinum rechallenge was 4.4 months (from 0.8 months to 34.9 months), significantly lower than previous reports. **Conclusions:** Patients who experienced disease progression following PARPi therapy showed a poor response to subsequent platinum-based chemotherapy, even when progression occurred more than 6 months after completion of their penultimate platinum-based chemotherapy. This supports the theory that PARPi resistance may be a surrogate for platinum resistance and raises concern for possible contribution of PARPi in the induction of platinum resistance in recurrent EOC. Research Sponsor: University of Ottawa Department of Obstetrics & Gynecology.

**5579** **Poster Session**

# Molecular and immune profiling of *TP53*-mutated ovarian cancers with non-*BRCA1/2* homologous recombination gene alterations.

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**Background:** Molecular alterations in homologous recombination (HR) pathway genes lead to HR deficiency (HRD) in ~50% of high grade serous ovarian carcinomas (HGSOC). The immune microenvironment of BRCA1/2-mutated HGSOC has been extensively characterized, in contrast to tumors with mutations in other HR genes. We evaluated a cohort of epithelial ovarian cancers (EOC) enriched for HGSOC and compared molecular and immune signatures of tumors with BRCA1/2 mutations (*BRCA*m) to those with non-BRCA1/2 HR gene mutations (NBHRD). **Methods:** We characterized 173 EOC by comprehensive genomic and immune profiling (CGIP) using panel-based next-generation DNA (523 genes) and RNA sequencing (384 genes), respectively. We enriched for HGSOC by selecting for *TP53* mutations and excluding tumors with non-serous histology or any mutation in *POLE*, *MLH1*, *PMS2*, *MSH2*, *MSH6*, or nucleotide excision repair genes. Tumors lacking *BRCA1/2*-mutations were classified as NBHRD if a reportable mutation was present in canonical HR genes. Mutational burden (TMB, mut/Mb) was estimated from detected SNV/indels. We calculated immune-related expression signatures, including tumor immunogenicity score (TIGS), cellular proliferation (CP), and cancer testis antigen burden (CTAB). PD-L1 expression was assessed by tumor proportion score (TPS) following 22C3 immunohistochemistry. Differences in TMB, TIGS, CP, CTAB, PD-L1 and gene expression rank were tested for using Wilcoxon rank-sum test. **Results:** Of 173 EOC, 84 cases had complete CGIP, including 11 (13%) *BRCA*m, 7 (8%) NBHRD (Table), and 66 (79%) lacking HR gene alterations. On average, NBHRD tumors harbored lower TMB (4.1±2.3 vs. 6.6±2.3 vs. p=0.03) and elevated TIGS (59.1±16.2 vs. 41.7±16.2 p=0.044) compared to *BRCA*m tumors. We found no difference in PD-L1 (p=0.21), CP (p=0.26), or CTAB (p=0.48). Expression changes were identified in 32 immune genes, of which 31 (97%) were substantially up-regulated (1.3-3.3 fold) in NBHRD compared to *BRCA*m tumors. **Conclusions:** Our findings showed our cohort of NBHRD tumors were more immunogenic but less mutagenic than *BRCA*m tumors, implying enhanced immunogenicity unrelated to neoantigen load. Given that immune checkpoint inhibitors have shown limited efficacy in ovarian cancer, our data suggest NBHRD tumors may have stronger and possibly distinct immune escape mechanisms compared to *BRCA*m tumors. Research Sponsor: Labcorp.

| | NBHRD mutations | |
|---|---|---|
| **NBHRD Case** | **Gene(s)** | **Mutation(s)** |
| **1** | ATM | 3085dupA (T1029fs) |
| | BRIP1 | 517C>T (R173C) |
| **2** | FANCA | 3494T>G (L1165*) |
| **3** | BRIP1 | 1871C>A (S624*) |
| **4** | BRIP1 | 2010dupT (E671*) |
| **5** | FANCF | 388dupC (Q130fs) |
| **6** | BRIP1 | 1489delG (V497fs) |
| **7** | CHEK2 | 1100delC (T367fs) |

**5580** **Poster Session**

## Exploring the significance of PARP inhibitor therapy after first-line chemotherapy in patients with homologous recombination proficient ovarian cancer: An extracted individual patient data and trial-level meta-analysis.

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**Background:** The use of poly (ADP-ribose) polymerase inhibitors (PARPi) as maintenance therapy in advanced epithelial ovarian cancer (EOC) patients (pts) has shown to delay cancer progression among patients with mutated BRCA (mBRCA) or homologous recombination deficiency (HRD), with debatable and divergent benefit among the subgroup of patients with homologous recombination proficiency (HRP). We aimed to further clarify the efficacy of PARPi after first-line chemotherapy (1L CT) in patients with HRP EOC. **Methods:** A systematic literature search of PubMed, Embase, The Cochrane Library until February 9$^{th}$ was conducted to identify articles or presentations of phase III clinical trials (P3CT) evaluating PARPi maintenance therapy after 1L CT in ovarian cancer. Individual patient data was reconstructed from Kaplan-Meier plots of progression-free survival (PFS) among pts with mBRCA, HRD and HRP through WebPlotDigitizer and R package IPDfromKM and futher combined. We also performed trial-level meta-analysis with a random effects model. Comparisons were made with Cox proportional hazards. Clinical benefit for each sub-group was accessed with the ESMO Magnitude of Clinical Benefit Formulary 2b (ESMO MBCS). **Results:** The literature search resulted in 513 items. After screening, 6 P3CT (SOLO1, PRIMA, VELIA, PAOLA, PRIME, and ATHENA-MONO) were selected, and the longer follow-up data of each trial was used. A total of 3205 pts were included in the analysis (2090 in PARPi arms, 1115 in control arms). HRP was associated with worse PFS regardless of the treatment arm (HRP vs mBRCA in PARPi arms: HR 1.92, 95% CI 1.62 – 2.21, P $<$ 0.001). Compared to control treatment arm, PARPi therapy was associated with a improved PFS in all subgroups, although the magnitude of benefit decreased from mBRCA to HRD and HRP (Table). Trial-level meta-analysis yielded similar results. PARPi therapy summed 4 out of 4 possible points at ESMO MBCS for mBRCA and HRD, but only 2 points among HRP pts, confirming a lower clinical benefit in this subgroup. **Conclusions:** This meta-analysis included additional P3CT recently presented and new data of subgroup analysis of previous studies. Results confirm a statistically significant benefit of PARPi maintenance after 1L CT for HRP EOC. Nevertheless, the relative and absolute gain in PFS is modest (9% in 2 years), while mBRCA and HRD subgroups have a substantial benefit. The worse prognosis of HRP pts, in addition to the small clinical benefit of PARPi therapy, highlights the need for new treatment strategies for this subgroup. Research Sponsor: None.

| | Median PFS (PARPi vs control) | 2-year PFS (PARPi vs control) | HR | 95% CI | P |
|---|---|---|---|---|---|
| **mBRCA** | 45.5 vs 16.6 mo | 69% vs 38% | 0.41 | 0.35 – 0.49 | $<$ 0.001 |
| **HRD** | 23 vs 15.6 mo | 49% vs 32% | 0.62 | 0.51 – 0.75 | $<$ 0.001 |
| **HRP** | 13.9 vs 10 mo | 28% vs 19% | 0.80 | 0.69 – 0.92 | 0.002 |

**5581** **Poster Session**

## Trends in the use of neoadjuvant chemotherapy for low-grade serous ovarian cancer in the United States.

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**Background:** Following the publication of randomized trials demonstrating its noninferiority, the use of neoadjuvant chemotherapy (NACT) for the treatment of advanced stage epithelial ovarian cancer has increased substantially in the United States. However, low-grade serous ovarian cancers (LGSOC) respond poorly to chemotherapy compared with high-grade serous carcinoma. For LGSOC, clinical guidelines favor surgical resection prior to adjuvant therapy. This study seeks to describe patterns and temporal trends in the use of NACT for LGSOC. **Methods:** This cohort study identified women treated for stage III or IV LGSOC in a Commission on Cancer accredited cancer program between January 1, 2004, to December 31, 2020. We fit Poisson regression models to evaluate temporal trends in the use of NACT and cytoreductive outcomes, and to identify factors associated with receipt of NACT. We considered age, race/ethnicity, Charlson Comorbidity Index, year of diagnosis, insurance status, income, facility type, census region, and stage as potentially associated with NACT. Due to the high rate of missingness in data describing cytoreductive outcomes after surgery, we undertook both multiply imputed and complete case analyses. **Results:** A total of 3,343 patients received treatment for LGSOC during the study period. The mean age at diagnosis was 54.8 year (SD 15.5) and most patients (82%) were white. The most commonly observed upfront treatment strategies were cytoreductive surgery followed by adjuvant chemotherapy (63.7%) and surgery without chemotherapy (19.2%). Treatment with NACT followed by interval cytoreductive surgery (13.0%) or chemotherapy alone (4.1%) were less common. The proportion of patients who received NACT increased from 9.5% in 2004 to 25.9% in 2020, corresponding to a statistically significant annual percent change (APC) of 7.2% (95% CI 5.6-8.9). Increasing decade of age (risk ratio [RR] 1.15; 95% CI 1.09-1.23), increasing calendar year of diagnosis (RR 1.07; 95% CI 1.05-1.08) and stage IV disease (RR 2.66; 95% CI 2.3-3.07) were associated with a higher probability of receiving NACT. Other variables were not associated with receipt of NACT. Among patients who underwent cytoreductive surgery, the proportion who achieved no gross residual disease remained stable over the course of the study period in both complete case (APC 0.5%; 95% CI -1.8 to 0.9) and multiply imputed (APC -0.1%; 95% CI -1.6 to 1.3) analyses. **Conclusions:** The use of NACT for patients with LGSOC increased substantially from 2004 to 2020. Despite increased utilization of NACT, the rate of complete cytoreduction has not improved over the study period, possibly calling into question the effectiveness of NACT in reducing tumor burden in this setting. Research Sponsor: None.

**5582** **Poster Session**

## Distinguishing primary mucinous ovarian tumors from metastases of non-gynecologic mucinous cancers: Can we leverage next-generation sequencing?

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**Background:** Primary mucinous ovarian cancers (MOC) are histopathologically challenging to differentiate from ovarian metastases of non-gynecologic origin, with this distinction being critical for appropriate management and prognosis. We compared the somatic gene variant landscape of MOC to that of non-gynecologic mucinous tumors. **Methods:** Data were extracted from the American Association for Cancer Research's (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE) database version 13.0 via cBioPortal. This publicly available, multi-institutional database provides next generation sequencing (NGS) genomic profiles of tumors. We queried this database for samples of MOC, mucinous colorectal cancer (MCRC), mucinous appendiceal cancer (MAC), mucinous breast cancer (MBC) and gastric type mucinous cancer (GMC). Frequencies of somatic gene variants including mutations, copy number alterations and structural variants were compared using Chi-squared or Fischer's exact tests, using the Benjamini-Hochberg method to control for multiple hypothesis testing with q-values reported. **Results:** A total of 883 tumors were included for analysis: 358 MCRC, 268 MAC, 157 MOC, 59 MBC and 41 GMC samples. Compared to MAC, MOC samples had higher variant frequencies of *CDKN2A* (33.3% vs 0.4%, $q<0.001$), *CDKN2B* (24.0% vs 0.0%, $q<0.001$), *TP53* (64.3% vs 23.5%, $q<0.001$), *ERBB2* (14.3% vs 1.1%, $q<0.001$) and *CDK12* (13.2% vs 0.0%, $q<0.001$), whereas *GNAS* variants were more common in MAC (45.5% vs 5.7%, $q<0.001$). Compared to MCRC, MOC samples had higher variant frequencies of *CDKN2A* (33.3% vs 2.3%, $q<0.001$), *CDKN2B* (24.0% vs 3.7%, $q<0.001$), *TP53* (64.3% vs 42.9%, $q<0.001$), *KRAS* (69.4% vs 51.1%, $q<0.001$) and *ERBB2* (14.3% vs 5.3%, $q<0.001$), whereas MCRC had higher variant frequencies of 57 genes, with the largest differentials among *APC* (48.8% vs 2.6%, $q<0.001$), *SMAD4* (25.2% vs 5.8%, $q<0.001$) and *TCF7L2* (19.0% vs 0.0%, $q<0.001$). Samples of MOC had significantly higher rates of *KRAS* variants compared to GMC (69.4% vs 31.7%, $q<0.001$) and lower rates of *STK11* variants (1.9% vs 22.0%, $q<0.001$). Compared to MBC, MOC samples had higher variant rates of *CDKN2A* (33.3% vs 3.4%, $q<0.001$), *TP53* (64.3% vs 10.2%, $q<0.001$) and *KRAS* (69.4% vs 0.0%, $q<0.001$), whereas MBC samples had higher variant frequencies of 11 genes, with the largest differentials among *GATA3* (32.1% vs 0.8%, $q<0.001$), *FGF3* (30.4% vs 2.4%, $q<0.05$) and *CCND1* (28.1% vs 1.6%, $q<0.001$). **Conclusions:** NGS demonstrates that MOCs carry a distinct genetic signature compared to mucinous tumors of non-gynecologic origin, most commonly with significantly higher variant frequencies of *CDKN2A*, *CDKN2B* and lower variant frequencies of *GNAS*, *APC*, *STK11* and *GATA3*. This provides rationale for prospective studies evaluating genetic signatures as an adjunct to histopathology in the diagnosis of primary MOC. Research Sponsor: None.

**5583** **Poster Session**

## Effectiveness of PARP inhibitor maintenance therapy (mPARPi) in advanced ovarian cancer (OC) by *BRCA1/2* and HRD signature in real-world practice.

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**Background:** mPARPi following surgery and platinum chemotherapy (PCT) is a standard of care treatment for newly diagnosed advanced OC. Clinical trials have demonstrated benefit of mPARPi for patients (pts) with and without *BRCA1/2* mutations (*BRCA*+/-). The degree of benefit of mPARPi for pts without homologous recombination deficiency (HRD) biomarkers detected remains in question. This study aimed to compare the effectiveness of mPARPi in real world practice defined by biomarker status (*BRCA*+/- mutation and a novel HRD signature [HRDsig]). **Methods:** This study included pts with advanced OC who received 1$^{st}$-line PCT with real-world progression-free survival (rwPFS) of at least 10 months after treatment initiation and received either mPARPi (without bevacizumab) or no maintenance therapy (nm). Pt data was obtained by the US-based de-identified Flatiron Health-Foundation Medicine real-world OC clinico-genomic database, originating from ~280 US cancer clinics (~800 sites of care) between 01/2015 and 09/2022. rwPFS and real-world overall survival (rwOS) were compared between pts +/- biomarkers by Cox models, adjusted for propensity scores accounting for disease stage at diagnosis, ECOG, age, and *BRCA* status (for the HRDsig analysis). HRDsig+ (Foundation Medicine) status was determined using a pre-specified cutoff. **Results:** Of 604 included pts, 128 pts received mPARPi (25.8% *BRCA*+ and 48.4% HRDsig+) and 476 received nm (14.3% *BRCA*+ and 35.5% HRDsig+). *BRCA*+ pts receiving mPARPi vs. nm had more favorable rwPFS (HR 0.44, 95% CI 0.24-0.79, p = 0.006), as did *BRCA*- pts (HR 0.7, 95% CI 0.51-0.95, p = 0.021). More favorable rwOS was not observed for either group (p = 0.7112, p = 0.2066 respectively). HRDsig+ pts receiving mPARPi vs. nm had more favorable rwPFS (HR 0.31, 95% CI 0.20-0.48, $p < 0.001$) and rwOS (HR 0.35, 95% CI 0.12-1.05, p = 0.061), while no differences were observed for those HRDsig- (rwPFS HR 0.99 0.71-1.40, p = 0.976 / rwOS HR 0.86, 95% CI 0.5-1.47, p = 0.575). A treatment interaction was observed for HRDsig+ vs. HRDsig- (rwPFS $p < 0.001$ / rwOS p = 0.042) but not for *BRCA*+ vs. *BRCA*- (rwPFS p = 0.213 / rwOS p = 0.596). Among *BRCA*- pts, those HRDsig+ receiving mPARPi vs nm had favorable rwPFS (HR 0.27, 95% CI 0.15-0.49, $p < 0.001$) and rwOS (HR 0.40, 95% CI 0.08-1.98, p = 0.216), while no difference was observed for those HRDsig- (rwPFS HR 1.02, 95% CI 0.72-1.44, p = 0.923 / rwOS HR 0.86, 95% CI 0.49-1.49, p = 0.590), with a treatment interaction observed for rwPFS ($p < 0.001$), but not for rwOS (p = 0.120). **Conclusions:** In this analysis of real-world practice, we observed improved outcomes among biomarker positive pts treated with mPARPi. HRDsig+ pts had improved outcomes, even among those who were *BRCA-,* while HRDsig- pts showed no enrichment for benefit with mPARPi, suggesting that a novel HRDsig might be able to predict benefit from mPARPi regardless of BRCA status. Research Sponsor: Foundation Medicine Inc.

**5584** **Poster Session**

## Triplet maintenance (olaparib, pembrolizumab, and bevacizumab) in *BRCA* non-mutated patients with platinum-sensitive recurrent ovarian cancer: A multi-center, single-arm phase II study (OPEB-01).

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**Background:** The optimal treatment of *BRCA* 1/2 non-mutated patients with platinum-sensitive recurrent ovarian cancer remains unknown. In this study, we evaluated the efficacy and safety of triplet maintenance therapy in *BRCA* non-mutated patients with platinum-sensitive recurrent ovarian cancer. **Methods:** *BRCA* 1/2 non-mutated patients with platinum-sensitive recurrent epithelial ovarian cancer, showing a complete/partial response after second-line platinum-based chemotherapy, were eligible. Triplet maintenance therapy (olaparib, bevacizumab, and pembrolizumab) was administered until disease progression or unacceptable toxicity. The primary endpoint was the progression-free survival (PFS) rate at six months after therapy initiation. The secondary endpoints were PFS, overall survival, and safety. The translational objectives included biomarker evaluation with respect to survival outcomes. **Results:** Forty-four patients were enrolled (median age 61 years), majority with high-grade serous carcinoma (93.2%) and partial response (75.0%) to second-line chemotherapy. Overall, 54.6% were homologous recombination deficiency (HRD)-positive (genomic instability score $\geq$ 42) and 63.6% had PD-L1 positive tumors (combined positive score [CPS] $\geq$ 1). At 6 months, the PFS rate was 88.6% (95% confidence interval [CI] 75.4–96.2). The median PFS has not been reached. The most common $\geq$ grade 3 treatment-related adverse events (AEs) were anemia (20.5%) and neutropenia (6.8%), but there were no grade 4 AEs. Exploratory analysis demonstrated remarkable survival outcomes regardless of HRD status, whereas patients with PD-L1 CPS $\geq$ 1 showed improved PFS compared to those with PD-L1 CPS $<$ 1 ($P = 0{\cdot}032$). Analysis of molecular consensus subtype of the pre-treatment tissue samples showed that patients with mesenchymal subtype demonstrated poor PFS, compared to non-mesenchymal subtypes (p = 0.0023). **Conclusions:** This is the first report on triplet maintenance therapy in *BRCA* non-mutated platinum-sensitive recurrent ovarian cancer. The results show that the triplet maintenance therapy is efficacious with manageable toxicity, showing a particular promise for patients with molecular consensus subtype other than mesenchymal. Clinical trial information: NCT04361370. Research Sponsor: MSD supported the study drugs; Korean government.

**5585** **Poster Session**

## The diagnostic landscape of HRD testing based on cross-sectional survey of physicians and molecular biologists conducting testing (INDICATOR ONE).

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**Background:** Homologous recombination deficiency (HRD) occurs in approximately 50% of epithelial ovarian cancer (OC) cases. As HRD-positive tumors are more sensitive to poly(ADP-ribose) polymerase inhibitors (PARPi), HRD testing (determined by BRCAm and genomic instability score) identifies advanced ovarian cancer (AOC) patients who will benefit most from PARPi treatment. The value of these tests is recognized by guidelines to inform PARPi maintenance treatment decisions following first-line chemotherapy. This study characterizes the current testing landscape. **Methods:** This non-interventional, cross-sectional, web-based survey will be repeated in three waves, 9-12 months apart. Reported results are from Survey Wave 1 open from July to November 2022 and conducted among physicians and clinical laboratory heads/molecular biologists in the US and Europe (UK, France, Germany, Austria). Participants were recruited from clinical sites/laboratories known to be conducting HRD testing and via a standing physician panel. **Results:** Responses were received from 287 eligible participants (representing invitees from ~9% sites and $<$ 2% panelists), 265 of whom completed the full survey (Europe: 153, US: 112; 228 physicians, 37 clinical laboratory heads/molecular biologists). Physicians ordered HRD testing for 70% $\pm$ 27% (mean $\pm$ SD) of newly diagnosed AOC patients. Nearly all physicians ordered the test to inform treatment decisions (n = 222; 97%). Physicians were most likely to conduct testing at stage 3 or 4 of OC diagnosis (Europe: n = 89, 64%; US: n = 63, 71%), followed by OC diagnosis regardless of stage (Europe: n = 51, 37%, US: n = 51, 57%). When European participants selected all types of tests used MyChoice CDx, Myriad Genetics (n = 82, 54%) was most commonly selected, followed by FoundationOne CDx, Foundation Medicine (n = 38, 25%). US participants used FoundationOne CDx (n = 62, 55%), followed by MyChoice CDx (n = 49, 44%), and QIAGEN QIASeq HRD (n = 38, 34%). Test costs were often partially (Europe: n = 47; 27%; US: n = 125; 53%) or fully covered (Europe: n = 89; 51%; US: n = 48; 21%). Results were received within 10 $\pm$ 6 (mean $\pm$ SD) working days in the US and 16 $\pm$ 11 working days in Europe. Testing guided treatment decisions 'always/often' (Europe: n = 117, 84%; US: n = 65, 73%) or 'sometimes' (Europe: n = 21, 15%; US: n = 23, 26%). Most European (n = 108, 78%) and US (n = 71, 80%) institutions offered genetic counselling. **Conclusions:** Among physicians and molecular biologists known to be conducting HRD testing, most newly diagnosed AOC patients were tested for HRD, and results usually played a role in treatment decisions. Variations in testing between the US and Europe include test types, test cost coverage, and time to receive results. Differences indicate potential areas for improvement in HRD testing to further benefit patients. Research Sponsor: This study was sponsored by AstraZeneca and is part of an alliance between AstraZeneca and Merck & Co., Inc., Kenilworth, NJ, USA.

**5586** **Poster Session**

## Immune features of ovarian tumors with a good response to neo-adjuvant chemotherapy in combination with an anti-PD-L1 alone or with an anti-CTLA4: Data from the randomized IneOV trial (a GINECO study).

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**Background:** We have shown that chemotherapy may have immunomodulatory properties and prime the tumor microenvironment (TME) by recruiting cytotoxic immune cells. We previously reported that neoadjuvant chemotherapy (NACT) associated with Durvalumab (D) +/- Tremelimumab (T) resulted in encouraging complete resection (70%) and complete pathological response (18%) rates in patients with unresectable ovarian cancer. Here, we aimed to 1) characterize the immune TME at baseline of responders compared to non-responders and 2) describe changes in immune TME in paired tumor samples at diagnosis and after 3 cycles of NACT with D +/- T in the randomized IneOV trial. **Methods:** Tumor samples from IneOV trial (55 at diagnosis, 40 after treatment) were analyzed for CD3+, CD68+ and CD20+ by multiplexed immunohistochemistry. Stromal and intra-epithelial TILs were scored as percentage of positive surface. Patients were classified as good pathological responders (pR) (CRS3) or pathological non-responders (pNR) (CRS1 or 2). Intra-tumoral T cell infiltration was described as High or Low (intraepithelial (ie)CD3+ $>$ median vs $<$ , respectively). Non parametric statistical tests were used. We evaluated the correlation of the markers with each others (Spearman test) and with pathological response rate (Mann-Withney test). **Results:** At diagnosis, in the intra-epithelial compartment of the TME, the most abundant cells were macrophages (median ieCD68+ = 3,4) compared to T (ieCD3+ = 1.1), B (ieCD20+ ND) ANOVA p-value = 0.002 and $<$ 0.0001 respectively . In individual tumors, infiltration by the 3 different immune subsets was poorly correlated suggesting immune TME heterogeneity in OC. Pathological response was evaluable in 64 patients: 19 pR and 45 pNR. At diagnosis, CD3+ (p = 0.02) and CD68+ (p = 0.006) infiltration was significantly higher in pR tumors compared to pNR. Most of pR (76%) had high intra-tumoral CD3+ infiltration versus 39% in pNR (p = 0.011). After treatment, tumors with pR showed significantly greater CD3+ intra-epithelial infiltration compared to pNR (p = 0.047). **Conclusions:** Our results suggest that good pathological response to NACT +D+/-T is associated with high levels of both T cells and macrophages in iTME at baseline, and increased intratumoral T cell infiltration post-treatment. Work is ongoing to further characterize the iTME, especially in pNR to identify other strategies to enhance the anti-tumor immune response. Clinical trial information: NCT03249142. Research Sponsor: AstraZeneca.

**5587** **Poster Session**

## Ovarian cancer and bevacizumab: Real-world use across western countries and effect on survival in high-risk subgroups.

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**Background:** Bevacizumab (bev) may be part of first-line treatment for patients with "high-risk" epithelial ovarian cancer (OC) (GOG-0218 and ICON7 trials). The prevalence of high-risk patient subgroups, including bev use and its effect on survival in a real-world setting is not well studied. **Methods:** The observational multi-country cohort study RESPONSE collected retrospectively medical record data on women with newly diagnosed advanced high-grade serous or endometrioid OC (DOI: 10.1002/cncr.34350). We analysed patients defined as 'high-risk' according to ICON7 definition as either 1) stage IV disease, 2) inoperable stage III disease or 3) sub-optimally debulked (>1 cm residual disease) stage III disease. Unadjusted Cox proportional hazards regression analysis was performed to estimate the association of bev with the risk of death. Follow up time was calculated from time between response assessment at the end of primary chemotherapy and death or 20 months follow-up, whichever occurred first. **Results:** Of 954 patients in total, we identified 386 high-risk patients (40%) treated with platinum-based chemotherapy. Of these, 132 (34%) received bev maintenance treatment. Baseline characteristics did not differ between patients receiving bev or no bev. Bev use was associated with a statistically significant reduction in risk of death with a HR of 0.49 (95%Ci: 0.18-0.78, p=0.002) in the total group of high-risk patients. The effect on survival was most evident among inoperable stage III/IV patients (n=151) with a 63% reduction in risk of death (HR 0.37; 95% CI (0.18-0.78, p=0.009). Risk estimates for additional subgroups are given in the table. **Conclusions:** Forty percent of this real-world population are considered high-risk according to ICON-7 and a majority of these patients did not receive bev during first-line treatment. In line with ICON 7, this analysis supports the beneficial effect of bev on overall survival in this high-risk population. Patients who do not receive surgery are underrepresented in clinical trials and this real-world study confirms the strong benefit of bev particularly in this subgroup. Any real-world study may be limited by the potential presence of selection bias of patients to receive bevacizumab or not. Research Sponsor: AstraZeneca, part of an alliance between AstraZeneca and Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc (Kenilworth, New Jersey).

**Effect estimates on overall survival in patients receiving platinumbased chemotherapy with or without bev.**

| Analysis set | Chemotherapy with bevacizumab (no. of pts) | Chemotherapy without bevacizumab (no. of pts) | Events N | HR 95% CI | p-value |
|---|---|---|---|---|---|
| High-risk* | 132 | 254 | 102 | 0.49 (0.31-0.77) | 0.002 |
| Inoperable (stage III/IV) | 34 | 117 | 62 | 0.37 (0.18-0.78) | 0.009 |
| Stage IV | 89 | 150 | 56 | 0.50 (0.28-0.91) | 0.023 |
| Stage III inoperable | 15 | 68 | 28 | 0.33 (0.10-1.10) | 0.069 |
| Stage III >1cm residual | 28 | 36 | 18 | 0.63 (0.25-1.6) | 0.324 |

*High-risk patients included stage IV disease, inoperable stage III disease or sub-optimally debulked (>1 cm) stage III disease

**5588** **Poster Session**

## Blinded-assessment of a solution to evaluate olaparib maintenance treatment efficacy in patients with ovarian cancer from the GINECO/ENGOT PAOLA-1 trial.

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**Background:** SOPHiA DDM Dx HRD Solution (SOPHiA GENETICS, SA) combines analysis of genomic instability with mutational status of HRR genes, including *BRCA1/2*, generated through a single genomic workflow in order to to predict Homologous Recombination Deficiency (HRD) status in ovarian cancer (OvCa) samples. Previous evaluation of SOPHiA DDM Dx HRD Solution demonstrated its results to be highly concordant with a reference HRD method. As part of the ENGOT HRD initiative, we present updated clinical relevance results of SOPHiA DDM Dx HRD Solution. **Methods:** GINECO/ENGOT-Ov25 PAOLA-1 trial randomized (2:1) 804 patients (pts) to receive after the end of first-line platinum-based chemotherapy either maintenance olaparib+bevacizumab or placebo+bevacizumab for up to 2 years. DNA from a sub-cohort of 384 formalin-fixed paraffin-embedded (FFPE) OvCa pts samples included in the PAOLA-1 clinical trial were analyzed using SOPHiA DDM Dx HRD Solution(*). We combined SOPHiA DDM Dx HRD Solution genomic instability score, with *BRCA* mutational status obtained from a Clinical Decision Support module, and clinical interpretation of Variants of Unknown Significance to establish the pts HRD status and investigated differences in progression-free survival (PFS) in the olaparib+bevacizumab and placebo+bevacizumab arms between pts with HRD positive or HRD negative test. **Results:** We determined the HRD status of 98.4% of pts using SOPHiA DDM Dx HRD Solution. The median PFS time for pts with HRD positive tumors was 35.7 months longer in the olaparib+bevacizumab arm than in the placebo+bevacizumab arm (hazard ratio [HR], 0.36; 95% confidence interval [CI], 0.25-0.51, $p< 0.001$), confirming the findings of our previous interim analysis. No significant difference in PFS was observed between treatment arms in pts with HRD negative test (HR, 1.02; 95% CI, 0.71-1.48; $p= 0.90$). **Conclusions:** These clinical relevance results from the SOPHiA DDM Dx HRD Solution evaluation on the PAOLA-1 samples further support the value of combining low-pass whole genome and targeted sequencing in a unique workflow for reliable and cost-effective HRD testing and future patient stratification. (*) Comparison data generated using the CE-IVD pipeline with Clinical Decision Support module for *BRCA* status only available in EU, Switzerland, UK. Research Sponsor: None.

**5589** **Poster Session**

# Predictors of long-term progression-free survival (PFS) in niraparib-treated patients (pts) from the PRIMA/ENGOT-OV26/GOG-3012 study.

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**Background:** Niraparib was approved as maintenance therapy for pts with advanced ovarian cancer (OC) after complete or partial response (CR/PR) to first-line (1L) platinum-based chemotherapy (CT) based on results from the PRIMA study. In this post hoc analysis, we identified factors associated with long-term PFS. **Methods:** PRIMA is a phase 3, randomized study of pts with newly diagnosed advanced high-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer at high risk for relapse with CR/PR after 1L platinum-based CT. Pts were randomized 2:1 to niraparib 200 or 300 mg or placebo QD, and stratified by best response to 1L CT (CR/PR), neoadjuvant CT (yes/no), and homologous recombination deficiency (HRD) status (deficient [HRd]/proficient or not determined [HRp/nd]). Investigator-assessed PFS was dichotomized in niraparib-treated pts with progressive disease (PD)/censoring $<2$ years vs PD/censoring $\geq 2$ years after randomization (data cut, Nov 17, 2021). Logistic regression modeling using backward elimination (significance level=0.15) was used to identify baseline covariates associated with long-term PFS. **Results:** Of 487 niraparib-treated pts, 152 (31%) had PD/censoring $\geq 2$ years after randomization. Odds ratios (OR) for PFS $\geq 2$ years by baseline subgroup are shown (Table). The logistic regression model showed that *BRCA* mutation and HRD status, International Federation of Gynecology and Obstetrics (FIGO) stage, fallopian tube as the site of the primary tumor, and absence of baseline nontarget lesions were associated with longer PFS. Eastern Cooperative Oncology Group (ECOG) performance score, body mass index, age, time from CT to randomization, number of target lesions, best response after CT, number of CT cycles, type of debulking surgery, and residual disease were not associated with PFS $\geq 2$ years. Safety has been reported previously (*Ann Oncol.* 2022;33[suppl 7]:S789). **Conclusions:** Results suggest that long-term PFS in pts treated with niraparib may be associated with BRCA/HRd biomarker status, FIGO stage, primary tumor site, and number of baseline non-target lesions. These data are hypothesis generating. Clinical trial information: NCT02655016. Research Sponsor: GSK.

| Variable | OR* (95% CI) N=487 | *P* Value |
|---|---|---|
| ***BRCA*/HRD status** | 3.73 (2.191–6.335) | <0.0001 |
| ***BRCA*1/HRd, n=105** | 10.75 (5.158–22.407) | <0.0001 |
| ***BRCA*2/HRd, n=47** | 2.49 (1.422–4.372) | 0.0014 |
| ***BRCAwt*/nd + HRd, n=95** | 1.00 | |
| ***BRCAwt* + HRp/nd,* n=240** | | |
| **FIGO stage** | | 0.0412 |
| **III, n=318** | 1.62 (1.019–2.568) | |
| **IV,* n=169** | 1.000 | |
| **Primary tumor site** | 0.53 (0.208–1.332) | 0.1755 |
| **Primary peritoneal, n=34** | 0.54 (0.275–1.052) | 0.0700 |
| **Fallopian tube, n=65** | 1.000 | |
| **Ovarian*, n=388** | | |
| **Baseline nontarget lesions** | 4.67 (2.076–10.485) | 0.0002 |
| **0, n=331** | 2.20 (0.857–5.649) | 0.1010 |
| **1, n=90** | 1.000 | |
| **≥2,* n=66** | | |

*Reference variable. †Higher OR indicates more likely to remain progression free; eg, OR of 1.63 is 63% more likely to remain progression free for ≥2 years vs reference. wt, wild type.

**5590** **Poster Session**

## Phase 1/1b study of PRGN-3005 autologous UltraCAR-T cells manufactured overnight for infusion next day to advanced stage platinum resistant ovarian cancer patients.

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**Background:** Relapsed or refractory (r/r) ovarian cancer patients (pts) have limited treatment options. PRGN-3005 UltraCAR-T cells express a chimeric antigen receptor (CAR) targeting unshed MUC16, membrane bound IL-15 (mbIL15) and a kill switch with robust activity in preclinical models. UltraCAR-T investigational therapies are manufactured overnight using the proprietary UltraPorator electroporation system at the medical center and administered to patients one day after gene transfer. **Methods:** The Phase 1/1b study of PRGN-3005 evaluates the safety and recommended Phase 2 dose (RP2D) of PRGN-3005 in pts with r/r ovarian cancer (NCT03907527). In Phase 1, pts received PRGN-3005 without lymphodepletion (LD) via Intraperitoneal (IP) infusion (Cohort 1, C1) or Intravenous (IV) infusion (Cohort 2, C2) at Dose level 1-3. Dose level 3, IV infusion was further evaluated in pts treated with cyclophosphamide LD (60mg/kg/day on days -4 to -3 (IV LD)). As of the February 6, 2023 data cut-off, 25 evaluable pts have been treated in C1 (n = 12), C2 (n = 6), and IV LD (n = 7). Pts had a median age of 64 years (38-76) and were heavily pre-treated with a median of 8 prior regimens (4-11). Pts treated in C1 received 1 to 65.5 x $10^5$ cells/kg, pts treated in C2 received 0.1 to 50 x $10^5$ cells/kg and pts treated in IV LD received 0.1 to 39 x $10^5$ cells/kg. **Results:** PRGN-3005 was well tolerated at up to 65.5 x $10^5$ cells/kg. There have been no deaths, dose-limiting toxicities, neurotoxicity, grade $\geq$3 Cytokine Release Syndrome (CRS), or unexpected on-target/off-target toxicities related to PRGN-3005, and no use of the kill switch as of data cut-off. Grade 1 CRS occurred in 3/7 IV LD pts and one pt had transient grade 2 CRS, which resolved in $<$ 24 hours. Plasma levels of IL-15 did not increase with treatment confirming mbIL15 is not shed. A dose dependent increase in PRGN-3005 was observed in peripheral blood of patients even in the absence of LD, and *in vivo* persistence of PRGN-3005 could be observed in some patients for up to 9 months post infusion. Response was evaluated per RECIST 1.1, and 20% of all subjects experienced a response in at least 1 target lesion. In the IV LD pts, the disease control rate (DCR) was 85.7% at first restaging, with a decreased target tumor burden in 4/7 (57%), and a 27.4% average decrease in CA125. One pt had a 28% decrease in target tumor burden after receiving a second infusion of PRGN-3005 after 12 months. **Conclusions:** PRGN-3005 UltraCAR-T targeting MUC16 has been well tolerated with minimal toxicity. PRGN-3005 demonstrated a dose-dependent expansion and persistence in blood with or without LD. Encouraging DCR rates and a reduction in overall tumor burden have been observed in heavily pretreated, ovarian cancer pts treated with LD. The study continues to enroll to the Phase 1b expansion phase and is treating pts at DL3 with LD with an option to receive a second dose. Clinical trial information: NCT03907527. Research Sponsor: Precigen, Inc.

**5591** **Poster Session**

# The role of Chemotherapy Response Score (CRS) in the decision making process for patients with advanced high grade serous ovarian cancer undergoing neoadjuvant chemotherapy.

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**Background:** The role of chemotherapy response score (CRS) in predicting PARP inhibitors (PARPi) response for high grade serous Advanced Ovarian Cancer (AOC) patients undergoing Neoadjuvant Chemotherapy (NACT) has never been investigated. Also, the correlation between CRS and Homologous Recombination status (HRs) is unclear. **Methods:** In this observational retrospective study, we collected data from patients with high grade serous AOC, FIGO stage III-IV, undergoing NACT and subsequent Interval Debulking Surgery (IDS) from 2017 to 2021. KELIM score, CRS and *BRCA* status were considered; additionally, HRs (Foundation test) was reported when available. Primary endpoint was Progression Free Survival (PFS) according to CRS (CRS 1/2 vs 3) in patients receiving PARPi. **Results:** We enrolled 309 patients; 102 had CRS3 and 193 had CRS1/2 (14 were undetermined). Patients with CRS3 and PARPi maintenance showed the best prognosis, compared to all other subgroups (median PFS Not Reached, $p$=0.014); additionally, in the *BRCA wild type* population, CRS3 was predictive of longer survival (median PFS for the CRS3+PARPi *BRCAwt* population 24 months compared with 15 months for the CRS1/2+PARPi *BRCAwt* patients, $p$=0.041). Furthermore, among the 44 patients with known HRs, 59.1% of HR Deficiency (HRD) positive patients had CRS3, conversely 22.7% of HRD negative ones had a CRS3 ($p$=0.048) Finally, we found out that a favorable KELIM was significantly associated with CRS3 in the all-comers patients ($p$=0.007) and in the *BRCAwt* ($p$=0.04), but it was not predictive of PARPi response. **Conclusions:** Our findings suggested that the higher the CRS at the interval cytoreduction, the better the subsequent PARPi response. CRS correlates with PARPi response, as the HRD test does in other clinical trials and it may be considered as a surrogate of HRD status. We have planned to retrospectively perform HR test on a total sample size of 77 patients who received PARPi to corroborate this hypothesis. Research Sponsor: Fondazione Policlinico Universitario Agostino Gemelli IRCCS.

| | Patients *(N)* | Median PFS *(months, CI 95%)* | *p* value |
|---|---|---|---|
| ***All-Comers*** | | | |
| **CRS 3 + PARPi** | 47 | NR | - |
| **CRS 1/2 + PARPi** | 106 | 26 | 0.014 |
| **CRS 3 - NO PARPi** | 23 | 18 | <0.001 |
| **CRS 1/2- NO PARPi** | 61 | 13 | <0.001 |
| ***BRCA-wt population*** | | | |
| **CRS 3 + PARPi** | 24 | 24 | - |
| **CRS 1/2 + PARPi** | 53 | 15 | 0.041 |
| **CRS 3 - NO PARPi** | 19 | 18 | 0.161 |
| **CRS 1/2 + No PARPi** | 48 | 13 | 0.001 |

**5592** **Poster Session**

## Real-world overall survival in second-line maintenance niraparib monotherapy vs active surveillance in *BRCA* wild-type patients with recurrent ovarian cancer.

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**Background:** The Phase 3NOVA trial assessed niraparib versus placebo as a maintenance treatment (tx) for patients (pts) with recurrent ovarian cancer (OC) who were platinum-sensitive after ≥2 regimens; progression-free survival was the primary endpoint and overall survival (OS) was a secondary endpoint (NCT01847274). The aim of this real-world study was to compare OS in a breast cancer gene wild-type (*BRCA*wt) population of pts with recurrent OC and who received second-line maintenance (2Lm) niraparib monotherapy or were under active surveillance (AS). **Methods:** This study used the US nationwide Flatiron Health de-identified electronic health record (EHR)-derived database. Pts diagnosed with epithelial OC between 1Jan2011–31May2021 who completed 2L therapy between 1Jan2017–2Mar2022 were eligible for inclusion. Pts were *BRCA*wt, had an ECOG PS score 0–1, epithelial histology, and platinum-sensitive disease with ≥6 months between end of first-line tx and start of 2L tx. Pts were assigned to 2Lm niraparib or AS cohorts based on their management following 2L non-maintenance therapy (≤120 days). Follow-up was measured from the index date (end of 2L non-maintenance therapy) until end of study (31May2022), last activity, or death, whichever came first. A target trial emulation cloned inverse probability of censoring weighting (IPCW) methodology was selected *a priori* to minimize bias. IPCW median OS and hazard ratios (HR) for 2Lm versus AS were estimated with Kaplan-Meier curves and Cox regression models. **Results:** Overall, 266 *BRCA*wt pts were included and received niraparib 2Lm (N=123) or were under AS (N=143). Across 2Lm and AS cohorts, prior to cloning and IPCW, 23.6% and 34.3% of pts were aged ≥75 years, and 26.0% and 16.8% had an EHR value for race as other than White, respectively. The majority of pts were from community practice (80.5% and 90.2%, respectively), had serous OC (79.7% and 81.1%) and had Stage III disease (53.7% and 60.8%). Homologous recombination deficiency status was unknown for 92.7% and 86.0% of pts in 2Lm and AS cohorts, respectively. Median follow-up for 2Lm and AS cohorts was 16.8 (Quartile [Q] 1, Q3: 10.4, 28.7) and 10.2 (Q1, Q3: 4.1, 23.7) months, respectively. IPCW median OS was 28.1 (95% confidence interval [CI]: 22.5, 43.2) and 21.5 (95% CI: 14.7, 27.0) months (HR: 0.63 [95% CI: 0.45, 0.88]) for niraparib 2Lm and AS cohorts, respectively and survival rates at 24 months were 58.2% (95% CI: 47.5, 67.6) and 46.1% (95% CI: 33.6, 57.7). **Conclusions:** This analysis provides real-world data on OS among pts with OC receiving niraparib 2Lm or under AS in the 2L setting following chemotherapy. Funding: GSK study (219306). Editorial support was provided by Fishawack Health, funded by GSK. Research Sponsor: GSK.

**5593** **Poster Session**

## Gynecologic-cancer analysis of *ARID1A* alterations detected in tissue and liquid biopsies.

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**Background:** The tumor suppressor gene *ARID1A* is an emerging target for new cancer treatment strategies including ATR inhibition. This study aimed to describe the landscape of *ARID1A* alterations (*ARID1A*mut) in gynecologic malignancies. **Methods:** Patients (pts) with a diagnosis of ovarian (OC) or uterine cancer (UC) of different histologies and comprehensive genomic profiling (CGP) by Foundation Medicine Inc. were included in this study. CGP of solid tissue biopsies (Tbx; FoundationOneCDx) included evaluation of genomic loss of heterozygosity (gLOH; gLOH-high as ≥16% as validated in OC), microsatellite instability (MSI), and tumor mutational burden (TMB; high as ≥10 mutations/Megabase). CGP of peripheral whole-blood liquid biopsies (Lbx; FoundationOneLiquidCDx) included evaluation of MSI and tumor fraction (TF), a measure of the relative quantity of circulating tumor DNA (ctDNA). TF was calculated by measures of aneuploidy and allele frequency and binned as TF < 1%, TF 1 to < 10%, or TF ≥10%. **Results:** Tbx Cohort: 5,778/30,212 (19.1%) cases were *ARID1A*mut. Pts had a median age of 63 (range 21-89) years. *ARID1A*mut were observed across many subtypes and most frequently in endometrial endometrioid (n = 3,052, 57.7%) and ovarian clear cell (n = 982, 57.6%) but rarely in serous (OC, n = 12,258, 2.8%; UC, n = 2,682, 8.9%). Pts frequently harbored more than one *ARID1A*mut (2,360/5,778, 40.8%). Of the 8,484 observed *ARID1A*mut, 97.6% were short variants (SV), 0.5% were deletions, and 1.9% were inactivating rearrangements. SV were primarily frameshifts (68.5%) and nonsense mutations (27.6%). The most frequent alterations observed were frameshifts at the D1860 codon. SV were predicted to be homozygous in 11.9%, heterozygous in 65.3%, or unknown zygosity in 22.8%. Overall, 16.6% of *ARID1A*mut cases with SV had at least one homozygous alteration. 6.6% of pts with homozygous *ARID1A*mut were MSI-high (MSI-H), while 39.4% of pts with only heterozygous or unknown zygosity *ARID1A*mut were MSI-H ($p < 0.0001$). Overall, 1,905 (33.0%) of *ARID1A*mut cases were MSI-H, and 2,183 (37.8%) were TMB high. For *ARID1A*mut cases with evaluable gLOH (n = 4745), the median gLOH was 2.7%, and 5.9% pts were gLOH-high. The most frequently altered co-occurring genes were *PTEN* (62.2%), PIK3CA (54.2%), and *TP53* (27.6%). 8.7% of *ARID1A*mut also harbored a *BRCA* alteration. Lbx Cohort: 59/967 (6.1%) cases were *ARID1A*mut. 17 (28.8%) were MSI-H. Frequency of *ARID1A*mut increased as TF increased, with a detected frequency of 1.3%, 6.7%, and 14.0% among Lbx with TF < 1%, TF 1 to < 10%, or TF ≥10% respectively. **Conclusions:** *ARID1A*mut are observed across a variety of Gynecologial cancer subtypes but are enriched in clear cell and endometrioid histologies and detected in both tissue and liquid biopsies. ARID1Amut were not associated with elevated gLOH but were often MSI-H and TMB ≥10mut/Mb. Clinical trials targeting *ARID1*A may wish to consider the context of co-occuring biomarkers. Research Sponsor: Foundation Medicine Inc.

**5594** **Poster Session**

## Healthcare access dimensions and uterine cancer survival: A National Cancer Database study.

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**Background:** Racial disparities persist throughout the continuum of care for Black patients with uterine cancer. Few studies have evaluated how multiple dimensions of healthcare access (HCA) contribute to these disparities in patients who present at an advanced stage and meet criteria for adjuvant therapy. **Methods:** Patients with Stage III-IV uterine cancer between 2004-2015 who received adjuvant therapy with complete sociodemographic and other relevant covariate data were identified in the National Cancer Database (NCDB). Race and ethnicity were defined as non-Hispanic (NH)-Black, Hispanic, and NH-White. Healthcare access dimensions of affordability, availability and accessibility were measured using variables defined in the NCDB. Overall survival was analyzed using Kaplan-Meier curves, log-rank test, and multivariable Cox proportional hazard models. **Results:** The study cohort included 43,134 patients: 78.8% NH-White, 15.3% NH-Black, and 5.9% Hispanic. Compared to NH-White and Hispanic patients, NH-Black patients were more likely to have Type II (75.6% vs. 53.9% and 55.4%) and Stage IV disease (40.8% vs. 30.7% and 32.3%). NH-Black patients were more likely to receive chemotherapy alone (53.5% vs. 43.1% and 46.2%) compared to NH-White and Hispanic patients. NH-Black patients were the most likely to have government funded insurance (58.6% vs. 50.3% and 50.4%) and live in the lowest income quartile (46.4% vs. 14.2% and 29.9%) compared to NH-White and Hispanic patients. NH-Black patients had a significantly higher risk of death than NH-White patients when adjusting for demographic/clinical characteristics and all three healthcare access dimensions (HR 1.29; 95% CI 1.24, 1.34). **Conclusions:** Healthcare access affordability predicts survival but does not fully explain racial disparities in survival rates of patients with advanced stage uterine cancer. NH-Black patients are more likely to have aggressive disease, receive chemotherapy alone, and have worse survival than NH-White patients regardless of pathogenic subtype. Investigating additional healthcare access dimensions may be critical to addressing disparities in uterine cancer. Research Sponsor: None.

**5595** **Poster Session**

## Preliminary antitumor activity of the combination of COM701 + BMS-986207 + nivolumab in patients with recurrent, metastatic MSS endometrial cancer.

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**Background:** There is a high unmet medical need for the treatment of patients [pts] with microsatellite stable [MSS], recurrent, metastatic, endometrial cancer [EC]. We reported encouraging preliminary antitumor activity with the triple combination of COM701 + BMS-986207 + nivolumab in patients with platinum resistant epithelial ovarian cancer [1]. COM701 is a novel, 1st-in-class immune checkpoint inhibitor [ICI] that binds to PVRIG, a DNAM-1 axis member, leading to activation of T-and NK-cells; BMS-986207 is an ICI of TIGIT. Nivolumab is an ICI of PD-1. We hypothesized that in pts with EC, the triple combination would demonstrate antitumor activity with a favorable safety and tolerability profile. We present encouraging preliminary results. **Methods:** As part of an expansion cohort, we enrolled 9 patients [pts] with EC. All pts received COM701 20 mg/kg + BMS-986207 480 mg + nivolumab 480 mg all IV Q4W. Primary objectives were safety/tolerability, with secondary objective of antitumor activity in pts with EC. Key inclusion criteria: Age $\geq$ 18 yrs, measurable disease, MSS by IHC or genomic testing, $\leq$2 prior systemic cytotoxic therapies, prior PD-1/PD-L1 permissible. Key exclusion criteria: prior receipt of anti-PVRIG, anti-TIGIT. Investigator assessed responses were per RECIST v1.1, safety per CTCAE v5.0. **Results:** Median age 71yrs, median of 2 prior lines of therapy, prior PD-1/PD-L1 3/9 [33%]. All pts received prior cytotoxic therapy. Objective response rate (ORR) 2/9 [22%] pts; 2 pts with SD. Disease control rate [CR + PR + SD] 4/9 [44%]. There were 2 pts with confirmed PR; 1 of these pts was refractory to prior receipt of lenvatinib + pembrolizumab [best response assessment of progressive disease]. Treatment related AEs were reported in 6/9 [67%] pts, the majority 4/6 [67%] were Grade 1 [1 pt each with chills, pyrexia, back pain and pruritus, lipase increased]. No new safety signals are reported. **Conclusions:** The combination of COM701 + BMS-986207 + nivolumab demonstrates encouraging preliminary signal of antitumor activity in pts with EC including in a pt refractory to prior exposure to lenvatinib + pembrolizumab. The triplet combination has a favorable safety/tolerability profile. Additional data analyses and pt follow up are ongoing and will be presented at the conference. Data extract 01/24/2023. 1. Moroney JW, Yeku O *et al*. Triple blockade of the DNAM-axis with COM701 + BMS-986207 + nivolumab demonstrates preliminary antitumor activity in patients with platinum resistant OVCA. Annals of Oncology (2022) 16 (suppl_1): 100104-100104. 10.1016/iotech/iotech100104. Clinical trial information: NCT04570839. Research Sponsor: Compugen Ltd.; Bristol Myers Squibb.

**5596** **Poster Session**

## Pathogenic germline variants in patients with endometrial cancer across diverse ancestries.

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**Background:** Racial/ethnic disparities in outcomes exist in endometrial cancer (EC), particularly amongst self-reported Black compared to Non-Hispanic White (NH-White) patients. However, the contribution of differences in germline pathogenic variants (gPV) and genetics care to disparities is unknown. We seek to describe the spectrum of gPV in unselected patients with EC by ancestry to characterize variations and describe any differences in subsequent genetic counseling follow-up. **Methods:** Germline assessment of ≥76 cancer predisposition genes was performed in patients with EC undergoing clinical tumor-normal MSK-IMPACT sequencing from 1/1/15-6/30/21. Self-reported data on race/ethnicity and Ashkenazi Jewish (AJ) ancestry were used to classify patients into mutually exclusive ancestry groups: AJ, Asian, Black, Hispanic, NH-White, or Unknown. Genetic ancestry was inferred from MSK-IMPACT, and those with single population ancestral fraction >0.8 were assigned to African (AFR), European (EUR), East Asian (EAS), Native American (NAM), South Asian (SAS), and AJ (ASJ) ancestry populations or considered admixed (Mixed). Clinicopathologic variables were reported using summary statistics and compared by ancestry using non-parametric tests. **Results:** Among 1,625 patients with EC, self-reported ancestry [202 AJ (12.4%), 124 (7.6%) Asian, 171 Black (10.5%), 124 Hispanic (7.6%), 927 NH-White (57.1%), and 77 missing (4.7%)] correlated with genetic ancestry. In those identifying as Black, 122 (71%) had >80% African ancestry, 45 (26%) were considered Mixed, and 4 (3%) had missing data. We observed gPV in 216 (13.3%) patients (73 high, 36 moderate and 107 low/uncertain penetrance), with 15 patients having >1 gPV. Rates of gPV varied significantly by self-reported ancestry [AJ: 40 (19.8%), Asian: 15 (12.1%), Black: 12 (7.0%), Hispanic: 15 (12.1%), NH-White: 129 (13.9%), Missing: 5; p=0.009] and genetic ancestry [AFR: 9 (6.4%), AJ: 53 (19.3%), EAS: 9 (11.0%), EUR: 112 (13.3%), NAM: 2 (40%), SAS: 7(20%), Mixed: 17 (8.6%), Missing: 7; p<0.001]. Self-reported Black patients had the lowest rate with 13 gPV observed in 12 patients (7.0%); 5 gPV had biallelic inactivation within the tumor (2 *MSH2*, 1 *MSH6*, 1 *BRCA2* and 1 *FANCA*). Biallelic inactivation was observed in 70 (32%) patients overall with highest rates in Black (42%), Asian (40%), AFR (67%) and SAS (71%) populations. In those with new gPV (n=114), 102 (89%) overall were seen in genetics clinic for follow-up care, with the lowest rates in patients identifying as Black (75%) and of AFR ancestry (67%). **Conclusions:** Although rates of gPV varied by ancestry, they are drivers of disease in all populations, emphasizing the importance of germline assessment in EC. Differences in gPV and subsequent genetics care may contribute to racial/ethnic disparities in outcomes in EC by affecting treatment and cancer prevention and should be studied further. Research Sponsor: U.S. National Institutes of Health; Robert and Kate Niehaus Center for Inherited Cancer Genomics.

**5597** **Poster Session**

## The effect of megestrol acetate ± pterostilbene in endometrial cancer: A prospective, randomized, window-of-opportunity clinical trial.

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**Background:** Pterostilbene (3,5-dimethoxy-40-hydroxystilbene) is a potent oral antioxidant found naturally at highest concentrations in blueberries. Its anti-tumor effects in preclinical studies of various solid tumors include carcinogenesis, inflammation, reactive oxygen species (ROS) formation, and antiproliferative effects. In endometrial cancer (EC), *in vitro* and *in vivo* studies demonstrated a synergistic antiproliferative effect of pterostilbene (PT) in combination with megestrol acetate (MA). No clinical trials testing the potential therapeutic benefit of pterostilbene in cancer have been completed. **Methods:** We performed a prospective, window-of-opportunity, randomized phase 2 clinical trial (NCT03671811) in patients with EC. Eligible patients had to be surgical candidates for treatment with hysterectomy and not have received prior therapy. The primary objective was to determine the effect of MA plus PT versus standard treatment of MA alone on tumor proliferation as measured by the Ki-67 index during the preoperative window. Patients were randomized 1:1 to one of two arms: MA+PT PO BID versus MA PO BID, for 3 weeks. The Ki-67 index was measured via hot-spot and H-score methodology in the preoperative tumor and hysterectomy specimen by two blinded pathologists whose measurements were averaged. The net change between pre- and post-operative specimens was calculated for each patient and expressed as a percentage. Toxicity was assessed using CTCAE grading. **Results:** A total of 44 patients with EC of all histologies were recruited to the study and included in the toxicity analysis. Median age was 61.9 years. Baseline demographics were comparable between both arms. Median treatment duration was 21 days (14-56), similar in both arms. One G3 hypertension was encountered in the MA arm; one G3 thromboembolic event in the MA+PT arm. Of 35 patients with sufficient treatment duration (>10 days) and available pre-and post-treatment specimens, 29 patients with endometrioid histology were evaluated for the ki67 analysis: 14 in the MA arm and 15 in the MA+PT arm. The MA+PT group demonstrated a -41.1% change in Ki-67 index by Hot Spot Score compared to -27.5% in the MA-only group (p=0.17). A similar trend was observed for the Ki-67 index by H Score methodology (-41.6% vs -26.7%, MA+PT vs MA, p=0.17). **Conclusions:** The combination of MA + PT in preoperative treatment of endometrial adenocarcinoma is well tolerated. The addition of Pterostilbene demonstrates a trend towards decreased Ki-67 index in endometrioid EC patients. Molecular studies are pending to delineate biomarkers associated with response. Clinical trial information: NCT03671811. Research Sponsor: internal funding.

# Overall survival and subsequent therapy from a phase II study of sintilimab and anlotinib in patients with advanced or recurrent endometrial cancer.

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**Background:** Although the combination of immunotherapy and antiangiogenic agents has been proved a promising strategy in endometrial cancer, studies in Chinese patients are limited. In the earlier phase II study (NCT04157491), Chinese patients with recurrent or advanced endometrial cancer treated with sintilimab + anlotinib had an objective response rate of 73.9% (95% confidence interval [CI]: 51.6% to 89.8%). Here we further updated overall survival (OS) and subsequent therapy for this study. **Methods:** Patients with endometrial carcinoma progressed after platinum-based chemotherapy were enrolled. Sintilimab 200 mg was supplied intravenously on day one, whereas anlotinib 12 mg was administered orally on day 1 - 14 every three weeks. **Results:** Twenty-three patients were enrolled in the study. 47.8% of patients received $\geq$ 2 lines of prior chemotherapy; microsatellite instability-high/mismatch repair deficiency (MSI-H/dMMR) and microsatellite instability stable/mismatch repair proficient (MSS/pMMR) accounted for 39.1% and 60.9% of patients, respectively. We observed a median OS of 17.8 months (95% CI, 9.4 to 26.3 months). Patients with microsatellite instability-high (MSI-H) had superior OS than their counterparts (not available vs. 13.3 months; HR 0.15, 95% CI, 0.33-0.70; P = 0.006). All patients had dropped out of the cohort [56.5% progression disease (PD), 13.0% adverse events (AE)]. Notably, five patients with partial responses (PRs) obtained pathological or radiography complete responses (CRs) in the follow-up. Pathological CRs were confirmed in three patients with long-lasting PRs who underwent surgery, consistent with PET/CT scans. Two patients with PR continued to have tumor shrinkage following treatment cessation due to AE and achieved CR during follow-up. Three out of four patients with CR experienced recurrences. There were no new grade 3-4 AEs associated with therapy. **Conclusions:** In terms of OS, combining sintilimab and anlotinib had promising therapeutic effects. Pathological CR was observed in patients with long-lasting PR, thus exploratory surgery may be required in selected patients. Clinical trial information: NCT04157491. Research Sponsor: None.

**Summary of subsequent therapies (N = 23).**

| Sintilimab and anlotinib | | Subsequent therapies | | | | |
|---|---|---|---|---|---|---|
| Best overall response | Patients, n | PD-1 inhibitor maintenance | Surgery | Chemotherapy | Other therapy | Overall survival |
| CR | 1 | Sintilimab | - | - | - | 37.0 m |
| | 1 | - | - | Paclitaxel plus carboplatin | Radiotherapy | 35.9 m |
| | 1 | Sintilimab | - | - | Olaparib | 35.7 m |
| | 1 | | | PD with no subsequent therapy | | 15.5 m |
| PR | 3 | - | Cytoreduction [a] | - | - | 29.9 to 31.0 m |
| | 1 | Sintilimab [b] | Cytoreduction [a] | Paclitaxel plus carboplatin | - | 31.9 m |
| | 1 | - | - | Paclitaxel | Pamiparib plus anlotinib | 30.9 m |
| | 1 | Sintilimab | - | - | - | 28.4 m |
| | 1 | - | - | NA | - | 13.8 m |
| | 6 | | | No subsequent therapy | | 3.3 to 37.5 m |
| SD | 1 | - | - | Paclitaxel | PARPi plus angiogenesis | 13.8 m |
| | 3 | | | No subsequent therapy | | 12.4 to 21.0 m |
| PD | 2 | | | No subsequent therapy | | 4.0 to 7.1 m |

[a] After PFS achieved 2 years. b After surgery.

**5599** **Poster Session**

# Preliminary results of a phase II trial with sacituzumab govitecan-hziy in patients with recurrent endometrial carcinoma overexpressing Trop-2.

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**Background:** Despite recent advances, there remains a significant need for targeted, efficacious treatments for advanced and recurrent endometrial carcinoma (EC). Trop-2 has been demonstrated to be overexpressed in several EC including grade 3 endometrioid adenocarcinoma (96%), and uterine serous carcinoma (65%). Trop-2 overexpression has been found to confer a worse prognosis and predicts disease recurrence. Sacituzumab govitecan-hziy (SG) is an antibody-drug conjugate comprised of a humanized anti-Trop-2 antibody conjugated with the active metabolite of irinotecan, a topoisomerase-I inhibitor. SG is currently FDA-approved for use in metastatic urothelial cancer and metastatic triple-negative breast cancer. **Methods:** We report results from the stage 1 of an open-label non-randomized phase 2 trial (NCT04251416) established to evaluate the clinical activity of SG in patients with persistent or recurrent EC of epithelial origin with Trop-2 overexpression. Criteria for study participation included radiographically confirmed and measurable persistent or recurrent EC, progression after or during platinum-based chemotherapy, and at least 2+ staining of Trop-2. One target lesion by RECIST v1.1 and adequate bone marrow, renal, and hepatic function were required. Patients were at least two weeks beyond prior treatment, major surgery, or high dose systemic corticosteroid use. Patients were given 10mg/kg of SG administered as an intravenous infusion once weekly on days 1 and 8 of 21-day treatment cycles. This 3-week cycle was continued without rest until disease progression or unacceptable toxicity. **Results:** Twenty-one patients were enrolled into stage 1. Ten patients (48%) had uterine serous carcinoma, seven (33%) had endometrioid adenocarcinoma, three (14%) had carcinosarcoma, and one patient had mixed serous and clear cell histology. All patients received at least one prior line of chemotherapy, (median 3 lines, range 1-6). At the time of submission, 20 patients were response-evaluable (Table); seven (35%) achieved objective response (5 out of 7 confirmed). Eighteen patients were evaluable for durable disease control; 7 (39%) achieved it. Follow-up durations had a median (IQR) of 15.6 (5.7–22.5) months. Median OS was 22.5 months, and median PFS was 5.7 months. The treatment was well-tolerated with no new or unexpected safety signals reported. **Conclusions:** Sacituzumab govitecan shows remarkable clinical activity against some of the most historically challenging and chemotherapy-resistant endometrial pathologies and demonstrates a favorable safety profile. With these promising results, we will begin the stage 2 expansion of this phase 2 trial. Clinical trial information: NCT04251416. Research Sponsor: Gilead.

**Overall disease response.**

| | | Evaluable | | |
|---|---|---|---|---|
| | | too soon | Yes | all 21 |
| **Best Response** | | 1 | . | 1 |
| | **N** | | | |
| **Complete Response** | **N** | . | 1 | 1 |
| **Progressive Disease** | **N** | . | 3 | 3 |
| **Partial Response** | **N** | . | 6 | 6 |
| **Stable Disease** | **N** | . | 10 | 10 |
| **—All–** | **N** | 1 | 20 | 21 |

**5600** **Poster Session**

## Racial and ethnic disparities in quality of diagnostic evaluation for uterine cancer among Medicare patients.

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**Background:** Uterine cancer is the most common gynecologic malignancy. As there is no routine screening for uterine cancer, appropriate evaluation of presenting symptoms is crucial for early diagnosis. We examined racial/ethnic disparities in the quality of diagnostic evaluation received by Medicare patients with uterine cancer. **Methods:** Using the Surveillance, Epidemiology and End Results (SEER)-Medicare database, we identified patients ≥65 years with uterine cancer diagnosed in 2008-2017 who presented with abnormal uterine bleeding (AUB, the most common symptom of uterine cancer). Patients with other cancer or unknown race/ethnicity were excluded. Race/ethnicity was categorized as White, Black, Hispanic, or Other (including American Indian/Alaska Native and Asian/Pacific Islander). Quality of diagnostic evaluation was measured by: 1) not receiving guideline-recommended diagnostic procedures (yes/no), and 2) number of days between AUB presentation and first diagnostic procedure. We compared these measures across racial/ethnic groups using multivariable regressions adjusting for patient sociodemographic characteristics, comorbid conditions, histology, and tumor grade. We further examined racial/ethnic differences in stage at diagnosis before vs. after accounting for these quality indicators. **Results:** The sample included 23,017 patients. Compared to White patients, Black, Hispanic, and Other patients were younger; more likely to reside in a metropolitan area, lack preventive care in the past year, or have comorbidities; and tended to have uterine cancer of non-endometrioid types and higher grade ($p<0.001$ for all). A larger proportion of Black than White patients did not receive guideline-recommended diagnostic procedures (Black: 9.6% vs. White: 5.0%, $p<0.001$; adjusted odds ratio [aOR] = 1.45, 95% CI: 1.20-1.74). Time from AUB presentation to first diagnostic procedure was longer for Black than White patients ($90^{th}$ percentile: 34 vs. 21 days, $p<0.001$; adjusted mean ratio = 1.38, 95% CI: 1.21-1.57). Black patients were more likely than White patients to be diagnosed at regional (aOR = 1.18, 95% CI: 1.04-1.33) or distant stage (aOR = 1.27, 95% CI: 1.06-1.52), rather than localized stage, even after adjusting for other characteristics. Further adjusting for quality of diagnostic evaluation slightly reduced Black-White differences in stage at diagnosis (regional: aOR = 1.16, 95% CI: 1.03-1.32; distant: aOR = 1.23, 95% CI: 1.03-1.48). Hispanic and Other patients also experienced delay in time to first diagnostic procedure, but they did not differ from White patients in receipt of guideline-recommended diagnostic procedures or stage at diagnosis. **Conclusions:** There were racial/ethnic disparities in the quality of diagnostic evaluation received by Medicare patients with uterine cancer, which may partially explain Black-White differences in their stage at diagnosis. Research Sponsor: U.S. National Institutes of Health.

**5601** **Poster Session**

## OATH trial: A phase II clinical trial evaluating the combination of onapristone with anastrozole for women with hormone receptor positive endometrial cancer—Preliminary results.

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**Background:** Endometrial cancer is the most common gynecologic cancer and is primarily treated with chemotherapy. Many endometrial cancers though express hormone receptors and may respond to hormonal therapy, a potentially attractive non-chemotherapy alternative in such a population of women. The aim of OATH is to investigate the potential of dual hormonal blockade through the combination of antiprogesterone and anti-estrogen therapy via the administration of onapristone extended release (ONA) plus anastrozole (ANA), respectively. OATH is an open-label, multicenter, investigator-initiated, non-randomized, phase 2 study to evaluate the safety and efficacy of ONA + ANA in patients (pts) with endometrial cancer (EC). ClinicalTrials.gov Identifier: NCT04719273. **Methods:** Pts received ONA 50 mg twice daily plus ANA 1 mg once daily and were treated until progressive disease (PD) or unacceptable toxicity. Co-primary endpoints were 4-month progression-free survival (PFS) rate and overall response rate (ORR). A sample size of 25 pts will achieve 80% power to detect an improvement in 4-month PFS estimates from 25% (historical) to 52% and an improvement in response rate from 15% (historical) to 37%, using two-sided exact test at 5% significance level. Secondary endpoints include PFS, disease control rate (DCR), and safety. **Results:** As of January 20, 2023, 14 pts were enrolled. Median age was 67 years (44-80). ECOG performance status was 0 (36%), and 1 (64%). Number of prior chemotherapy regimens was 0 (1 pt,7%), 1 (9 pts, 64%) and 2 (4 pts, 29%). Seven (50%) pts received radiotherapy and 3 (21%) pts received prior checkpoint inhibitor therapy. Median treatment duration was 4.2 (1.0-19.9) months, and 8 pts remain on treatment. Adverse events were mainly grade 1 and 2. The most common treatment-related adverse events (AEs) and abnormal laboratory values were hot flashes (36%), alanine transferase (ALT) increased (29%), aspartate aminotransferase (AST) increased (29%), nausea (29%), and diarrhea (21%). No treatment-related serious AE, deaths on treatment, or treatment-related drug discontinuations were reported. The 4-month PFS Kaplan-Meier rate was 63.5%. Among 13 pts who had at least one tumor assessment after baseline, the best overall response was: 1 complete response, 1 partial response (response rate: 15.4%), 9 (69%) stable disease, and 2 (15.4%) progressions. Updated results will be presented. **Conclusions:** Preliminary results of dual hormonal blockade using ONA and ANA in heavily pretreated pts with EC suggest that this combination ONA + ANA has promising activity and is well tolerated. Clinical trial information: NCT04719273. Research Sponsor: Thomas Jefferson University; Context Therapeutics.

**5602** **Poster Session**

## Correlation of cardiovascular disease with racial disparities in endometrial cancer outcomes.

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**Background:** Survival for Black women with endometrial cancer (EC) is shorter than that for non-Hispanic White (NHW) women, with a rate ratio for mortality of 1.98 per the American Cancer Society. Cardiovascular risk factors and disease are also more prevalent in Black women than NHW women. In women with breast cancer, Black patients received less optimal management of comorbidities and experienced increased cardiovascular disease (CVD)-related mortality as compared to White women. Similar to breast cancer, we hypothesize that CVD contributes to EC mortality disparities for Black women. **Methods:** In this retrospective cohort study, SEER and institutional data were utilized to investigate the contribution of CVD to outcomes for Black EC patients. The primary outcome was the contribution of cardiovascular mortality to the overall survival of Black patients. Secondary outcomes included identifying rates of new cardiovascular diagnoses, renal dysfunction, and adequacy of blood pressure control. The SEER cohort was defined using SEER*Stat 8.4.0.1. Uterine cancer patients were identified from the 2020 SEER Research Data. Survival by cause of death and proportion of deaths by cause of death were analyzed. Raw and adjusted hazard ratios for cardiovascular mortality were calculated. Next, institutional data was used to investigate survival, CVD diagnoses, renal dysfunction, and HTN in EC patients. **Results:** The SEER cohort contained 192,465 patients. Of these, 153,878 (80.8%) were White and 19,906 (10.3%) were Black. Black race was associated with decreased survival among patients who died of cardiovascular causes (HR 1.51, 95% CI 1.4 - 1.63, $p < 2*10^{-16}$). When adjusted for age, stage, and histology, the hazard for decreased survival remained elevated for Black patients who died of cardiovascular causes (adjusted HR 1.65, 95% CI 1.52-1.77, $p < 2*10^{-16}$). Our institutional cohort included 1491 patients, 1263 (84.7%) White and 151 (10.0%) Black. Black patients had a relative risk of death of 1.92 (95% CI 1.38 - 2.61) compared with White patients. Among patients with CVD, the hazard for death was 2.02 (95% CI 1.39 - 2.80). Black patients had significantly higher blood pressure, creatinine, and eGFR measurements. **Conclusions:** Racial outcome disparities in EC are multifactorial. CVD management will become increasingly important with the use of targeted therapies including lenvatinib and trastuzumab. Our study highlights an additional area of disparity and suggests possible interventions. Research Sponsor: None.

**5603** **Poster Session**

## Association of the Duffy-null allele and endometrial cancer characteristics: An effort to explore racial disparity in Black women with endometrial cancer.

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**Background:** Efforts are needed to identify factors that account for the disparately high mortality in Black women with endometrial cancer. The Duffy antigen receptor for chemokines (DARC) is expressed on erythrocytes and endothelial cells and modulates levels of inflammatory chemokines in circulation and in tissues. The African ancestry-specific Duffy-null allele, in which erythrocyte expression and function of DARC is lost, is associated with worse breast cancer phenotypes and survival. Here, we characterize Duffy-null status and associated prognostic and clinical outcomes in patients with endometrial cancer. **Methods:** Patients with endometrial cancer were prospectively consented, and germline DNA was extracted from saliva or blood samples. Duffy-null genotype was determined using an allelic discrimination assay. Associations between Duffy-null genotype status and clinicopathologic characteristics were performed using Fisher's Exact analysis. **Results:** 33 patients were enrolled (Table); 17 (51.5%) were Duffy-null, 5 (15.2%) were Duffy-null allele carriers, and 11 (33.3%) were non-carriers. Compared with non-carriers, Duffy-null patients were more likely to be Black (100% v 9.1%, $p<0.0001$) and have non-endometrioid histology (64.7% v 10%, p=0.0173). There was a trend towards higher rates of grade 3 histology (70.6% v 36.6%), intact tumor mismatch repair (MMR) (86.7% v 54.6%), estrogen receptor (ER) negative tumor status (25% v 10%), advanced stage (37.5% v 18.2%), and positive lymph nodes (25% v 0%) (Table). Over a minimum of 12 months of follow up, only Duffy-null individuals died from disease (4 v 0, p=0.0006). **Conclusions:** Duffy-null status was associated Black race, aggressive histologic subtypes, intact MMR mechanisms, and worse survival. Further investigation is needed to explore the underlying mechanism of the Duffy-null phenotype on endometrial cancer outcomes to better elucidate risk factors and underlying causes that may contribute to endometrial cancer disparities. Research Sponsor: U.S. National Institutes of Health.

**Patient characteristics and Duffy-null status.**

| Patient Characteristic, n (%) | Duffy-null homozygous | Duffy-null allele carriers | Non-carriers | p-value |
|---|---|---|---|---|
| **Race** | | | | **<0.0001** |
| **Black** | 17 (100.0) | 3 (60.0) | 1 (9.1) | |
| **Asian** | 0 | 0 | 2 (18.2) | |
| **White** | 0 | 2 (40.0) | 8 (72.7) | |
| **Stage** | | | | 0.1946 |
| **I or II** | 10 (62.5) | 2 (40.0) | 9 (81.8) | |
| **III or IV** | 6 (37.5) | 3 (60.0) | 2 (18.2) | |
| **Grade** | | | | 0.1831 |
| **1** | 3 (17.7) | 1 (20.0) | 2 (18.2) | |
| **2** | 2 (11.8) | 0 | 5 (45.5) | |
| **3** | 12 (70.6) | 4 (80.0) | 4 (36.4) | |
| **Histology** | | | | **0.0173** |
| **Clear** | 2 (11.8) | 1 (20.0) | 1 (10.0) | |
| **Endometrioid** | 6 (35.3) | 3 (60.0) | 9 (90.0) | |
| **Serous** | 9 (52.9) | 1 (20.0) | 0 | |
| **Tumor ER status** | | | | 0.1429 |
| **Positive** | 12 (75.0) | 2 (40.0) | 9 (90.0) | |
| **Negative** | 4 (25.5) | 3 (60.0) | 1 (10.0) | |
| **Tumor MMR status** | | | | 0.0813 |
| **Intact** | 13 (86.7) | 5 (100) | 6 (54.6) | |
| **Deficient** | 2 (13.3) | 0 | 5 (45.5) | |
| **Lymph node status** | | | | 0.2922 |
| **Disease** | 4 (25.0) | 1 (25.0) | 0 | |
| **No disease** | 12 (75.5) | 3 (75.5) | 9 (100.0) | |
| **Clinical status** | | | | **0.0006** |
| **Alive** | 13 (76.5) | 4 (100.0) | 11 (100.0) | |
| **Deceased** | 4 (23.5) | 0 | 0 | |

**5604** **Poster Session**

## The impact of cause of mismatch repair deficiency and other molecular markers on clinical outcomes with the use of durvalumab in advanced endometrial cancer in the phase 2 PHAEDRA trial (ANZGOG1601).

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**Background:** In the single arm phase 2 PHAEDRA trial, MMR deficiency (dMMR) was predictive of response to durvalumab (1500mg IV Q4W), with an objective tumor response rate (OTR; defined by iRECIST) of 47% in dMMR compared with 3% in MMR-proficient (pMMR) advanced endometrial cancer (AEC). This substudy of the PHAEDRA trial investigates MMR molecular subtypes and other genomic tumor features and their correlation with treatment outcomes. **Methods:** Testing was performed to determine molecular subtypes of dMMR, including germline pathogenic variants in DNA MMR genes (Lynch syndrome), somatic biallelic MMR gene inactivation through somatic mutation and somatic hypermethylation of the *MLH1* gene promoter. DNA from formalin-fixed paraffin-embedded tumor tissue and matched peripheral blood was available from 41/71 (25 dMMR, 16 pMMR) participants for testing on a custom capture-based 298-gene targeted panel (2.005Mb) including the MMR genes and key somatic AEC driver genes. The derived tumor genomic features included microsatellite instability (MSI), tumor mutational burden (TMB), COSMIC v.3.2 tumor mutational signatures and insertion/deletion (Indel) somatic mutation count. **Results:** Of the 71 patients recruited, 35 were dMMR and 36 were pMMR. Median follow-up was 44 vs 52 months in dMMR vs pMMR participants, respectively. The dMMR molecular subtypes were 4 (11.4%) Lynch syndrome, 4 (11.4%) somatic MMR mutation, 25 (71.4%) *MLH1* methylated and 2 (5.7%) dMMR-uncategorised. The OTR rate was 100% (4/4; 95%CI 40-100%) for Lynch, 75% (3/4; 95%CI 22-99%) for somatic MMR mutations and 40% (10/25; 95% CI 22-61%) for *MLH1* methylated groups. The median TMB (assessed in 41/71) was higher in those with a confirmed radiological response (37, IQR:26-50) vs non-responders (16, IQR:9-25; $p < 0.001$). Within the *MLH1* methylated group, TMB was also higher in responders vs non-responders (40 *v* 21; $p = 0.03$). Somatic mutations in *KRAS*, *PTEN*, *PIK3CA*, *ARID1A* and *TP53* were not associated with OTR rate. **Conclusions:** dMMR-*MLH1* methylated AEC demonstrated greater heterogeneity in OTR to single agent durvalumab than the dMMR-Lynch and dMMR-somatic MMR mutation molecular subtypes. Higher TMB was seen in responders, and specifically within dMMR-*MLH1* methylated responders, compared to non-responders. Clinical trial information: ANZGOG1601. Research Sponsor: Australia and New Zealand Gynaecological Oncology Group.

**5605** **Poster Session**

## Laparoscopic versus open-surgery in FIGO stage II endometrioid endometrium cancers: Is there a prognostic effect?

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**Background:** Based on two randomized trials (LACE and LAP2) minimal invasive surgery has turned into the surgical standard in early stage endometrial cancer including "high-risk" patients. However, these recommendations are predominately based on "low-risk" cancers, which are mainly represented in both trial collectives. We herein provide a retrospective study, which focuses on potential differences in clinical outcome in early stage endometrioid endometrial cancers with distinct risk constellations treated by laparoscopy or open surgery. **Methods:** 420 early stage endometrial cancers were retrospectively dichotomized according to the surgical approach and correlated to the recurrence rate and clinical outcome. In addition, subgroup analyses were performed according relevant clinical risk parameters, namely FIGO stage, grading and LVSI. **Results:** The analyzed collective consisted of 73.8% stage IA, 19.5% stage IB, and 6.7% stage II cases. Twenty-tree percent of patients exhibit G3 tumors and LVSI was detected in 12.4%. Minimal invasive surgery was performed in 54.5% of study patients. During a median follow-up of 5.0 years, recurrence or death were observed in 8.3% and 6.7%, respectively. Recurrences were predominately located in the vaginal cuff (n = 21; 60.0%), to a minor extent in loco-regional lymph nodes (n = 11; 31.4%), and in three patients (8.6%) in both sides. No distant metastases were detected at first recurrence. Also under consideration of the mentioned clinicopathologic parameters, the surgical approach in FIGO stage I did not influence the recurrence rate and patients' survival. However, in a subgroup analysis of stage II disease, the laparoscopic approach was clearly associated with a significant higher recurrence rate (85.7% vs. 14.3%; p = 0.013). All of the recurrences were located in the vaginal cuff, and in one case, additional relapse was found in loco-regional lymph nodes. Moreover, laparoscopic surgery in stage II disease was associated with impaired progression-free and overall survival (HR 8.86 (1.008 – 20.85) and HR 6.36 (1.102 – 28.61), respectively). **Conclusions:** We herein demonstrate that a minimal invasive surgical approach in stage II endometrial cancer is associated with higher recurrence rates and impaired clinical outcome. These data could be interpreted to be in line with the results of the LACC trial in cervical cancer. Although, grounded on a retrospective analysis, these hypothesis-generating results warrants a confirmatory trial, which is ongoing in a much larger collective of stage II endometrial cancer patients. Research Sponsor: None.

**5606** **Poster Session**

## Impact of best practice advisory on genetic counseling referral patterns for patients with endometrial cancer.

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**Background:** The National Comprehensive Cancer Network (NCCN) recommends that patients with endometrial cancer under age 50 undergo germline genetic testing. Despite this recommendation, completion rates are suboptimal for patients with gynecologic malignancies. The reasons for failure to complete testing are unknown, but oncology providers may not refer patients to genetic counselors, who frequently order this testing. Best practice advisories (BPAs) in electronic medical records can alert providers of patients who meet guideline-based treatments and testing criteria. It is unknown how oncology providers interact with a BPA indicating patients with endometrial cancer meet NCCN germline testing criteria. The objective of this study is to evaluate genetic counseling referral patterns after implementing a BPA. **Methods:** Our team developed a BPA to prompt oncology providers to order genetic counseling referrals for patients diagnosed with endometrial or uterine cancer under age 50. We reviewed all provider-BPA interactions between go-live (January 2022) and January 2023. Patient demographic, histopathologic, and cancer treatment data were collected. Provider actions, including BPA cancellation and order placement, were collected. The Chi-Square goodness of fit test was used to identify differences in referral rates by patient or disease characteristics. **Results:** The BPA displayed 1121 times for 103 patients. Attending physicians received 535 alerts, fellow physicians – 269, and advanced practice providers (APPs) – 317. The median number of alerts per patient was 7 (range 1-87). Of the 103 patients, 23 were excluded from analysis due to no diagnosis of endometrial cancer, patient declined referral, previously completed, or a lack of provider visits within the study period. Of the 80 eligible patients, 36 (45%) received referrals; 18 were placed by attending physicians, 17 by fellows, and one by an APP. Patients under age 40 versus age 40-49 were more likely to be referred (65% vs. 35%; $p = 0.011$). Patients with active disease were more likely to be referred than those in surveillance (65% vs. 18%; $p < 0.001$). There were no differences in referral rates by primary language, race, body mass index $\geq 40$, fertility-sparing versus definitive treatment, stage I versus stage II-IV disease, or grade 1-2 versus three tumors. **Conclusions:** Despite implementing a BPA, only 45% of eligible patients received indicated referrals. Attending and fellow physicians frequently manage patients with active disease and often order referrals; however, APPs frequently manage patients in surveillance and infrequently place referrals, highlighting an opportunity for education. In addition, patients aged 40-49 are less likely to be referred, suggesting a need for new strategies to improve referral rates. Further research is indicated to identify referral barriers for patients undergoing active treatment. Research Sponsor: None.

**5607** **Poster Session**

## Impact of surgical weight loss treatments on care burden among obese endometrial cancer survivors.

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**Background:** Among obesity-related cancers globally, 40% of disability adjusted life years lost are attributed to endometrial cancer (EC). EC patients are more likely to die of obesity-related complications rather than the cancer itself. Metabolic and bariatric surgery (MBS) is an effective weight loss treatment that has been shown to reduce prevalence and severity of many obesity-related chronic conditions. However, there is limited evidence on MBS on EC survivors. We examined the burden of patient healthcare utilization among EC survivors who did and did not undergo MBS. **Methods:** We utilized the SEER-Medicare database to identify 31,437 patients diagnosed with endometrial cancer between 2015 and 2017. We selected 9,229 (29.4%) patients with documented obesity (ICD codes) among whom 75 (0.8%) patients underwent MBS after completing EC treatment (2017-2019). EC survivors with and without a history of MBS were matched on age at EC diagnosis. We examined annualized Medicare inpatient and provider claims payments among EC-MBS (starting 3 months after the surgery, n=66) and EC-no MBS patients (2017-2019) and used Wilcoxon Rank-Sum tests to examine differences in payments in a 1:5 matched sample. **Results:** EC-MBS patients were younger (59.9 years) at the time of cancer diagnosis compared to EC-no MBS patients (68.2 years, $p<0.01$). In an age-matched sample, annualized median inpatient and provider claim payments among EC-MBS patients ($1,824) were lower than that of EC-no MBS patients ($2,920, $p<0.01$). **Conclusions:** Surgical weight loss achieves rapid and effective weight loss and has the potential to lower healthcare utilization among EC survivors but less than 1% of eligible patients receive the surgery. Further research is needed to better understand patient, provider, and access barriers to surgical weigh loss in patients with obesity-related cancers. Research Sponsor: NYS DOH.

| Matched on age | Endometrial Cancer | | |
|---|---|---|---|
| **Demographics** | **MBS Surgery N = 66** | **No MBS Surgery N=330** | **P** |
| **Age at EC Diagnosis** | 59.9 (10.2) | 60.2 (9.3) | .95 |
| **Race** | | | .51 |
| **White** | 59 (89.4) | 274 (83.0) | |
| **Black** | 6 (9.1) | 43 (13.0) | |
| **Other** | 1 (1.5) | 13 (3.9) | |
| **Outcomes** | | | |
| **NCH Claim Provider Payment Amount** | | | <.01 |
| **Mean (SD)** | 2,634.57 (2,960.95) | 4,626.66 (8,332.06) | |
| **Min** | 35.92 | 0 | |
| **Q1** | 735.48 | 1,241.43 | |
| **Median** | 1,824.43 | 2,920.58 | |
| **Q3** | 2,989.84 | 5,289.31 | |
| **Max** | 15,629.97 | 98,045.38 | |
| **NCH Carrier Claim Submitted Charge Amount** | | | <.01 |
| **Mean (SD)** | 13,158.50 (18361.08) | 19,659.33 (26,420.96) | |
| **Min** | 92.00 | 164.68 | |
| **Q1** | 2,700.91 | 5,447.73 | |
| **Median** | 6,776.86 | 12,975.62 | |
| **Q3** | 15,771.21 | 23,664.66 | |
| **Max** | 98,302.92 | 255,705.11 | |

**5608** **Poster Session**

## Efficacy and safety of anlotinib in overall and disease-specific advanced gynecological cancer: A real-world study.

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**Background:** Anlotinib is a novel oral small-molecule multi-target tyrosine kinase inhibitor that has been approved for treating non-small cell lung cancer. However, its efficacy and safety among patients with advanced gynecological cancer. We conducted this study to address this issue in the real-world setting. **Methods:** Data from patients treated with anlotinib for persistent, recurrent or metastatic gynecological cancer including cervical, endometrial, and ovarian cancer were collected from 17 centers from August 2018. The database lock-time was on March 2022. Anlotinib was administered orally on days 1–14 every 3 weeks until disease progression, severe toxicity occurred, or death. The outcomes included objective response rate (ORR), disease control rate (DCR), and progression-free survival (PFS). **Results:** A total of 249 patients were analyzed, with a median follow-up of 14.46 months. The overall ORR and DCR were 28.1% (95% CI 22.6% to 34.1%), and 80.7% (95% CI 75.3% to 85.4%), respectively. Specifically, the ORR varied from 19.7% to 34.4% and the DCR differed from 81.7% to 90.0% in disease-specific advanced gynecological cancer. The median PFS was 6.1 months and ranged from 5.6 to 10.0 months in the overall and disease-specific advanced gynecological cancer, respectively. Larger cumulative dosage of anlotinib (>700 mg) was in general associated with longer PFS in the overall and disease-specific advanced gynecological cancer. The most common adverse event related to anlotinib use was pain/arthralgia (18.3%). **Conclusions:** In conclusion, anlotinib holds promise in treating patients with advanced gynecological cancer, such as cervical, endometrial, and ovarian cancer, with reasonable efficacy and tolerable safety. Research Sponsor: None.

**5609** **Poster Session**

## A multicenter, single-arm, phase 2 study of surufatinib plus toripalimab for patients with advanced endometrial cancer.

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**Background:** Several immunotherapy monotherapies, or combined with antiangiogenic inhibitors, have shown antitumor efficacy in endometrial cancer (EMC) and been approved by FDA. However, therapeutic options for EMC after failure of first-line treatment remain scarce in China. The open-label, multi-cohort, single-arm phase 2 study was performed to evaluate the efficacy and safety of the combination of surufatinib (a small-molecule inhibitor of VEGFR 1-3, FGFR1 and CSF-1R) with toripalimab (an anti-PD-1 antibody) for Chinese patients (pts) with EMC after failure of one or more prior lines of systemic treatment. **Methods:** Pts with EMC who progressed or were intolerable after at least one prior line of systemic antitumor therapy were eligible and enrolled. They received 21-day cycles of surufatinib 250 mg orally, QD, plus toripalimab 240 mg IV, Q3W, until disease progression or reaching the maximum treatment duration with toripalimab of 24 months, or other protocol-specified criteria. The primary endpoint was objective response rate (ORR) per RECIST 1.1. **Results:** From August 2020 to March 2022, 28 pts were enrolled and received the combination treatment (median duration: 4.6 months). Median age was 58 years (range: 50-71), and 22 (78.6%) pts were endometrioid adenocarcinoma at diagnosis. 9 (32.1%) pts had received ≥2 prior lines of therapy. As of 28 Dec 2022, the median follow-up duration was 16.8 months. Microsatellite status was available in 25 pts. 20 with mismatch repair-proficient (pMMR) and 5 with mismatch repair-deficient (dMMR) were determined. All 28 pts were evaluable with at least one post-baseline tumor assessment. Efficacy results were: confirmed ORR, 28.6% (8 partial response [PRs]); DCR, 82.1%; mDoR, 5.7 months; mPFS (95%CI), 5.4 months (2.7, 8.3); 12-month OS rate, 71.0%. Among pts with pMMR, the confirmed ORR was 25.0%; DCR was 85.0%; mDoR was 4.2 months; mPFS (95%CI) was 4.0 months (2.7, 8.3); 12-month OS rate was 75.4%. All pts experienced at least one treatment-emergent adverse event (TEAE), and 19 (67.9%) of them reported grade ≥3 TEAEs. The most common (≥5% pts) grade ≥3 TEAEs were hypertension (28.6%), aspartate aminotransferase increased (14.3%), alanine aminotransferase increased (10.7%), proteinuria (7.1%), Gamma-glutamyltransferase increased (7.1%) and malignant neoplasm progression (7.1%). No new safety signals were observed. **Conclusions:** Surufatinib plus toripalimab had a promising antitumor activity and a manageable safety profile in pts with EMC after failure of one or more prior lines of systemic therapy. Clinical trial information: NCT04169672. Research Sponsor: HUTCHMED Limited.

**5610** **Poster Session**

## TROPiCS-03: A phase 2 basket study of sacituzumab govitecan (SG) in patients (pts) with metastatic solid tumors—Early analysis in pts with advanced/metastatic endometrial cancer (EC).

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**Background:** Pts with advanced/metastatic EC who progressed on or after platinum (PT)-based and anti–PD-(L)1 therapies have a poor prognosis with limited treatment options. SG is a Trop-2–directed antibody-drug conjugate. In the open-label, phase 1/2 IMMU-132-01 basket study, SG monotherapy resulted in a 22% objective response rate (ORR) with a manageable safety profile in 18 pts with metastatic EC who had relapsed after or were refractory to ≥1 prior standard therapeutic regimen (Bardia et al. *Ann Oncol.* 2021). Here, we report early data in pts with advanced/ metastatic disease from the EC cohort of the TROPiCS-03 Ph2 study. **Methods:** TROPiCS-03 (NCT03964727) is a multicohort, open-label, Ph 2 basket study in pts with metastatic solid tumors. Adult pts in the EC cohort progressed after prior PT-based chemotherapy and anti–PD-(L)1 directed therapy [requirement for PD-(L)1 progression added in amendment], had ECOG PS 0-1 and creatinine clearance ≥30 mL/min. Pts received 10 mg/kg of SG on D1 and D8 of a 21-D cycle. The primary endpoint was ORR by investigator's assessment per RECIST 1.1. Secondary endpoints included duration of response (DOR), clinical benefit rate (CBR), and progression-free survival (PFS) per investigator's assessment, overall survival, and safety. The safety population included pts who received ≥1 dose of SG; the efficacy population included pts receiving ≥1 dose of SG and had ≥13 weeks of follow-up. **Results:** As of data extraction on October 11, 2022, 28 pts received ≥1 dose of SG. Median study follow-up was 5.3 mo (range, 0.4-13.1); median age 69 y (range, 44-83), 57% ECOG PS 1,14% microsatellite instability high. Pts received a median of 3 prior therapies (range, 1-6); 100% received prior PT-based chemotherapy, 61% prior immunotherapy, 54% prior targeted agents, and 11% prior hormonal therapy. In 20 pts with ≥13 weeks of follow-up, ORR was 25% (95% CI, 8.7-49.1). Regarding best overall response, all responses were partial response (PR). In addition, stable disease (SD) was 40% and progressive disease was 15%; CBR (confirmed complete response + PR + SD ≥ 6 mo) was 35% (95% CI, 15.4-59.2). Median PFS was 5.6 mo (95% CI, 2.3 mo-not reached [NR]) and median DOR was NR (95% CI, 2.76 mo-NR; n = 5). Treatment was ongoing for 50% of pts. Grade ≥3 treatment-related adverse events (TRAEs) occurred in 64% of pts; most common grade ≥3 TRAEs were neutropenia (25%), febrile neutropenia (14%), and diarrhea (14%). Discontinuation rate due to TRAEs was 7%. While on treatment, two deaths occurred due to causes unrelated to SG. **Conclusions:** Preliminary findings showed encouraging efficacy of SG with a manageable toxicity profile in a pretreated population with advanced/metastatic EC. Safety signals were consistent with the known SG safety profile. This early analysis will be updated with the full dataset. Clinical trial information: NCT03964727. Research Sponsor: Gilead Sciences, Inc.

**5611** **Poster Session**

## Clinical and genomic landscape of *RAS* pathway mutations in gynecologic cancers.

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**Background:** We aimed to describe *RAS* mutations in gynecologic cancers as they relate to clinicopathologic features, subtypes, co-mutations, and implications for therapy. **Methods:** Patients with gynecologic cancers who had next-generation sequencing at our institution between Feb 2010 and Aug 2022 were included. Clinical, histopathologic, and sequencing data were collected and analyzed. Overall survival was estimated using the Kaplan-Meier model. **Results:** Of the 3310 gynecologic cancer patients tested, 522 (15.8%) harbored a *RAS* mutation. For patients with mutation, median age was 56 (18-87) years, with cancer types including ovarian (43.5%), endometrial (43.4%), cervical (9.2%), and vulvovaginal (2.9%). Most patients (92.2%) had recurrence. The most common histology for each cancer included endometrioid in endometrial (60.8%), low grade serous in ovarian (34.4%), adenocarcinoma in cervical (60.4%), and melanoma in vulvovaginal (66.7%). Mucinous and clear cell differentiations were overrepresented (12.5% each). Median overall survival for all *RAS*-mutated patients was 69 months (95%CI 59-82), which was significantly better than in wildtype control of 56 months (95%CI 52-59, p = 0.022). Mutations observed were in *KRAS* (85.8%), *NRAS* (12.8%), and *HRAS* (3.3%). The most common mutant alleles for each were KRAS G12D (34.5%), KRAS G12V (31.7%), NRAS Q61R (34.3%), and HRAS G12S (17.6%). Of note, the incidence of KRAS G12C was 5.6% (0.8% overall). The most common co-mutations for *RAS* were *PIK3CA* (35.7%), *PTEN* (33.3%), *TP53* (32.4%), and *ARID1A* (20.8%). This trend held for each mutation and cancer type. Of these, 64.7% were potentially actionable alterations, including 91.1% of *PIK3CA*, 83.7% of *PTEN,* and 50.0% of *ARID1A*. *RAS* pathway targeted therapies were administered to 62 patients (57 MEK, 5 BRAF, 5 KRAS G12C, 4 SHP2). The median overall survival for these patients was significantly improved (101 months, 95%CI 78-160) compared to *RAS*-mutated patients who did not receive a *RAS* pathway inhibitor (66 months, 95%CI 53-79, HR 0.7, p = 0.031). Of interest, novel KRAS G12C inhibitors showed durable benefit in 3 ovarian (high grade serous, low grade serous, clear cell) and 2 endometrial (mixed endometrioid, clear cell; mixed endometrioid, serous, mucinous) cancers with a clinical benefit rate of 100%, duration of objective response of 22 months, and ongoing responses at 5 and 16 months. **Conclusions:** Gynecologic cancers with *RAS* mutations have distinct histopathologic distribution and portend improved overall survival. The most commonly actionable co-mutations were *PIK3CA, PTEN*, and *ARID1A*, which may aid in combination therapy design. *RAS* pathway targeted therapy is associated with improved overall survival in this cohort and should be considered. Research Sponsor: None.

| *RAS*-pathway Inhibitor | *RAS*-mutated GYN Cancer Patients (n) | Median Overall Survival (months, 95% CI) | HR (95% CI) | p |
|---|---|---|---|---|
| **Received** | 62 | 101 (78-160) | 0.67 (0.47-0.96) | 0.031 |
| **Not received** | 460 | 66 (53-79) | | |

**TPS5612** **Poster Session**

## ARTISTRY-7: A phase 3, multicenter study of nemvaleukin alfa in combination with pembrolizumab versus chemotherapy in patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer (GOG-3063; ENGOT-OV68).

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**Background:** ARTISTRY-7 will evaluate the novel engineered cytokine nemvaleukin alfa (nemvaleukin, ALKS 4230) in patients (pts) with gynecologic cancers. Ovarian cancer (OC) is the 8th most common cause of cancer mortality in women. OC is an area of high unmet need, as many pts become resistant/refractory to frontline platinum-based chemotherapy. In the platinum-resistant setting, standard of care chemotherapy and anti-PD-1 therapy in clinical trials have modest response rates ranging from ~6% to 20% and ~7% to 12%, respectively. Nemvaleukin was designed to selectively bind to the intermediate-affinity interleukin-2 (IL-2) receptor, preferentially activating antitumor $CD8^+$ T and natural killer cells with minimal regulatory T cell expansion. This selectivity may provide enhanced tumor killing and improved safety/tolerability vs high-dose IL-2. In clinical studies, nemvaleukin, as monotherapy and in combination with pembrolizumab, has shown clinical benefit in multiple tumor types, including OC. In ARTISTRY-1, in 14 evaluable patients with OC, 4 responses were observed with nemvaleukin + pembrolizumab, including 2 complete responses and 2 partial responses (ORR 28.6%; DCR 71.4%; median DOR 53.4 wks). Nemvaleukin monotherapy activity was also observed (6 melanoma and 4 renal cell carcinoma responses). **Methods:** ARTISTRY-7 (NCT05092360) is an ongoing phase 3, multicenter, randomized study of nemvaleukin and/or pembrolizumab vs chemotherapy. Eligible pts are women ($\geq$18 y) with histologically confirmed epithelial OC (high-grade serous, endometrioid, clear cell), fallopian tube cancer, or primary peritoneal cancer. Pts must have had $\geq$1 prior line of systemic therapy (platinum-sensitive setting), $\leq$5 prior lines (platinum-resistant setting), and prior bevacizumab, with radiographic progression on most recent therapy. Pts with primary platinum-refractory disease (progression on first-line platinum therapy) or primary platinum resistance (progression $<$3 months after first-line platinum therapy completion) are excluded. Approximately 376 pts will be randomized (3:1:1:3) to receive nemvaleukin 6 $\mu$g/kg IV (days 1-5) + pembrolizumab 200 mg IV (day 1) of each 21-day cycle, pembrolizumab or nemvaleukin monotherapy, or chemotherapy, and stratified by PD-L1 status, histologic subtype, and chemotherapy (paclitaxel vs other). Pts will continue treatment until disease progression or intolerable toxicity (maximum 35 pembrolizumab cycles; nemvaleukin can be continued). The primary endpoint is investigator-assessed PFS (RECIST v1.1) in the nemvaleukin + pembrolizumab vs chemotherapy arms. Secondary/exploratory endpoints include overall survival, other antitumor measures, safety, health-related quality of life, and PK/PD effects. Clinical trial information: NCT05092360. Research Sponsor: Alkermes, Inc.

**TPS5613** **Poster Session**

## UPGRADE-A: Phase 1 expansion trial of the NaPi2b-directed antibody drug conjugate (ADC) upifitamab rilsodotin (UpRi) in combination with carboplatin in patients with high-grade serous ovarian cancer (HGSOC).

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**Background:** UpRi is a first in class NaPi2b ADC with a novel scaffold-linker-payload that is designed to enable high drug-to-antibody ratio and controlled bystander effect. NaPi2b is a sodium-dependent phosphate transporter protein broadly expressed in HGSOC, with limited expression in healthy tissues. Interim data from a previous phase 1b study of heavily pretreated HGSOC patients reported clinical activity and tolerability data for UpRi as a monotherapy, most notably in patients with NaPi2b positive tumors (TPS≥75). Based on these emerging single-agent safety and efficacy data, it is hypothesized that UpRi in combination with carboplatin may provide additional clinical benefit for patients in earlier lines of treatment. UPGRADE-A is a Phase 1 dose escalation (DES) and expansion (EXP) study to evaluate UpRi and carboplatin followed by UpRi maintenance in recurrent platinum-sensitive HGSOC. The DES portion of UPGRADE-A has completed enrollment, and the EXP portion is ongoing. **Methods:** The EXP cohort of UPGRADE-A is enrolling patients with recurrent or metastatic PSOC (defined as having achieved a PR or CR to 4+ cycles in their last platinum containing regimen) who have received 1-3 prior lines of therapy. Up to 1 non-platinum based prior chemotherapy regimen is allowed, provided it is not the most recent line of chemotherapy. The primary objective of EXP is feasibility of UpRi + carboplatin at the RP2D, defined as 60% of patients completing at least 4 cycles of UpRi + carboplatin without discontinuing treatment early for reasons other than disease progression. Secondary objectives include the safety/tolerability, pharmacokinetics, and preliminary anti-neoplastic activity of the UpRi + carboplatin combination. Tumor tissue must be provided (archival or fresh sample) for retrospective NaPi2b assessment. UpRi 30mg/m2 + carboplatin (AUC 5) will be administered IV every 28 days for up to 6 cycles, followed by UpRi maintenance monotherapy until disease progression or unacceptable toxicity. Up to 30 patients are expected to enroll in EXP, and the trial is currently open for enrollment. NCT04907968. Clinical trial information: NCT04907968. Research Sponsor: Mersana Therapeutics.

**TPS5614** **Poster Session**

## UP-NEXT (GOG-3049/ENGOT-Ov71-NSGO-CTU): A study of upitifamab rilsodotin (UpRi), a NaPi2b-directed antibody drug conjugate (ADC), in platinum-sensitive recurrent ovarian cancer.

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**Background:** UpRi is a first-in-class NaPi2b-targeting ADC with a novel scaffold-linker-payload that enables high drug-to-antibody ratio and controlled bystander effect. NaPi2b is a sodium-dependent phosphate transporter protein broadly expressed in high-grade serous ovarian cancer (HGSOC) with limited expression in healthy tissues. It is estimated that the majority of HGSOCs have high NaPi2b expression. Studies are being conducted to evaluate UpRi safety and efficacy in platinum-resistant ovarian cancer (PROC), but there remains an unmet need in the maintenance setting for patients with recurrent platinum-sensitive ovarian cancer (PSOC), particularly for patients who have received prior maintenance therapy, are at high-risk of early relapse, and where close monitoring after platinum-based therapy would generally be considered preferable. **Methods:** UP-NEXT is a Phase 3 study evaluating UpRi monotherapy as post-platinum maintenance treatment in recurrent PSOC, enrolling patients with NaPi2b-positive tumors (defined as TPS $\geq$75). Patients must have received 2-4 prior lines of platinum containing chemotherapy, achieved a partial or complete response in their penultimate platinum regimen, and progressed $>$6 months after completion of the last dose of platinum in the penultimate regimen. Patients may be enrolled if their best response to the last line of treatment is no evidence of disease, complete or partial response, or stable disease. Prior PARPi treatment is required for patients with a BRCA mutation. Patients who received bevacizumab in combination with their most recent platinum containing regimen are excluded. Patients are randomized 2:1 to UpRi 30mg/m2 or placebo, given IV Q4W. The primary endpoint is PFS assessed by BICR, with key secondary endpoint of OS. UP-NEXT is conducted in collaboration with GOG(3049) and ENGOT(Ov71-NSGO-CTU). Approximately 350 patients will be enrolled globally. NCT05329545. Clinical trial information: NCT05329545. Research Sponsor: Mersana Therapeutics.

**TPS5615** **Poster Session**

## A randomized trial of olaparib, durvalumab, and cancer vaccine, UV1, as maintenance therapy in patients with BRCAwt with recurrent ovarian cancer: ENGOT-OV56/NSGO-CTU-DOVACC trial.

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**Background:** Most ovarian cancers (OC) are diagnosed at an advanced stage and despite initial therapy, the disease will often relapse and require further treatment Thus, there is a need for novel therapeutic options. PARP inhibitors lead to increasing tumour neoantigen, and modulation of the tumour microenvironment, which may facilitate a more profound antitumour immune response. UV1 is a therapeutic cancer vaccine directed against telomerase. Since telomerase is an essential enzyme and universally expressed by most tumor cells, it represents a unique cancer antigen as a basis for immunotherapy (IO). The rationale for integrating immunotherapy as maintenance therapy following chemotherapy is based on preclinical studies which have shown that chemotherapy induces immunogenic cell death leading to increased recognition of the tumor by the immune system. The proposed study is evaluating the use of the therapeutic cancer vaccine UV1 in combination with olaparib and the PD-L1 inhibitor, durvalumab as maintenance therapy after response to platinum-based chemotherapy.
**Methods:** The primary objective is to demonstrate efficacy of UV1-olaparib-durvalumab combination maintenance therapy against olaparib in maintenance after platinum combination therapy for BRCAwt patients with relapsed ovarian cancer. Key eligibility criteria include: histologically confirmed, platinim sensitive recurrent OC in response to last platinum-containing chemotherapy, BRCAwt. Patients may be previously treated with PARPi, however prior IO is not permitted. Patients are stratified by HRD status and previous use of PARPi. 184 patients are randomized to three arms (1:1:2): arm A: olaparib single agent, arm B: olaparib-durvalumab and arm C: olaparib, durvalumab-UV1. Duration of therapy: olaparib until progression of disease; durvalumab for 24 months; intradermal UV1, 8 doses within 5 months. Intradermal sargramostim is used as vaccine adjuvant. Primary endpoint is progression-free survival (PFS) of arm C versus arm A. Key secondary endpoints include PFS arm B versus C, patient reported outcomes, and overall survival. This NSGO-CTU sponsored trial is enrolling patients in 11 countries. The following cooperative groups are participating: NSGO-CTU (DK, FIN, NOR, SWE, LTU), BGOG (BE), HeGOG (GRC, CYP), NOGGO (DE), AGO-A (AUT) & DGOG (NL). Clinical trial information: NCT04742075. Research Sponsor: Ultimovacs; Astra Zeneca.

**TPS5616** **Poster Session**

## A phase 1/2 open-label, multicenter, dose escalation and expansion study of AVB-001, an intraperitoneally administered, cell-generated, human IL-2 immunotherapy in patients with platinum-resistant, high-grade, serous adenocarcinoma of the ovary, primary peritoneum, or fallopian tube.

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**Background:** The potential of cytokines as cancer therapeutics has been limited by short half-life and severe adverse effects associated with high systemic exposure when delivered intravenously. Many strategies are being explored to overcome these limitations. A locoregional delivery approach to achieve high sustained local concentrations in the tumor microenvironment with minimal systemic exposure could widen the therapeutic window. Early experience with free recombinant human IL2 (rhIL-2) given intraperitoneally (IP) showed meaningful clinical activity in relapsed ovarian cancer. Still, the cumbersome delivery procedure requiring indwelling catheters and need for high volume IP infusions leading to frequent complications and poor patient compliance limited the utility of this approach. To overcome these shortcomings, we developed a clinically translatable localized delivery LOCOcyte platform composed of polymer encapsulated allogeneic epithelial cells engineered to produce immune effector molecules for local delivery with temporal regulation. The first product, AVB-001, produces native hIL-2, for the treatment of ovarian cancer and other peritoneal malignancies. IP AVB-001 inhibited tumor growth and improved survival in an *in vivo* ID8 ovarian cancer murine model. Sustained IL-2 production with well tolerated high IP concentrations were achieved, with >100x differential concentration vs. systemic blood levels in both mice and non-human primates. Strong local and systemic immune activating effects, optimized T cell profile and immune memory were observed without concomitant increase of T regs. The first in human study of AVB-001 in patients with advanced ovarian cancer (NCT05538624) is described here. **Methods:** Part 1 dose escalation exploring 4 ascending dose levels (capsules target production of 0.6, 1.2, 2.4, and 3.6 ug hIL2/kg/d) with a Bayesian Optimal Interval 3+3 design, in patients with recurrent high grade serous adenocarcinoma of the ovary, primary peritoneum, or fallopian tube. A minimum of 12 and up to 24 patients will be enrolled to receive one dose of AVB-001 administered IP. The primary objective is to evaluate safety (Incidence and severity of adverse events per NCI CTCAE v5.0), tolerability, and feasibility of delivering AVB-001 IP, and establish the RP2D. Secondary objectives include assessment of antitumor activity (RECIST v1.1, iRECIST), pharmacokinetics, and pharmacodynamic correlates of immune activation. Part 2 will enroll 20 patients at the RP2D with efficacy as the primary objective. This multicenter study will be conducted at 5 sites, currently two sites are open. The first patient was dosed in December 2022. Recruitment in dose level 1 cohort continues. Clinical trial information: NCT05538624. Research Sponsor: Avenge Bio.

**TPS5617** **Poster Session**

## CRI-CCTG-0003/IND.240: An immunotherapy platform study in platinum-resistant high grade serous ovarian cancer (IPROC).

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**Background:** Identifying new treatments for patients with platinum-resistant high grade serous ovarian cancer (HGSC) is a priority. Although several biological features of HGSC suggest inherent immunogenicity, immunotherapy has had limited efficacy to date. IPROC is an adaptive platform trial designed to evaluate multiple immunotherapy combinations selected and informed by an expert panel. IPROC accommodates both biomarker-agnostic and biomarker-directed combinations. Protocol and sub study specific translational studies are conducted on archived diagnostic tissue and serial prospective blood and tumor sample collection. **Methods:** IPROC is an open-label, multi center, phase II platform trial. Eligibility includes HGSC histology; progression within 6 months of the last platinum regimen; $<1$ prior line of chemotherapy for platinum resistant disease (unlimited prior lines for platinum sensitive); prior treatment with immunotherapy allowed (provided not discontinued for toxicity), ECOG 0/1. Patients must be willing and able to undergo study procedures. The primary endpoint is ORR (RECIST1.1). Secondary endpoints include iRECIST ORR, RECIST/iRECIST progression free and overall survival and safety. Exploratory objectives include whole exome sequencing and immune profiling of tumor and blood samples to identify biomarkers and new immunotherapy strategies/combinations for future evaluation. Tumor biopsy occurs at baseline, cycle 2 and progression (voluntary) with blood and plasma collected at each cycle and on progression. All sub studies use Simon 2-stage design with 10 patients (pts) enrolled in each stage. At the end of stage 1, in the absence of response, a modified cohort based on biomarker selection may be created through protocol amendment. In each substudy a null hypothesis that the objective response rate (ORR) is $\leq$5% is tested against a one-sided alternative that the ORR is $\geq$ 25%. A combination would be accepted as active if $\geq$4/20 pts respond with $\alpha$=0.02 and power of 0.76. As of January 19, 2023, 2 sub studies are open and 12 patients have accrued. Sub study A is evaluating the combination of durvalumab and BA3011, a conditionally active anti-AXL humanized monoclonal antibody (IgG1) conjugated to monomethyl auristatin E (MMAE) in AXL overexpressing HGSC. Sub study B is evaluating durvalumab plus BA3021, a CAB anti-receptor tyrosine kinase orphan receptor 2 (ROR2) humanized monoclonal antibody (IgG1) conjugated to MMAE in ROR2 overexpressing HGSC. Further sub studies are planned (NCT04918186). Clinical trial information: NCT04918186. Research Sponsor: Cancer Research Institute.

**TPS5618** **Poster Session**

## TEDOVA/GINECO-OV244b/ENGOT-ov58 trial: Neo-epitope based vaccine OSE2101 alone or in combination with pembrolizumab vs best supportive care (BSC) as maintenance in platinum-sensitive recurrent ovarian cancer with disease control after platinum.

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**Background:** Besides PARP inhibitors and bevacizumab, there are no approved maintenance therapies after platinum based chemotherapy for patients with a platinum sensitive relapsed epithelial ovarian cancer (OC). Immune checkpoint inhibitors (ICI) as single agents have limited activity in OC. One attractive strategy is to turn OC from immunogenic "cold" to "hot" tumors via vaccination with tumor-associated antigens (TAAs). OSE2101 is a multiple-neoepitope vaccine restricted to HLA-A*02-positive patients (45% of OC patients) targeting 5 TAAs: TP53, MAGE2, MAGE3, CEA and HER2. These neo-epitopes are modified to increase both major histocompatibility complex and the T cell receptor binding affinity. The proof of concept for this approach was recently demonstrated with OSE2101 improving overall survival in a phase III trial in lung cancer progressing after ICI (Besse *et al.* 2021[1]). The combination of OSE2101 with an ICI may most effectively harness anti-tumor immunity.
**Methods:** TEDOVA is an international randomized open-label, phase II trial evaluating the benefit of maintenance by OSE2101 alone or in combination with PD1 inhibition (pembrolizumab) after platinum based chemotherapy in relapsed OC, previously treated with bevacizumab (if eligible) and a PARP inhibitor (if eligible). Patients (N=180) with CR/PR/SD at the end of chemotherapy are randomized (1:1:2) to: Observation/BSC (Arm A), OSE2101 alone (Arm B), or OSE2101 in combination with pembrolizumab (Arm C). Experimental treatments are continued until progression, or intolerance, for up to 2 years. The primary endpoint is progression-free survival (PFS). Secondary endpoints include overall response rate, safety, time to subsequent first or second treatment (TTST-1, TTST-2) and overall survival. 180 HLA-A*02 positive patients will be randomized. HLA-A*02 negative patients will be followed in a separate observational cohort. The sample size is calculated to provide 90% power to detect an improvement in PFS for Arm C vs Arm A with a HR of 0.57. Three one-sided Log-rank tests will be considered in a pre-defined sequence: H1: C (OSE2101+pembrolizumab) vs A (BSC); H2: C (OSE2101+pembrolizumab) vs B (OSE2101) and H3: B vs A. The type I error will be $\alpha$=5%. The type II error will be $\beta$=10%. Tests will be one-sided. Status: The TEDOVA/GINECO-OV244b/ENGOT-ov58 trial is currently recruiting. Clinical trial information NCT04713514. 1. Besse B, Garcia MR, Cobo MA, Quoix E, Madroszyk A, Felip E, et al. LBA47 - Activity of OSE-2101 in HLA-A2+ non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (IO): Final results of phase III Atalante-1 randomised trial. Annals of Oncology 2021;32(suppl_5) : S1283-S1346. Clinical trial information: NCT04713514. Research Sponsor: OSE Immunotherapeutics; Merck Sharp & Dohme Corp.

**TPS5619** **Poster Session**

## Uncovering mechanisms of response of pembrolizumab and lenvatinib for the treatment of platinum-resistant high grade serous ovarian cancer.

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**Background:** Despite initial response to conventional platinum-containing therapies, the majority of high grade serous ovarian cancer (HGSOC) patients will eventually develop treatment resistance. Despite interest for immune checkpoint inhibitor alternatives, pembrolizumab monotherapy is poor with objective response rates (ORR) ranging between 4.1 - 10%. Poor response may be linked to higher expression of immunosuppressive factors (e.g. VEGF, TGF-β) in the tumor microenvironment (TME). In an immunosuppressive TME, monotherapy with PD-1 inhibitors can induce T-cell dysfunction and apoptosis, leading to innate resistance to pembrolizumab. Preclinical studies of other tumors have demonstrated that lenvatinib can improve T-cell activation and reduce the tumor-associated macrophage population and TGF-β/VEGF/FGF-signaling. In HGSOC, mechanisms of resistance to pembrolizumab and whether this resistance can be overcome by the addition of lenvatinib remain unknown. The objective of this investigation is to uncover the immunologic basis and synergistic mechanisms of action underlying clinical efficacy of pembrolizumab and lenvatinib in HGSOC. Specifically, we will evaluate the dynamic changes in proliferative and dysfunctional T-cell populations in the peritoneal TME (p-TME) of HGSOC patients receiving monotherapy with pembrolizumab or lenvatinib followed by combination therapy. **Methods:** All patients will receive a cycle of monotherapy (pembrolizumab 200 mg IV every 3 weeks or lenvatinib 20 mg po daily) followed by combination therapy (both) up to 35 cycles. Enrolled patients will receive intra-peritoneal port placement for serial peritoneal fluid evaluations (cycle 0 day 1, cycle 0 day 8, cycle 1 day 8, cycle 2 day 1, cycle 3 day 1, cycle 5 day 1, then day 1 of every 3rd cycle) for multichannel flow cytometry and single-cell RNA sequencing. Our primary translational objective is to estimate both the individual and combined effects of pembrolizumab and lenvatinib on T-cell dysfunction (PD1+ CD38+) and proliferation (ki67+) in the p-TME using multichannel flow cytometry on the peritoneal fluid. Secondary clinical objective is ORR. Secondary translational objectives include individual and synergistic effects of monotherapy and combination therapy on T-cell effector function, T-cell memory, and myeloid cell subpopulations. Exploratory objectives include evaluating the dynamic changes in immune and non-immune cells in the p-TME for exceptional responders and non-responders using single cell RNA sequencing. Key eligibility criteria include 1) histologic diagnosis of high grade serous ovarian, peritoneal, or fallopian tube cancer 2) platinum-resistant disease and 3) no prior lenvatinib therapy. The trial is open with 10 patients enrolled at the time of submission. Clinical trial information: NCT05114421. Research Sponsor: Merck.

**TPS5620** **Poster Session**

# First trial of chemotherapy de-escalation in ovarian cancer (OC): A phase III randomized, open label study of niraparib maintenance after carboplatin and paclitaxel in patients with optimally debulked advanced (homologous recombination deficient) HRD high-grade ovarian cancer in first line therapy (N-PLUS/NOGGO-ov53/ENGOT-ov62).

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**Background:** OC is the fifth most common cause of death from cancer in women. More than 70% of the patients are diagnosed with advanced disease and less than 40% of women with OC are cured. Currently, the standard therapy in HRD OC is surgical debulking followed by 6 cycles of chemotherapy with subsequent maintenance treatment with poly ADP ribose polymerase (PARP) inhibitors. Within the last decades, no focus was set on the benefits of fewer cycles of chemotherapy, even though there is evidence for comparable efficacy and less toxicity in comparison to more cycles. Chemotherapies are usually associated with side effects, which can be severe and even lead to therapy discontinuation. The data available about the needed number of chemotherapy cycles is weak, especially in the context of PARP inhibition. Furthermore, patients with stage III/IV with optimal cytoreduction are underrepresented in previous studies. In the N-PLUS trial, we hypothesize that recurrence-free survival (RFS) in patients receiving 3 cycles of chemotherapy followed by maintenance with niraparib is not inferior to 6 cycles of chemotherapy followed by niraparib in advanced HRD high-grade OC patients with no visible disease following primary tumor debulking. **Methods:** In this multicenter, randomized, open-label study 650 patients with advanced HRD high-grade OC with no residual tumor mass following primary tumor debulking will be enrolled. Patients will be randomized 1:1 to receive either 3 cycles carboplatin + paclitaxel and maintenance therapy with niraparib (Arm A) or 6 cycles carboplatin + paclitaxel and maintenance therapy with niraparib (Arm B) for a maximum of 36 months. Randomization will be performed according to the results of the NGS analysis and stratified either to BRCAm/LOH-independent or BRCAwt/LOHhigh, FIGO stage III vs. IV, and participating countries. The primary endpoint will be RFS, secondary endpoints will be OS, TFST, TWIST, PFS2, Quality of Life and safety assessments. Clinical trial information: NCT05460000. Research Sponsor: GSK.

**TPS5621** **Poster Session**

## Oregovomab and non-platinum chemotherapy in PARP inhibitor-resistant ovarian, fallopian tube, or primary peritoneal cancer patients not candidates for platinum retreatment: A multicenter, two-cohort, single-arm phase 2 trial (OPERA/KGOG 3065/APGOT-OV6).

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**Background:** As PAPR inhibitors (PARPis) are becoming the standard of care option for epithelial ovarian cancer (EOC), PARPi-resistant patients are increasing. Moreover, non-platinum single agent chemotherapy in these patients has been found to elicit poor survival outcomes. Oregovomab, an investigational murine monoclonal antibody directed against CA-125, has shown promising efficacy in the previous phase II study of combinational front-line adjuvant chemotherapy. The aim of the present study is to investigate the efficacy of oregovomab + non-platinum-based chemotherapy in PARPi-resistant EOC patients not suitable for platinum-based therapy. **Methods:** OEPRA is a multi-centre, investigator-initiated, two-cohort, single-arm phase II trial recruiting PARPi-resistant EOC patients from five sites in South Korea. The trial includes patients with recurrent EOC who have experienced disease progression despite treatment with PARPis and who have either received bevacizumab or are not eligible for bevacizumab treatment. Mucinous histology type is excluded. Patients who have received one to three prior lines of chemotherapy are to be assigned to Cohort 1 (oregovamab 2 mg [C1,2,3,5,7 for five doses] + pegylated liposomal doxorubicin [PLD] 40 mg/m$^2$ q4w, n = 28), while patients who have received more than three prior lines of chemotherapy are to be assigned to Cohort 2 (oregovamab 2 mg [C1,2,3,5,7 for five doses] + weekly paclitaxel 80 mg/m$^2$ [D1,8,15 q4w], n = 28). A total of 56 patients will be recruited and treated with oregovomab + PLD / weekly paclitaxel until disease progression, unacceptable toxicity, or withdrawal of patient consent. The primary endpoint is objective response rate by RECIST 1.1. Accrual is expected to be completed in 2023, followed by presentation of results in 2024. The study is registered with Clinicaltrials.gov (NCT05407584). Clinical trial information: NCT05407584. Research Sponsor: CANARIABIO Inc.; Yonsei University.

**TPS5622** **Poster Session**

## GLORIOSA: A randomized, open-label, phase 3 study of mirvetuximab soravtansine with bevacizumab vs. bevacizumab as maintenance in platinum-sensitive ovarian, fallopian tube, or primary peritoneal cancer.

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**Background:** Elevated folate receptor-alpha (FR$\alpha$) expression is a characteristic of epithelial ovarian cancer (EOC), thereby providing a rational target for antibody drug conjugate (ADC) development in ovarian cancer. Mirvetuximab soravtansine (MIRV) is an ADC comprising a FR$\alpha$-binding antibody, cleavable linker, and the maytansinoid DM4, a potent tubulin-targeting agent that has received accelerated approval for patients with FR$\alpha$ positive platinum resistant ovarian cancer. MIRV in combination with BEV has demonstrated clinically meaningful activity, along with acceptable tolerability, in patients with FR$\alpha$ expressing ovarian cancer.[1] **Methods:** GLORIOSA is a randomized, open-label, phase 3 study designed to evaluate the efficacy of in combination with bevacizumab compared with bevacizumab alone as maintenance for patients with FR$\alpha$-positive recurrent platinum-sensitive epithelial ovarian, fallopian tube, or peritoneal cancers who have not progressed after second line platinum-based chemotherapy plus bevacizumab (which may be given on protocol for patients with high FR$\alpha$ tumor expression). Confirmation of high FR$\alpha$ positivity by immunohistochemistry using the Ventana FOLR1 CDx Assay (high expression; $\geq$ 75% of viable tumor cells staining at 2+ intensity) and 1 prior line of therapy is required for inclusion. GLORIOSA is designed to randomize 418 patients, 1:1 receiving intravenous MIRV at a dose of 6 mg/kg adjusted ideal body weight plus bevacizumab 15mg/kg every 3 weeks or receiving bevacizumab 15mg/kg every 3 weeks until disease progression or unacceptable toxicity. Radiological assessments will be conducted every 9 weeks ($\pm$ 2 weeks) for 72 weeks, and subsequently every 18 weeks ($\pm$ 3 weeks) until progressive disease (PD), death, the start of new anticancer therapy, or withdrawal of consent from the study (whichever occurs first). The primary efficacy endpoint is progression-free survival by investigator and will also be assessed as a sensitivity analysis. The secondary endpoints include objective response rate, quality of life, overall survival, and safety and tolerability. GLORIOSA is a global study that opened for enrollment in December 2022.
Reference: 1. Gilbert L, Oaknin A, Matulonis UA, et al. Safety and efficacy of mirvetuximab soravtansine, a folate receptor alpha (FR$\alpha$)-targeting antibody-drug conjugate (ADC), in combination with bevacizumab in patients with platinum-resistant ovarian cancer. Gynecol Oncol. 2023; 170: 241–247 Clinical trial information: NCT05445778. Research Sponsor: ImmunoGen, Inc.

**TPS5623** **Poster Session**

## Exactis-03: A phase I trial of the combination of olaparib and navitoclax in women with high grade serous ovarian cancer and triple negative breast cancer.

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**Background:** Identifying new therapeutic options for patients (pts) with high grade serous ovarian cancer (HGSC) and triple negative breast cancer (TNBC) is a priority. For pts with pathogenic variants in *BRCA*, the PARP inhibitor (PARPi) olaparib is used to treat TNBC and as maintenance for HGSC. PARPi can induce a senescence-like phenotype in cancer cells with cell survival dependent on anti-apoptotic proteins. The intrinsic apoptotic pathway is regulated by the Bcl-2 family composed of anti-apoptotic proteins (including Bcl-2, Bcl-xL), pro-apoptotic effectors and the pro-apoptotic BH3-only proteins. Increased expression of Bcl-xL occurs in 88% of HGSC. Olaparib and navitoclax, a Bcl-2/Bcl-xL inhibitor, are synergistic in pre clinical models of HGSC and TNBC. Exactis- 03 investigates targeting, olaparib-induced sensecence as a treatment strategy for pts with HGSC and TNBC. **Methods:** Exactis-03 is a multi-centre phase I trial determining if olaparib can be safely combined with navitoclax in pts with TNBC who have somatic or germline mutations in *BRCA1/2* or *PALB2* and pts with recurrent HGSC who have progressed $\geq$ 6 months since their last platinum based chemotherapy. Additional eligibility criteria include : $\geq$3 prior lines of treatment for TNBC (no limit for HGSC); for pts with HGSC prior PARPi is allowed provided there was no progression on or $\leq$6 months since discontinuation of the PARPi; ECOG PS $\leq$2; ability to absorb study medication and pts must be willing and able to undergo study related procedures. The primary endpoint is identification of the recommended phase II dose (RP2D) of olaparib combined with navitoclax. Olaparib 200mg bid is administered alone for the first 2 weeks. Tumor biopsies will be performed at baseline and on day 7-12 (prior to navitoclax) to evaluate senescence and apoptosis biomarkers and to create 3D organoids and ex vivo microdissected tumor (MDT) models for functional assessment of drug response. Navitoclax is dose escalated with a fixed dose of olaparib in 28-day cycles with 3 pts initially treated at each dose level. If no dose limiting toxicity (DLT) is observed, the dose level will be escalated until $\geq$ 1/3 or $\geq$ 2/6 patients experience DLT. The RP2D will be defined as the dose level below the one where $\geq$ 1/3 or $\geq$ 2/6 patients experience DLT. The 2-week lead-in with olaparib alone and one full cycle of the combination (navitoclax/olaparib) must be completed before dose escalation is permitted. Blood samples are collected for pharmacokinetics and serial evaluation of plasma biomarkers. There is an optional tumor biopsy on progression. Exploratory objectives include determining levels of pro- and anti- apoptotic proteins in biopsy samples and evaluation of cell fate decision biomarkers in biopsy tissue and blood (senescence secretome). Patient-derived organoids and ex vivo MDT will be used to explore drug response and sequencing (NCT05358639). Clinical trial information: NCT05358639. Research Sponsor: Grant from Exactis (Networks of Centres of Excellence (NCE), Canadian Institutes of Health Research (CIHR), Natural Sciences and Engineering Research of Council of Canada (NSERC), Social Sciences and Humanities Research Council via Exactis PMT; Philanthropic Donation; Ovarian Cancer Canada (Federal).

**TPS5624** **Poster Session**

# First-in-human phase 1/2 study of ubamatamab, a MUC16xCD3 bispecific antibody, administered alone or in combination with cemiplimab in patients with recurrent ovarian cancer.

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**Background:** Mucin-16 is a cell surface glycoprotein that is overexpressed in epithelial ovarian cancer (OC). Ubamatamab (REGN4018) is a mucin-16 x cluster of differentiation 3 (MUC16xCD3) bispecific antibody that promotes T cell–mediated cytotoxicity by facilitating contact between cancer cells and T cells. In mouse model studies, ubamatamab demonstrated dose-dependent antitumor activity against MUC16-expressing OC tumor cells.[1] Cemiplimab is an anti–programmed cell death-1 monoclonal antibody. In a Phase 1 study (NCT03564340) in patients with recurrent OC, ubamatamab monotherapy demonstrated an acceptable safety profile, durable clinical activity across a range of doses between 20 mg and 800 mg intravenous (IV) weekly (as measured by RECIST and cancer antigen 125 [CA-125] response rates), and linear pharmacokinetics up to 800 mg IV weekly.[2] These clinical data support further evaluation of a once every 3-week (Q3W) regimen of ubamatamab alone and in combination with cemiplimab. The study is currently recruiting patients to combination dose escalation, monotherapy dose expansion, and the randomized Phase 2 cohort. **Methods:** In Phase 2, up to 150 patients with advanced platinum-resistant OC and elevated serum cancer antigen-125 will be randomized to three arms (1:1:1) to receive ubamatamab 250 mg IV Q3W or 800 mg IV Q3W as monotherapy, or ubamatamab 250 mg IV Q3W in combination with cemiplimab 350 mg Q3W. All arms will include weekly step-up dosing of ubamatamab (1 mg week 1, 20 mg week 2, and full dose weeks 3 and 4) to limit risk of cytokine release syndrome prior to proceeding to Q3W dosing. Expansion cohorts will use a Simon 2-stage study design, with an interim analysis after the first 20 patients. Any arm with $\geq$3 objective responses will be expanded to 50 patients. The primary objective of the dose expansion phase is to assess the preliminary efficacy of ubamatamab as monotherapy or in combination with cemiplimab, separately by cohort. Secondary objectives include characterization of the safety profile by cohort, and the pharmacokinetics of ubamatamab alone or in combination with cemiplimab, as well as patient-reported outcomes for all cohorts. In this dose expansion phase the primary endpoint will be the objective response rate for each arm as defined by RECIST 1.1 criteria. Secondary endpoints include evaluation of duration of response and progression-free survival as well as further evaluation of safety and pharmacokinetics. Exploratory endpoints include evaluation of baseline tumor MUC16 immunohistochemistry expression and other biomarkers as predictors of response. The impact of ubamatamab on quality of life and physical functioning will also be assessed. References: 1. Crawford A et al. Sci Transl Med. 2019;11:eaau7534. 2. Annals of Oncology (2022) 33 (suppl_7): S235-S282. 10.1016/annonc/annonc1054. Clinical trial information: NCT03564340. Research Sponsor: Regeneron Pharmaceuticals, Inc.

**TPS5625** **Poster Session**

## FLORA-5/GOG3035: Chemo-immunotherapy (paclitaxel-carboplatin-oregovomab [PCO] vs chemotherapy (paclitaxel-carboplatin-placebo [PCP]) as front-line treatment in patients with advanced epithelial ovarian cancer (EOC)—Phase III, double blind, placebo controlled, global, multinational study.

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**Background:** Oregovomab, a murine IgGκ1 monoclonal antibody with high affinity binding to tumor associated antigen CA125, renders the target antigen CA125 more immunogenic or "neoantigen-like". The proposed mechanism action is enhanced antigen processing and presentation to specific T cells. This phenomenon is hypothesized to bypass tumor-associated immune suppression when oregovomab is combined with chemotherapy. In a randomized phase II study, oregovomab, in combination with paclitaxel and carboplatin, (PC) induced tumor immunity and demonstrated significant improvement in median PFS (41.8 months(m) PCO vs 12.2 m PC, HR 0.46, p = 0.0027) and median OS (N.E. PCO vs 43.2 m PCP, HR 0.35, p = 0.043) in patients with previously untreated EOC. Patients receiving adjuvant chemotherapy were included. Oregovomab combined with PC had a favorable toxicity profile. FLORA-5/GOG3035, the definitive confirmatory global registration trial, is currently recruiting patients in the front-line setting. **Methods:** In this phase 3, multicenter, double-blind, placebo-controlled trial, optimally debulked patients with FIGO III/IV EOC and serum CA125 $\geq$ 50 U/ml receiving adjuvant (Cohort 1) or patients receiving neoadjuvant chemotherapy post-interval cytoreductive surgery (Cohort 2) will be randomized to PC + oregovomab or placebo (PCO vs. PCP). Patients with germline *BRCA1/2* mutations are excluded. Chemotherapy will be administered every 3 weeks in both cohorts. Oregovomab/placebo is administered simultaneously at cycles 1, 3, and 5 of chemotherapy with an additional dose at 12 weeks following cycle 5 in Cohort 1. Neoadjuvant patients will be administered oregovomab/placebo after debulking surgery at cycles 4 and 6 with two additional doses at 6- and 18-weeks following cycle 6 in Cohort 2. No other front-line maintenance therapy is permitted. The primary objective is PFS determined by RECIST 1.1. Cohort 1 will recruit 372 patients with a 90% power to detect a difference with an alpha of 0.025 and a hazard ratio of 0.65 when 252 PFS events have been observed. Cohort 2 will be analyzed separately recruiting 232 patients with a 90% power to detect a difference with an alpha of 0.025 and a hazard ratio of 0.60 when 165 PFS events have been observed. An interim futility analysis will be performed. Secondary objectives include OS, frequency and severity of AEs, and QoL. Exploratory objectives include iRECIST, TFST, TSST, PFS2, and evaluation of correlative biomarkers. The study is actively enrolling in the US, Canada, Belgium, Italy, Spain, Czech Republic, Hungary, Poland Korea, Taiwan, Mexico Argentina, India and Chile. 518 of the planned 602 patients were enrolled at the time of submission. Clinical trial information: NCT04498117. Research Sponsor: CanariaBio, Inc.

**TPS5626** **Poster Session**

## A phase II, randomized, double-blind study of the use of rucaparib vs placebo maintenance therapy in metastatic and recurrent endometrial cancer.

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**Background:** There are currently no approved maintenance therapies for metastatic and recurrent endometrial cancer, which carries a dismal long-term prognosis. The PARP inhibitor drug class has demonstrated significant clinical benefit as a maintenance therapy for patients with germline/somatic BRCA mutations or homologous recombination deficiency (HRD) in ovarian cancers. However, BRCA mutations are not common in endometrial cancer. Loss of function of the tumor suppressor gene PTEN has been demonstrated in greater than 80% of endometrioid endometrial cancers [1]. PTEN loss of function is well known to lead to activation of the PI3K-AKT-mTOR pathway but has also been shown to lead to defects in homologous recombination (HR) DNA repair of double strand breaks [2]. Specifically, PTEN silencing leads to decreased RAD51 foci formation. Based on this mechanism, in vitro data on endometrial cancer cell lines has demonstrated sensitivity to PARP inhibitors. Notably, sensitivity of PARP inhibition in PTEN loss of function is independent of microsatellite instability (MSI) [3]. **Methods:** This is a multi-center phase II, placebo controlled, double-blinded study of the use of rucaparib as maintenance therapy in patients with metastatic or recurrent endometrial cancer. A maximum of 138 patients will be randomized 1:1 to receive rucaparib at starting dose of 600mg BID dosing vs. placebo. Standard dose reductions of known toxicities will be followed based on FDA approved indications of rucaparib. Patients will remain on therapy until progression of disease or toxicity induced discontinuation. Eligible patients will have Stage III/IV or recurrent endometrial cancer and must have received one or two prior lines of chemotherapy. All histologic subtypes, including carcinosarcoma will be included. Treatment arms will be stratified on histology, number of lines of prior therapy, and complete vs partial response to prior line of therapy. The primary endpoint is progression free survival (PFS). Secondary endpoints include overall survival (OS), overall response rate (ORR), and toxicity. To date, 79 patients have been enrolled. 1. Mutter GL, Lin MC, Fitzgerald JT, et al. Altered PTEN expression as a diagnostic marker for the earliest endometrial precancers. *J Natl Cancer Inst.* 2000;92(11):924-930. 2. Shen WH, Balajee AS, Wang J, et al. Essential role for nuclear PTEN in maintaining chromosomal integrity. *Cell.* 2007;128(1):157-170. 3. Dedes KJ, Wetterskog D, Mendes-Pereira AM, et al. PTEN deficiency in endometrioid endometrial adenocarcinomas predicts sensitivity to PARP inhibitors. *Sci Transl Med.* 2010;2(53):53ra75. Clinical trial information: NCT03617679. Research Sponsor: Clovis Oncology.

**TPS5627** **Poster Session**

## ENGOT-EN20/GOG-3083/xport-EC-042: A phase 3, randomized, placebo-controlled, double-blind, multicenter trial of selinexor in maintenance therapy after systemic therapy for patients with P53 wild-type, advanced or recurrent endometrial carcinoma.

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**Background:** Patients (pts) with first-line metastatic or recurrent endometrial cancer (EC) have a poor prognosis. Selinexor is an oral XPO1 inhibitor, which leads to nuclear accumulation of tumor suppressor proteins, including p53. Selinexor is FDA-approved for use in multiple myeloma and diffuse large B-cell lymphoma, and has shown clinical activity in previously treated, advanced EC. Molecular characterization of EC is critical in directing treatment for advanced and recurrent disease. Of the EC molecular subtypes, *TP53* wild type (wt) tumors represent 50% of advanced and recurrent tumors. A recent phase 3 study in maintenance after chemotherapy found that, despite the primary endpoint (PFS) not reaching statistical significance, prolonged PFS of oral once-weekly selinexor versus placebo (13.7 months and 3.7 months, respectively) was observed in a prespecified exploratory subgroup analysis of patients with advanced or recurrent *TP53*wt EC. **Methods:** XPORT-EC-042 (NCT05611931) is a Phase 3 randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of selinexor as maintenance therapy in pts with *TP53*wt advanced or recurrent EC, who have achieved a partial response or complete response per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 after completing at least 12 weeks of platinum combination chemotherapy $\pm$immunotherapy for primary stage IV or recurrent disease. Eligible pts must be $\geq$18 years of age, have histologically confirmed EC, and *TP53* wt disease based on NGS sequencing assessed by Foundation Medicine. Pts will be randomized 1:1 with either selinexor 60 mg or placebo once weekly in 28-day cycles until progressive disease, toxicity, or 3 years if in complete response. A total of 220 pts will be enrolled at sites across the United States, Canada, Europe, and Israel. The primary objective is to compare PFS in pts treated with selinexor compared to placebo based on RECIST v1.1 criteria as assessed by the Investigator. Key secondary objective is overall survival. Other secondary objectives are safety, time to first subsequent therapy, time to second subsequent therapy, time from randomization until the second progression event (PFS2), and PFS by a blinded independent central review. Patient enrollment is ongoing. Clinical trial information: NCT05611931. Research Sponsor: Karyopharm Therapeutics.

**TPS5628** **Poster Session**

## A phase 2, two-stage study of avelumab and axitinib in patients with mismatch repair–proficient (MMR-P) recurrent or persistent endometrial cancer (EC).

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**Background:** Despite significant strides in understanding the molecular pathogenesis of EC, there remain few effective therapies for recurrent disease. Deeper insight into the roles of disordered tumor vasculature and HIF1$\alpha$- and VEGF-mediated immunosuppressive effects on myeloid-derived suppressor cells, T-cells, and PD-L1 expression contributed to the development of new targeted regimens. By inhibiting VEGF receptor (VEGFR) and PD-L1 signaling, immunologically "cold" tumors may become inflamed. The combination of the anti-PD-L1 antibody avelumab with axitinib, an inhibitor of VEGFR 1-3 and PDGFR with more potent $IC_{50}$ inhibitory activity than lenvatinib, has also shown synergistic activity and is FDA approved as first line treatment for patients with renal cell cancer. We therefore hypothesized that this combination would be well tolerated and efficacious in recurrent MMR-P EC. Objectives:This is a non-randomized two-stage phase 2 study in patients with MMR-P EC evaluating the activity of combined avelumab and axitinib, as assessed by the co-primary endpoints of (1) frequency of patients surviving progression-free for at least 6 months (PFS6), and (2) the objective response rate (ORR) as measured by RECIST 1.1. **Methods:** Patients must have MMR-P EC and have received at least one chemotherapeutic regimen, with no upper limit on the number of prior lines received. Prior use of immune checkpoint inhibitors (ICI) is excluded. Eligible patients received avelumab 800 mg IV every 2 weeks and axitinib 5 mg orally twice daily until disease progression or unacceptable toxicity. In the first stage of the study, 16 patients were enrolled; if there were $\geq$2 objective responses or $\geq$2 PFS6 responses, accrual continued to the second stage with enrollment of an additional 19 patients. The combination of avelumab/axitinib would be considered worthy of further study if overall there were $\geq$4 objective responses or $\geq$8 PFS6 responses. **Results:** As of the data-cutoff in September 2022, a total of 28 patients had received study treatment; one patient withdrew from the study due to toxicity, prior to her first radiographic assessment. The median number of prior lines was 1 (range 1-4). Median follow-up was 12.7 months. Of the 28 patients receiving study treatment, eleven patients (39.3%, 95% CI 21.5%-59.4%) achieved a PR [11/28; 8 confirmed PR (28.6%) and 3 unconfirmed PR (10.7%)]. An additional 39.3% (11/28) had stable disease as best response. Median PFS was 7.3 months (95% CI 3.9-9.0). PFS6 was 59.3% (95% CI 35.7%-76.7%) and at 6 months, 10 patients were still alive and progression-free. Updated efficacy data and safety data will be reported at the time of the meeting. **Conclusions:** With 8 confirmed PRs and 10 PFS6 responses, the co-primary endpoints were met and the combination of avelumab/axitinib is considered worthy of further study in this population of MMR-P EC. Clinical trial information: NCT02912572. Research Sponsor: Pfizer.

**TPS5629** **Poster Session**

# A randomized phase II study comparing single-agent olaparib, single-agent cediranib, and the combinations of cediranib/olaparib, olaparib/durvalumab (MEDI4736), cediranib/durvalumab (MEDI4736), and olaparib/AZD5363 (capivasertib) in women with recurrent, persistent, or metastatic endometrial cancer.

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**Background:** Identifying new approaches for the treatment of advanced endometrial cancer (EC) is a priority. A platform study design allows for a faster investigation of novel drug combinations. NRG-GY012 is an ongoing platform study investigating drug combinations with the PARP inhibitor olaparib (O) and the anti-angiogenic agent cediranib (C). Results from the first set of arms established improved PFS for combination cediranib/olaparib over C alone, but did not meet its prespecified statistical significance. In this second set of arms, based on preclinical data, we are investigating the combination of O with an AKT inhibitor (capivasertib), O with durvalumab and C with durvalumab compared to the reference arm of C alone. **Methods:** This is a multicenter randomized four arm study for patients with recurrent, metastatic or persistent EC. Patients are randomized 1:1:1:1 to cediranib PO 30 mg Daily; olaparib 300 mg PO BID and capivasertib 400mg 4 day on/3 off schedule; olaparib 300 mg PO BID and durvalumab 1500mg q28 days; or the combination of cediranib 20 mg PO Daily 5 days on/2 days and durvalumab 1500mg q28. All treatment cycles are 28 days. Primary endpoint is progression free survival (PFS). The study is powered to detect a doubling in median PFS from 3.6 (based on cediranib alone) to 7.2 months with 90% power, using a one-sided test with $\alpha = 0.05$ per comparison. Forty patients will be enrolled per arm, with an interim futility analysis planned at 50% information time. Eligibility includes endometroid, serous, and mixed histology EC; at least 1 prior line of chemotherapy (no more than 2 lines for metastatic disease), prior endocrine or immunotherapy alone is allowed; prior treatment with lenvatinib and pembrolizumab is excluded. Archival tumor tissue and blood samples are being collected for translational studies. The study is open across the NRG network; 76 of a planned 168 patients are enrolled to date. Safety analysis at the time of 36 patients enrolled did not demonstrate any new safety signals and the study was approved to continue enrollment. Clinical trial information: NCT03660826. Research Sponsor: U.S. National Institutes of Health.

**TPS5630** **Poster Session**

## Randomized phase III trial in MMR deficient (MMRd) endometrial cancer (EC) patients comparing chemotherapy (CT) alone versus dostarlimab in first line advanced/metastatic setting: DOMENICA study (GINECO-EN105b/ENGOT-en13 study).

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**Background:** The standard treatment for advanced EC is still platinum-based combination CT, regardless of the histology, molecular status and the patient's profile. However, EC patients are a particularly frail group of patients, often with co-morbidities. Tolerance of CT can be difficult and induce long-term toxicities. In advanced EC disease, MMRd/MSI-H tumors represent 15 to 20 % of cases. Preclinical data suggest that these tumors are more resistant to platinum. On the other hand, anti-PD1 immunotherapy has shown impressive results among MMRd/MSI-H EC patients after platinum-based CT. The aim of this study is to de-escalade the first line advanced/metastatic treatment of patients with MMRd/MSI-H endometrial cancer with the objective to avoid carboplatin-paclitaxel related toxicities by substituting CT with the PD1 inhibitor dostarlimab. **Methods:** DOMENICA is an ongoing international randomized, open-label, phase III trial. 142 patients with MMRd/MSI-H EC Stage III or Stage IV or first recurrent disease without curative treatment (surgery, radiation therapy, +/- adjuvant CT) will be randomized (1:1) to receive either 4 cycles of dostarlimab 500mg every 3 weeks followed by dostarlimab 1000mg every 6 weeks as maintenance up to 2 years or 6 cycles of carboplatin-paclitaxel. A cross over is allowed from the CT arm to the dostarlimab arm at first progression. The maximum treatment duration with dostarlimab will be 24 months. Stratification factors are prior adjuvant CT, prior pelvic radiotherapy. The primary endpoint is the progression-free survival (PFS). Secondary endpoints include overall survival (OS), PFS2, quality of life, best objective response rate, disease control rate, duration of response rate, safety, tolerability, time to first and second subsequent therapy, efficacy of second systemic therapies, pharmacokinetics description and immunogenicity determination. The study is designed to expect a 17.8-months PFS in dostarlimab arm and a 10-months PFS in the CT arm, translating to a hazard ratio of 0.58. A protocol amendment is submitted to increase patient population (with extended eligibility criteria, PFS hypothesis). Status: The DOMENICA/GINECO-EN105b/ENGOT-en13 trial is currently recruiting, the first patient was randomized in April 2022. Clinical trial information: NCT05201547. Research Sponsor: GlaxoSmithKline.

**TPS5631** **Poster Session**

## RT-PACE: Phase I/II study of adjuvant whole pelvic hypofractionated radiotherapy for non-metastatic cervical and endometrial cancer.

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**Background:** Whole pelvic radiation therapy (WPRT) improves locoregional control in women with high-intermediate and high-risk endometrial cancer. The standard treatment course consists of 25-28 fractions (5-5.5 weeks) of 1.8-2 Gy/fraction, and is delivered using intensity-modulated radiation therapy (IMRT), which allows for superior sparing of normal tissue with a subsequent lower rate of acute and late toxicity compared to less conformal treatment techniques. Moderate hypofractionation (HF, $>$2 Gy/fraction) has been studied in other disease sites, such as breast and prostate cancer, and is associated with lower or comparable toxicity, improved patient convenience, and greater cost savings compared to standard fractionation. However, HF has not been well-studied in the setting of WPRT for gynecologic cancers. **Methods:** This phase I/II multi-institutional study evaluates the feasibility, safety, and toxicity profile of HF-WPRT in women with non-metastatic cervical or endometrial cancers who have undergone curative hysterectomy and are recommended adjuvant WPRT by their treating physician. Concurrent chemotherapy is not allowed, but can be administered sequentially prior to or after WPRT. Para-aortic radiation or nodal boosts are not allowed, however vaginal brachytherapy boost is permissible. Phase I is a safety study of increasing dose-per-fraction. All treatment regimens have an approximate biologic effective dose of 53 Gy ($\alpha/\beta = 10$). A keyboard design is utilized to identify the maximum tolerated dose-per-fraction (MTD), defined in this study as the regimen that is associated with a CTCAE grade 3+ gastrointestinal/genitourinary toxicity rate of $\leq$10% on the last day of WPRT. There are 3 dose cohorts of increasing dose-per-fraction. Phase II will accrue 64 evaluable patients to HF-WPRT using the MTD determined in phase I. The primary endpoint is to evaluate the change in patient-reported gastrointestinal toxicity from baseline to the last day of WPRT using the EPIC bowel score. The study is powered to compare results to the RTOG 1203 IMRT standard fractionation arm. The phase 1 portion of the study completed accrual; the phase II portion opened in April 2022 with a fractionation of 42.56 Gy in 16 fractions. Secondary endpoints include genitourinary toxicity (EPIC, CTCAE), quality of life (FACT-Cx, PRO-CTCAE), financial toxicity (FACIT-COST), and decision-making (Decision Regret Scale). Pelvic control at 2 years is an exploratory endpoint. Clinical trial information: NCT04683653. Research Sponsor: University of Chicago Comprehensive Cancer Center.

**TPS5632** **Poster Session**

## CCTG EN10: A phase II study of tailored adjuvant therapy in *POLE*-mutated and p53-wildtype/NSMP early-stage endometrial cancer (EC)—RAINBO BLUE and TAPER.

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**Background:** Molecular classification of EC provides an opportunity to personalize treatment for patients with early disease based on prognosis. We hypothesize that de-escalated adjuvant treatment in patients with early-stage *POLE*-mutated (*POLE*mut) or p53wt/NSMP (p53 wildtype/no specific molecular profile) EC is feasible and associated with favourable disease control, QOL and health economics. **Methods:** EN.10 is a Canadian Cancer Trials Group led phase II trial that enrolls two independent cohorts of patients with early stage EC based on tumour molecular status: *POLE*mut (substudy A) and p53wt/NSMP (substudy B). The primary objective is to estimate the 3-year rate of pelvic recurrence. Secondary objectives include estimated 3-year isolated vaginal recurrence, para-aortic recurrence, distant metastasis, survival (recurrence-free, EC-specific, overall survival) and to describe the patient decisional conflict and fear of recurrence. Tertiary objectives: QOL, economic evaluation and interrogation/discovery of additional prognostic biomarkers. Statistical Design: Registration to Substudy A or B is based on molecular classification. Treatment will be deescalated in both substudies; to surveillance-only (all early stage *POLE*mut, and a proportion of NSMP), or vaginal brachytherapy (proportion of NSMP), with NSMP stratification based on histological grade, and lymphovascular invasion. Substudy A can enroll endometrioid, serous, clear cell, un/dedifferentiated and carcinosarcomas whereas Substudy B is confined to endometrioid histotype. Both arms require ECOG 0-2 and hysterectomy+BSO with nodal assessment required for stage II and grade 3 EC. A total of 120 patients with *POLE*mut (Sub-study A) and 180 with p53wt/NSMP ER+ (Sub-study B) EC will be recruited in 3 years. If the upper 95% confidence limit is less than 5% in either of Substudy A, Cohort A1 and Substudy B or both, it will be concluded that patients in one or both groups have an acceptable low risk of pelvic recurrence at 3 years with molecularly-tailored de-escalated adjuvant treatment An additional estimated 25 patients with higher risk *POLE*mut EC will be enrolled for an exploratory analysis. Conduct to Date: Study activation Dec 19 2022. Enrollment January 31, 2023: 36 Supported by Canadian Cancer Society, Canadian Institutes of Health Research, Gynecologic Cancer Initiative, BC Cancer Foundation. Clinical trial information: NCT05640999. Research Sponsor: Canadian Cancer Society, Canadian Institutes of Health Research, Gynecologic Cancer Initiative, BC Cancer Foundation.

**TPS5633** **Poster Session**

# The RAINBO MMRd-GREEN trial (GCIG/DGOG/ENGOT-EN14$^2$): A phase III trial on the addition of adjuvant durvalumab to radiotherapy in patients with high-risk MMRd endometrial cancer.

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**Background:** The molecular class of endometrial cancer (EC) is both prognostic and predictive in high-risk EC (HREC). The TransPORTEC research consortium showed that patients with MMRd HREC did not benefit from adjuvant chemotherapy added to radiotherapy. MMRd tumors are particularly sensitive to immunotherapy. We hypothesize that adjuvant durvalumab added to standard radiotherapy will increase recurrence-free survival (RFS) in patients with MMRd HREC. **Methods:** MMRd-GREEN is an international, open-label, randomized phase III trial and part of the RAINBO program (NCT05255653). Eligible patients will be allocated (1:1) to adjuvant durvalumab 1500 mg once every 4 weeks for 1 year combined with radiotherapy or standard radiotherapy alone. The primary endpoint is RFS at 3 years. Secondary endpoints are pelvic, vaginal and distant RFS, EC-specific survival, overall survival, treatment-related toxicity, health-related quality of life and exploratory translational research. Main inclusion criteria include histologically confirmed stage IB/II with (substantial) lymph-vascular space invasion (LVSI) or stage IIIA-C MMRd EC, after hysterectomy and bilateral salpingo-oophorectomy (regardless of lymphadenectomy or sentinel lymph node biopsy) without macroscopic residual disease. Molecular classification must be performed according to the WHO 2020 algorithm. The target accrual is 316 patients, accounting for a total drop-out rate of 12%. This sample size yields 80% power to detect a 13% increase in the 3-year RFS (hazard ratio 0.58) as a result of the addition of durvalumab, with an accrual duration of 48 months and follow-up period of 30 months. No interim analysis is planned; an independent data monitoring committee will routinely monitor recurrences and adverse events. Enrollment: Since August 2022, the trial is open for recruitment in the Netherlands and per February 10$^{th}$ 2023, the first 3 patients have been enrolled. Activation of more international centers is ongoing. Clinical trial information: NCT05255653. Research Sponsor: KWF Dutch Cancer Society; AstraZeneca.

**TPS5634** **Poster Session**

## AFT-50 EndoMAP: A phase IB/II multi-cohort study of targeted agents for patients with recurrent or persistent endometrial cancer.

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**Background:** The prognosis for women with recurrent or persistent EC after progressing on first-line chemotherapy is poor, with a median overall survival (OS) of 12 months, highlighting the need for more efficacious therapies for this population. Immune checkpoint inhibitors either as monotherapy or when combined with kinase inhibitors have recently demonstrated encouraging response rates in pts with microsatellite instability-high (MSI-H)/mismatch repair-deficient (dMMR) and MS-stable (MSS)/MMR-proficient (MMRp) EC, respectively. Atezo is a humanized monoclonal anti-programmed cell death ligand 1 (PD-L1) inhibitor that has demonstrated monotherapy antitumor activity with an acceptable safety profile in relapsed recurrent EC. Atezo has shown compelling clinical efficacy for pts with certain solid tumors (e.g., urothelial, NSCLC, triple negative breast cancer) as monotherapy and as part of combinatorial therapy. The AFT-50 EndoMAP trial is a platform trial designed to evaluate the efficacy and safety of Atezo in combination with biomarker-defined targeted agents in pts with recurrent or persistent EC. Recognizing pts may have either progressed through or received a checkpoint inhibitor in a prior line of therapy, a non atezo cohort will also be open to enrollment. **Methods:** This is a phase IB/II non-randomized, multicenter, multicohort, biomarker-driven platform study consisting of two cohorts: A (atezo containing) and B (non atezo). Eligible pts have recurrent or persistent EC and have received no more than 2 prior lines of therapy. FoundationOne CDx (F1CDx) NGS assay will be used for genomic tumor profiling. In cohort A, pts may be eligible for one of the following doublets: Atezo+ipatasertib (PIK3CA/PTEN/AKT1-altered cancers), Atezo+talazoparib (tumors with genomic loss of heterozygosity (LOH) $\geq$16%), Atezo+Trastuzumab emtansine (ERBB2/HER2 mutated and/or amplified tumors), Atezo+Tiragolumab (MSI-H and/or TMB$>$10 mut/MB), and Atezo+bevacizumab (biomarker unmatched). Pts will receive Atezo in addition to the targeted agent (at the study approved dosing schedule) until progression, unacceptable toxicity, pt or physician decision to withdraw from the study, death, or study termination. Pts in cohort B, will be eligible for inavolisib (PIK3CA/PTEN/AKT1-altered cancers) + letrozole. Each cohort will enroll ~20 pts; however, the exact size of the cohort may be adjusted. The primary endpoint for Cohort A is confirmed overall response rate (ORR) for each cohort, and for Cohort B is progression free survival at 6 months. Secondary endpoints include disease control rate, duration of response, OS, safety and tolerability, 6-month PFS (cohort A). As a platform study, additional arms may be added, as supported by evolving understanding of EC and molecular targets. EndoMAP is actively enrolling at 17 sites in the US with a target of 25 sites nationwide. Clinical trial information: NCT04486352. Research Sponsor: Genentech; Alliance Foundation.

**TPS5635** **Poster Session**

## GCIG SB-001/NSGO-CTU-PEACE/ANZGOG 1923/2020: Palliation in gynae-oncology—Patients' expectations and assessment of care.

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**Background:** Patients with advanced gynaecological cancers who are approaching end of life (EOL) have a high symptom burden and following several prior lines of therapy, a low likelihood of response to further anti-cancer treatment. Despite this, 20-30% of women with gynecological cancer received chemotherapy in the last 30 days of life, with potentially detrimental effects on health and quality of life. Little is known about patients' and carers' perceptions and preferences in this phase of illness. Eliciting patient's values and preferences for EOL care and shared decision-making are central elements of GCIG SB-001/NSGO-CTU-PEACE with the aim of improving patient-centered EOL care. The primary aim of PEACE is to assess the feasibility of collecting data on patient satisfaction towards EOL. Secondary aims include collecting data on patient and carer satisfaction with care, as well as prospective collection of details of their care. **Methods:** PEACE will prospectively enroll patients in Norway and Australia. Key eligibility criteria include: Patients with gynaecological cancer at an advanced stage with a predicted life expectancy of approximately 4 months. Patients may be on anti-cancer treatment or may be under observation/palliative care. In addition, the patient must be able (both physically and cognitively) to complete patient-reported outcome measures independently. The study will also include an appointed carer (not mandatory). Patient and carer satisfaction with care and the importance of domains of care will be assessed with the CANHELP-Lite individualized (Canadian Health Care Evaluation Project) instrument and FACIT (Functional Assessment of Chronic Illness Therapy). Carer's perception of the bereavement period and the quality of the patient's death will be assessed with the CANHELP lite bereavement and the Quality of Death and Dying questionnaire. The study will prospectively collect data on EOL treatment. Patient and carer satisfaction with care and quality of the dying process will be summarized by standard descriptive statistical measures. A sample size of 65 patients would have at least 80% power with 95% confidence to rule out a 60% completion rate in favour of the more interesting 75% rate. Assuming a 10% drop-out rate, PEACE will enrol 73 patients. Enrolment commenced in December 2022. ClinicalTrials.gov Identifier: NCT05142150 Clinical trial information: NCT05142150. Research Sponsor: Radiumhospitalets Legater; Private Practice Fund, Canberra Hospital.