Society of Gynecologic Oncology 2020 Annual Meeting on Women's Cancer
Abstracts for Oral Presentation

Scientific Plenary I: Shaping the Future with Innovative Clinical Trials: A Clearer Vision Ahead in Gynecologic Cancer

1 - Scientific Plenary
Sentinel lymph node biopsy versus lymphadenectomy for high-grade endometrial cancer staging (SENTOR trial): A prospective multicenter cohort study

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Objective: It is unclear whether sentinel lymph node biopsy (SLNB) can replace complete lymphadenectomy in women with high-grade endometrial cancer (EC). We performed a prospective multicenter cohort study (the SENTOR trial) to evaluate the performance characteristics of SLNB using indocyanine green (ICG) in stage I high-grade EC (ClinicalTrials.gov ID: NCT01886066).

Method: Patients with clinical stage I grade 2 endometrioid or high-grade EC (grade 3 endometrioid, serous, clear cell, carcinosarcoma, undifferentiated, or mixed tumors) undergoing laparoscopic or robotic surgery at 3 cancer centers in Toronto, Canada, were prospectively recruited for SLNB with ICG. After SLNB, high-grade EC patients underwent pelvic and paraaortic lymphadenectomy (PLND/PALND), and grade 2 endometrioid EC patients underwent PLND only. All SLNs were submitted for standardized ultrastaging. The study was powered using a Fleming 2-stage design to accurately determine patient-specific sensitivity of the SLNB algorithm as the primary outcome; secondary outcomes were the negative predictive value (NPV), false negative rate (FNR), and bilateral detection rate.

Results: We accrued 156 patients (high-grade EC, *n* = 126) with mean age 64 years (range 40–86 years) and BMI 28 (range 18–47). All patients had SLNB and PLND, and 106/126 patients (84%) with high-grade EC had PALND. Median numbers of SLNs, PLNs, and PALNs removed per patient were 3 (IQR 2–5), 16 (IQR 12–20), and 6 (IQR 4–10), respectively. SLN detection rates were 99% per patient (95% CI 95–100), 88% per hemipelvis (95% CI 83–91), and 77% bilaterally (95% CI 70–83). Of 26 patients (17%) with nodal metastases, 25 were identified by the SLNB algorithm, for a patient-specific sensitivity of 96% (95% CI 80–100), FNR of 3.9% (95% CI 0–19), and NPV of 99% (95% CI 96–100). Only one patient (0.6%) would have been misclassified by the SLNB algorithm.

Conclusion: SLNB has excellent performance characteristics and the potential to replace lymphadenectomy in high-grade EC patients with an increased risk of lymph node metastases. Randomized trials comparing oncologic outcomes and morbidity between SLNB alone and complete lymphadenectomy are needed.

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2 - Scientific Plenary
Validation of sentinel lymph biopsy in patients with early stage vulvar cancer: A prospective trial of 1552 women (GROINSS-V II/GOG270)

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Objective: The sentinel lymph node (SLN) procedure in vulvar cancer has become standard of care since our first GROINSS-V study reported a groin recurrence rate of 2.3%. In GROINSS-V II/GOG270, a study that investigated the safety of radiotherapy in patients with metastases in their SLN, all SLN-negative patients were registered in order to confirm our previous findings. Here we present the analysis of the patients with a negative SLN.

Method: A prospective observational trial was performed in patients with early-stage squamous cell carcinoma of the vulva (diameter <4 cm), without suspicious lymph nodes at palpation or imaging, and planned for surgery (radical local excision in combination with an SLN procedure). In case of a metastatic SLN (metastasis of any size), radiotherapy was given to the

groin(s) to a total dose of 50 Gy. In case of a negative SLN, patients were followed up for 2 years. Stopping rules were formulated in order to monitor the groin recurrence rate.

Results: From December 2005 until October 2016, 1,708 patients were included in GROINSS-V II/GOG270. After exclusion of 156 ineligible patients, 1,552 patients were available for analysis. The SLN was negative in 1,222 patients (78.7%). During follow-up, 144/1,222 (11.8%) patients were diagnosed with local recurrence, of whom 16/144 (11%) also had groin metastasis. Isolated groin recurrences were diagnosed in 38/1,222 patients (3.1%). In 6/38 patients, clear protocol violations were observed: incomplete treatment of groin (*n* = 3); primary tumor >4 cm (*n* = 1); not all SNs visualized on the lymphoscintigram were removed (*n* = 2). Prognostic factors related to groin recurrences will be presented.

Conclusion: In the largest prospective series of SLN-negative vulvar cancer patients ever reported, the safety of omitting inguinofemoral lymphadenectomy after a negative SLN could be confirmed with a groin recurrence rate of 3.1% (after exclusion of the protocol violations 2.7%), comparable to the data of our first GROINSS-V study.

LBA 3 - Scientific Plenary

Radiotherapy as an alternative treatment for inguinofemoral lymphadenectomy in vulvar cancer patients with a metastatic sentinel node: Results of GROINSS-V II.

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Objective: In order to reduce treatment-related morbidity, the GROINSS-V II trial investigated whether radiotherapy is a safe alternative for inguinofemoral lymphadenectomy (IFL) in vulvar cancer patients with a metastatic sentinel node.

Method: GROINSS-V II was a prospective multicenter phase II trial, including patients with early-stage squamous cell carcinoma of the vulva (diameter <4 cm) without suspicious lymph nodes at imaging, who had primary surgical treatment with sentinel node procedure. In case of a metastatic sentinel node (metastasis of any size), radiotherapy was given to the groin (50 Gy). Stopping rules were defined to monitor groin recurrence rate.

Results: From December 2005 until October 2016, 1,708 patients were registered. Overall 1,552 patients were eligible, of whom 324 (21%) had a metastatic sentinel node. After 54 months of inclusion, the stopping rule was activated; interim analysis showed an increased risk for groin recurrence in case of sentinel node metastasis >2 mm and/or with extranodal extension (ENE). The protocol was amended, with patients only with micrometastasis ≤2 mm receiving radiotherapy from then on, and those >2 mm undergoing IFL (with radiotherapy if >1 metastasis or ENE). Final analysis after ≥2 years revealed 6 isolated groin recurrences in 157 patients with a sentinel node micrometastasis (3.2%). Four could not be considered radiotherapy failures: 2 developed recurrence in the contralateral (sentinel node-negative) groin; 2 refused radiotherapy. Twenty-eight patients did not undergo radiotherapy. Among 129 patients who received radiotherapy to the groin, 2 isolated groin recurrences were diagnosed (1.6%). Radiotherapy to the groin after sentinel node procedure showed only minimal toxicity: 5/118(4.2%) had grade 3 toxicity, while no grade 4 or 5 toxicity was observed.

Conclusion: Radiotherapy to the groin is a safe alternative for IFL in patients with sentinel node metastasis ≤2 mm, with minimal toxicity. For patients with sentinel node metastasis >2 mm, radiotherapy with a total dose of 5 0Gy was no safe alternative for IFL; dose escalation and/or chemoradiation should be investigated in these patients.

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4 - Scientific Plenary

Phase II OVARIO study of niraparib + bevacizumab therapy in advanced ovarian cancer following front-line platinum-based chemotherapy with bevacizumab

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Objective: Niraparib improves progression-free survival (PFS) in newly diagnosed and recurrent ovarian cancer (OC) in patients after platinum-based chemotherapy in all biomarker-defined subgroups. OVARIO (NCT03326193) is a single-arm study evaluating niraparib + bevacizumab treatment in advanced OC after response to first-line platinum-based chemotherapy + bevacizumab.

Method: All patients with newly diagnosed FIGO stage IIIB–IV OC who had a complete or partial response (CR or PR) after first-line platinum-based chemotherapy + bevacizumab were eligible. Patients receiving neoadjuvant chemotherapy, as well as primary debulking surgery, were eligible. All patients underwent tissue testing for homologous recombination deficiency or proficiency (HRd or HRp) at enrollment. Bevacizumab dosage was 15 mg/kg every 3 weeks up to 15 months, including time on first-line chemotherapy. Niraparib, 300 or 200 mg once daily, based on baseline body weight and platelet count, was started within 12 weeks of completing first-line treatment and continued for 3 years or until progressive disease (PD) or unacceptable toxicity. The primary endpoint is PFS at 18 months from treatment initiation. An interim analysis of PFS at 6 months from treatment initiation was performed after all patients had had 2 scans after starting treatment.

Results: Enrollment was completed at 105 patients. Median age and body weight were 60 years and 68 kg, respectively. Most patients received neoadjuvant chemotherapy (63%), were stage III (79%), and had serous histology (95%). Overall, 49% of patients had pre-existing hypertension, and 47% of patients were HRd, including HRd-*BRCA*mut and HRd-*BRCA*wt. Starting dose was 200 mg in 78% of patients. At 6 months, the PFS rate was 89.5%. Grade ≥3 related treatment-emergent adverse events included thrombocytopenia, anemia, and hypertension, similar to the AVANOVA trial, which used the same combination.

Conclusion: Safety of the niraparib + bevacizumab combination was consistent with the known side effects of each drug as monotherapy, and the combination did not appear to cause cumulative toxicities. Median PFS in advanced OC following first-line platinum-based chemotherapy + bevacizumab has not been reached.

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5 - Scientific Plenary

A pilot study of nivolumab in combination with front-line neoadjuvant dose-dense paclitaxel and carboplatin chemotherapy in patients with high-grade serous ovarian cancer

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Objective: In patients with epithelial ovarian cancer (EOC), increased intratumoral T cells are associated with a better prognosis, generating a rationale for combining chemotherapy with PD-1 blockade, such as nivolumab. In this study, we investigated the combination of nivolumab with neoadjuvant carboplatin and weekly paclitaxel for the upfront treatment of EOC. The primary objective was to measure safety and tolerability as determined by the rate of dose-limiting toxicities (DLTs). Secondary objectives included the complete gross resection rate (CGR), chemotherapy response score (CRS), progression-free survival (PFS), overall survival, and a range of translational parameters.

Method: Patients with FIGO stage 3–4 EOC who were judged to be candidates for neoadjuvant chemotherapy with interval debulking surgery (IDS) were eligible. Patients were treated with IV weekly paclitaxel (80 mg/m^2), with carboplatin (AUC6) and nivolumab (360 mg) given q3 weeks. Three to six cycles were allowed prior to surgery, for a total of 6–8 cycles. After completion of chemotherapy, maintenance nivolumab could be continued for 1 year. Adverse events were graded as per

CTCAE v4.0. The CRS (from 1 to 3) was graded at time of IDS as previously published. Multiplexed immunofluorescence (IF) was performed on pre- and post-treatment tumor samples.

Results: A total of 21 patients were enrolled; median age was 64 years (range 38–77 years); the majority were white (81%) with high-grade serous histology (90%) and stage IV disease (67%). One patient was replaced given G3 infusion reaction with cycle 1. Therapy was well tolerated; two patients (9.5%) had DLTs that delayed IDS, including G4 pneumonitis and G4 myositis. Other grade 3–4 adverse events attributed to nivolumab included rash (10%), fever (5%), and fatigue (5%); 19% of patients had G2 hypothyroidism; 90% achieved an optimal CGR; 35% had a CRS of 3. Median PFS has not been reached; 71.9% of patients are progression free at 1 year with a median follow-up of 14.3 months (6.3–19.8). All patients remain alive. Treatment was associated with tumor microenvironment conversion to an "inflamed" phenotype, with a significant increase in percentage CD8+ T cells (P = 0.0002) (**Figure 1**).

Conclusion: In a high-risk population of EOC patients, the addition of nivolumab to upfront chemotherapy led to promising PFS and favorable changes in the tumor microenvironment.

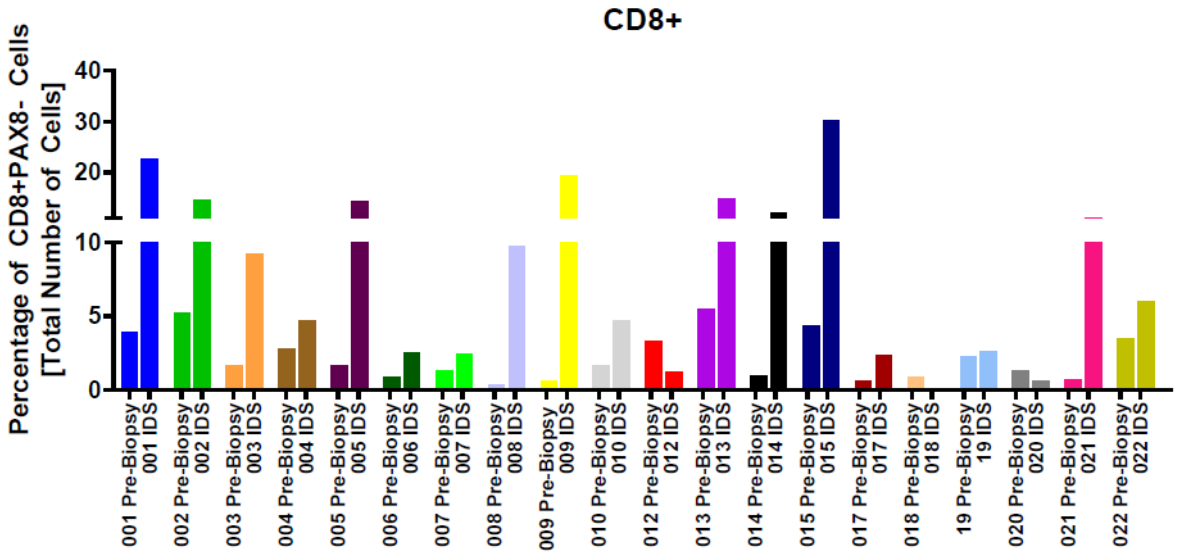

Fig. 1.

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6 - Scientific Plenary

Phase II study of durvalumab alone or in combination with ADXS11-001 (AXAL) in recurrent/persistent or metastatic cervical cancer

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Objective: Our goal was to evaluate the safety, tolerability, and efficacy of PD-L1 immune checkpoint blockade (durvalumab) alone or in combination with a tumor-selective vaccination (ADXS11-001) in patients with persistent-recurrent or metastatic cervical cancer (PRmCC) and metastatic HPV+ SCCHN in part A (dose escalation) or with PRmCC in part B (dose-expansion). Part B results are reported here.

Method: This was an open-label, randomized trial comparing durvalumab versus durvalumab + ADXS11-001 in patients with PRmCC. ADXS11-001, an attenuated *Listeria monocytogenes,* expresses HPV E7 protein, to induce HPV-specific cytotoxic T cells to infiltrate the tumor. ADXS11-001 (1×10^9 CFU) was dosed IV q4 weeks. Durvalumab (10 mg/kg) was dosed IV q2 weeks. The primary objectives were objective response rate (ORR), progression-free survival (PFS) according to RECIST v. 1.1, and safety by NCI CTCAE v 4.03.

Results: A total of 54 PRmCC patients were enrolled and randomized 1:1 to each arm. Twenty (74.1%) and 22 (81.5%) were evaluable for tumor response in the durvalumab and durvalumab + ADXS11-001 arms, respectively. Fewer patients had received 4 or more prior regimens for recurrent/metastatic disease or palliation in the durvalumab arm compared to the durvalumab + ADXS11-001 arm (3.7% vs 25.9%). The confirmed ORR was similar for both groups with 2 partial responses in durvalumab (10 %) and 1 partial response and 1 complete response in durvalumab + ADXS11-001 (9%). Median PFS was numerically higher in durvalumab than in durvalumab + ADXS11-001: durvalumab was 5.0 months (95% CI 1.9–6.9) and durvalumab + ADXS11-001 was 2.1 months (95% CI 1.7–3.8). The incidence of grade ≥3 treatment-related adverse events was lower in subjects in the durvalumab arm (2 [7.4%] of 27 subjects) than in the durvalumab + ADXS11-001 arm (7 [25.9%] of 27). The most common grade ≥3 treatment-related adverse events in the durvalumab arm included thrombocytopenia, thyroiditis, diabetic ketoacidosis, and type I diabetes mellitus (1.3% each); in the durvalumab + ADXS11-001 arm they included anemia (14.8%), hypotension (11.1%), and acute respiratory failure, fatigue, nausea, vomiting, and pain (1.3% each). One grade 5 event (acute respiratory failure) occurred in the durvalumab + ADXS11-001 arm and was deemed possibly related to either or both agents.

Conclusion: The combination of durvalumab + ADXS11-001 appears to be safe and tolerable but requires close monitoring. The ORR was similar across arms, and the PFS in the durvalumab arm was numerically higher than that observed with durvalumab + ADXS11-001. Two objective responses were previously reported in subjects in part A, dose escalation of the study (ADXS11-001 at 1×10^9 CFU + MEDI 3 mg/kg, $n = 4$), including a complete response. The evaluation of *Lm*-constructs in combination with an anti-PD-1/-L1 antibody or other agents is ongoing.

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7 - Scientific Plenary

A phase II trial of the Wee1 inhibitor adavosertib (AZD1775) in recurrent uterine serous carcinoma

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Objective: Uterine serous carcinoma (USC) is an aggressive subtype of endometrial carcinoma characterized by frequent TP53 mutations (>90%), often concomitantly with oncogenic mutations or amplifications that can increase replication stress. We hypothesized that USCs would therefore be uniquely sensitive to further interference of cell cycle regulation by Wee1 inhibition. This 2-stage single-arm phase 2 study was conducted to assess the activity of the oral Wee1 inhibitor adavosertib as monotherapy in recurrent USCs.

Method: Women with recurrent USC were eligible for this study; cancers with any component assessed as serous (with the exception of carcinosarcomas) were considered eligible. Patients were required to have had at least 1 prior platinum-based chemotherapy regimen; those with MSI-H/MMRd disease were required to have already received prior therapy with a PD1/PDL1 therapy or to be ineligible for such therapy. There was no upper limit on the number of prior lines patients could have received. All patients were required to have RECIST measurable disease. Patients received adavosertib 300 mg daily on days 1 through 5 and 8 through 12 of a 21-day cycle. In a planned total accrual of 35 patients, if at least 4 patients had confirmed response or 8 patients were progression-free at 6 months (PFS6), the trial would be considered positive, with an alpha of 10% and a beta of 15% to detect coprimary endpoints of an at least 20% overall response rate (ORR) or a 30% PFS6 rate.

Results: Between October 11, 2018, and August 20, 2019, 27 patients were enrolled in the study. Median follow-up was 3.5 months. The median number of prior lines was 3 (range 1–7). As of August 20, 2019, 21 patients were evaluable for response. In these patients, 6 confirmed responses were observed, for an ORR of 30% (95% CI 12%–54%), with 1 additional patient having an unconfirmed response. Data are not mature for PFS. **Figure 1** shows the waterfall plot of best responses. The most frequently observed adverse events included anemia (67%), diarrhea (67%), nausea (58%), and fatigue (50%). Frequently observed grade 3 or higher adverse effects included anemia (21%), neutropenia (21%), and syncope (21%). Updated data will be presented.

Conclusion: Adavosertib monotherapy demonstrated clinical activity in women with USC, with a preliminary response rate of 30%. Further studies in this patient population are warranted.

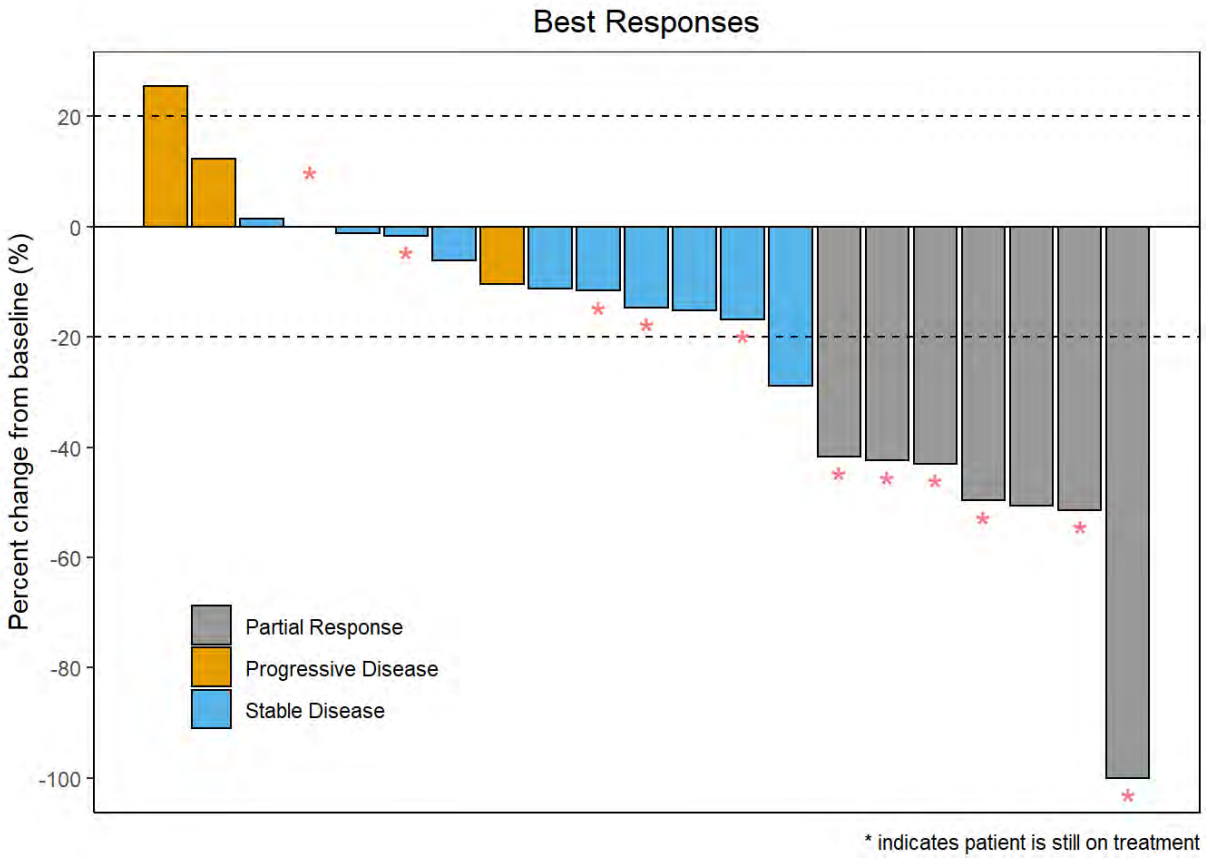

Fig. 1.

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8 - Scientific Plenary

Dkn-01 treated patients with recurrent epithelial endometrial (EEC) or ovarian (EOC) cancers which harbor Wnt activating mutations have longer progression-free survival and improved clinical benefit

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Objective: Dickkopf-1 (DKK1) is a secreted modulator of Wnt signaling that promotes tumor cell proliferation, angiogenesis, and metastasis and contributes to an immune suppressive tumor microenvironment. Activating mutations of the Wnt/Beta-catenin dependent signaling pathway result in increased tumor production of DKK1. We assessed whether patients whose tumors harbor Wnt-activating mutations have improved clinical outcomes to DKN-01 (DKK1 antibody).

Method: Patients with recurrent EEC or platinum-resistant/refractory epithelial ovarian cancer (EOC; ≥1 therapy for recurrent disease) were treated with DKN-01 as monotherapy (mono) or in combination with paclitaxel (combo) in a phase 2 basket trial (NCT03395080) whereby ≥50% must have had a Wnt-signaling alteration. Patients with available tumor genetics were included, and the frequency of Wnt-activating mutations (CTNNB1, APC, RNF43, AXIN, RSPO, and ZNRF3) was assessed in EEC, EOC, and overall. Univariate/multivariate logistic regression and Cox-PH models were used to study the association of Wnt-activating mutations with clinical benefit (partial response or stable disease), progression free survival (PFS), and overall survival (OS) to DKN-01 based treatments.

Results: Of 92 patients enrolled, 88 had genetics available; 21 patients (24%) had Wnt-activating mutations (18 EEC and 3 EOC); CTNNB1 was the most frequent (*n* = 16). In a pooled analysis, patients with Wnt-activating mutations had clinical benefit: 66.7% (14/21) of patients versus 40.3% (27/67) of patients without activating mutations; OR = 2.96 (95% CI 1.09–8.73) and adjusted (for mono/combo and tumor type) OR = 4.61 (95% CI 1.50–15.70). The median PFS was 175 days in patients with Wnt-activating mutations versus 63 days for those without; HR = 0.46 (95%CI 0.23–0.92) and adjusted (for mono/combo and tumor type) HR = 0.41 (95% CI 0.20–0.83). and a median OS for patients was not reached (3 events/21 patients) versus 321 days for those without activating mutations (18 events/67 patients); HR = 0.48 (95% CI 0.14–1.6) and adjusted (mono/combo) HR = 0.50 (95% CI 0.15–1.7). See **Figure 1.**

Conclusion: EEC patients more commonly had Wnt-activating mutations, mostly CTNNB1, while a lower frequency was seen in EOC patients. Wnt-activating mutations were associated with improved clinical benefit and longer PFS for DKN-01 based therapies, independent of tumor and treatment type. There were a limited number of deaths as of July 30, 2019, and overall survival follow-up is ongoing.

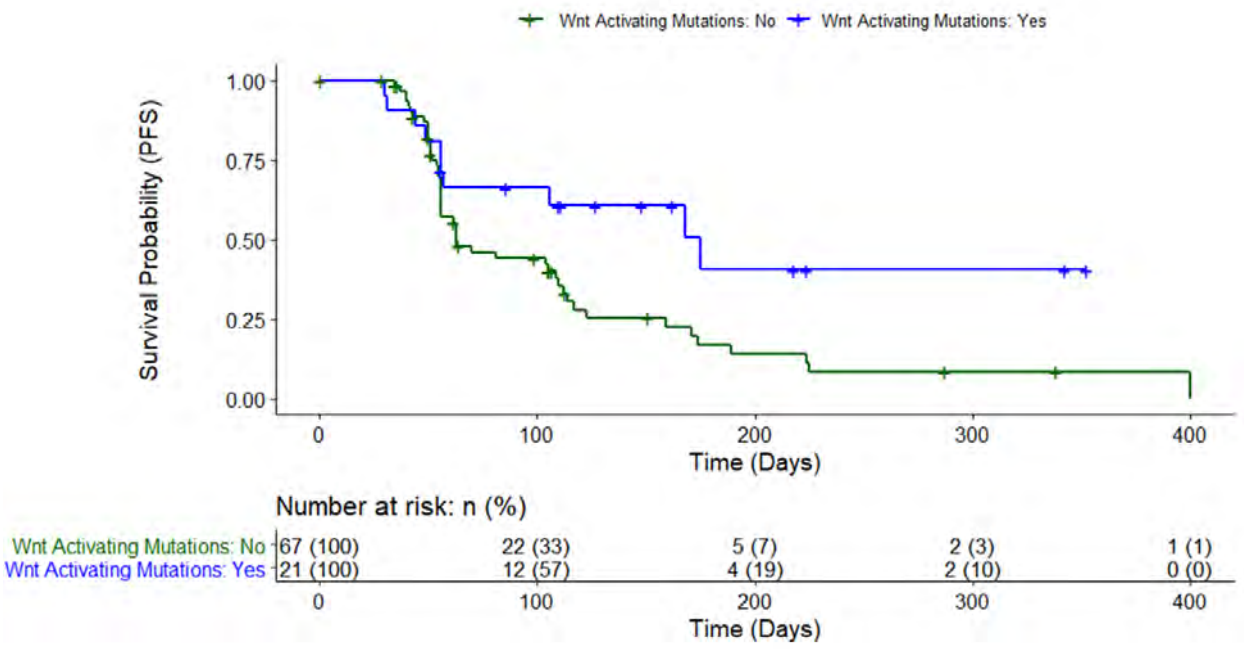

Fig. 1.

Scientific Plenary II: Shining a light on the problem: rare tumor trials and inequity in gynecologic cancer care

LBA 9 - Scientific Plenary

Safety and efficacy of the anti–PD-1 monoclonal antibody dostarlimab in patients with recurrent or advanced dMMR endometrial cancer

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Objective: Dostarlimab (TSR-042) is a humanized programmed death (PD)-1 receptor monoclonal antibody that blocks interaction with PD-1 ligands, PD-L1 and PD-L2. The objective of this interim analysis is to assess the safety and efficacy of dostarlimab in patients with mismatch repair (MMR)-deficient endometrial cancer who are enrolled in the GARNET trial (NCT02715284).

Method: Patients with MMR-deficient endometrial cancer, as confirmed by immunohistochemistry, with recurrent or advanced disease that progressed on a platinum doublet regimen, were enrolled. Patients received 500 mg Q3W of dostarlimab for the first 4 cycles, then 1,000 mg Q6W until disease progression or discontinuation. The primary endpoints were objective response rate (ORR) and duration of response (DOR), as assessed against Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 by blinded independent central review.

Results: Seventy patients with MMR-deficient endometrial cancer treated with dostarlimab, with measurable disease at baseline and ≥6 months of follow-up by the data cutoff date (July 8, 2019), were included in this interim analysis. Median age was 64.5 years. ORR was 43%: 9 (13%) patients had a confirmed complete response and 21 (30%) had a confirmed partial response (**Table 1**). Of the responders, 77% remained on treatment at data cutoff. The Kaplan–Meier estimated likelihood of maintaining response was 96% at 6 months and 77% at 12 months. The disease control rate was 59%. With median follow-up of 11.2 months at data cutoff, median DOR was not reached. Fifty patients (71%) experienced ≥1 treatment-related adverse event (TRAE); the most common were fatigue, diarrhea, and nausea (each, 16%). Ten (14%) patients had a grade ≥3 TRAE; lipase increased, transaminases increased, and colitis, diarrhea, and anemia (each, 3%) were the most common. Two (3%) patients discontinued treatment due to TRAEs. Immune-related TRAEs were reported in 19 (27%) patients, and grade ≥3 immune-related TRAEs were reported in 7 (10%) patients; diarrhea (6%) was the most common immune-related TRAE. There were 4 (6%) deaths due to adverse events; none were assessed as related to dostarlimab.

Conclusion: Preliminary data for dostarlimab demonstrated clinical activity in patients with previously treated recurrent or advanced MMR-deficient endometrial cancer with an acceptable safety profile.

Table 1.

Best overall response by RECIST v1.1, *n* (%)	**dMMR EC *n* = 70**
CR	9 (13)
PR	21 (30)
SD	11 (16)
PD	26 (37)
NE	3 (4)
CR = complete response; dMMR = mismatch repair deficient; EC = endometrial cancer; NE = not evaluable; PD = progressive disease; PR = partial response; SD = stable disease	

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10 - Scientific Plenary (Seminal)

Lenvatinib plus pembrolizumab in patients with advanced endometrial cancer: Final analysis of a multicentre, open-label, single-arm, phase 2 trial

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LBA 11 - Scientific Plenary

A randomized phase II/III study of paclitaxel/carboplatin/metformin versus paclitaxel/carboplatin/placebo as initial therapy for measurable stage III or IVA, stage IVB, or recurrent endometrial cancer: An NRG Oncology/GOG study

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Objective: Obesity and diabetes are associated with increased risk and worse outcomes for endometrial cancer. Paclitaxel and carboplatin is the standard initial therapy for advanced and recurrent endometrial cancer. Thus, we evaluated the efficacy and tolerability of the addition of the antidiabetic drug metformin to paclitaxel and carboplatin in endometrial cancer patients.

Method: In this randomized phase II–III trial, up to 540 patients with chemotherapy-naïve stage III–IVA (with measurable disease) and stage IVB or recurrent (with or without measurable disease) endometrial cancer were to be randomly assigned to treatment with paclitaxel and carboplatin with metformin (850 mg BID) versus paclitaxel and carboplatin with placebo. After completion of up to 10 cycles of paclitaxel and carboplatin with metformin or placebo, metformin or placebo was continued as maintenance therapy until disease progression. The primary endpoint of phase II was progression-free survival (PFS). The primary endpoint of phase III was overall survival (OS). The phase II study had 90% power with 20% alpha. The phase II–III study had 88% power with 5% alpha. Secondary endpoints were objective response, duration of response, and toxicity.

Results: From March 17, 2014, to February 1, 2018, 469 patients were randomized to the phase II and III studies. The phase II study deemed metformin worthy of further investigation in the phase III study. An interim phase III analysis stopped accrual for futility. Paclitaxel and carboplatin with metformin was well tolerated, with no unexpected serious toxicity. The addition of metformin to paclitaxel and carboplatin did not significantly improve OS (log rank one-sided *P* = 0.185, HR = 0.886, 95% CI 0.676–1.161) or PFS (HR = 0.885, 95% CI 0.711–1.101). At a median follow-up of 28 months and 215 deaths, median OS was 30 and 35 months, on paclitaxel and carboplatin with placebo and pPaclitaxel and carboplatin with metformin, respectively. Objective response rates were also similar between the paclitaxel and carboplatin with metformin and the paclitaxel and carboplatin with placebo arms (62% and 60%, respectively). BMI was neither prognostic nor predictive of response to paclitaxel and carboplatin with metformin. The OS HR for BMI was 0.987 per unit increase (95% CI 0.965–1.010) among patients treated with metformin.

Conclusion: PFS and OS were not significantly increased with the addition of metformin to paclitaxel and carboplatin for the treatment of advanced and recurrent endometrial cancer. Additional translational studies are underway to identify potential biomarkers of endometrial cancer patients that may have benefited from metformin treatment.

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12 - Scientific Plenary

Randomized phase II trial of carboplatin-paclitaxel compared to carboplatin-paclitaxel-trastuzumab in advanced or recurrent uterine serous carcinomas that overexpress HER2/Neu (NCT01367002): Updated survival analysis

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Objective: HER2/Neu is a growth-factor receptor expressed in 30% of uterine serous carcinomas (USC). Based on the preliminary results of a multicenter, randomized phase II trial, trastuzumab (a humanized monoclonal antibody targeting HER2/Neu) in combination with carboplatin/paclitaxel is now recognized as an alternative standard in treating advanced or recurrent HER2/Neu+ USC. Herein, we report updated survival data.

Method: Eligible patients had primary stage III–IV or recurrent, HER2/Neu+ disease. Patients were randomized to receive carboplatin/paclitaxel (control) for 6 cycles ± intravenous trastuzumab (experimental) until progression or toxicity. The primary endpoint was progression-free survival (PFS), and secondary endpoints were toxicity and overall survival (OS). Survival differences between treatment arms were assessed for significance via 1-sided log-rank tests.

Results: Forty-three progressions and 38 deaths (44 PFS events) occurred among 58 evaluable patients; median follow-up was 25.9 months (range 0.33–91 months). Among all patients, updated PFS continued to favor the trastuzumab arm, with medians of 8.0 (control) versus 12.9 (experimental) months (*P* = 0.005, HR = 0.46, 90% CI 0.28–0.76). Similarly, updated median PFS was 9.3 (control) versus 17.7 (experimental) months among 41 stage III–IV patients undergoing primary treatment (*P* = 0.015, HR = 0.44, 90% CI 0.23–0.83), and was 7.0 (control) versus 9.2 (experimental) months among 17 patients with recurrent disease (*P* = 0.004, HR = 0.12, 90% CI 0.03–0.48). Among all patients, OS was significantly higher in the trastuzumab arm than in the control arm, with medians of 24.4 (control) versus 29.6 (experimental) months, respectively (*P* = 0.046, HR = 0.58, 90% CI 0.34—0.99; **Figure 1**). This benefit was particularly striking in stage III–IV patients, who had OS medians of 25.4 months (control) versus not reached (experimental, *P* = 0.041, HR = 0.49, 90% CI 0.25–0.97). In a subgroup analysis, no significant OS benefit from trastuzumab was observed in patients with recurrent disease. Finally, long-term toxicity was not different between treatment arms.

Conclusion: In this updated survival analysis of a randomized phase II trial, the addition of trastuzumab to carboplatin/paclitaxel increased PFS and OS in women with advanced/recurrent, HER2/Neu+ uterine serous carcinoma. The greatest benefit was observed in women with stage III–IV disease who were treated upfront.

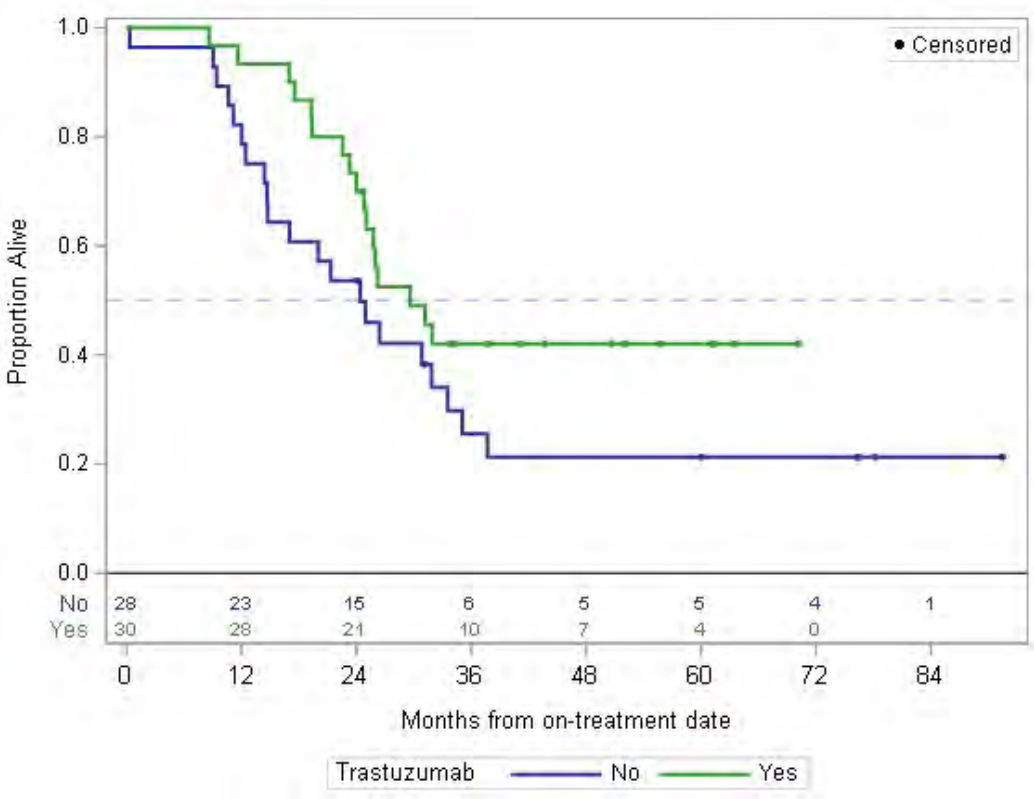

Fig. 1. Overall survival vs trastuzumab, all evaluable subjects (with number of subjects at risk).

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13 - Scientific Plenary

Differences in the molecular landscape of uterine cancer between African American and Caucasian patients

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Objective: While the cause of uterine cancer disparities in African-American women is multifactorial, there is significant evidence suggesting a genetic basis of disparity. Racial differences in the molecular landscape of uterine cancer have yet to be fully characterized. We aim to examine uterine cancer tumors stratified by race and to identify potential therapeutic targets.

Method: A total of 288 uterine cancer samples underwent tumor profiling with NextGen DNA sequencing (NextSEQ on 592 genes), RNA sequencing, in situ hybridization, and immunohistochemistry (Caris Life Sciences, Phoenix, AZ, USA). Tumor mutation burden (TMB) was calculated based on somatic nonsynonymous missense mutations, and microsatellite instability (MSI) was evaluated by fragment analysis, immunohistochemistry (IHC) and next-generation sequencing (NGS). Patient race was collected from treating physicians and analyzed using the χ^2 test.

Results: Tumors from 124 (43%) African-American and 164 (57%) white patients were included. Serous carcinoma was most common (SC, n = 112), followed by endometrioid (EC, n = 87), carcinosarcoma (CS, n = 49), and leiomyosarcoma (LMS, n = 40). Mean age was similar for African-American (63.3) and white (62.5) patients. SC was more common in African-American patients, while EC was more common in white patients ($P < 0.0001$ and $P = 0.0023$, respectively). There were no differences in immunogenic markers (TMB, MSI, mismatch repair [MMR], PD-L1) between races. In epithelial carcinomas (EC, SC, CS), mutations in the PI3K pathway (*PIK3CA*, *PTEN*, *PIK3R1*, *AKT1*) were more common in white patients (60% vs 37%, P =

0.0007), while TP53 mutations were more common in African-American patients (76% vs 53%, *P* = 0.0004). Among CS, there was a trend toward higher ER and PR expression among African-American patients (*P* = 0.077 and *P* = 0.07, respectively). Among EC, mutations in *NF1*, *NFE2L2*, *MRE11*, *SETD2*, *FANCE*, *PRDM1,* and *DNMT3A* were significantly higher in African-American patients. In leiomyoscarcoma (LMS), there was a trend toward higher MED12 mutations in African-American patients although not statistically significant (46% vs 15%, *P* = 0.09). In SC, *BRCA2* mutations were significantly more prevalent in white patients (8% vs 0%, *P* = 0.023), while differences in Her2 over-expression were not found. SC and LMD had few markers of immunogenicity overall. See **Table 1**.

Conclusion: Unique molecular profiles were identified between white and African-American patients. Differences in PI3K pathway upregulation, ER/PR expression, *BRCA* and *MED12* mutations, as well as similar immunogenicity and HER2 expression between races may have clinical implications. Additional studies are needed to explore these findings.

Table 1.

Cancer Type	Gene	% AA	% CC	p value
Serous		49%	31%	0.0023
Endometrioid		15%	42%	<0.001
Combined Epithelial Histologies	PIK3CA	33%	41%	0.1701
	PTEN	11%	38%	<0.001
	PIK3R1	8%	19%	0.0205
	AKT1	0%	4%	0.0540
	PIK3CA/ PTEN/PIK3R1/AKT1	37%	60%	0.0007
	TP53	76%	53%	0.0004
Carcinosarcoma	ER (IHC)	31%	10%	0.0770
	PR (IHC)	24%	5%	0.0700
Endometrioid	NF1	25%	7%	0.0503
	NFE2L2	18%	3%	0.0199
	MRE11	15%	2%	0.0225
	SETD2	13%	0%	0.0023
	FANCE	8%	0%	0.0366
	PRDM1	6%	0%	0.0367
	DNMT3A	6%	0%	0.0491
Serous	BRCA2	0%	8%	0.0230
	Her2 (IHC)	16%	11%	0.4686
Leiomyosarcoma	MED12	46%	15%	0.0892

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14 - Scientific Plenary

Understanding mechanisms of disparities in gynecologic malignancies

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Objective: The difference in cancer morbidity and mortality between individuals of different racial groups is a complex issue often understood in terms of health disparities. This study explores the hypothesis that societal health disparities mediate interactions between the environment and tumor epigenomes and genomes that contribute to differential health outcomes.

Method: The newly developed Cancer Genetic Ancestry Atlas (TCGAA) encodes Cancer Genome Atlas (TCGA) data by ethnic ancestry allowing for systematic analysis of sequencing data along ancestry lines. We investigated differences in methylation,

gene, and microRNA expression between tumors of European and African ancestry in individual gynecologic cancers and across all gynecologic malignancies.

Results: Tumor samples from 1,424 patients of European ancestry and 315 patients of African ancestry with breast, cervical, ovarian, and uterine malignancies were pooled, and differential mRNA expression analysis was performed. Tumors of African ancestry across all gynecologic tumor types showed downregulated expression of cell adhesion molecules, DNA damage repair molecules, and PI3K signaling pathway members. African ancestry tumors also showed notable downregulated expression of transcripts with microRNA binding motifs including known tumor-associated microRNAs such as miR-19, miR-203, and miR-181. We then analyzed microRNA sequencing data directly and found tumor type specific alterations in the expression level of microRNAs between European and African ancestry tumors. For example, breast cancers (both triple negative and nontriple negative) and uterine cancers showed variant patterns of microRNA expression in African ancestry compared to European ancestry tumors. These two tumor types shared multiple commonly altered microRNAs including mirR-154 and let-7. Finally, we investigated DNA methylation alterations in our population. This analysis identified a trend toward hypomethylation in African ancestry tumor samples compared to European ancestry samples; analysis of relationship between specific loci of methylation (intergenic, promoter, UTR) and specific expression changes is ongoing.

Conclusion: This study suggests new mechanisms of morbidity and mortality via environmental interactions and identifies novel possible therapeutic targets for future investigation.

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15 - Scientific Plenary

Compensation differences by gender in gynecologic oncology

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Objective: Women represent nearly 1/3 of all practicing physicians. Despite the critically important roles of women in the physician workforce, their salaries have lagged behind those for men, even when corrected for years of experience. The purpose of this study was to determine whether a compensation discrepancy exists between male and female gynecologic oncologists.

Method: An anonymous survey was distributed to members of the Society of Gynecologic Oncology to evaluate compensation of gynecologic oncologists by gender stratified by practice setting. Demographic information, compensation model, and practice volume were compared between practice settings and gender. Logistic regression modeling was used to identify significant contributors to the odds of making at or above the median salary.

Results: Of the 263 respondents, 41% were female and 59% were male. More than 97% of both genders reported full-time practice. A higher percentage of female respondents reported working in an academic institution (47.0% vs 43.0%, $P = 0.028$). There were no differences between genders with respect to group size, percentage of protected research time, frequency of call, or geographic location of the respondents, although men were more likely to be compensated for extra call ($P = 0.03$) and were more likely to respond to obstetrical emergencies ($P = 0.04$). The reported median salary was $380,000 for women and $500,000 for men, representing a difference of $120,000 (95% CI $84,706–$169,103). The discrepancy in compensation when adjusted for frequency of call and practice volume was noted only in the academic practice setting ($P = 0.04$). More than 75% of female providers in academic practice make below the median salary for gynecologic oncologists observed in this survey. Male gender remained a statistically significant contributor to compensation when adjusted for age and years post-fellowship, the only differences between male and female academic gynecologic oncologists with the odds of making above the median salary at 1.54 ($P < 0.0001$, 95% CI 1.27–1.87). See **Figure 1.**

Conclusion: A significant discrepancy in compensation exists between men and women in gynecologic oncology in academic settings. Policy reform is required to ensure equitable compensation.

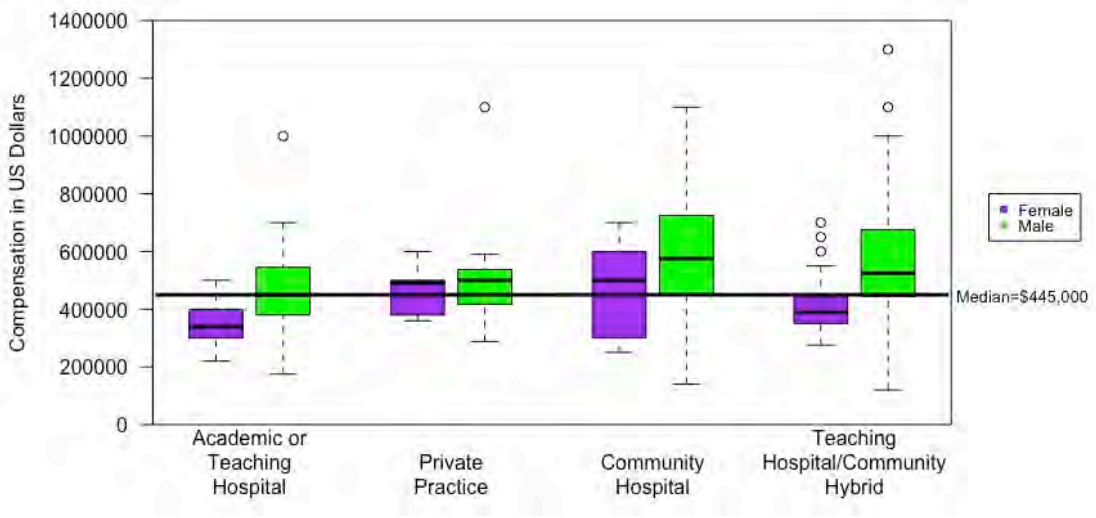

Fig. 1. Compensation by practice setting and gender.

Education Forum I: Which way do we go? How to identify patients for first line PARPi maintenance and genetic counseling

18 - Education Forum
Video-assisted genetic counseling in patients with ovarian, fallopian, and peritoneal carcinoma: A prospective, randomized controlled trial

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Objective: Our goal was to evaluate the proportion of patients with ovarian, fallopian tube, or peritoneal carcinoma (EOC) who receive genetic testing after observing a genetic counseling video compared to traditional referral for genetic counseling.

Method: Patients with ovarian, fallopian, or peritoneal cancer who had undergone surgical staging and received at least 2 cycles of adjuvant therapy were eligible for enrollment at a tertiary referral center from July 2017 to June 2019. Patients were randomized to video-assisted counseling (VAC) followed by the option of immediate genetic testing or video-assisted introduction followed by referral to formal genetic consultation. All patients received a 3-part questionnaire encompassing sections of knowledge revisions (KR), perceived personal control (PPC), and the impact of events-intrusion (IEI) before and after intervention. The primary outcome was the proportion of patients who received genetic testing. Secondary outcomes included retention of key concepts, changes to perceived control, and the impact of events-intrusion items. SPSS 2013 was used to analyze the data through *t* test comparisons for continuous data and χ^2 for discrete data. See **Table 1**.

Results: A total of 80 patients (median age 67 years) were randomized to either VAC followed by immediate testing (n = 40) or formal genetic counseling (n = 40). The majority of subjects were stage IIIC. Median time since initial diagnosis to genetic testing was 5.8 months. Both arms showed significant improvement in knowledge scores and PPC scores when pre-education and post-education surveys were compared. Changes in pre and post scores were not significantly different between the two arms. The VAC group resulted in a significantly higher proportion of patients who chose to receive testing when compared to the formal consultation group (95% vs 75%, $P < 0.005$).

Conclusion: Using a genetic counseling video followed by an immediate testing option significantly increased the proportion of patients with ovarian, fallopian, or peritoneal carcinoma who underwent genetic testing while providing similar changes in knowledge and other patient-reported outcomes when compared to standard counseling methods.

Table 1. Demographics of the patients enrolled in the Video-Assisted Genetic Counseling Prospective Trial

Age at diagnosis, median (range)	67 years (21 – 85 years)

Race, % (n)	
White, non-Hispanic	63.75% (51)
African American	35% (28)
Asian-American	1.25% (1)
BMI (kg/m^2), median (range)	30.3 (18.5 – 52.6)
Smoking Status, % (n)	
Never	72.5% (52)
Current	10% (8)
Former	17.5% (14)
Histology, % (n)	
High Grade Serous	65% (52)
Low Grade Serous	1.25% (1)
Clear Cell	7.5% (6)
Endometrioid Adenocarcinoma	25% (20)
Carcinosarcoma	1.25% (1)
Diagnosed Stage, n	
IA	4
IB	2
IC	11
IIA	3
IIB	1
IIC	2
IIIA	0
IIIB	0
IIIC	37
IVA	15
IVB	5
Vital Statistics at last contact, % (n)	
Alive	86.25% (69)
Deceased	13.75% (11)
First Degree Relative with Cancer, % (n)	57.5% (46)
Mutation Identified, n	
Major (BRCA+, BRIP, MUTYH, APC)	8
VUS	11

Education Forum II: Novel radiation therapeutic strategies for gynecologic cancers in 2020 and beyond

19 - Education Forum
A randomized phase II study of chemoradiation and pembrolizumab for locally advanced cervical cancer: Presentation of safety data

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Objective: There is a strong rationale for using immune checkpoint inhibitors (ICI) in locally advanced cervical cancer (LACC), particularly in combination with SOC chemoRT (CRT). The question of sequential versus concurrent use has not been addressed prospectively. Moreover, the safety of combining ICI with pelvic CRT has not been established. The current study was designed in part to evaluate the safety of the combination.

Method: This is a randomized, phase II, open-label multicenter study. Patients ≥18 years with LACC, stages IB-IVA (FIGO 2009) were randomized 1:1 to pembrolizumab (pembro) after CRT (arm 1) or pembro during CRT (arm 2). CRT therapy was identical for both arms with standard weekly cisplatin dosing. Pembro 200 mg was administered as a 30-minute infusion Q3 weeks for 3 doses: beginning week 9 (arm 1) after CRT or week 1 during CRT (arm 2). All patients receiving any protocol treatment were evaluated for safety. Safety assessments included incidence and severity of adverse events and occurrence of

dose-limiting toxicities (DLTs) as defined per protocol. Blood and tumor were collected at defined time points for translational study.

Results: As of August 2019, 60 (of planned 88) patients have begun treatment; 52 completed and have complete adverse event data (24 arm 1; 28 arm 2). Overall there were 22 G3 and 11 G4 treatment-related adverse events: most common was lymphopenia (8 arm 1; 12 arm 2). Adverse events of special interest are presented in **Table 1**. Two patients had grade 3 diarrhea, 1 in each arm. Two patients experienced 3 DLTs (both arm 2): grade 3 diarrhea (1), grade 3 nausea (1), grade 3 vomiting (1). Most patients completed 6 cisplatin treatments (100% arm 1 vs 82% arm 2); 83% in both arms completed 3 infusions of pembro. All but 2 patients completed radiation (2 patients in arm 2 withdrew from protocol), 79% and 75% in <8 weeks in arms 1 and 2, respectively.

Conclusion: With complete safety data for 52 patients, we have demonstrated the safety and feasibility of the combination of ICI and pelvic CRT. Based upon these data, no major differences in total number of adverse events of special interest are evident by arm. The safety stopping bounds were not crossed, and the study is continuing with accrual. At study completion, we will address the scientific question of which treatment regimen is the most biologically promising.

Table 1. Adverse events of clinical interest; possibly, probably or definitely related to pembrolizumab

		Arms														
		N=24 Arm 1 (Pembro after CRT)					N=28 Arm 2 (Pembro during CRT)					N=52 ----- Total				
Category	AE	G1	G2	G3	G4	G5	G1	G2	G3	G4	G5	G1	G2	G3	G4	G5
GASTROINTESTINAL	ABDOMINAL DISTENSION						1					1				
	ABDOMINAL PAIN	3					2					5				
	BLOATING	1										1				
	COLITIS							1					1			
	COLONIC STENOSIS									1					1	
	CONSTIPATION	2					2	1				4	1			
	DIARRHEA	12	3	1			15	3	1			27	6	2		
	DRY MOUTH		1				1					1	1			
	DYSPEPSIA						1					1				
	GASTROESOPHAGEAL REFLUX DISEASE						1					1				
	MUCOSITIS ORAL	3	1									3	1			
	NAUSEA	9	10	1			7	8	2			16	18	3		
	PROCTITIS						2					2				
	RECTAL PAIN						2					2				
	STOMACH PAIN						1					1				
	VOMITING	4	6	1			3	3	1			7	9	2		
REPRODUCTIVE/BREAST	DYSPAREUNIA	1										1				
	OTHER		1										1			
	PELVIC PAIN	1	2									1	2			
	PERINEAL PAIN	1										1				
	VAGINAL DISCHARGE	2	2									2	2			
	VAGINAL HEMORRHAGE	1										1				
	VAGINAL PAIN		1										1			
	VAGINAL PERFORATION								1					1		
RESPIRATORY/THORACIC/MEDIASTINAL	OTHER	1										1				
	SORE THROAT	1										1				
SKIN/SUBCUTANEOUS TISSUE	ALOPECIA	1					1					2				
	HYPERHIDROSIS	1						1				1	1			
	OTHER	2					1					3				

		Arms														
		N=24 Arm 1 (Pembro after CRT)					N=28 Arm 2 (Pembro during CRT)					N=52 ----- Total				
Category	AE	G1	G2	G3	G4	G5	G1	G2	G3	G4	G5	G1	G2	G3	G4	G5
	PRURITUS	1					2					3				
	RASH ACNEIFORM						1					1				
	RASH MACULO-PAPULAR						2					2				
OVERALL MAXIMUM – Highest grade	****	8	13	2			9	10	3	1		17	23	5	1	

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20 - Education Forum

Age matters when predicting overall survival benefit of combined chemotherapy and radiation versus radiation alone in high risk endometrial cancer: A study of 20,000 women using PORTEC-3 criteria

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Objective: Our goal was to evaluate the interplay of age, histology, and stage in predicting overall survival (OS) in high-risk endometrial cancer patients treated with combined chemotherapy and radiation versus radiation alone in 1,500+ Commission on Cancer®-Accredited facilities, after accounting for prognostic clinical factors.

Method: High-risk endometrial cancer patients diagnosed in 2004–2014 in the National Cancer Data Base were identified. Patients had stage IA–IB grade 3 endometrioid endometrial cancer (EEC) ± lymphovascular space invasion (LVSI), stage II–III EEC, or stage I–III serous/clear cell uterine cancer and began therapy within 60 days of diagnosis. All were treated with pelvic beam radiation and/or radioactive implants. Combined chemotherapy and radiation patients also received multiple chemotherapy agents. Inverse probability of treatment weighting based on propensity score and weighted Kaplan-Meier and Cox modeling evaluated age, histology, and stage in predicting OS, after balancing for 11 clinical and demographic factors. Patients with missing survival data were excluded. Interaction tests evaluated heterogeneity of treatment effects in subgroups.

Results: A total of 20,015 women with high-risk endometrial cancer were eligible: 10,009 in the combined chemotherapy and radiation group and 10,006 in the radiation alone group. After balancing of clinical factors, adjusted 5-year OS was 76.6% versus 71.8% for patients after combined chemotherapy and radiation versus radiation alone (HR = 0.85, 95% CI 0.81–0.88). The survival benefit varied in age, histology, and stage subgroups ($P < 0.0001$ for interaction tests). The largest benefit for combined chemotherapy and radiation was in elderly patients ≥70 years old (HR = 0.67, 95% CI 0.63–0.72) versus <60 years (HR = 0.97, 95% CI 0.89–1.06) or 60–69 years old (HR = 0.94, 95% CI 0.87–1.02). In patients <70 years old, combined chemotherapy and radiation was associated with a 16% higher risk of death in stage I–II EEC (95% CI 1.04–1.29), but a 34% lower risk of death for stages I–III serous/clear cell carcinoma (HR = 0.66, 95% CI 0.56–0.79). In contrast, in patients ≥70 years old, the combined chemotherapy and radiation benefit was higher in stage III versus stage I–II EEC (HR = 0.61, 95% CI 0.54–0.68 versus HR = 0.80, 95% CI 0.72–0.89) and in stage III versus stage I–II serous/clear cell carcinoma (HR = 0.54, 95% CI 0.46–0.64 versus HR = 0.73, 95% CI 0.61–0.88). See **Figure 1**.

Conclusion: Age matters in the selection of adjuvant therapy for high-risk endometrial cancer patients. The largest benefit of combined chemotherapy and radiation was predicted in elderly patients with stage III endometrioid or in serous or clear cell carcinoma. Caution should be exercised when considering combined chemotherapy and radiation for younger patients with stage I–II high-risk EEC because of the observed increased risk of death.

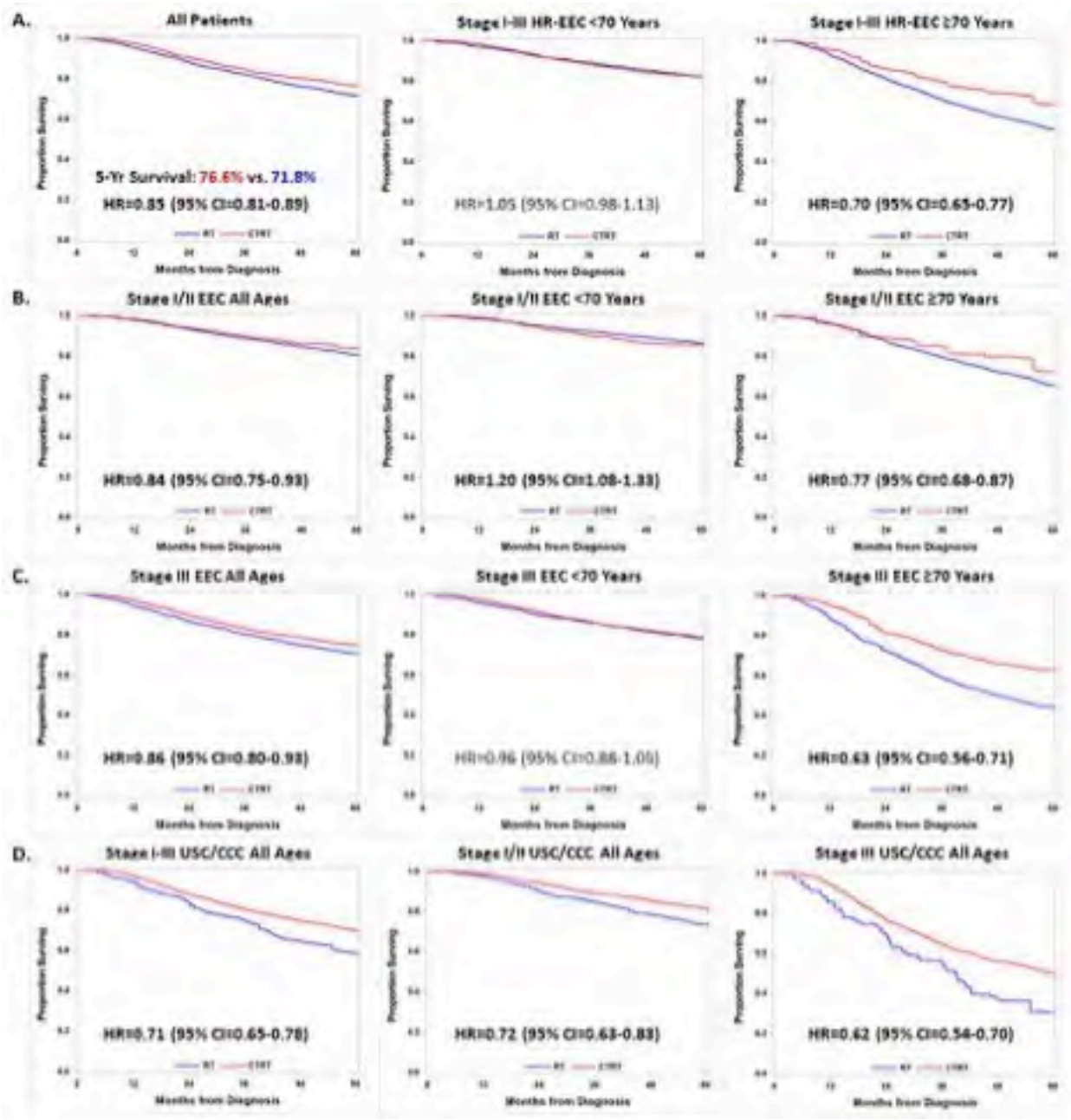

Fig. 1. Survival distributions and adjusted hazard ratio (HR) and 95% confidence interval (CI) for CTRT vs. RT.

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21 - Education Forum

Outcomes of MSI high advanced-stage endometrial cancer treated with chemotherapy and radiation versus chemotherapy alone

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Objective: Our goal was to determine whether microsatellite instability (MSI) high advanced-stage endometrial cancer responds better to chemotherapy followed by radiation or chemotherapy alone.

Method: A multicenter retrospective analysis of patients with stage III and IV endometrial cancer from 2000 to 2016 was performed. Inclusion criteria were patients undergoing hysterectomy, bilateral salpingoophorectomy ± staging procedure followed by adjuvant chemotherapy or chemotherapy and radiation. Differences in the frequencies of histology, stage, and

cytoreduction status were identified using the Pearson χ^2 test. Two-year progression-free survival (PFS) was calculated using Kaplan-Meier estimates.

Results: Final analysis included 37 patients receiving postoperative adjuvant therapies: 55% (*n* = 20) chemotherapy followed by radiation; 29.5% (*n* = 17) chemotherapy alone. The median age was 62 years (range 51–81 years); histology included 48.6% endometrioid, 40.5% serous, and 10.7% clear cell tumors. Of these patients, 92% underwent optimal cytoreduction. There was no difference in the frequency of histologic subtypes (*P* = 0.83) and stage (*P* = 0.12) between the 2 treatment arms. There was a significant improvement in 2-year PFS (log rank *P* = 0.04) in patients receiving chemotherapy followed by radiation over chemotherapy alone. See **Figure 1**.

Conclusion: Chemotherapy and radiation given for advanced-stage MSI high endometrial cancer is associated with a higher 2-year PFS than chemotherapy alone.

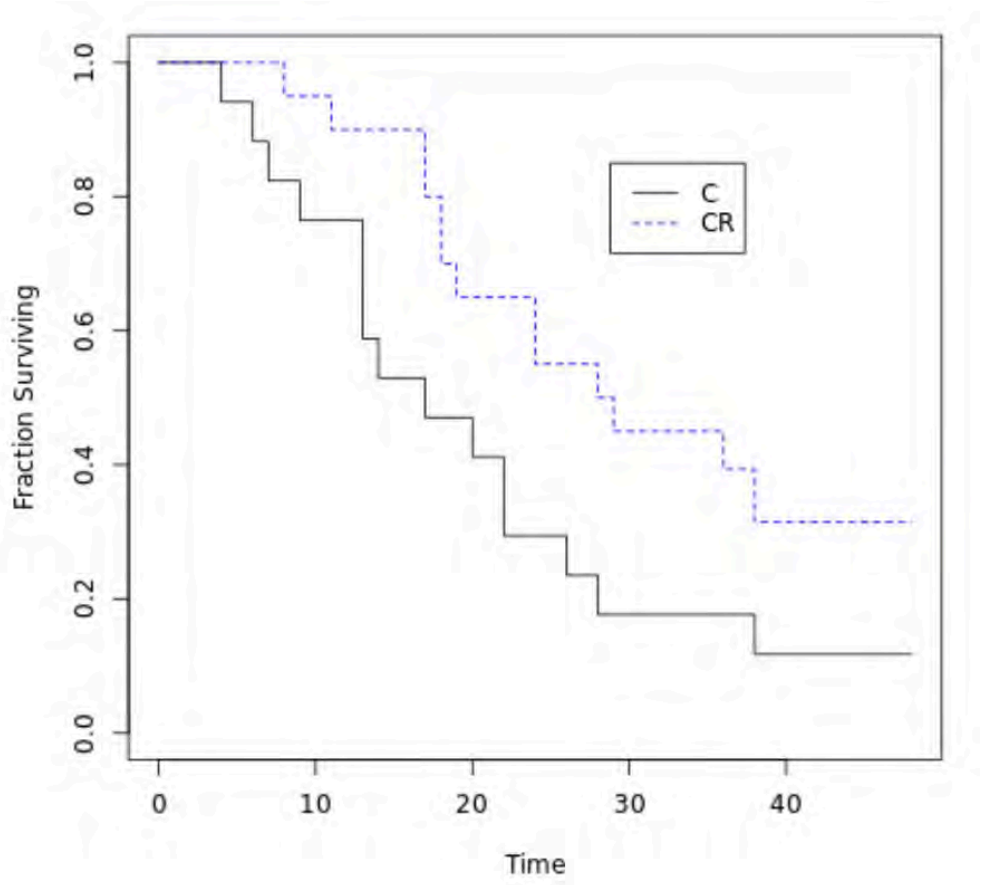

Fig. 1. Kaplan-Meier survival by group.

Scientific Plenary IV: Fighting Cancer with Fitness and the Immune System

22 – Scientific Plenary
Behavioral weight loss intervention effectiveness in gynecologic oncology clinics is minimal; nearly half of obese endometrial cancer survivors gain weight over 12 months
E.M. Wilson, A.S. Zamorano, J. Liu, A. Leon, L.M. Kuroki, P.H. Thaker, C.K. McCourt, K.C. Fuh, L.S. Massad, M.A. Powell, D.G. Mutch, G.A. Colditz and A.R. Hagemann. *Washington University School of Medicine in St. Louis, St. Louis, MO, USA*

Objective: Obesity is a major risk factor for all-cause mortality in endometrial cancer (EC) survivors. A previous randomized controlled behavioral weight-loss trial (ScaleDown) from our academic gynecologic oncology practice found no difference in weight change from baseline in a text-based intervention group or a "usual care" control group; 49.2% of all participants gained weight. We compared clinical characteristics and weight change between ScaleDown participants and EC survivors who declined participation in order to guide future interventions and test the hypothesis that nonparticipants gained more weight than participants.

Method: Clinic visits from May to December 2017 were previously screened for EC survivors with BMI ≥ 30 kg/m^2. We obtained Institutional Review Board approval for a retrospective assessment of eligible patients who declined to participate in the trial. Kruskall-Wallis and Fisher's exact tests were performed to compare demographics and weight change at 6 and 12 months between participants and nonparticipants.

Results: Among 358 eligible obese EC survivors, 80 women participated in ScaleDown and 278 declined. Those who declined were older (63.4 vs 59.3 years, $P < 0.001$), more likely to be Caucasian ($P = 0.019$), and on more medications (median 7 vs 4, $P < 0.001$) and had a lower median BMI (39.1 vs 41.7 kg/m^2, $P = 0.011$). Patients who declined were also more likely to have recurrent cancer (15.2% vs 5.1%, $P = 0.021$) and less likely to have had genetic counseling (10.8% vs 20%, $P = 0.038$). There were no differences in cancer histology, stage, or receipt of initial chemotherapy or radiation therapy. At 6 and 12 months, there was no difference in BMI change from baseline between participants and nonparticipants ($P = 0.77$ and $P = 0.76$, respectively). At 12 months, 47% of nonparticipants gained weight. See **Table 1**.

Conclusion: EC survivors who choose to participate in behavioral weight-loss interventions are more likely to be younger, of non-white race, and on fewer medications and to have participated in other proactive health care, such as genetic counseling. Regardless of participation in behavioral weight-loss interventions, nearly half of EC survivors gain weight over a 12-month follow-up. As obesity-related mortality increases, urgent efforts at more intensive weight management interventions for obese EC survivors are warranted.

Table 1.

	Participants	Non-participants	p-value
Age (mean)	59.3	63.4	<0.001
Race (n, %)			0.019
Caucasian	62 (77.5)	243 (87.4)	
Black	15 (18.6)	32 (11.5)	
Asian	2 (2.5)	0 (0)	
Other	1 (1.3)	3 (1.1)	
Number of active medications (median)	4	7	<0.001
Baseline BMI (kg/m^2, median)	41.7	39.1	0.011
Cancer stage (n, %)			0.113
IA	49 (63.6)	149 (54.8)	
IB	9 (11.7)	59 (21.7)	
II	1 (1.3)	15 (5.5)	
III	14 (18.2)	39 (14.3)	
IV	4 (5.2)	10 (3.7)	
Cancer histology (n, %)			0.715
Endometrioid, grade 1-2	65 (81.3)	62 (82.7)	
Endometrioid, grade 3	6 (7.5)	3 (4.0)	
Serous	1 (1.3)	4 (5.3)	
Clear cell	1 (1.3)	1 (1.3)	
Carcinosarcoma	6 (7.5)	4 (5.3)	
Mixed endometrioid/serous	1 (1.3)	1 (1.3)	
Recurrent cancer			0.021
Yes	4 (5.1)	42 (15.2)	
No	75 (94.9)	235 (84.8)	
Received genetic counseling			0.038
Yes	16 (20.0)	30 (10.8)	
No	64 (80.0)	247 (89.2)	
Change in BMI from Baseline (kg/m^2, median)			
At month 6	0.00	0.04	0.77
At month 12	0.00	0.00	0.76
Change in Weight from Baseline after 12 months (n, %)			0.433
Gained weight	32 (49.2)	79 (47.0)	
Lost 0% to 2.5% of weight	9 (13.9)	39 (23.2)	
Lost 2.5% to 4% of weight	7 (10.8)	12 (7.1)	

Lost 4% to 5% of weight Lost 5% or more of weight	2 (3.1) 15 (23.1)	8 (4.8) 30 (17.9)	

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23 - Scientific Plenary

Increased physical activity promotes CD8+ lymphocyte infiltration and improves survival in a murine model of ovarian cancer

S. Lynam, A.E. Stenzel, E. Zsiros, A. Sen and K. Odunsi. *Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA*

Objective: The beneficial effects of physical activity on immune responses have been well characterized in a variety of diseases. However, there is a paucity of data describing the mechanisms by which exercise influences antitumor responses in gynecologic cancers. We sought to characterize the role of exercise in a murine model of ovarian cancer and its impact on the immune system.

Method: Wildtype C57BL/6 (control) and PD1$^{-/-}$ knockout (KO) mice were injected intraperitoneally using syngeneic ID8-derived ovarian cancer cells and randomized to wheel-running versus sedentary lifestyle post-inoculation. To determine baseline physical activity characteristics and the influence of voluntary exercise on tumor kinetics, wheel running distance was assessed daily with biweekly measurement of abdominal circumference and weight until moribund. Immunohistochemistry (IHC) analysis was performed at endpoint on omental tumor to characterize CD3, CD4, and CD8 expression. Overall survival (OS) comparison using Kaplan-Meier and log rank analyses was performed using SAS.

Results: There were 15 wildtype controls and 31 PD1KO developed widely metastatic tumors. Average daily running distance ranged from 7 to 12 km in the wheel/active group. Median OS for wildtype mice was similar between the wheel group and sedentary controls (42 vs 39 days, $P = 0.29$). Interestingly, in PD1KO mice, significantly increased CD8+ T cell infiltration was seen in the wheel group compared to the sedentary group ($p = 0.04$). Physical activity in conjunction with higher CD8 infiltration was also associated with improved survival in CD8-high/wheel mice demonstrating median OS of 75 days compared to 40 days in CD8-high/sedentary mice (HR = 0.57, 95% CI 0.19–1.67).

Conclusion: To our knowledge, this is the first study to investigate the association between physical activity, immune checkpoint blockade, and survival in murine models of ovarian cancer. Voluntary exercise, specifically in PD1KO mice, favorably affects survival in a subpopulation with increased tumoral CD8+ lymphocyte infiltration. Our findings confirm previous work demonstrating beneficial effects of tumor-infiltrating lymphocytes in ovarian cancer while suggesting the potential of physical activity to enhance immune responses to further improve survival.

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24 - Scientific Plenary

Water-only fasting and its effect on chemotherapy administration in gynecologic malignancies

C.J. Riedinger, K.J. Kimball, L.C. Kilgore, C. Bell, E. Heidel and J.D. Boone. *University of Tennessee Medical Center, Knoxville, TN, USA*

Objective: The utility and duration of chemotherapy treatment may be limited by side effects. Starvation is a nonpharmacological method that may improve tolerability as organisms withdraw energy from growth and reproduction to focus on cellular maintenance. Cancer cells function independently of these nutrition-signaling pathways and are unable to mount this protective response. This differential response has been theorized as an adjunct to improve the response of cancer cells to treatment and reduce side effects. We sought to investigate the feasibility and effect of a 48-hour water-only fast in patients receiving chemotherapy for gynecologic malignancy.

Method: With Institutional Review Board approval, a nonblinded randomized controlled trial was performed. Patients with biopsy proven gynecologic malignancy receiving at least 6 cycles of chemotherapy were included. Fasting patients maintaining a water-only fast for 24 hours before and 24 hours following each chemotherapy cycle were compared to nonfasting patients. Abstracted data included patient demographics, treatment regimens, treatment modifications, and side effect profile. Patient functional status and quality of life (QOL) were evaluated by using the NCCN-FACT FOSI-18 questionnaire.

Result: Analysis included 110 cycles of chemotherapy from 20 patients. The mean age was 59, and the majority of patients were stage 3 or 4 (80.9%). Ten patients had ovarian, 9 had uterine, and 1 had cervix cancer. All patients received at least

doublet chemotherapy, with 91.7% receiving taxane and platinum-based agents. There was no significant difference in weight loss between treatment groups (−1.1 kg vs −0.4 kg, *P* = 0.226). Unanticipated hospitalizations were similar; however, fewer dose reductions and/or delays were seen in the fasting group. There was no significant difference in mean QOL scores (57.45 in fasting group, 57.06 in control group, *P* = 0.89). See **Table 1**.

Conclusion: A 48-hour fast was found to be well tolerated without increasing weight loss, hospital admissions, or chemotherapy dose reduction/delays. This study did not demonstrate an improvement in QOL, but the water-only fast resulted in less than half of the treatment modifications seen in the nonfasting group. Larger studies may be considered to further analyze the effect on QOL in cancer patients undergoing chemotherapy.

Table 1.

	Fasting (n=10)	**Non-fasting (n=10)**	
Age Mean (years)	 59.4	 60	p=0.89
BMI Mean (kg/m^2)	 27.8	 30	p=0.37
Cancer Type Ovary Uterus Cervix	 4 (40%) 5 (50%) 1 (10%)	 6 (60%) 4 (40%)	p=0.42
Stage Stage 1 Stage 2 Stage 3 Stage 4	 2 (20%) 6 (60%) 2 (20%)	 1 (10%) 1 (10%) 7 (70%) 1 (10%)	p=0.73
Weight loss Mean (kg)	-0.48	-1.09	p=0.226
NCCN-FACT FOSI -18 score (max 72)	57.45	57.06	p=0.89
Hospital admission	1	2	
Dose delay or reduction	3	7	

Scientific Plenary V: Novel Ovarian Cancer Regimens: Tomorrow's Treatment?

LBA 25 - Scientific Plenary

Avelumab in combination with and/or following chemotherapy vs chemotherapy alone in patients with previously untreated epithelial ovarian cancer: Results from the phase 3 javelin ovarian 100 trial

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Objective: This randomized, open-label, phase 3 trial (JAVELIN Ovarian 100; NCT02718417) evaluated avelumab in combination with and/or following chemotherapy versus chemotherapy alone in patients with previously untreated epithelial ovarian cancer (EOC).

Method: Patients with stage III–IV EOC (post debulking surgery or candidates for neoadjuvant chemotherapy) were randomized 1:1:1 to receive 6 cycles of chemotherapy (carboplatin AUC 5 or 6 intravenously, IV, every 3 weeks, Q3W with paclitaxel 175 mg/m^2 Q3W or 80 mg/m^2 weekly—investigators' choice) followed by avelumab maintenance (10 mg/kg IV every 2 weeks, Q2W; chemotherapy → Ave), chemotherapy with avelumab (10 mg/kg IV Q3W) followed by avelumab Q2W maintenance (chemotherapy with → Ave), or chemotherapy followed by observation (chemotherapy → O, control). The primary endpoint was progression-free survival (PFS) by blinded independent central review per Response Evaluation Criteria in Solid Tumors v1.1.

Results: A total of 998 patients were randomized. At interim analysis (data cutoff September 7, 2018), median follow-up for PFS (95% CI) was CTx → Ave, 11.1 months (95% CI 10.3–12.2); CTx + Ave → Ave, 11.0 months (95% CI 10.5–11.9); and CTx → O, 10.2 months (95% CI 9.5–10.8). In both avelumab arms, PFS was not improved versus control, prespecified futility boundaries were crossed, and the trial was stopped. Hazard ratios (95% CI) for PFS in avelumab arms versus control were 1.43 ((95% CI 1.051–1.946) for CTx → Ave and 1.14 ((95% CI 0.832–1.565) for CTx+Ave → Ave. Median PFS was 16.8 months (95% CI 13.5–NE) for CTx → Ave, 18.1 months (95% CI 14.8–NE) for CTx+Ave → Ave, and NE (18.2–NE) for CTx → O. Subgroup analyses based on baseline characteristics and biomarkers (PD-L1, CD8, and *BRCA*) did not identify subsets with clear benefit in either avelumab arm. Overall survival data were immature, and median values were not reached. Objective response rates were 30.4% (95% CI 25.5–35.7) for CTx → Ave, 36.0% (95% CI 30.8–41.4) for CTx+Ave → Ave, and 30.4% (95% CI 25.6–35.7) for CTx → O. No new safety signals were observed. In the CTx → Ave, CTx+Ave → Ave, and CTx → O arms, grade ≥3 treatment-emergent adverse events of any causality occurred in 66.5%, 70.8%, and 62.6%, respectively.

Conclusion: This first phase 3 trial of a checkpoint inhibitor in patients with previously untreated EOC did not meet its primary endpoint of improving PFS in either avelumab arm. No new safety signals were identified. Translational analyses to further understand the role of checkpoint inhibitors in this setting are ongoing.

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26 - Scientific Plenary

Demcizumab combined with paclitaxel for platinum-resistant ovarian, primary peritoneal, and fallopian tube cancer (EOC): The SIERRA multi-institutional open-label phase Ib trial

K.F. Handley[a], K.N. Moore[b], R.A. Burger[c], G.Z. Dal Molin[d], R. Stagg[e], A.K. Sood[a] and R.L. Coleman[a]. *[a]The University of Texas MD Anderson Cancer Center, Houston, TX, USA, [b]The University of Oklahoma Stephenson Cancer Center, Oklahoma City, OK, USA, [c]University of Pennsylvania, Philadelphia, PA, USA, [d]A Beneficência Portuguesa de São Paulo, São Paulo, Brazil, [e]Oncomed Pharmaceuticals, Redwood City, CA, USA*

Objective: Our goal is to evaluate the safety of demcizumab (DLL4 targeted IgG2 humanized monoclonal antibody; potent inhibitor of the Notch pathway) in combination with weekly paclitaxel in platinum-resistant EOC; to estimate the maximum tolerated dose (MTD) or maximum administered dose (MAD); and to determine the recommended phase two dose. Objective response rate (ORR) was a secondary objective.

Method: We conducted a 3+3 dose-escalation trial in patients with recurrent, platinum-resistant EOC with RECIST v. 1.1 measurable disease and four or fewer prior chemotherapy regimens. Two dosing cohorts (2.5 mg/kg and 5 mg/kg) were initially targeted; however, an intermediate dose level (3.5 mg/kg) was prescribed if the 5 mg/kg dose was not tolerable. Demcizumab was administered intravenously on days 1 and 15 and paclitaxel (80 mg/m^2 IV) weekly on days 1, 8, and 15 for each of three 28-day cycles: the three-cycle doublet could be repeated once if safe. Thereafter, paclitaxel was administered until unacceptable toxicity or disease progression was reached.

Results: Nineteen patients were enrolled (3 at each dose level). No dose-limiting toxicity (DLT) was observed; however, an intermediate dose level (3.5 mg/kg) was enrolled (n = 3) and expanded (n = 10) based on emerging safety data from other studies in the demcizumab program. The most common adverse events of any grade were diarrhea (68%), fatigue (58%), peripheral edema (53%), and nausea (53%). Grade ≥3 adverse events included hypertension (26%), abdominal pain, anemia, neutropenia, and urosepsis (11% each). Demcizumab-related adverse events of any grade were fatigue (42%), hypertension (37%), diarrhea (32%), and headache (32%). Pulmonary hypertension, grade 2 (n = 2) and grade 1 (n = 1), was observed. No DLTs were recorded, and the MTD was not reached. ORR was 21% (95% CI 6–45%); clinical benefit rate (CBR) was 42% (95% CI 20–66%). Two of five patients with prior bevacizumab treatment had an objective response, and two others had confirmed stable disease (≥12 weeks). See **Figure 1**.

Conclusion: Demcizumab in combination with paclitaxel has a manageable toxicity profile and showed activity in patients with heavily pretreated platinum-resistant ovarian cancer. Ongoing investigation is evaluating the next-generation bispecific VEGF/DLL4 antibody, navicixizumab, in combination with paclitaxel.

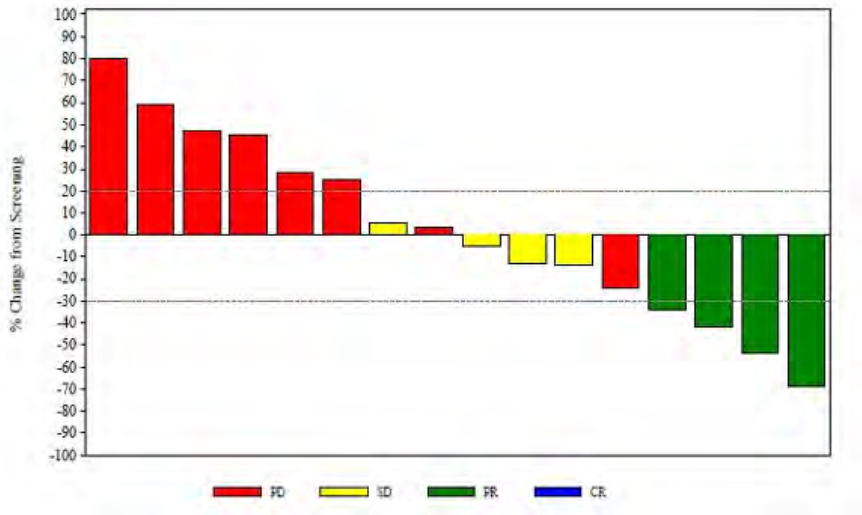

Fig. 1. Waterfall pot of the maximum percent decrease in tumor size by best overall response. PD: progressive disease; SD stable disease; PR: partial response; CR: complete response.

26.5 - Scientific Plenary

A phase Ib study of navicixizumab and weekly paclitaxel in heavily pretreated platinum resistant ovarian, primary peritoneal or fallopian tube cancer

S. Fu[a], R.A. Burger[b], E. Hamilton[c], B.R. Corr[d], R.W. Naumann[e], R.M. Wenham[f], M.A. Morgan[g], R. Stagg[h] and K.N. Moore[i]. *[a]The University of Texas MD Anderson Cancer Center, Houston, TX, USA, [b]University of Pennsylvania, Philadelphia, PA, USA, [c]Sarah Cannon Research Institute Tennessee Oncology, Nashville, TN, USA, [d]University of Colorado Denver, Aurora, CO, USA, [e]Levine Cancer Institute, Charlotte, NC, USA, [f]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA, [g]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA, [h]OncoMed Pharmaceuticals, a fully owned subsidiary of Mereo BioPharma, Redwood City, CA, USA, [i]The University of Oklahoma Stephenson Cancer Center, Oklahoma City, OK, USA*

Objective: Anti-VEGF and anti-DLL4 have both demonstrated single-agent activity in ovarian cancer. Navicixizumab is an anti-DLL4/VEGF IgG2 bispecific monoclonal antibody that had a response rate of 25% (3/12) in heavily pretreated ovarian cancer patients in an earlier single-agent phase 1a trial. This is an ongoing phase 1b study designed to assess the safety and efficacy of paclitaxel and navicixizumab in platinum-resistant ovarian cancer patients who received at least 3 prior therapies and/or bevacizumab.

Method: Paclitaxel 80 mg/m^2 was given on days 1, 8, and 15, and navicixizumab was given on days 1 and 15 of every 28-day cycle. This study was designed as a dose escalation trial assessing navicixizumab doses of 3 or 4 mg/kg followed by an expansion cohort. The expansion cohort was undertaken with 3 mg/kg of navicixizumab as higher doses did not show increased activity, but did result in more pronounced chronic toxicity in the phase 1a study. A standardized treatment algorithm for hypertension is being employed.

Results: Forty-four patients were treated; 5 are still ongoing. The median number of prior therapies was 4 (range 2–12). All 44 patients had received prior paclitaxel; 68% had received bevacizumab; and 41% had received a PARP inhibitor. One patient (2%) had a RECIST 1.1 complete response; 18 patients (41%) had a partial response; 15 (34%) had stable disease; 7 (16%) had progressive disease; and 3 (7%) were NE. The clinical benefit rate was 77%. Twenty-four of 36 (75%) patients with an elevated CA-125 had a GCIG-defined response. The median duration of response was 5.7 months, and the median time to progression was 7.3 months. The related adverse effects (all grades) that occurred in >15% of the patients were hypertension (68%), fatigue (48%), headache (27%), neutropenia (21%), pulmonary hypertension (18%), and diarrhea (16%), Other related adverse events of significance were infusion reaction (9%), grade 4 thrombocytopenia (2%), and grade 4 gastrointestinal perforation (2%). Antidrug antibody was detected in 4 of 25 patients who have been evaluated and had at least 1 follow-up ADA sample; drug exposure was affected in 3 patients.

Conclusion: These interim efficacy data in heavily pretreated platinum-resistant ovarian cancer patients are encouraging. The safety profile appears to be manageable with hypertension being the most common adverse event related to navicixizumab. Final data will be presented.

27 - Scientific Plenary

A randomized phase II evaluation of weekly gemcitabine plus pazopanib versus weekly gemcitabine alone in the treatment of persistent or recurrent epithelial ovarian, fallopian tube or primary peritoneal carcinoma

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Objective: Angiogenesis inhibition is a valuable strategy for ovarian cancer (EOC). Pazopanib is a potent small molecular inhibitor of VEGF-1, -2, -3, PDGFR, c-kit, and has activity as a single agent in ovarian cancer. We designed a trial to assess the benefit of adding pazopanib to gemcitabine in patients with recurrent EOC.

Method: An open-label, randomized, multisite, phase 2 trial was conducted (NCT01610206) including patients with platinum-resistant or sensitive disease, 3 or fewer prior lines of chemotherapy, and measurable/evaluable disease. Patients were randomly assigned to weekly gemcitabine 1,000 mg/m^2 on days 1 and 8 of a 21-day cycle, with or without pazopanib 800 mg QD, stratified by platinum sensitivity and number of prior lines (1 vs 2 or 3). The primary endpoint was progression-free survival (PFS).

Results: A total of 148 patients were enrolled 2012–2017. Median age was 63 years (30–82 years); 60% were platinum-resistant; and surveillance was 13 months (0.4–54 months). Median PFS was 5.3 (95% CI 4.2–5.8) versus 2.9 months (95% CI 2.1–4.1) in the gemcitabine arm. The PFS effect was most pronounced in the platinum-resistant group (5.32 *vs* 2.33 months Tarone-Ware, $P < 0.001$). There was no difference in overall survival (OS). Overall recurrence rate (PR 20% vs 11%, χ^2 $P = 0.02$) and DCR (80% vs 60%, χ^2 $P < 0.001$) were higher in the combination. High-grade adverse events in the combination arm included grade 3 or lower: hypertension (15%), neutropenia (35%), and thrombocytopenia (12%).

Conclusions: The addition of pazopanib to gemcitabine enhanced anti-tumor activity; those with platinum-resistant disease derived the most benefit from combination therapy, even in the setting of receiving prior bevacizumab.

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28 - Scientific Plenary

Tolerability and adverse events experienced by women with ovarian cancer treated with intravenous or intraperitoneal chemotherapy plus veliparib and bevacizumab based on *BRCA* status

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Objective: Our goal is to evaluate how women, dichotomized by *BRCA* status, tolerate intravenous (IV) or intraperitoneal (IP) chemotherapy given with veliparib and bevacizumab (BEV) on a GOG phase I study (GOG 9923, NCT00989651).

Method: This is an Institutional Review Board approved, multiinstitutional, prospective study of women treated with IV carboplatin, paclitaxel, and BEV every 21 days (regimen 1), weekly IV paclitaxel with carboplatin and BEV (regimen 2), or IV paclitaxel and BEV with IP cisplatin (regimen 3). BEV was continued as maintenance in all arms. Veliparib was given with cytotoxic chemotherapy either twice daily for the entirety of each cycle (continuous) or on days −2 to 5 (intermittent). Primary endpoints of maximum tolerated dose (MTD) and recommended phase 2 dose were presented at ASCO 2019. This is an unplanned, post hoc analysis of clinical characteristics and toxicity data based on *BRCA* status. Descriptive statistics and Kaplan-Meir methods were used.

Results: A total of 424 patients were evaluable. Of these, 173 (40.8%) were treated on regimen 1, 128 (30.2%) on regimen 2, and 123 (29%) on regimen 3. The majority of patients were 50–69 years old and Caucasian and had a performance status of 0–1. Serous histology (77.6%) was most common, followed by endometrioid (7.5%) and clear cell (5.9%). Eighty-five percent of patients in regimen I had grade 4–5 toxicities; 50% in regimen 2; and 45.5% in regimen 3. Ten percent of patients treated on regimen 1, 12% on regimen 2, and 19.8% on regimen 3 were *BRCA* positive. *BRCA*-positive patients, when compared to wildtype patients, experienced similar rates of anemia (29.3% vs 27.2%, *P = 0.73*), febrile neutropenia (8.8% vs 9.1%, *P = 0.92*), abdominal pain (8.6% vs 4.8%, *P = 0.26*), colonic perforation (1.7% vs 1%, *P = 0.62*), nausea (6.9% vs 6.2%, *P = 0.85*), vomiting (5.2% vs 4.8%, *P = 0.89*), and peripheral sensory neuropathy (0% vs 1.4%, *P = 0.36*). Median progression-free survival was not significantly different between *BRCA*-positive and -negative patients (HR = 0.96, 95% CI 0.65–1.42), although this study's primary aim was not to evaluate outcomes.

Conclusion: Germline *BRCA* mutations positively affect chemosensitivity in epithelial ovarian cancer, but may also affect toxicities experienced by women with this disease. In this population with newly diagnosed ovarian cancer, however, we show that therapy is well tolerated among both *BRCA*-positive and -negative patients.

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29 - Scientific Plenary

Outcomes based on treatment regimen in newly diagnosed ovarian, primary peritoneal and fallopian tube cancer receiving intravenous or intraperitoneal platinum-based chemotherapy in combination with veliparib and bevacizumab

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Objective: Our goal was to determine whether differences in progression-free survival (PFS) or overall survival (OS) were seen in patients based on regimen of chemotherapy received among epithelial ovarian, peritoneal, or fallopian tube cancer (EOC) patients enrolled on GOG 9923, a phase I study of every-21-day carboplatin/paclitaxel (C/T), weekly C/T, or intravenous and intraperitoneal (IP) paclitaxel/cisplatin in combination with continuous or intermittent/ABT-888 and bevacizumab (BEV) in newly diagnosed previously untreated EOC.

Method: Three regimens (6 cohorts) were evaluated in this study. Each regimen had 2 subcohorts to evaluate continuous veliparib dosing twice daily PO days 1–21 or intermittent dosing twice daily PO days −2 to 5. Veliparib was administered only during chemotherapy. Regimen 1 treated patients with C/T, BEV 15 mg/kg IV day 1 (starting cycle 2). Regimen 2 used weekly C/T, BEV 15 mg/kg IV day 1 (starting cycle 2). Regimen 3 used IV/IP paclitaxel and cisplatin, BEV 15 mg/kg IV day 1 (starting cycle 2). All regimens were followed by BEV maintenance cycles 7–22. Primary endpoints of maximum tolerated dose (MTD) and recommended phase 2 dose along with adjusted PFS and OS were presented at ASCO 2019. This study evaluates oncologic outcomes separately in each chemotherapy cohort.

Results: A total of 424 patients were enrolled, 90% of whom were white and 74% of whom had serous histology. Of these, 312 (73.6%) patients had stage III disease. Fifty-nine (13.7%) patients had a *BRCA 1* or *2* mutation; 210 (48.7%) patients were *BRCAwt*; and 162 (37.6%) had unknown *BRCA* status. Ninety-one percent of patients experienced thrombocytopenia in regimen 1 compared to 59% in regimen 2 and 63% in regimen 3. Adverse events were otherwise similar in treatment groups. PFS was 24.5 and 26.1 months for regimen 1 continuous and intermittent dosing, respectively. PFS was 23.5 and 24.4 months for regimen 2 continuous and intermittent dosing, respectively. PFS was 43.2 and 39.6 months for regimen 3 continuous and intermittent dosing, respectively. OS was 65.2 and 59.9 months for regimen 1 continuous and intermittent dosing, respectively. OS was 66.5 and 67.2 months for regimen 2 continuous and intermittent dosing, respectively. OS has not been reached for regimen 3.

Conclusion: It is important to note that the primary outcome of this study was the determination of a recommended phase 2 dose of veliparib in combination with chemotherapy for EOC; however, patients receiving regimen 3 consisting of IP cisplatin + IV/IP paclitaxel showed promising PFS and OS when compared to patients receiving regimen 1 and regimen 2. Differences may be reflective of selection bias toward patients enrolled on the IP chemotherapy arm. There was not a significant difference

between continuous and intermittent dosing of veliparib.

Scientific Plenary V: Endometrial Cancer: Moving beyond grade and changing care?

16 - Scientific Plenary
How do uterine cancer NGS results impact patient outcomes?
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Objective: Our goal was to describe next-generation sequencing (NGS) outcomes for uterine malignancies to identify predictive biomarkers and response to therapies.

Method: Records of patients with a uterine malignancy and NGS testing between 2016 and 2019 at a single institution were reviewed. Extracted information included somatic mutation profile, clinical course, response to platinum therapy, and utilization of targeted therapy or clinical trial enrollment based on NGS results.

Results: NGS results were available for 106 unique uterine cancers with predominance of carcinoma to sarcoma (*n* = 83 vs 23). Most were stage I at the time of diagnosis (*n* = 42, 39.6%). A total of 92 (86.8%) patients had at least 1 targetable therapy identified with a mean of 1.94 targetable mutations per tumor. Based on NGS results, 40 patients were prescribed targeted therapy or enrolled on a clinical trial. A median of 2 lines of conventional chemotherapy were given prior to therapy based on NGS results. Nearly half (*n* = 51, 48.1%) of patients had a response to platinum-based therapy. These patients had a trend toward more mutations in *PTEN* (20 vs 11, *P* = 0.050) and the Fanconi's anemia pathway (9 vs 3, *P* = 0.11). Somatic mutation profile patterns varied across histological subtypes. The most commonly prescribed targeted therapy in this patient population was everolimus. Of these 21 patients, 47.6% had a durable response greater than 6 months with 8 patients experiencing more than 1 year of progression-free survival. Among patients with endometrioid histology, CTNNB1 was more likely to be found in low-grade disease confined to the uterus (67% vs 25%, *P* = 0.049).

Conclusion: Somatic NGS identified a targeted therapy option for the majority of uterine carcinomas and sarcomas. Pooling mutations for *PTEN* and those associated with homologous recombination provide a trend toward prediction of response to platinum therapy. Durable response was seen in patients treated with everolimus based on NGS results. The presence of CTNNB1 in low-risk endometrial adenocarcinoma may help predict risk for recurrence and therefore benefit of adjuvant therapy. Consideration of early implementation of NGS testing in patients with uterine cancer should be considered to clarify prognosis, predict response to conventional therapy, and suggest targeted therapy options that have potential for prolonged response.

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17 - Scientific Plenary
Turning ProMisE into practice: Predicting response in medically managed endometrial cancers via molecular classification
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Objective: Our goal was to determine whether molecularly classifying endometrial cancers (EC) predicts response when treated with a levonorgestrel intrauterine system (LNG-IUD).

Method: Patients treated with LNG-IUD for medical management of EC or endometrial intraepithelial neoplasia (EIN) with adequate tissue available from 2013 to 2018 were included in a retrospective study. Indications for medical management were fertility preservation and medical comorbid conditions precluding surgery. Patients were classified into 4 molecular subgroups according to the Proactive Molecular Classifier for EC (ProMisE) algorithm: polymerase-ε (POLE) mutated, mismatch repair-deficient (MMR-D), tumor protein 53 (p53) wildtype/POLE wildtype (copy-number low), and p53 abnormal (copy-number high). Immunohistochemistry was performed for mismatch repair proteins and p53. Single-gene sequencing to detect mutations in the polymerase-ε (POLE) exonuclease domain was performed. Subgroups were assessed relative to the primary outcome, months to progression/definitive therapy.

Results: We identified 48 patients with EC/EIN treated with LNG-IUD. The median age was 55.4 years (range 24–91 years); median follow-up time was 16.9 months. Twenty-six patients were diagnosed with EIN prior to LNG-IUD treatment; 20 had grade 1 endometrioid EC; 2 patients had grade 2 EC. The majority of patients (62.5%) treated with LNG-IUD had medical comorbid conditions precluding surgery. We classified 34 (71%) patients as copy-number low, 6 (12.5%) as MMR-D, 4 (8%) as

copy-number high, and 4 (8%) as POLE mutated. Of the copy-number high cases, 3/4 had EIN with strong and diffuse p53 staining consistent with a missense mutation. Twelve patients (25%) underwent definitive therapy after attempted medical management: 8 (17%) had progression, and 4 (8%) had stable disease without regression. Of those patients who progressed/underwent definitive treatment, 8/34 (23.5%) of their tumors were classified as copy-number low; 2/6 (33%) were MMR-D; 2/4 (50%) were copy-number high; and 1/4 (25%) were POLE mutated. Compared to other subgroups, copy-number high tumors had shorter time to progression/definitive therapy ($P = 0.03$).

Conclusion: Patient tumors with endometroid EC/EIN in the copy-number high subgroup demonstrate a shorter time to definitive therapy/progression when managed with LNG-IUD than tumors in other molecular subgroups. Molecular classification of EC/EIN prior to management with LNG-IUD may predict patients at increased risk of progression or needing definitive therapy.

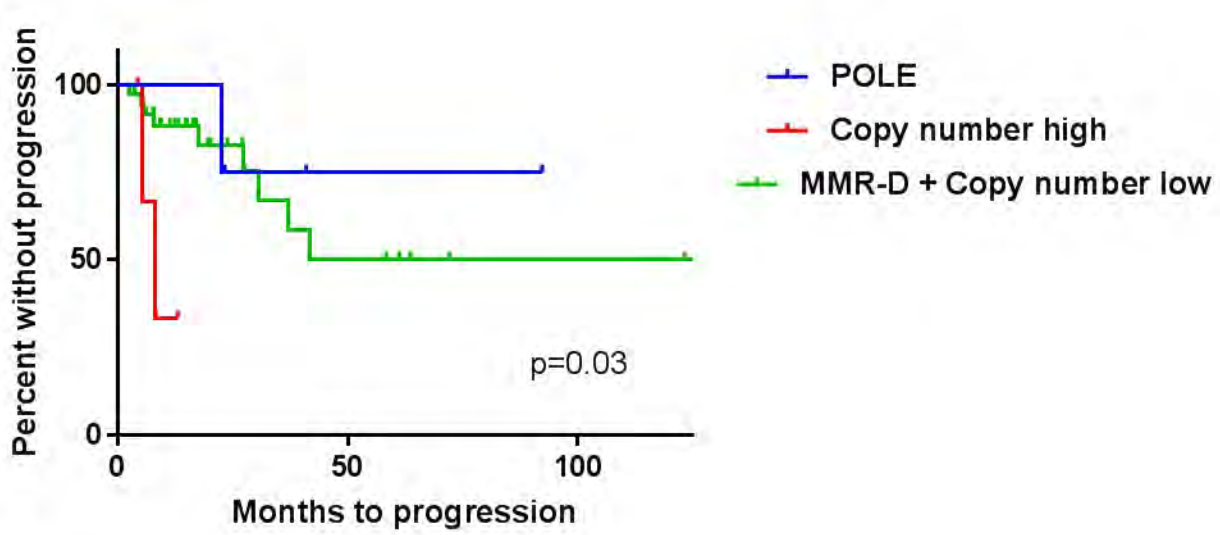

Fig. 1.

Seminal Abstracts: 2020: The Rise of PARP for all???

30 – Seminal Abstracts
Randomized phase II CLIO study on olaparib monotherapy versus chemotherapy in platinum-sensitive recurrent ovarian cancer.
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Objective: The CLIO trial (NCT02822157) evaluated Olaparib single-agent therapy versus standard-of-care chemotherapy in platinum-sensitive recurrent epithelial ovarian cancer (relapse ≥6 months after platinum-based chemotherapy) (PSOC).

Method: Eligible patients with measurable germline *BRCA* wildtype PSOC disease and ≥1 prior line of chemotherapy were randomized 2:1 to olaparib (OLA) monotherapy (300-mg tablets, BID) or physician's choice chemotherapy (CT; carboplatin AUC 5 pegylated liposomal doxorubicin 30 mg/m^2 q4w or carboplatin AUC 4 d1 gemcitabine 1,000 mg/m^2 d1 d8 q3w). Response was evaluated according to RECIST v1.1. Prior bevacizumab was allowed. Disease control rate (DCR) was defined as response or stable disease at 12 weeks

Results: A total of 60 patients were randomized 2:1 to OLA ($n = 40$) or CT ($n = 20$). Baseline characteristics, summarized in **Table 1**, were not significantly different between both arms. Objective response rate (ORR) was 40% (14/40) for OLA and 60% (12/20) for CT ($P = 0.12$). DCR was 80% (32/40) for OLA and 85% (17/20) for CT. Progression-free survival (PFS) was similar in both arms (median PFS 6.4 vs 8.5 months for OLA and CT, respectively, HR = 1.11, 95% CI 0.60–2.04, $P = 0.7$) as well as for overall survival (OS; median OS 23.9 vs 27.7, respectively, HR = 1.01, 95% CI 0.40–2.51). Adverse events in the OLA and CT arms did not reveal any unexpected events. Somatic *BRCA* testing is ongoing and will be presented at the meeting.

Conclusions: PFS and OS were similar between olaparib monotherapy and chemotherapy in recurrent germline *BRCA* wildtype platinum-sensitive epithelial ovarian cancer.

Table 1.

Baseline characteristics	**OLAPARIB**	**CHEMOTHERAPY**
Number of patients	40	20
Median age at randomization (years)	70 (IQR 63-76)	66 (IQR 58-73)
WHO score		
0	25 (62.5%)	12 (60%)
1	15 (37.5%)	8 (40%)
Histology		
High-grade serous	38 (95%)	19 (95%)
Clear-cell	1 (2.5%)	1 (5%)
Carcinosarcoma	1 (2.5%)	0 (0%)
Median months since diagnosis	34.1 (IQR 19.8-52.9)	43.3 (IQR 22-60)
Median prior lines	2 (IQR: 1-2.3, range 1-6)	2 (IQR:1-3, range 1-5-)
1	16 (40%)	7 (35%)
2	14 (35%)	5 (25%)
3	5 (12.5%)	4 (20%)
4 or more	5 (12.5%)	4 (20%)
Prior bevacizumab	21 (52.5%)	10 (50%)
Prior PARPi/placebo (in trial)	0	1 (5%)

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31 – Seminal Abstracts

Efficacy of niraparib therapy in patients with newly diagnosed advanced ovarian cancer by BRCA and homologous recombination status: PRIMA/ENGOT-OV26/GOG-3012 study

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Objectives: Niraparib improves progression-free survival (PFS) in patients (pts) with newly diagnosed advanced ovarian cancer after first-line (1L) platinum-based chemotherapy (CT). We report the efficacy of niraparib in pts by biomarker status.

Methods: This double-blind, placebo (PBO)-controlled, phase 3 study randomized 733 pts with newly diagnosed advanced ovarian, primary peritoneal, or fallopian tube cancer with a complete or partial response (CR or PR) to 1L platinum-based CT. Stratification factors were best response to the 1L CT (CR/PR), receipt of neoadjuvant CT (yes/no), and homologous recombination status (deficient/proficient/not determined). Pts received niraparib or PBO once daily. The primary endpoint of PFS assessed by blinded independent central review was analyzed using a stratified Cox proportional hazards model and hierarchically tested in homologous recombination deficient pts, then the overall population. Biomarker subgroup analysis of PFS was a prespecified exploratory analysis, and was performed using a stratified log-rank test and summarized using Kaplan-Meier methodology.

Results: Of 733 randomized pts (niraparib, 487; PBO, 246), 373 (51%) were homologous recombination deficient (niraparib, 247; PBO, 126) and 249 (34%) were homologous recombination proficient (niraparib, 169; PBO, 80). Overall, 35% had stage IV disease, 67% received neoadjuvant CT, and 31% had a PR to 1L CT. Niraparib-treated pts in all the biomarkers groups had a statistically significant and clinically meaningful benefit in PFS (Table). The most common grade ≥3 adverse events were anemia (31%), thrombocytopenia (29%), and neutropenia (13%).

Conclusions: Niraparib improved PFS as evidenced by reduction in the risk of recurrence or death due to any cause in the overall population of advanced ovarian cancer. No new safety signals were identified

Table 1.

Biomarker Subgroup	Hazard Ratio (95% CI)	*P* Value
Overall	0.62 (0.502-0.755)	<0.0001
Homologous recombination deficient	0.43 (0.310-0.588)	<0.0001
*BRCA*mut	0.40 (0.265-0.618)	<0.0001
*BRCA*wt	0.50 (0.305-0.831)	0.0064
Homologous recombination proficient	0.68 (0.492-0.944)	0.0203

mut = mutated; wt – wild type.

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32 – Seminal Abstracts

Time to first subsequent therapy (TFST) and progression-free survival 2 (PFS2) from the phase 3 randomized, double-blind PRIMA/ENGOT-OV26/GOG-3012 study in patients with newly diagnosed ovarian cancer

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Objective: Niraparib improves progression-free survival (PFS) in patients with newly diagnosed advanced ovarian cancer after response to first-line platinum-based chemotherapy. We report the key secondary endpoints of the PRIMA/ENGOT-OV26/GOG-3012 study.

Method: This double-blind, placebo-controlled, phase 3 study randomized 733 patients with newly diagnosed advanced ovarian, primary peritoneal, or fallopian tube cancer with a complete or partial response (CR or PR) to first-line platinum-based chemotherapy. Patients received niraparib or placebo once daily for 36 months or until disease progression. The primary endpoint was PFS assessed by blinded independent central review. TFST and PFS2 were key secondary endpoints.

Results: In the overall population, median TFST was 6.6 months longer in patients receiving niraparib than in patients receiving placebo (HR = 0.65, 95% CI 0.52–0.80, *P* = 0.0001; **Table 1**). In the patients with homologous-deficient tumors, median TFST had not been reached for patients receiving niraparib, compared with 13.7 months in patients receiving placebo (HR = 0.46, 95% CI 0.33–0.64, *P* < 0.0001). In patients with homologous recombination-proficient tumors, the median TFST was 3.7 months longer in patients receiving niraparib than in patients receiving placebo (HR = 0.64, 95% CI 0.46–0.90, *P* < 0.0105). PFS2 data show point estimates HR < 1, as shown in **Table 1** (20% data maturity in overall population).

Conclusion: Preliminary data on TFST and PFS2 were supportive of a clinical benefit of niraparib therapy in a broad population of patients with ovarian cancer following response to first-line chemotherapy.

Table 1.

	Homologous Recombination Deficient		**Homologous Recombination Proficient**		**Overall Population**	
Endpoint	**Niraparib (*n* = 247)**	**Placebo (*n* = 126)**	**Niraparib (*n* = 169)**	**Placebo (*n* = 80)**	**Niraparib (*n* = 487)**	**Placebo (*n* = 246)**
Time to first subsequent therapy (47% data maturity in overall population)						
Median (95% CI) – mo	NE (24.7-NE)	13.7 (11.6-19.3)	11.6 (9.7-14.2)	7.9 (6.6-10.4)	18.6 (15.8-24.7)	12.0 (10.3-13.9)
HR (95% CI)	0.46 (0.33-0.64)		0.64 (0.46-0.90)		(0.65-0.80)	
Progression-free survival 2 (20% data maturity in overall population)						
HR (95% CI)	0.84 (0.49-1.45)		0.56 (0.34-0.91)		0.81 (0.58-1.14)	

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33 – Seminal Abstracts

Phase III PAOLA-1/ENGOT-ov25: maintenance olaparib with bevacizumab in patients with newly diagnosed, advanced ovarian cancer treated with platinum-based chemotherapy and bevacizumab as standard of care

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34 – Seminal Abstracts

Maintenance olaparib plus bevacizumab (bev) after platinum-based chemotherapy plus bev in patients (pts) with newly diagnosed advanced high-grade ovarian cancer (HGOC): Efficacy by timing of surgery and residual tumor status in the Phase III PAOLA-1 trial

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Objective: In the PAOLA-1/ENGOT-ov25 (NCT01844986) trial, the addition of the PARP inhibitor olaparib to bevacizumab (BEV) maintenance therapy following first-line platinum-based chemotherapy plus BEV led to a statistically significant progression-free survival (PFS) benefit in patients with advanced high-grade ovarian cancer (HR = 0.59, 95% CI 0.49–0.72) (Ray-Coquard et al. *Annals Oncol* 2019: abst LBA2_PR). This analysis evaluates olaparib plus BEV efficacy in PAOLA-1 by timing of surgery and presence of residual tumor after surgery.

Method: PAOLA-1 is a randomized, double-blind, phase 3 trial in patients with newly diagnosed, FIGO stage III–IV, high-grade serous or endometrioid ovarian, fallopian tube, or primary peritoneal cancer. Patients had received platinum-based chemotherapy plus BEV and were in clinical complete or partial response. Patients were randomized to olaparib tablets (300 mg bid for up to 24 months) plus BEV (15 mg/kg q3w, for 15 months in total) or placebo plus BEV, stratified by first-line treatment outcome and tumor *BRCA* mutation status. PFS was assessed by investigators and blinded independent central review (modified Response Evaluation Criteria in Solid Tumors [RECIST] v1.1).

Results: A total of 537 patients were randomized to olaparib plus BEV and 269 to placebo plus BEV. Median follow-up was 22.9 months. Of these, 51% and 42% of patients had upfront and interval surgery, respectively, and 60% and 33% had no residual and residual macroscopic disease, respectively, after surgery regardless of timing (7% of patients had no surgery). For PFS, HR = 0.52 (95% CI 0.40–0.69, median 29.6 vs 18.2 months [olaparib plus BEV placebo plus BEV]) in patients undergoing upfront surgery; HR = 0.66 (0.50–0.87, median 21.4 vs 16.7 months) in patients undergoing interval surgery; HR = 0.54 (0.42–0.71, median 29.6 vs 19.3 months) in patients with no residual macroscopic disease after cytoreductive surgery; and HR = 0.63 (0.47–0.85, median 18.2 vs 12.9 months) in patients with residual macroscopic disease after cytoreductive surgery. Results of analyses combining timing of surgery, residual disease status, and/or disease stage are presented in **Table 1.**

Conclusion: Maintenance olaparib plus BEV improved outcomes compared with BEV alone in patients with newly diagnosed advanced high-grade serous ovarian cancer regardless of the timing of surgery or residual disease status after surgery. However, the magnitude of the PFS benefit is greatest when surgery achieved complete surgical debulking, particularly in the upfront setting.

Table 1.

	Median PFS, months		HR (95% CI)
	Olaparib + bev arm	Placebo + bev arm	*P* value
PFS, investigator-assessed (*n* = 806)	22.1	16.6	0.59 (0.49-0.72) *P* <0.0001
Upfront surgery and no residual disease (*n* = 245)	39.3	22.1	0.47 (0.29-0.75)
Interval surgery and no residual disease (*n* = 238)	22.1	17.7	0.61 (0.41-0.91)
Interval surgery with residual disease (*n* = 100)	18.7	12.3	0.70 (0.41-1.2)
Upfront surgery with residual disease (*n* = 164)	17.6	13.0	0.74 (0.48-1.15)
PFS, assessed by blinded independent central review (*n* = 806)	26.1	18.3	0.63 (0.51-0.77) *P* <0.0001
Stage III pts with upfront surgery and no residual disease (*n* = 211)	NR	24.9	0.45 (0.27-0.75)

Stage III pts with upfront surgery and residual disease or who had received NACT and stage IV pts† (*n* = 595)	22.0	16.6	0.65 (0.51-0.82)

NACT, neoadjuvant chemotherapy; NR, not reached

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35 – Seminal Abstracts

Population adjusted indirect comparison of the SOLO1 and PAOLA-1/ENGOT-ov25 studies of olaparib with or without bevacizumab, bev alone and placebo in the maintenance treatment of women with newly diagnosed stage III/IV ovarian cancer with BRCA mutation

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Objective: Our goal was to assess the comparative efficacy of olaparib with versus without bevacizumab, olaparib versus bevacizumab, and bevacizumab versus placebo in the maintenance treatment of newly diagnosed advanced ovarian cancer with *BRCA* mutation.

Method: An unanchored population-adjusted indirect comparison (PAIC) was performed on the endpoint of progression-free survival (PFS) (Response Evaluation Criteria to Solid Tumor [RECIST] version 1.1), according to the study investigator, using individual patient data from the SOLO1 (olaparib versus placebo phase 3 trial and pooled with individual patient data from the *BRCA* mutation subset of the PAOLA-1/ENGOT-ov25 (olaparib plus bevacizumab versus placebo plus bevacizumab) phase 3 trial. Inverse probability of treatment weights was used to match each arm of PAOLA-1 to the SOLO1 cohort, such that key baseline clinical and demographic characteristics were similar across populations. All analyses were performed in patients with complete baseline data. Weighted Cox regression analysis was performed to estimate the comparative efficacy of different treatment strategies and was supplemented by weighted Kaplan-Meier analyses.

Results: Data for 380 patients with complete baseline data from SOLO1 (*n* = 254 olaparib, *n* = 126 placebo) were pooled with data from 222 *BRCA*-mutated patients with complete baseline data in PAOLA-1 (*n* = 151 olaparib plus bevacizumab, *n* = 71 bevacizumab plus plaebo). Prior to matching, PFS at 2 years was 76% olaparib plus bevacizumab, 73% olaparib, 44% bevacizumab, and 36% placebo. The weights allocated to the PAOLA-1 cohort ranged from 0.12 to 3.98 (median 0.88), with an effective sample size of 166. The matched PAOLA-1 cohort had baseline data comparable to SOLO1, with 85% FIGO stage III, 81% complete response after first-line chemotherapy, and 75% no residual disease after surgery. **Table 1** presents the results of the matched comparison.

Conclusion: The results of the PAIC suggest that the combination of olaparib plus bevacizumab leads to a potentially meaningful improvement in PFS versus olaparib alone in women with *BRCA*-mutated newly diagnosed ovarian cancer. The relative clinical benefit of bevacizumab appears to be additive and consistent across regimens, such that its use leads to a similar level of benefit when combined with olaparib and compared with olaparib alone or used as monotherapy and compared with placebo. Despite matching, the results of this analysis should be viewed with the limitation that it is a nonrandomized comparison.

Table 1. Results of PAIC.

Regimen 1	Regimen 2	Kaplan-Meier estimate of PFS at 24 months for regimen 1 [95% confidence interval]	Kaplan-Meier estimate of PFS at 24 months for regimen 2 [95% confidence interval]	Hazard Ratio for regimen 1 versus regimen 2 [95% confidence interval]**
Olaparib plus bevacizumab*	Olaparib	82% [76% to 89%]	73% [68% to 79%]	0.71 [0.45 to 1.09]
Olaparib	Bevacizumab plus placebo*	73% [68% to 79%]	50% [39% to 64%]	0.48 [0.30 to 0.75]
Bevacizumab plus placebo*	Placebo	50% [39% to 64%]	36% [28% to 45%]	0.65 [0.43 to 0.95]

Table note: *Results based on weighted outcomes after matching tumour location status, ECOG status, FIGO stage, type of surgery (interval versus initial), residual disease status after surgery (yes or no), response to first-line treatment and age to SOLO1; **Confidence intervals generated via bootstrapping.

36 – Seminal Abstracts

Integration of veliparib (V) with front-line chemotherapy and maintenance in women with high-grade serous carcinoma of ovarian, fallopian tube, or primary peritoneal origin (HGSC)

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37 – Seminal Abstracts

Safety of veliparib in combination with chemotherapy and as maintenance in front-line ovarian cancer: Results in BRCAm, hrd, and whole populations from the velia trial

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Objective: The phase 3 VELIA trial demonstrated that veliparib dosed concurrently with carboplatin/paclitaxel and continued as maintenance monotherapy resulted in a statistically significant improvement in progression-free survival compared to carboplatin/paclitaxe alone in patients with newly diagnosed stage III–IV high-grade serous ovarian, fallopian tube, and peritoneal cancer. It has been hypothesized that while DNA repair deficiencies may improve response to PARP inhibition, they may also render patients with *BRCA* mutations *(BRCAm)* or homologous recombination-deficient (HRD) tumors more sensitive to treatment-related toxicities.

Method: Patients were eligible regardless of biomarker status and were randomized to 1 of 3 treatment arms. This analysis is limited to patients randomized to carboplatin/paclitaxel plus veliparib followed by veliparib maintenance. Patients received 6 cycles (21 days/cycle) of carboplatin (AUC 6) and paclitaxel (175 mg/m^2 q3w or 80 mg/m^2 weekly). Veliparib was continuously dosed at 150 mg BID PO with carboplatin/paclitaxel and then at 300 mg BID, increasing to 400 mg BID if tolerated, for 30 additional cycles. Patients receiving ≥1 dose of study drug were included in safety analyses. Adverse events in patients randomized to carboplatin/paclitaxel plus veliparib followed by veliparib maintenance are reported for the whole patient population, as well as for the *BRCAm* and HRD patient subsets.

Results: During the entire treatment period (combination chemotherapy and maintenance), grade 2–4 nonhematologic adverse events were predominantly gastrointestinal. Grade 3–4 hematologic adverse events included neutropenia and anemia in more than one-third of patients. Frequency of common adverse events was generally comparable in the whole population and the *BRCAm* and HRD patient subsets. Frequency of adverse events leading to dose reduction was also comparable. In the whole population, the prevalence of all-grade neutropenia, anemia, thrombocytopenia, and nausea decreased substantially from cycles 7–9 to cycles 10–12 (in which cycle 7 was the first cycle of monotherapy maintenance). See **Table 1**.

Conclusion: In VELIA, adverse event frequencies were generally similar among the whole patient population and biomarker-positive patient subsets.

Table 1. Common treatment-emergent AEs during entire treatment period (combination and maintenance) in patients randomized to veliparib in combination with C/P and continued as maintenance monotherapy.

Adverse event, *n* (%)	**Whole Population (*n* = 377)**	***BRCA*m Population (*n* = 106)**	**HRD Population (*n* = 211)**
AE leading to dose reduction	89 (23.6)	26 (24.5)	55 (26.1)
Hematologic AEs (Grade 3-4)			
Neutropenia	218 (57.8)	67 (63.2)	129 (61.1)
Anemia	144 (38.2)	39 (36.8)	80 (37.9)
Thrombocytopenia	105 (27.9)	27 (25.5)	56 (26.5)
Leukopenia	66 (17.5)	18 (17.0)	38 (18.0)

Non-hematologic AEs (Grade 2-4)			
Nausea	167 (44.3)	46 (43.4)	100 (47.4)
Fatigue	137 (36.3)	44 (41.5)	73 (34.6)
Alopecia	126 (33.4)	37 (34.9)	75 (35.5)
Vomiting	70 (18.6)	19 (17.9)	40 (19.0)
Peripheral sensory neuropathy	63 (16.7)	17 (16.0)	37 (17.5)
Urinary tract infection	61 (16.2)	16 (15.1)	32 (15.2)
Diarrhea	58 (15.4)	27 (25.5)	37 (17.5)
Constipation	47 (12.5)	17 (16.0)	30 (14.2)

Education Forum IV: PARP me now or PARP me later? Upfront treatment vs. Maintenance vs. Recurrence

38 - Education Forum

Out-of-pocket costs for PARP inhibitor treatment: Are ovarian cancer patients at risk for financial toxicity?

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Objective: PARP inhibitors offer substantial clinical benefit to ovarian cancer (OC) patients in multiple treatment settings. However, their price is considerable, and patients may be at risk for financial toxicity. For other disease sites, a $10 increase in out-of-pocket costs for oral anticancer treatment is associated with a 10%–20% increased likelihood of treatment discontinuation/delay. The amount of cost-sharing OC patients may experience while receiving PARP treatment is not well understood.

Method: OC patients who were treated from 2014 to 2017 with PARP were identified in MarketScan, a national health insurance claims database. Data were collected on demographics, type of insurance, treatment duration, out-of-pocket costs, and total costs. Treatment duration was from the first PARP drug claim to the final drug claim plus the supply duration of the final PARP prescription. Cost estimates were adjusted to 2018 dollars. The primary outcome was mean out-of-pocket cost for PARP treatment.

Results: A total of 503 patients with a mean age of 56 years were treated with olaparib (*n* = 315, 55%), niraparib (*n* = 175, 31%), or rucaparib (*n* = 82, 14%). Median PARP treatment duration was 88 days (IQR 27–199 days). Mean out-of-pocket cost for PARP was $305/month (SD $2,275, median $39). Mean out-of-pocket cost for care overall was $470/month (SD $2,407, median $125). Mean total drug cost for PARP treatment was $12,966/month (SD $17,734, median $12,718), and total cost for care overall was $20,239/month (SD $23,354, median $15,307). Most patients (65%) had conventional insurance (HMO, PPO); 18% had a high-deductible plan. The out-of-pocket cost for PARP treatment was similar for those with high-deductible (median $41/month) or conventional coverage (median $39/mo).

Conclusion: OC patients experienced high out-of-pocket costs for PARP treatment. Substantial variation in the out-of-pocket patients' experience was also observed, suggesting that some patients may be at significant risk for financial toxicity. In addition to drug costs, overall health care spending by patients and third-party payers for PARP treatment was also very high. Cost-sharing may be an obstacle to some patients receiving this highly effective treatment. The effect of cost-sharing for PARP on treatment adherence, oncologic endpoints, and social outcomes is unknown.

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39 - Education Forum

Upfront maintenance with anti-vascular versus PARP inhibitors in advanced ovarian cancer: A cost-effective analysis

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Objective: Our goal was to evaluate the cost-effectiveness of upfront maintenance bevacizumab versus niraparib versus olaparib in advanced-stage ovarian cancer patients.

Method: Markov models were established based on GOG 218, SOLO1, PRIMA, and PAOLA-1. Incremental cost-effectiveness ratios (ICERs) were estimated based on progression-free life-year saved (PF-LYS).

Results: In wildtype *BRCA* patients, the estimated cost of chemotherapy is $535/cycle; chemotherapy + bevacizumab is $10,092/cycle for 6 cycles and $9,557/cycle for 14 (median) maintenance bevacizumab cycles. With an estimated 6-month improvement in PFS, the ICER of bevacizumab was $416,051 PF-LYS. The estimated cost of niraparib is $14,750/month for maintenance therapy. Since most patients were unable to tolerate full dose, we calculated niraparib at the lower dose of 200 mg at a cost of $9,883/month. Based on hypothetical results of PRIMA with a 6- 12-, or 24-month improvement in PFS for *wtBRCA*, the ICER of niraparib would be $707,976, $353,988, or $176,994, respectively. In the *mBRCA* patients, the estimated cost of olaparib is $16,178/month for 2 years of maintenance based on SOLO1. With an estimated 48-month improvement in PFS, the ICER of olaparib would be $96,000 PF-LYS. With hypothetical results of PRIMA at 36-, 48-, or 60- month improvement in PFS for *mBRCA* patients, the ICER of niraparib (200 mg) would be $117,996, $88,497, or $70,798, respectively. Using hypothetical results of PAOLA-1 at a 36-, 48-, or 60-month increase in PFS, the ICER of bevacizumab combined with olaparib would be $347,428, $270,222, or $221,090 PFS-LYS, respectively. After the ESMO presentations, a precise model will be generated according to the actual PFS gain associated with molecular signatures: *BRCA* vesus HRD-non-*BRCA* versus signature negative.

Conclusion: Maintenance with targeted therapies in advanced ovarian cancer can be cost-effective, particularly with companion biomarker guidance.

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40 - Education Forum

Just OK is not OK: How well does PARP inhibitor frontline maintenance therapy need to work in biomarker negative ovarian cancer for universal treatment to represent a value-based therapeutic option?

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Objective: Media coverage of clinical trials evaluating PARP inhibitor (PARPi) frontline maintenance therapy (FMT) for women with advanced ovarian cancer has reported a progression-free survival (PFS) benefit regardless of biomarker status. It is uncertain whether the benefits derived from universal PARPi FMT will enhance outcomes for all patients relative to the cost of delivery. We aimed to determine whether a PARPi for all rather than a biomarker-based FMT approach represents a feasible value-based care strategy.

Method: A Markov-based decision model simulating the publicly available study designs of the PAOLA-1, VELIA, and PRIMA trials was used to evaluate the cost-effectiveness of 2 PARPi FMT strategies: (1) MT until progression for all (PARPi for all) and (2) biomarker-based MT only for germline/somatic *BRCA* mutations and HRD + tumors (BBMT). The primary outcome was the improvement in PFS with PARPi FMT in the biomarker-negative cohort that would be necessary to render a PARPi-for-all strategy cost-effective in each trial. The effectiveness outcome was PFS; costs and toxicities of MT were incorporated. Cost-effectiveness was reported as the incremental cost-effectiveness ratio (ICER) in U.S. dollars/quality-adjusted life-year (QALY) gained.

Results: PARPi for all was more costly and more effective than BBMT in all three trials. PARPi for all in PRIMA was associated with $321,214/QALY compared to BBMT, while PAOLA-1 and VELIA demonstrated $400,569/QALY and $562,691/QALY, respectively. At current drug costs, the HR for PARPi benefit in the biomarker-negative cohort must be <0.4 for niraparib and <0.23 for olaparib to make PARPi for all cost-effective. Veliparib would need to cost $7,500/month or less for a HR < 0.25 to render universal PARPi cost-effective. These results are insensitive to changes in assumptions about the effectiveness of each PARPi in biomarker-positive patients and relatively insensitive to the proportion of high-grade serous cancers that are biomarker-positive.

Conclusion: Universal PARPi FMT can be cost-effective only if biomarker-negative patients achieve an improvement in PFS approaching that seen in biomarker-positive patients. These results highlight the importance of reporting the effectiveness of PARP inhibitors in the cohort that is biomarker-negative.

Education Forum VI: Rare Tumors: Emerging Therapies and Challenges in Trials

41 - Education Forum

MILO/ENGOT-ov11: Phase-3 Study of Binimetinib versus Physician's Choice Chemotherapy in Recurrent or Persistent Low-grade Serous Carcinomas of the Ovary, Fallopian Tube, or Primary Peritoneum

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Objective: Low-grade serous ovarian carcinomas (LGSOC) have historically low chemotherapy responses. Alterations affecting the MAPK pathway, most commonly KRAS/BRAF, are present in 30%–60% of LGSOC. A phase II study of the MEK inhibitor selumetinib showed promising response rate of 15% in LGSOC, and binimetinib, a potent MEK1/2 inhibitor, has demonstrated activity across multiple cancers.

Method: MILO (MEK-inhibitor in low-grade serous ovarian cancer)/ENGOT-ov11 was an open-label, 2:1-randomized study of binimetinib (45-mg BID) versus PCC in LGSOC. Eligible patients had recurrent or persistent measurable LGSOC following ≥1 prior platinum-based chemotherapy, ≤3 prior chemotherapy lines, and no prior MEK or BRAF inhibitor. The primary endpoint was progression-free survival (PFS) by blinded central review; additional assessments were overall survival (OS), overall response rate (ORR), duration of response (DOR), clinical-benefit rate, biomarkers, and safety.

Results: A total of 303 patients were randomized (201 binimetinib, 102 PCC). Median PFS was 9.1 months (95% CI 7.3–11.3) for binimetinib and 10.6 months (95% CI 9.2–14.5) for PCC (HR = 1.21, 95% CI 0.79–1.86, closed early for futility). Secondary efficacy endpoints were similar in the 2 groups: ORR = 16% (complete/partial responses, CR/PRs, 32) versus 13% (CR/PRs =13), median DOR 8.1 months (range 0.3–12.0+ months) versus 6.7 months (0.3–9.7+ months), and median OS 25.3 versus 20.8 months for binimetinib and PCC, respectively. Safety results were consistent with known safety profile of binimetinib; most common grade ≥3 events were blood CK increased (20%) and hypertension (20%). Post-hoc analysis suggests a possible association between KRAS mutation and response to binimetinib.

Conclusion: Although MILO did not meet its primary endpoint, binimetinib showed activity in LGSOC across the efficacy endpoints evaluated. Chemotherapy responses were higher than predicted. Further evaluation is warranted.

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42 - Education Forum

A Randomized Phase II/III Study to Assess the Efficacy of Trametinib in Patients with Recurrent or Progressive Low-Grade Serous Ovarian or Peritoneal Cancer

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Objective: Low-grade serous carcinoma of the ovary/peritoneum (LGSOC) is a rare subtype, accounting for 5%–10% of all serous cancers and is characterized by alterations in the MAPK pathway, relative chemoresistance, and prolonged overall survival (OS) compared to high-grade serous carcinoma. NRG Oncology in the United States and the National Cancer Research Network (NCRN) in the United Kingdom collaborated on a phase II–III trial to assess the efficacy of a MEK inhibitor trametinib (TRAM) compared to physician's choice standard of care (SOC) in recurrent LGSOC.

Method: Patients were randomized 1:1 to receive either TRAM 2 mg daily or 1 of 5 SOC options (weekly paclitaxel, PLD, topotecan, letrozole, or tamoxifen) until disease progression. Patients who progressed on SOC were allowed to cross over to TRAM. The primary objective tested the progression-free survival (PFS) superiority of TRAM versus SOC. Secondary objectives included toxicity, quality of life (QOL), and objective response rate (ORR) by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Exploratory objectives were OS and PFS and ORR after crossover. PFS and OS curves were estimated using the Kaplan-Meier method and compared by a 1-sided, $\alpha = 0.025$ log rank test.

Results: A total of 260 patients (48.1% had >3 prior lines of therapy) were enrolled between February 2014 and April 2018. Median follow-up was 31.4 months. PFS was significantly improved for TRAM compared to SOC (median 13.0 vs 7.2 months, HR = 0.48, 95% CI 0.36–0.64, $P < 0.0001$). ORR was 26.2% for TRAM versus 6.2% for SOC (OR = 5.4, 95% CI 2.39–12.21, $P < 0.0001$). Response duration for TRAM was significantly better than that for SOC (median 13.63 months, 95% CI 8.08–18.76, vs 5.88 months, 95% CI 2.76–12.19). Preliminary analysis of QOL patient-reported outcomes shows no significant therapy effects. Main grade >3 adverse events in TRAM versus SOC were hematologic toxicity (13.4% vs 9.4%), gastrointestinal toxicity (27.6% vs 29%), skin toxicity (15% vs 3.9%), and vascular toxicity (18.9% vs 8.6%). Median OS for TRAM versus SOC was 37.0 months (95% CI 30.3–NE) versus 29.2 months (95% CI 23.5–51.6) (HR = 0.75, 95% CI 0.51–1.11). For 88 patients who crossed over to TRAM, median PFS was 10.8 months (95% CI 7.3–12.0), and ORR was 15% (95% CI 0.07–0.22).

Conclusion: Compared to physician's choice SOC, TRAM was associated with significantly improved PFS and ORR in women with recurrent LGSOC.

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Phase II study of enzalutamide in androgen receptor positive (AR+) recurrent high-grade and low-grade serous ovarian cancer

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Objective: This was a single-institution, phase II, Simon 2-stage with safety lead-in study of the oral androgen-receptor (AR+) antagonist, enzalutamide, in patients with recurrent AR+ ovarian cancer with measurable disease and 1–3 prior lines of chemotherapy. The primary objective was to determine the proportion of patients surviving progression free for 6 months (PFS6) and overall response rate by Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria, with 7/58 responses or PFS6 of 13 being considered a positive study.

Method: Following consent, archival tissue was screened for AR+ by immunohistochemistry with ≥5% considered positive. Enrolled patients were treated with enzalutamide 160 mg po daily until progression of disease or treatment discontinuation. A cycle was 28 days. Adverse events were graded by Common Terminology Criteria for Adverse Events (CTCAE) V 4.0.

Results: Between November 2013 and July 2018, 160 patients were screened, and 59 patients (45 high-grade serous [HGS], 14 low-grade serous [LGS]) consented to treatment on the study (1 patient was replaced; efficacy cohort = 58, safety cohort = 59). There were 1 confirmed and 1 unconfirmed partial responses (PR); PFS6 was 22% (90% CI 15.1%–100%) with PFS6 for those with HGS 19.8% (90% CI 12.7%–100%) and for LGS 38.5% (21.7%–100%). Median PFS was 3.5 months. There were no toxicities >grade 3 related to the study drug. Related grade 3 toxicities occurred in 6 patients (1 fatigue, 2 rash, 1 hypertension, 1 anemia, and 1 transaminase elevation).

Conclusion: The study met its primary endpoint, with 13 patients (22%) remaining progression free at 6 months. However, the response rate was low. Enzalutamide was well tolerated and may offer a well-tolerated treatment option in select patients.

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44 - Education Forum

Phase II study of pembrolizumab for high-grade neuroendocrine tumors of the cervix and vulva

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Objective: The aim of this study was to investigate the efficacy and safety of pembrolizumab in women with metastatic high-grade neuroendocrine tumors of the lower genital tract.

Method: This was a prespecified cohort of an open-label, investigator-initiated phase II basket trial of pembrolizumab in patients with rare tumors. Patients must have failed prior treatment in the past 6 months before study enrollment. Patients were enrolled from August 2016 to October 2018. The primary endpoint was nonprogression rate (NPR) at 27 weeks. Subjects were evaluated every 9 weeks (3 cycles) with radiographic imaging to assess response to treatment.

Results: Seven patients (6 cervix, 1 vulva) were included in this cohort. No patients met the primary endpoint of nonprogression at 27 weeks. At first radiologic assessment, 1 patient had stable disease while 6 patients had progression. The single patient with stable disease at 9 weeks went on to have disease progression at 14 weeks. The median progression-free survival was 2.1 months (range 0.8–3.3 months). Severe treatment-related adverse events (≥grade 3) were seen in 2 of 7 patients (29%). One patient had asymptomatic elevation of serum alkaline phosphatase, while the other had asymptomatic elevation of serum alanine aminotransferase.

Conclusion: Pembrolizumab alone showed minimal activity in women with high-grade neuroendocrine tumors of the lower genital tract. Treatment was well tolerated in the majority of study participants with low rate of severe adverse events.

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45 - Education Forum

A phase IB trial of paclitaxel and carboplatin + galunisertib in patients with uterine and ovarian carcinosarcoma

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Objective: The aim of this study was to determine the feasibility of delivering 4 cycles of paclitaxel/carboplatin in combination with galunisertib to patients with gynecologic carcinosarcoma.

Method: Patients with newly diagnosed or recurrent stage I–IV carcinosarcoma of the uterus, ovary, fallopian tube, or peritoneum who were otherwise candidates for combination paclitaxel/carboplatin were included. Intravenous paclitaxel/carboplatin was given in 28-day cycles with galunisertib 150 mg orally twice daily on days 4–17. The primary objective was to determine feasibility of galunisertib with receiving 4 cycles of paclitaxel/carboplatin. Secondary objectives included adverse event frequency and progression-free survival (PFS). The exploratory objective was to determine whether H-score criteria of nuclear phospho-smad levels after cycle 1 are associated with response to galunisertib therapy.

Results: All 20 planned patients have been enrolled. Eighteen had newly diagnosed disease; 75% were stage III–IV; 18/20 patients received 4 cycles of galunisertib with paclitaxel/carboplatin; 2 patients had disease progression before this time point and were removed from study. Best response was 5% complete response, 20% partial response, 25% stable disease, 20% progressive disease, and 30% not yet evaluable. Median PFS has not yet been reached. Of these patients, 30% had ≥grade 3 adverse events, most frequently including urinary tract infection, venous thromboembolism, dyspnea, and pneumonia. One patient died from interstitial pneumonitis attributed to underlying lung disease. Translational work is underway.

Conclusion: Galunisertib was well tolerated with paclitaxel/carboplatin for patients with gynecologic carcinosarcoma. Results of pre- and post-treatment biopsies will be correlated with response to therapy.

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Genomic landscape, clonal evolution and chemoresistance of ovarian yolk sac tumors: Data from Chinese national center of rare diseases

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Objective: The aim of this study was to investigate the genomic landscape, evolutionary pattern, and chemo-resistance-related mechanism of ovarian yolk sac tumors (YSTs).

Method: We performed whole-exome and transcriptome sequencing on 43 tumors and germline DNA samples from 30 patients with ovarian YSTs, which were categorized as chemo-sensitive or chemo-resistant groups. Meanwhile, we established a three-dimensional organoids model from YST patient biopsy specimens and investigated the function of the top 5 mutation genes by using CRSISPR-Cas9 knockout, invasion, migration, wound healing, and tumor clone formation. Moreover, patient-derived xenografts (PDXs) were applied for further validation in vivo.

Results: Ovarian YSTs exhibited a moderate level of mutational burden, which was very similar to that of ovarian epithelial cancer, but significantly higher than that of testicular germ cell tumors. Tumor mutation burden of relapse samples is significantly higher than that of primary samples. And the microsatellite instability score of primary samples in the chemo-resistant group was significantly higher than that in the chemo-sensitive group. More than half of primary YSTs were detected missense or frame shifting mutations in genes of neuroblastoma breakpoint family (NBPF), in which NBPF10 showed the highest mutation frequency of 24%. Knockout of NBPF10 enhanced YST tumor cell lines (NOY1) migration and invasion. Three-dimensional organoids results showed that the deficient of NBPF10 increased tumor clone formation, which was further confirmed by PDXs in vivo. *TP53* and *KRAS* alterations were present exclusively in the chemo-resistant group and detected in only 2 patients with Swyer syndrome. Clonality analysis revealed relapsed YSTs evolved either from 1 of the subclones of primary tumors at very early time or new clones emerged after initial treatments.

Conclusion: Our sequencing data of YSTs indicated differences in mutational profiling between primary and relapsed tumors. *NBPF10* may have acted as 1 of the driver genes, promoting tumorigenesis. We also confirmed that *TP53* alterations were associated with chemotherapy resistance, which was previously reported in testicular germ cell tumors. Two different clonal evolution patterns suggested different mechanisms of chemo-resistance and a multistep process causing YST recurrence.

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Response to first-line single agent chemotherapy impacts subsequent response to second-line therapy in low-risk gestational trophoblastic neoplasia

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Objective: The aim of this study was to compare outcomes for patients with low-risk gestational trophoblastic neoplasia (GTN) based on initial response to first-line single agent chemotherapy.

Method: This was a retrospective study of low-risk GTN cases treated at a regional trophoblastic disease reference center over 45 years. Patients failing to achieve a normal hCG with first-line therapy were defined as resistant. Patients achieving hCG remission but recurring were defined as relapse. Primary endpoints were complete remission rate with second-line therapy and time to complete remission. Univariate and multivariate analyses were performed to define prognostic factors.

Results: Among 877 low-risk GTN patients, 124 (14.8%) were resistant and 22 (2.6%) relapse. Complete remission rates with second-line therapy were similar between relapse (77.3%) and resistant (76.6%) patients ($P = 0.95$), but resistance was associated with a longer time to reach complete remission (median 8.3 weeks vs 4.9 weeks, $P = 0.024$). In multivariate analysis, the only significant prognostic factors for time to second-line remission were primary chemoresistance (HR = 0.37, 95% CI 0.16–0.86, $P = 0.02$), hCG at second-line ≥ 10,000 IU/L (HR = 0.44, 95% CI 0.21–0.92, $P = 0.03$), and number of chemotherapy cycles (HR = 0.73, 95% CI 0.63–0.85, $P < 0.001$). With additional lines of therapy, durable complete remission rates for relapse and resistant patients rose to 90.9% (20/22) and 99.2% (123/134), respectively ($P = 0.059$), without significant differences in overall time to complete remission. See **Figure 1**.

Conclusion: Second-line therapy for resistant or relapse low-risk GTN is able to achieve complete remission in a large percentage of patients. Although time to complete remission for relapse disease was shorter than that for resistant disease, relapse disease had a lower rate of overall remission. Further study to understand the biologic differences between resistant and relapse disease is warranted.

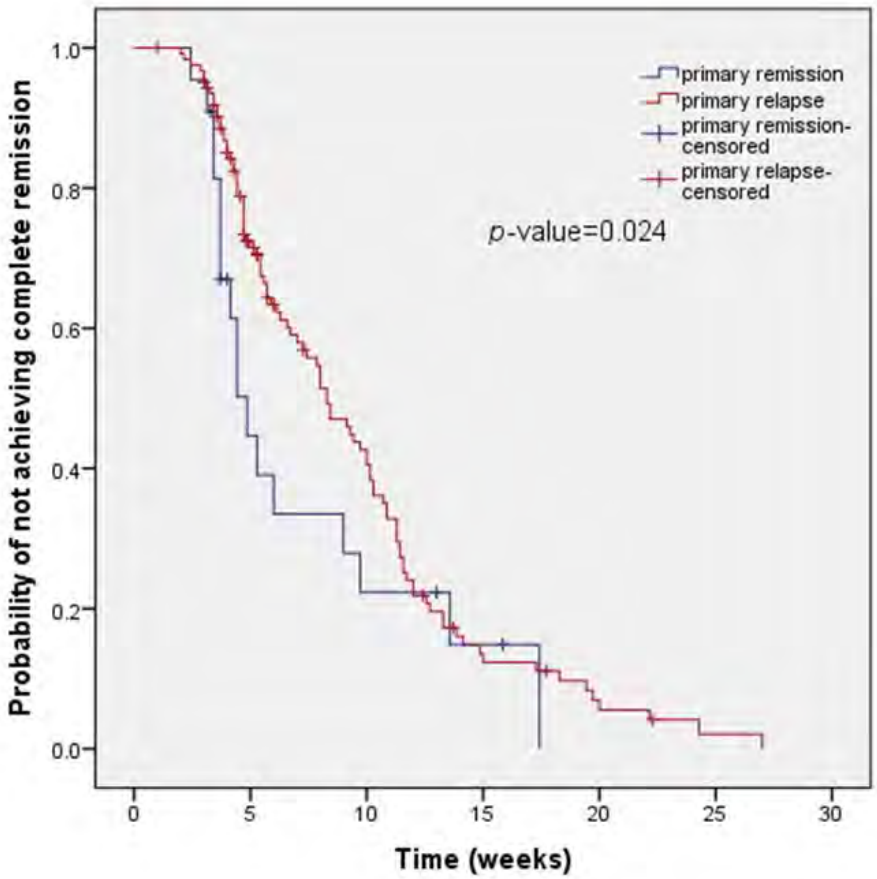

Fig. 1.

Featured Poster Session I

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Isolation of ovarian cancer circulating tumor cells using an epitope independent microfluidic cell capture device and their interrogation using a multiplex gene expression assay or immunofluorescence

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Objective: The current study was designed to evaluate the ability of an epitope independent microfluidic cell capture device to isolate circulating tumor cells (CTCs) from the blood of women with stage III–IV high-grade serous ovarian cancer (HGSOC) that could subsequently be evaluated using either a highly multiplexed gene expression assay or by immunofluorescence (IF).

Method: Blood from 37 HGSOC patients and 38 healthy women was collected into 10-mL K_2EDTA vacutainers and either processed within 8 hours of collection or stored at room temperature for ~96 hours before being processed. Cells captured by the Parsortix system based on their size and deformability were either eluted directly into lysis buffer for subsequent molecular evaluation or into specially designed cell capture chambers or deposited onto glass slides using a cytocentrifuge for subsequent IF staining. Lysates were processed using the HyCEAD Ziplex assay to simultaneously assess the expression levels of 48 different genes. Gene expression data were evaluated using multivariate logistic regression (MLR) and receiver operating curve (ROC) analyses. CTCs captured in the chambers or deposited on cytology slides were visualized by 4-color IF staining using a combination of epithelial-specific, ovarian cancer-related, blood cell-related markers and DAPI.

Results: The blood from the HGSOC patients and healthy women (~9 mL of blood per sample) was successfully processed through the Parsortix system up to 96 hours post blood draw, with average processing times of 71 minutes for 0- to 8-hour samples (average 2.4 hours post draw) and 91 minutes for 96-hour samples (average 94 hours post draw). Gene expression data demonstrated clear discrimination between ovarian cancer and healthy volunteer populations: MLR analysis resulted in predictive models having ROC curves with AUCs of 93.3% (4 genes, sensitivity = 88%, specificity = 86%, PPV = 85%, NPV = 89%) and 94.5% (3 genes, sensitivity = 92%, specificity = 80%, PPV = 81%, NPV = 91%) for blood samples processed within 8 and 96 hours after collection, respectively. Four-color IF evaluation identified CTCs (range 1–25) in 50% of the HGSOC blood samples tested. See **Figure 1**.

Conclusion: The present study demonstrated the ability to isolate CTCs from the blood of HGSOC patients up to 96 hours after collection. CTCs could be identified by both the multiplexed gene expression assay and 4-color IF staining.

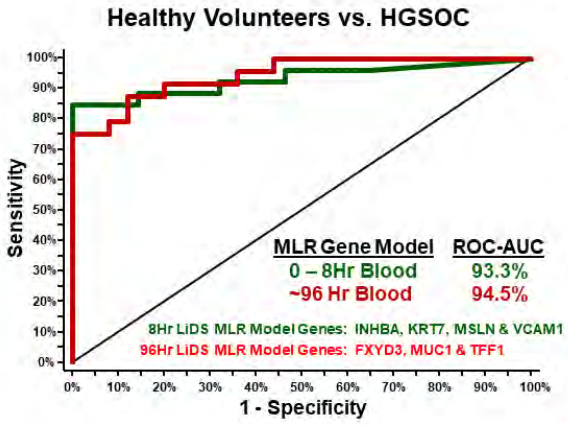

Figure 1. To the left are the Receiver Operating Characteristic (ROC) curves from multivariate logistic regression models using gene expression data from cells isolated either 0 – 8 hours after collection or ~96 hours after collection to predict presence of high grade serous ovarian cancer. Below are examples of IF stained cells captured from HGSOC patients.

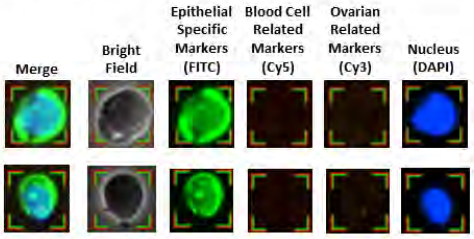

Fig 1.

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Improvement in MIA (OVA1) testing for detection of ovarian malignancy
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Objective: The aim of this study was to determine whether reflex testing of multivariate index assay (MIA) OVA1 by MIA2G (Overa) can improve specificity in detection of malignancy in women with adnexal masses. MIA consists of 5 proteins to evaluate risk of malignancy in women with adnexal masses. MIA2G consists of 5 proteins with substitution of 2 different proteins than MIA. Algorithms have been developed and FDA approved for both tests to generate a risk score.

Method: A total of 1,076 serum samples from two prospective studies of MIA (OVA1) were analyzed to determine sensitivity, specificity, and positive and negative predictive values in patients with intermediate results by reflex testing to MIA2G (Overa). Results of MIA of 5–7 in premenopausal women and 4.4–6 in postmenopausal women were reflexed to MIA2G. Of the 1,076 samples, 366 were in the borderline positive range. Results were reclassified as negative if MIA2G was less than 5. Statistics were calculated with DTCompair package.

Results: Reflex testing to MIA2G of intermediate-range MIA results improved specificity of testing to 72.01% (95% CI 68.91–75.12). See **Table 1**. Of 161 postmenopausal false positive tests, 74 reflexed to MIA2G, and of 152 false positive tests, 59 reflexed. This represents elimination of 57.5% of false positive tests of MIA.

Conclusion: Our results demonstrate that reflex testing with MIA2G can decrease false positive results in the intermediate range of MIA testing. MIA was developed to have high sensitivity in order to refer all potential cancers to gynecologic oncologists. Concerns existed that specificity was low and false positive results led to increased referrals. Reflex testing with second-generation testing has decreased false positive results without significant reduction in sensitivity. Current reports list MIA results as low risk or high risk and CA-125 results are given. If MIA is in the intermediate range, it is reported as reflexed and MIA2G results are given as well as CA-125. This provides clinicians with better information to guide surgical management or referral.

Table 1. Results Reflex Testing with MIA2G.

Menopausal Status	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
All	87.87% (83.99 - 91.75)	72.01% (68.91 - 75.12)	51.51% (46.96 - 56.06)	94.61% (92.82 - 96.40)
Pre	84.71% (77.05 - 92.36)	78.48% (74.78 - 82.18)	41.38% (34.06 - 48.70)	96.62% (94.82 - 98.42)
Post	89.30% (84.88 - 93.73)	62.73% (57.51 - 67.94)	57.59% (51.90 - 63.27)	91.19% (87.50 - 94.88

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Feasibility of using menstrual cups to detect endometrial pathology

K. Gotimer, H. Chen and V. Kennedy. *UC Davis Medical Center, Sacramento, CA, USA*

Objective: Endometrial sampling techniques are invasive and uncomfortable and require expertise to perform. Menstrual cups are capable of collecting vaginal, cervical, and endometrial secretions for cytological and pathological analysis. It is hypothesized that endometrial cells collected by menstrual cup could be used to screen for endometrial cancer and that patients may prefer this technique. The objectives of this pilot study are to evaluate the feasibility of using a menstrual cup to diagnose endometrial cancer, to compare patient-reported comfort/preference, and to obtain preliminary data to power a larger study.

Method: Patients with biopsy-confirmed endometrial cancer, scheduled to undergo hysterectomy were approached. Participants were asked to wear a menstrual cup for 3 hours. Cup contents underwent cytologic and molecular analysis. Results were compared to pathology from the original biopsy and final hysterectomy specimen. Patients completed a survey regarding comfort and acceptability of this approach.

Results: To date, 6 participants have been enrolled. Average age and BMI were 56.8 years and 32.6, respectively; 67% were postmenopausal. All reported recent bleeding; however, only 2 reported bleeding on the day of collection. The original method of diagnosis was EMB in 5 participants and D&C in 1. Four of 6 participants had abnormal cells identified on cytology collected by the menstrual cup, 2 of which were consistent with final pathology (**Table 1**). Neither of the 2 participants with adenocarcinoma identified on menstrual cup pathology reported bleeding on the day of collection. Average response for discomfort of menstrual cup insertion and removal was 2.8 (on a scale where 0 = no discomfort and 10 = extreme discomfort). Average discomfort associated with EMB/D&C was rated 5.8. Of all patients, 67% preferred the menstrual cup method to EMB/D&C.

Conclusion: Menstrual cups may provide a novel, less invasive, and more comfortable approach for the diagnosis of endometrial cancer. Endometrial pathology may be detectable even in patients who are not actively bleeding at the time of sample collection. Study recruitment and molecular analysis of samples is ongoing.

Table 1. Pathology results.

	Original diagnosis	**Final diagnosis**	**Menstrual Cup Cytology**
MC001	Grade 1 endometrioid adenocarcinoma	Stage 1B grade 1 endometrioid adenocarcinoma	NILM
MC002	Grade 1 endometrioid adenocarcinoma	Stage IIIC2 grade 3 endometrioid adenocarcinoma	NILM
MC003	Grade 2 endometrioid adenocarcinoma	Stage 1B grade 2 endometrioid adenocarcinoma	Adenocarcinoma
MC004	Grade 2 endometrioid adenocarcinoma	Stage 1A grade 3 serous carcinoma of the uterus	Atypical cells
MC005	Grade 1 endometrioid adenocarcinoma	Stage 1A grade 2 endometrioid adenocarcinoma	Rare atypical squamous cells
MC006	Grade 1 endometrioid adenocarcinoma	Stage 1A grade 2 endometrioid adenocarcinoma	Adenocarcinoma

NILM = Negative for Intraepithelial Lesion or Malignancy

104 - Featured Poster Session

Reading between the lines: The interpretation of immunohistochemical staining for mismatch repair proteins and its effect on clinical decision making in endometrial cancer

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Objective: Up to 5% of endometrial cancers (EC) are associated with germline mutations in mismatch repair (MMR) genes. Screening for Lynch syndrome (LS) may be performed using clinical screening guidelines, microsatellite instability testing, or immunohistochemical (IHC) staining for MMR proteins (MMRP). Under current College of American Pathology (CAP) guidelines, any positive IHC MMR staining should be reported as intact expression. However, tumors may exhibit partial expression of MMRP, so-called heterogenous staining. Our objective was to examine the frequency of LS in patients with EC exhibiting heterogenous staining versus complete loss of staining for MMRP.

Method: A retrospective review of 455 patients with EC who underwent a hysterectomy from 2012 to 2017 was performed. Patients with complete MMRP loss and heterogenous MMRP staining were identified. Patients' medical and family history, MLH1 hypermethylation status, and genetic test results were recorded. Statistical analysis was performed using SPSS Version 25.

Results: Of 455 patients, 92 had complete loss, 48 heterogenous (27/48 reported as heterogenous), and 315 no loss of MMRP staining. Of these, 13 (2.86%) patients were found to have LS, similar to nationally reported rates. Of patients with LS, 3/13 (23%) had heterogenous staining and 10/13 (77%) complete loss of staining. When the frequency of LS in patients with reported heterogenous staining (3/27) was compared, there was no statistically significant difference from that found in complete loss of MMRP staining (10/92, $P = 0.398$). There was also no significant difference between the groups with heterogenous and complete loss staining when separated by individual protein (MLH1/PMS2, $P = 0.349$; MSH6, $P = 0.303$). See **Table 1**.

Conclusion: Strict interpretation of IHC staining for MMRP according to current CAP guidelines may neglect patients at risk for LS. In our population, 3/27 patients with reported heterogenous MMRP staining were diagnosed with LS. All had at least 20% intact MMRP staining and would have been considered low probability risk for LS according to current guidelines. Our data suggest genetic testing for LS in patients with heterogenous IHC staining for MMRP should be considered. Current reporting guidelines regarding MMRP expression in endometrial cancer patients need to be reevaluated.

Table 1. Correlation of patterns of loss of MMR protein IHC expression with Lynch Syndrome genetic testing results.

Pattern of MMR protein loss by IHC		**Genetic testing not performed**	**Genetic testing performed**		
			Negative	**VUS**	**Positive**
No MMRP loss (n=315)		303	9	3	0
Heterogenous MMRP (n=48)					
***Heterogenous reported as intact MMRP (n=21)**		18	3	0	0
Heterogenous reported as heterogenous MMRP staining (n=27)	***MLH1/PMS2 (n=22)***				
	MLH1/PMS2 (n=12) Positive methylation	12	N/A	N/A	N/A
	MLH1/PMS2 (n=5) Negative methylation	3	1	0	**1**
	MLH1/PMS2 (n=5) Methylation not tested	1	4	0	0
	MSH6 (n=2)	0	0	0	**2**
	MSH2/MSH6 (n=3)	2	1	0	0
Complete loss of MMRP (n=92)					
MLH1/PMS2 (n=76)					
MLH1/PMS2 (n=52) Positive methylation		51	0	1	0
MLH1/PMS2 (n=3) Negative methylation		0	3	0	0
MLH1/PMS2 (n=21)		14	6	0	**1**

Methylation not tested				
MSH6 (n=11)	1	3	1	**6**
MLH2/MSH6 (n=3)	0	1	0	**2**
PMS2 (n=2)	0	1	0	**1**
Total number of cases (n=455)	405	32	5	**13**
Abbreviations: IHC = immunohistochemistry; MMR = Mismatch repair; MMRP = mismatch repair protein * In accordance with guidelines, intact MMRP would not indicate need for genetic testing				

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Development of novel biomarkers for early detection of high-grade serous ovarian cancer in high-risk women using exosomal miRNAs

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Objective: The aim of this study was to identify unique circulating exosomal miRNA signatures in high-grade serous ovarian cancer (HGSC) patients with germline *BRCA1* or *BRCA2* mutations and determine the performance of each candidate miRNA in combination with CA-125 for early detection of ovarian cancer.

Methods: Plasma samples from patients with known germline *BRCA1* or *BRCA2* mutations were obtained preoperatively from women with HGSC and healthy women (controls) in accordance with an Institutional Review Board-approved protocol. Exosomal RNA was isolated from plasma, and RNAseq performed on 20 patients and 20 age-matched controls. Logistic regression model was used to classify patient and control groups based on expression of differential miRNAs. Next, candidate miRNA expressions were validated by quantitative postoperative chemotherapy (PCR) analyses on an independent cohort of plasma samples obtained from 70 patients (47 with *BRCA1* mutations and 23 with *BRCA2*) and 51 controls (37 with *BRCA1* mutations and 14 with *BRCA2*). Random forest model in glmnet R package was used to test the prediction accuracy for the validated miRNAs in combination with CA-125.

Results: Logistic regression analysis on the top 7 miRNAs (hsa-mir-378a, hsa-mir-191, hsa-let-7a-3, hsa-mir-320b-1, hsa-mir-218-2, hsa-mir-16-1, and hsa-mir-451a) identified from the training cohort achieved an area under the curve (AUC) of the receiver operating characteristic (ROC) curve equal to 0.93. Plasma from 121 patients was assessed for validation. All miRNA sequences showed decrease in Ct values in the HGSC cohort compared to healthy patients, corresponding to increased relative expression, while 6 sequences were statistically significant (Mir-378a, 40.18 vs 44.4, $P = 0.011$; Mir-191, 38.56 vs 42.9, $P = 0.037$; Let-7a-3, 38.5 vs 42.55, $P = 0.027$; Mir-320b-1, 39.29 vs 43.68, $P = 0.017$; Mir-16-1, 46.69 vs 49.23, $P = 0.030$; and Mir-451a, 33.15 vs 38.81, $P = 0.003$). Random forest model showed improved AUC of CA-125 combined with 4 of the miRNA (miR-451a, miR-16-1, miR-218-2, and let-1a-3).

Conclusion: In HGSC patients with *BRCA1/2* mutations, we have identified upregulated expression of 6 exosomal miRNA. When combined with CA-125, 4 miRNA each improve the AUC of CA-125, suggesting that these may complement the early detection of ovarian cancer in combination with CA-125 levels. Further validation in prospectively collected serial samples is ongoing.

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Metal tube combined with ultrasound-guided accurate interstitial brachytherapy for postoperative pelvic side-wall recurrences of cervical cancers: Technique and outcome

H. LIU, S. Niu Sr., X. Chen, Z. Fang and Y. Guo. *Fourth Hospital of Hebei Medical University, Shijiazhuang, China*

Objective: Our goal was to describe and evaluate the metal tube-assisted ultrasound-guided accurate interstitial brachytherapy technique (TUG-ISBT) and the clinical outcome of a transvaginal treatment without anesthesia modality for the treatment of women with postoperative pelvic sidewall recurrences of cervical cancer.

Method: Between 2016 and 2018, 16 patients with pelvic wall recurrent after primary surgery underwent TUG-ISBT in order to boost radiation doses following external beam radiotherapy (EBRT). The histologic type was squamous cell carcinoma in 14 and adenocarcinoma in 2 patients. All patients started with EBRT (45~50 Gy/25 fractions) to the planning target volume (PTV) in pelvic first, and the gross tumor volume (GTV) synchronously boosted the dose to 60 Gy. All patients received boost TUG-ISBT (24~ 28Gy/4 fractions) after external radiation. The median cumulative RT dose at implantation site (equivalent dose in 2 Gy/f; EQD2) was 97 Gy (92–100 Gy). Each implant needle, guided by ultrasound, can be placed accurately assisted by metal tube into the site of recurrent pelvic wall lesions. The needles can be implanted transvaginally without anesthesia following completion of therapy.

Results: Mean patient age was 56.2 years. The local control rate is 75%; about 12 patients achieved complete remission (Fig.1). Two of these patients developed pulmonary metastasis within 6 months after treatment despite complete local tumor disappearance. The 2-year postradiation disease-free survival rate (62.5%) has been excellent with only 4 local progress and 2 patients dead of pulmonary metastasis. The implant procedure was completed transvaginally in all patients. There were no major intraoperative complications. The multivariate analysis indicated shape of tumor brachytherapy coverage index > 0.8 and prescribed total dose > 95 Gy being positive predictors for local control.

Conclusion: Under the guidance of ultrasound, the insertion of pelvic sidewall tumors through vaginal stump can be easily realized by using metal tube. This kind of treatment pattern is quick and simple and does not require anesthesia. More aggressive treatment modalities such as higher radiation doses boosted by interstitial brachytherapy are needed for recurrences with infiltration of the pelvic wall tumor.

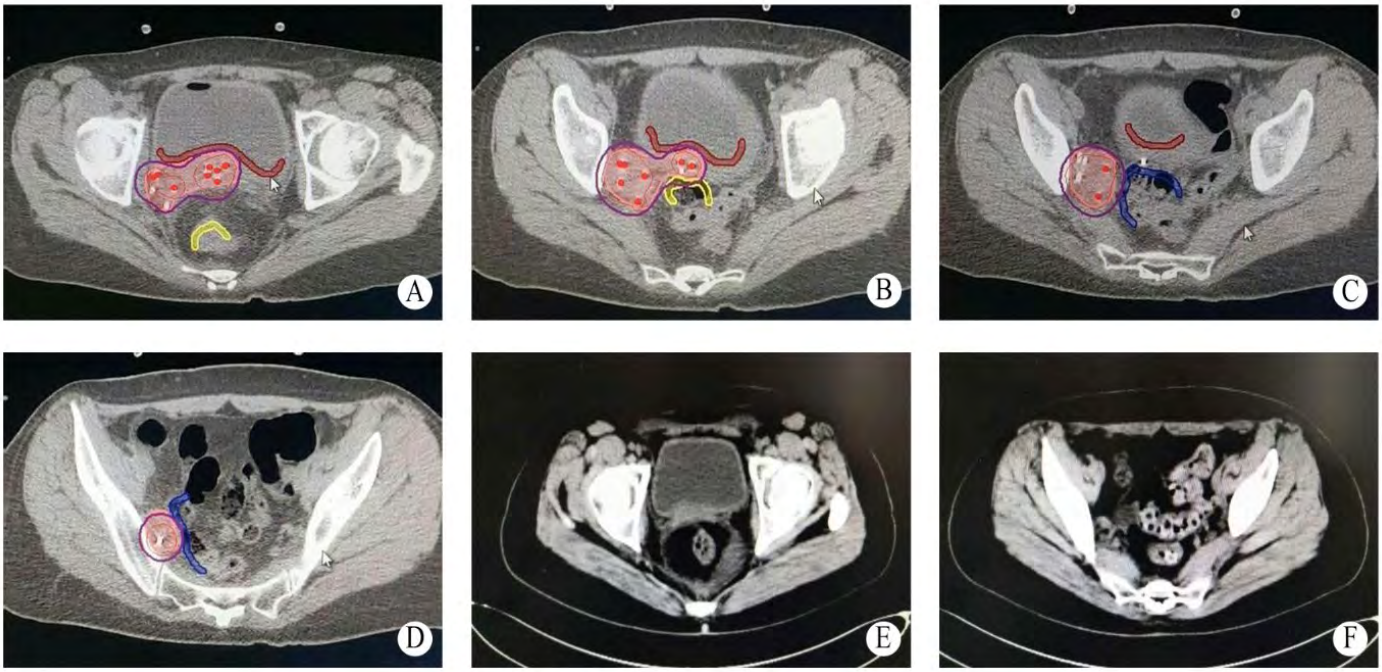

Fig. 1. (A, B, C, D) Dose distribution of interstitial brachytherapy on CT image. The red dose line is 7Gy. (E, F) Two months after radiotherapy on CT image. The tumor disappeared completely.

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Decreasing incidence of cervical cancer in United States and Taiwan: Have we left anyone behind?

W.C. Huang[a], J.K. Chan[b], D.S. Kapp[c], W.S. Liou[a] and C.I. Liao[a]. *[a]Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, [b]California Pacific and Palo Alto Medical Foundation/Sutter Health Research Institute, San Francisco, CA, USA, [c]Stanford University School of Medicine, Stanford, CA, USA*

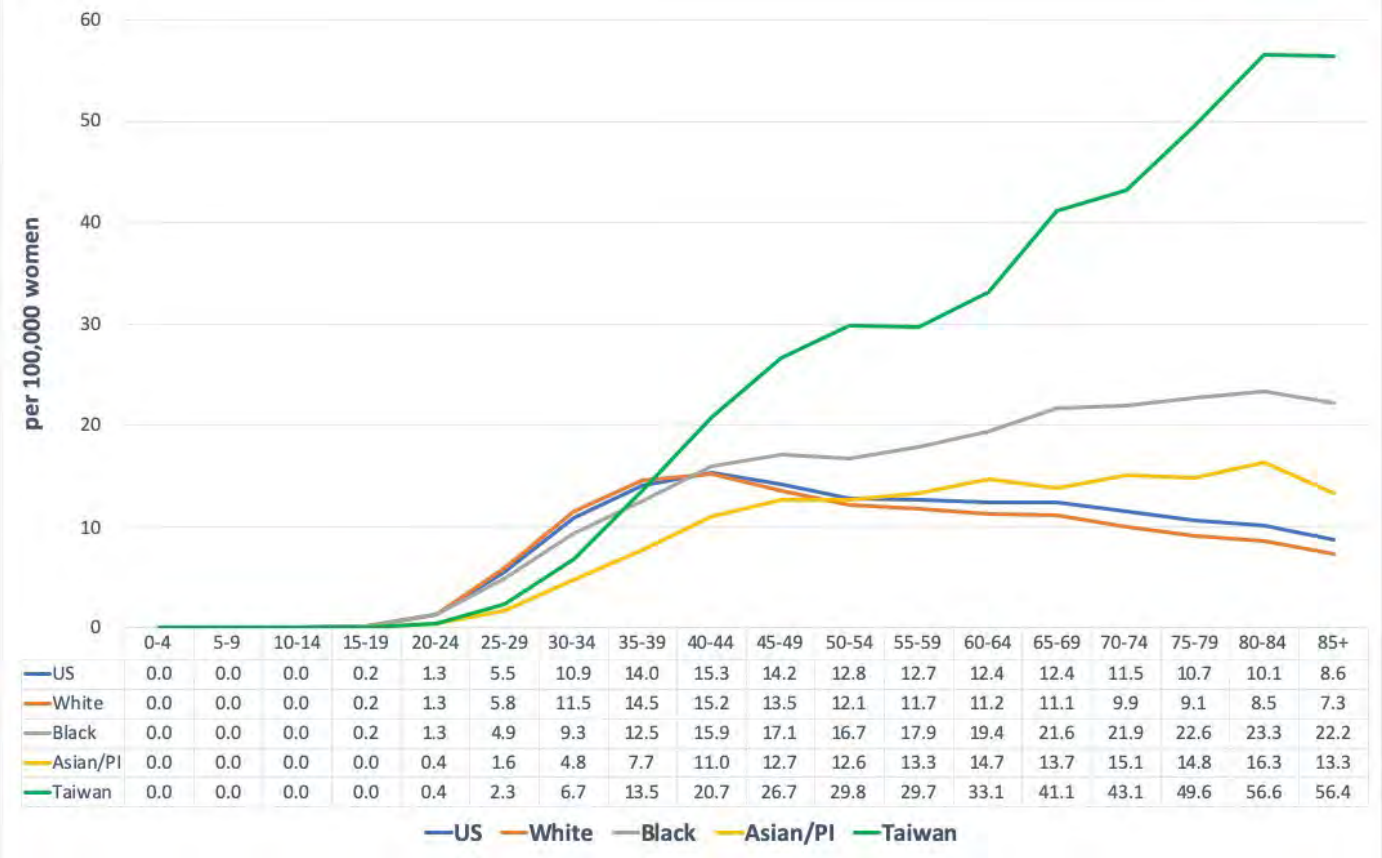
Objective: The aim of this study was to determine the differences in the trends of cervical cancer incidence in United States and Taiwan using population-based data.

Method: Cancer registries data from 2001 to 2015 were obtained by using United States Cancer Statistics (USCS) and Taiwan Health and Welfare Data Science Center (HWDC) and were adjusted by World (WHO 2000–2025) Standard Million (18 age

groups). NCI's Surveillance, Epidemiology and End Results registry (SEER) Stat 8.3.6 and Joinpoint regression programs 4.6.0.0 were used to evaluate the trends in age-adjusted cervical cancer (ICD-10 = C53) incidence expressed per 100,000 women.

Results: From 2001 to 2015, the age-adjusted incidence of cervical cancer decreased in Taiwan and the United States with average annual percentage changes (AAPC) of −6.2% and −1.0% ($P < 0.05$), respectively. Of the U.S. patients, white, black, and Asian patients had a decrease in incidence with AAPCs of −1.0%, −2.4%, and −2.7% ($P < 0.05$), respectively. With respect to cell type, there was an increase in the incidence of white patients with adenocarcinoma with an AAPC of 0.6%. ($P < 0.05$). We determined the age group at greatest rate of cervical cancer diagnosis and showed the 40- to 44-year-olds in the United States (15.3/100,000) and the 80- to 84-year-olds in Taiwan (56.6/100,000) had the highest rates. With respect to racial groups in the United States, the age group with the highest rate was 40–44 years for white patients (15.2/100,000), 80–84 years for Asian patients (16.3/100,000), and 80–84 years for black patients (23.3/100,000). See **Figure 1**.

Conclusion: The incidence of cervical cancer is decreasing in the United States and Taiwan. In the United States, the age and racial disparities in the diagnosis of white patients at a younger age compared to those for Asian and black patients suggest potential differences in screening practices, clinical presentation, and tumor biology.



	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
US	0.0	0.0	0.0	0.2	1.3	5.5	10.9	14.0	15.3	14.2	12.8	12.7	12.4	12.4	11.5	10.7	10.1	8.6
White	0.0	0.0	0.0	0.2	1.3	5.8	11.5	14.5	15.2	13.5	12.1	11.7	11.2	11.1	9.9	9.1	8.5	7.3
Black	0.0	0.0	0.0	0.2	1.3	4.9	9.3	12.5	15.9	17.1	16.7	17.9	19.4	21.6	21.9	22.6	23.3	22.2
Asian/PI	0.0	0.0	0.0	0.0	0.4	1.6	4.8	7.7	11.0	12.7	12.6	13.3	14.7	13.7	15.1	14.8	16.3	13.3
Taiwan	0.0	0.0	0.0	0.0	0.4	2.3	6.7	13.5	20.7	26.7	29.8	29.7	33.1	41.1	43.1	49.6	56.6	56.4

Fig. 1. Age-specific incidence of cervical cancer in the US and Taiwan, 2001-2015.

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Sequential use of epigenetic therapy helps to shorten duration of classic chemotherapy in the treatment of ovarian cancer and minimizes damage to normal tissue

L. Chang, J. Schweinsburg, K. Hunter, J.K. Aikins, S.A. Brown and O. Ostrovsky. *Cooper University Hospital, Camden, NJ, USA*

Objective: Combined usage of epigenetic drugs with classic chemotherapy is effective against ovarian cancer, but has adverse effects on normal tissues. We aim to determine the optimal sequence of classic chemotherapy with epigenetic drugs that target ovarian cancer and limit toxicity to normal cells. We also investigate whether epigenetic treatment can shorten the exposure to classic chemotherapy, as it is nonspecific to all rapidly dividing cells.

Method: Classic chemotherapy, paclitaxel and cisplatin, is administered in combination or in sequence with epigenetic drugs—5-azacytidine (AZA) and/or suberoylanilide hydroxamic acid (SAHA)—to the following normal cells: adipocyte-derived stem cells (ASC), primary fibroblasts (PF), and human intestinal epithelial cells (HIEC-6). The least toxic regimens to normal cells were then administered to the ovarian cancer cell lines *Caov-3*, *SKOV-3*, and *OVCAR-3*. The treatment effects on cell viability were assessed using the 3-(4,5-dimethylthiazol-2yl)-2,5-diphenyltetrazolium bromide (MTT) and cell count assays. Secretome analysis of conditioned medium collected from the treated ovarian cancer cells was performed using enzyme-linked immunospot asay (ELISA).

Results: The combination of paclitaxel and cisplatin with AZA and SAHA targeted all ovarian cancer cell lines (82%–99% cell death), but also caused significant normal cell death (66%–100%). In contrast, paclitaxel and cisplatin followed by AZA or SAHA is less toxic to ASC and PF (up to 96% viability) when compared to a tetracocktail therapy (1% viability, $P < 0.0001$). Paclitaxel and cisplatin followed by SAHA was least toxic to HIEC-6 (100% viability, $P = 0.0356$). Paclitaxel and cisplatin followed by epigenetic drugs targets ovarian cancer cells more efficiently than 2 rounds of paclitaxel and cisplatin ($P < 0.001$). Levels of VEGF and IL-6 were significantly downregulated after treatment with paclitaxel and cisplatin followed by SAHA in most ovarian cancer cells, *SKOV-3* and *OVCAR-3*.

Conclusion: Sequential treatments of classic chemotherapy with epigenetic drugs, specifically SAHA, preserve the viability of normal cells, efficiently target ovarian cancer, and also minimize exposure to classic chemotherapy.

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110 - Featured Poster Session

Photoimmunoconjugate nanoparticle, mechanism-based therapy for intraperitoneal treatment of carcinomatosis

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Objective: Photoimmunoconjugate nanoparticles (PICNP) consist of antibody-bound photosensitizers conjugated to small molecule inhibitors or other cytotoxic agents as nanoparticles. Antibody targeting achieves specificity of delivery to cancer cells. The photosensitizer may then be activated by near-infrared light to selectively induce tumor destruction mediated by mitochondrial membrane destruction conferring a pro-apoptotic state that sensitizes the cells to the cargo. In this work, we develop a novel PICNP consisting of cetuximab (anti-epidermal growth factor receptor, EGFR), benzoporphyrin derivative (BPD), and inhibitors of EP4 (EP4i)—a modulator of inflammation and the cyclo-oxygenase (COX) pathway (**Figure 1A**). EGFR is known to be upregulated in 35%–70% of ovarian cancers, and we have previously shown strong EP4 expression by immunohistochemistry in approximately 64% of serous, 40% of endometrioid, and 100% of clear cell carcinomas.

Method: Expression of EGFR and EP4 were confirmed by Western blot in ovarian cancer cell lines. Scratch assays were performed using an automated system (Biotek, Vermont). Gap closure was measured following treatment with various concentrations and combinations of PIC and EP4 inhibitor with and without *hv*. Cellular viability was assessed using MTT assays. A luciferase-based bioluminescence assay using an ovarian cancer cell line xenograft in mice was used to test effects of EP4 inhibitor on tumor burden.

Results: Most ovarian cancer cell lines over-express EGFR and EP4 (**Figure 1B**). At 18 hours, migration of OVCAR5 is impaired by both EP4i as well as the PIC, and inhibition is greatest when these agents are used in combination followed by light exposure (**Figure 1C**).Viability was not significantly affected (not shown). In mice, oral gavage twice daily with EP4i resulted in a dose-dependent decrease in tumor growth relative to control. Representative images of tumor burden are shown for control versus dose B (**Figure 1D**) and illustrated graphically over 3 weeks.

Conclusion: Photodynamic therapy using cetuximab-BPD in conjunction with EP4 inhibition impedes ovarian cancer cell migration in vitro. EP4 inhibitors reduce tumor burden in vivo. PICNPs are a promising strategy for intraperitoneal treatment at the time of primary or interval debulking. Further development of the approach is warranted and ongoing.

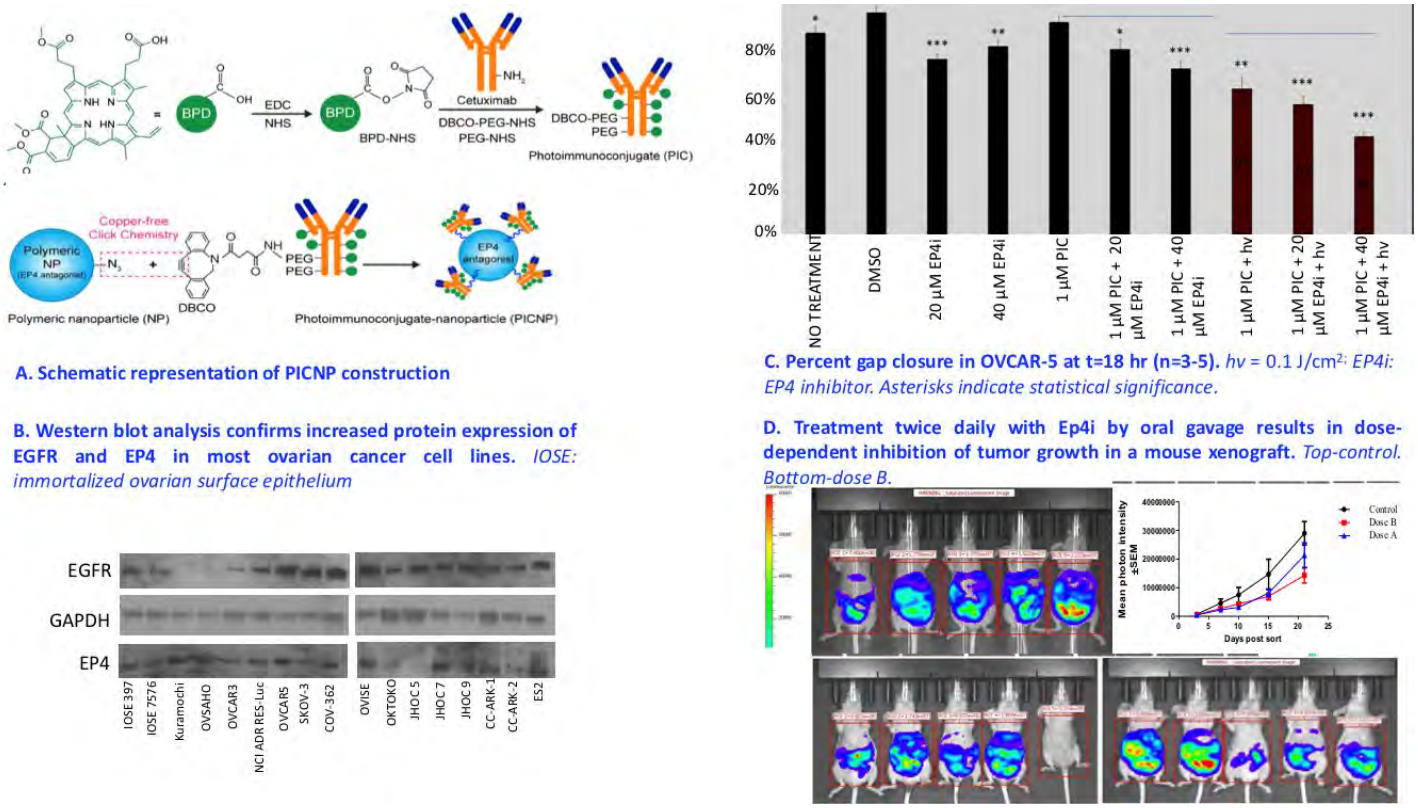

Fig. 1.

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ONC201 has anti-tumorigenic activity in obesity-driven epithelial ovarian cancer

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Objective: ONC201 is an orally bioavailable dopamine receptor 2 antagonist that has demonstrated antitumorigenic activity without significant toxicity in phase 1 and 2 trials. Thus, we evaluated the antitumorigenic effects of ONC201 in ovarian cancer (OC) cell lines and a high-grade serous OC mouse model [K18-gT$_{121}^{+/-}$; p53$^{fl/fl}$; Brca1$^{fl/fl}$ (KpB)] using both obese and lean mice.

Method: Four human OC cell lines, *OVCAR3*, *SKOV3*, *IGROV-1*, and *OVCAR5*, were used. Cell proliferation and apoptosis were assessed by MTT and cleaved caspase assays. Cell cycle was measured by Cellometer. Reactive oxygen species (ROS), JC-1, and TMRE assays were used to assess cellular stress and mitochondrial membrane potential. Adhesion and invasion were assessed by laminin and wound healing assays. KpB mice were fed a low-fat (lean) or high-fat (obese) diet. Following tumor onset, obese and lean mice were treated with vehicle or ONC201 (130 mg/kg qwk, oral) for 4 weeks. Immunohistochemistry was performed to assess signaling targets of ONC201, including mitochondrial caseinolytic protease P (ClpP) and the mTOR/MAPK pathways.

Results: ONC201 decreased cell proliferation in a dose-dependent manner in all four cell lines (IC50s 1–10 mM). Treatment with ONC201 induced cell cycle G1 arrest and increased Annexin V and cleaved caspase 3, 8, 9 activity ($P < 0.05$). ONC201 increased ROS levels and decreased JC1 and TMRE levels. ONC201 reduced cell adhesion and migration ($P < 0.05$). Obesity promoted OC tumor growth in KpB mice ($P < 0.05$). ONC201 decreased tumor weight in obese (73%) and lean (65%) mice. ONC201 decreased expression of Ki-67 and phosphorylated S6 and 42/44 and increased expression of ClpP in the OCs of obese and lean mice ($P < 0.05$).

Conclusion: ONC201 inhibited OC cell proliferation and tumor growth in obese and lean KpB mice, via effects on diverse signaling mechanisms such as the mTOR/MAPK pathways and mitochondrial ClpP. Thus, ONC201 holds promise as a novel targeted therapy in the treatment of OC.

112 - Featured Poster Session

Utilization and prognostic impact of somatic tumor testing in ovarian cancer: A single-institution experience

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Objective: Comprehensive genomic profiling (CGP) to identify potential therapeutic targets in treatment of ovarian cancer has allowed for individualized treatment approaches in a new era of personalized medicine. This analysis reflects the application of CGP in the treatment of gynecologic malignancies at our institution and reveals novel mutation patterns that may reflect differential survival outcomes in women with ovarian cancer.

Method: Between August 2016 and July 2019, 363 patients diagnosed with ovarian, fallopian tube, or primary peritoneal cancer received CGP using Foundation One or OmniSeq next-generation sequencing (NGS). Testing was obtained at provider discretion in management of recurrent or treatment-refractory disease. Patient demographics, histopathologic data, and treatment history including use of targeted therapy were retrospectively analyzed using electronic medical records. Patients with inadequate follow-up data were excluded from survival analyses. Actionable mutations were defined as alterations associated with FDA-approved therapies.

Results: A total of 363 patients were identified over this study period, with 233 patients undergoing Foundation One (FO) testing compared to 137 receiving OmniSeq. High-grade serous histology was most common in this population (72.4%, *n* = 263) followed by clear cell (5.4%, *n* = 20). *TP53* mutations were most commonly identified (70.3%, *n* = 260), while pathogenic *BRCA1/2* mutations occurred in 23.5% (*n* = 87). Statistical frequency and prognostic effect of pathogenic mutations were analyzed as a function of overall survival from test date to endpoint and are reflected in **Figure 1**. Combined FO and Omniseq data demonstrate 53% (*n* = 193) of patients had an actionable mutation, with an average of 1.5 qualifying mutations for FDA-approved therapies. PARP inhibitors were the most commonly prescribed targeted therapy due to CGP (14.8%, *n* = 54), followed by mTOR inhibitors (1.9%, *n* = 7).

Conclusion: Genomic profiling using NGS through commercially available platforms allows for identification of novel therapies in challenging treatment-refractory gynecologic cancers. Ongoing evaluation of usage patterns and patient survival as a result of CGP will become increasingly beneficial as we strive to identify women most likely to benefit from targeted therapy.

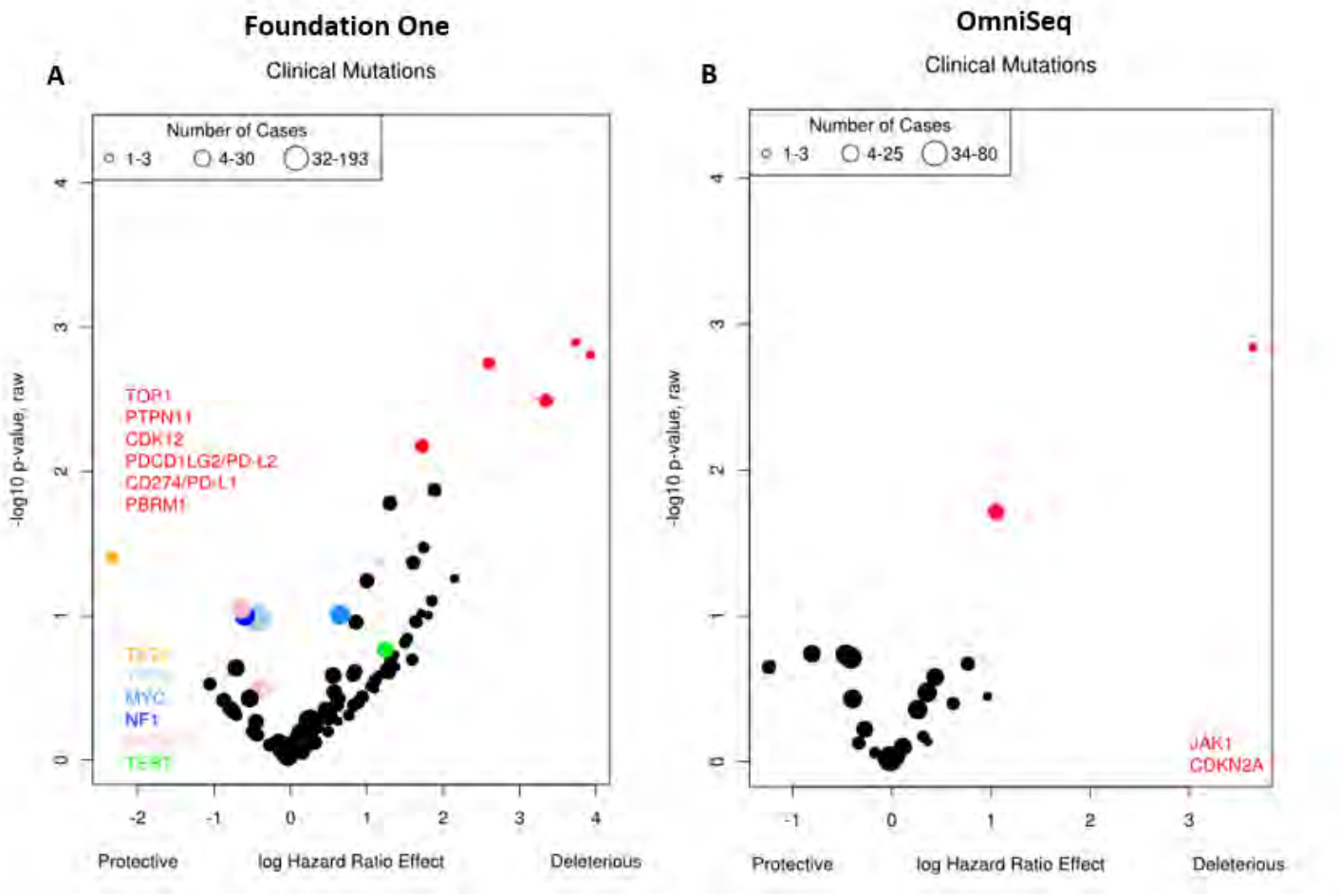

Fig. 1. Volcano plots demonstrating relative proportion, prognostic effect (x axis), and statistical significance of mutation (y axis) of clinically significant mutations. Significant mutations with greater than 1-fold increase in HR effect highlighted in red. A) Foundation Medicine -*TOP1, PTPN11, PD-L1, PD-L2 and PBRMi*. B) OmniSeq – *JAK1 and CDKN2A*.

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113 - Featured Poster Session

Patterns and adoption of *BRCA* testing in ovarian cancer in the real world: Observations from Flatiron Health

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Objective: Limited real-world information exists on *BRCA* testing among ovarian cancer (OC) patients. Given changes in available treatment options and lack of clarity regarding how to sequence germline and somatic testing, we sought to determine temporal trends, timing, and results of germline (*gBRCA*) and somatic (*sBRCA*) testing in OC patients reflective of a broad U.S. community setting.

Method: We included OC patents diagnosed from January 1, 2011, to May 31, 2018, who received front-line treatment and were followed for ≥1 year in the Flatiron Health EHR-derived database, a nationwide U.S. database comprising de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction. Lines of therapy were derived algorithmically based on dates of surgery and chemotherapy. We used descriptive statistics for all analyses.

Results: Among 1,921 front-line OC patients of all stages, 69% had ≥1 documented *BRCA* test in follow-up. Among tested patients, 68% had only *gBRCA* testing, 9% had only *sBRCA,* and 30% received >1 test in follow-up. Among patients diagnosed in 2011, 25% received a *BRCA* test within 1 year of diagnosis (*gBRCA*, 23%; *sBRCA*, 1%). In 2018, proportions increased to 69%, 61%, and 20% for any *BRCA*, *gBRCA,* and *sBRCA* test, respectively. *BRCA1* mutation (*BRCA1m*) was found in 10% of tested patients, and *BRCA2m* was found in 8% of tested patients. The majority of *BRCA1m* and *BRCA2m* were *gBRCA* (**Table 1**). Most

patients underwent testing either before (10%) or during (46%) front-line therapy. However, "catch up" testing after front-line therapy was seen. Among 1,076 patients who received second-line therapy during follow-up, 172 (16%) underwent *BRCA* testing during second-line therapy; this was the first observed test for 100 (9%) second-line patients. Among 700 patients who received third-line therapy, 81 (12%) were tested during third-line therapy; this was the first observed test for 46 (7%) third-line patients.

Conclusion: Both *gRBCA* and *sBRCA* testing among OC patients increased in the last decade, with >2/3 of patients tested within 1 year of diagnosis in 2018. Yet only 68% received any form of *BRCA* testing, and only 21% received *sBRCA* testing, suggesting missed opportunities to identify patients appropriate for targeted therapy and offer genetic counselling to family members. Further studies are warranted to understand predictors of *BRCA* testing, the optimal testing sequence and implications of testing on disease progression, treatment sequencing, and response.

Table 1. BRCA testing patterns among US OC patients treated in real world clinical practice.

	Ever	**Before 1L**	**During 1L**	**During 2L**	**During 3L**
Patients under observation in this period	**1921[1]**	**1921[1]**	**1921[1]**	**1076[2]**	**700[3]**
Total tests in this period	1793	223	1063	194	95
Patients tested in this period	1328 (69%)	201 (10%)	883 (46%)	172 (16%)	81 (12%)
The following percentages are based on all patients tested in the respective period.					
gBRCA[4] tests only	897 (68%)	172 (86%)	700 (79%)	92 (53%)	40 (49%)
sBRCA[4] tests only	115 (9%)	17 (8%)	71 (8%)	70 (41%)	34 (42%)
Both, gBRCA first	181 (14%)	5 (2%)	54 (6%)	6 (3%)	< 5 (< 6%)
Both, sBRCA first	50 (4%)	< 6 (< 2%)	25 (3%)	< 5 (< 3%)	< 5 (< 6%)
Not documented	85 (6%)	< 6 (< 2%)	33 (4%)	< 5 (< 3%)	< 5 (< 6%)
≥ 1 BRCA1m result	129 (10%)	32 (16%)	73 (8%)	17 (10%)	< 5 (< 6%)
gBRCA only	83 (6%)	28 (14%)	52 (6%)	12 (7%)	< 5 (< 6%)
sBRCA only	19 (1%)	< 5 (< 2%)	11 (1%)	< 5 (< 3%)	< 5 (< 6%)
Both gBRCA & sBRCA	15 (1%)	< 5 (< 2%)	5 (1%)	< 5 (< 3%)	< 5 (< 6%)
Not documented	12 (1%)	< 5 (< 2%)	5 (1%)	< 5 (< 3%)	< 5 (< 6%)
≥ 1 BRCA2m result	100 (8%)	20 (10%)	60 (7%)	9 (5%)	5 (6%)
gBRCA only	68 (5%)	16 (8%)	49 (6%)	< 5 (< 3%)	< 5 (< 6%)
sBRCA only	18 (1%)	< 5 (< 2%)	7 (1%)	< 5 (< 3%)	< 5 (< 6%)
Both gBRCA & sBRCA	5 (1%)	< 5 (< 2%)	< 5 (< 1%)	< 5 (< 3%)	< 5 (< 6%)
Not documented	9 (1%)	< 5 (< 2%)	< 5 (< 1%)	< 5 (< 3%)	< 5 (< 6%)

[1]All patients diagnosed 1/1/2011-5/31/2018 followed for at least 12 months who received FL treatment while in the Flatiron network.
[2]Subset of all patients for whom we observed 2L therapy
[3]Subset of all patients for whom we observed 3L therapy
[4] A test was considered germline (gBRCA) if the sample was from blood or saliva. A test was considered somatic (sBRCA) if the sample was from tissue. If sample type was unknown, we used the specific test name to determine sample type and germline vs. somatic test.

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114 - Featured Poster Session

Performance characteristics of screening strategies to identify Lynch syndrome in women with non-serous and non-mucinous ovarian cancer

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Objective: The third most common cancer for women with Lynch syndrome (LS) is nonserous/nonmucinous ovarian cancer (OC). The incidence of LS and the optimal method for identifying LS in women with newly diagnosed OC has not been determined. We compared the performance characteristics between immunohistochemistry (IHC) for MMR proteins, microsatellite instability (MSI), and family history compared to germline mutation status to determine the best strategy to identify LS in this population.

Method: Women with newly diagnosed nonserous/nonmucinous OC (*n* = 212) were prospectively recruited from 3 cancer centers in Ontario, Canada. Tumors were reflexively assessed for MMR deficiency (MMRd) by IHC and MSI. All women completed a family history assessment and underwent germline testing for mutations in the MMR pathway. The sensitivity, specificity, and positive and negative predictive values (PPV and NPV) were compared among the four screening strategies.

Results: Of 212 women, 182 had OC alone (86%), and 30 had synchronous OC and endometrial cancers (14%). Complete germline data were available for 153 women (72%). Twenty-four OC were MMRd (12%, *n* = 203); 2 (1%) were equivocal; and 18 (12%, *n* = 146) were MSI-high (MSI-H). Twenty-two (14%) met SGO 20%–25% family history criteria, and 30 (20%) met Ontario Ministry of Health criteria for genetic assessment. Twelve women (7.8%, *n* = 153) had germline mutations: 3 *MLH1*, 7 *MSH6*, 1 *MSH2,* and 1 *PMS2*. Combined IHC and MSI testing was the best screening strategy with sensitivity of 91.7%, specificity of 89.4%, PPV of 42.3%, and NPV of 99.2% (**Table 1**). MSI had the lowest performance characteristics with sensitivity of 80%.

Conclusion: The rate of MMRd in nonserous/nonmucinous OC was lower than expected; however, mutation rate is significant and warrants screening for LS. The most superior screening strategy to identify women with LS in this population is combined IHC and MSI testing and should be considered standard of care.

Table 1. Performance characteristics of screening strategies for Lynch syndrome in women with nonserous/nonmucinous ovarian cancer

Screening strategy	No.	Sensitivity (95%CI)	Specificity (95% CI)	PPV (95%CI)	NPV (95%CI)
IHC	152	83.3 (51.5-97.9)	89.3 (82.9-93.9)	40 (21.1-61.3)	98.4 (94.4-99.8)
MSI	116	80 (44.3-97.4)	92.5 (85.6-96.7)	50 (24.6-75.3)	98 (92.9-99.8)
eFHQ	115	88.9 (51.7-99.7)	82.1 (73.4-88.9)	29.6 (13.7-50.2)	98.8 (93.8-99.9)
IHC + MSI	153	91.7 (61.5-99.7)	89.4 (83.1-93.9)	42.3 (23.3-63.1)	99.2 (95.7-99.9)

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115 - Featured Poster Session

Use of a genetic navigator to maximize Lynch syndrome detection in women with endometrial and non-serous/mucinous ovarian cancer

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Objective: Despite recommendations for reflex immunohistochemistry (IHC) for mismatch repair (MMR) proteins to identify Lynch syndrome (LS), uptake of genetic counselling by those who meet referral criteria is low. Our objective was to use a multipronged approach including a genetics navigator to increase uptake of genetic testing for LS in endometrial (EC) and nonserous/mucinous ovarian cancer (OC) patients.

Method: Women with newly diagnosed EC or OC were prospectively recruited from 3 cancer centres in Ontario, Canada. Family history questionnaires (eFHQ) were used to assess LS-specific family history. Reflex IHC for MMR proteins was performed, with inclusion of clinical directives in pathology reports. A genetics navigator initiated a genetic counseling referral on behalf of the treating physician and facilitated genetic referrals to the closest genetic counseling centre (**Figure 1**).

Results: A total of 838 (643 EC, 167 OC, and 28 synchronous EC/OC) patients consented to the study; 193 (23%) were MMR-deficient by IHC (MMRd). The MMRd rate for OC was 9%; EC, 26%; and synchronous EC/OC, 39%. Overall, 162 (19%) women were eligible for genetic assessment for LS: 36 based on family history alone, 22 based on family history and IHC, 78 based on IHC alone, and 26 based on clinical discretion. After adjusting for patients who died (*n* = 5) or pending genetic counseling (*n* = 7), 137 (91%, *n* = 150) have completed genetic counseling, and 97 were offered and completed genetic testing. Thirty women (3.6% of total cohort; 30.9% of those with genetic testing) were diagnosed with LS: 5 MLH1, 9 MSH2, 13 MSH6, and 3 PMS2.

While OC had the lowest rate of MMRd, the rate of LS in women with OC was high compared to EC (33.3% OC, 12% EC, 36.4% EC/OC).

Conclusion: Introduction of a genetic navigator into the genetics referral process resulted in a high rate of genetic counseling (>90%) in gynecologic cancer patients at risk for LS. The MMRd was low in nonserous/mucinous OC; however, the pretest probability of having LS was very high, warranting reflex MMR IHC for this population.

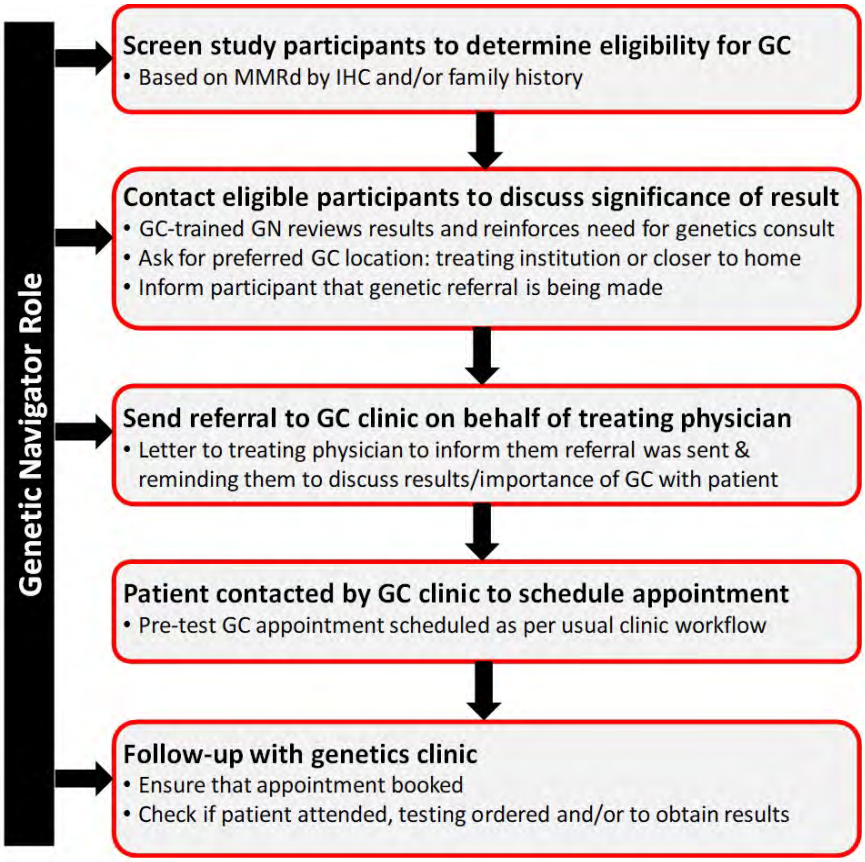

Fig. 1. Facilitation of GC referrals for eligible participants by the study genetic navigator (GN). The role of our dedicated GN at several steps throughout the genetic referral process is highlighted. This individual was trained by a certified genetic counsellor prior to contacting study patients.

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116 - Featured Poster Session

Application and outcomes of sentinel lymph node biopsy in early-stage cervical cancer

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Objective: Our goal was to investigate the use of sentinel lymph node biopsy (SLN) in early-stage cervical cancer, comparing perioperative and survival outcomes to patients undergoing standard lymph node dissection (LND).

Method: Patients who underwent primary hysterectomy for early-stage cervical cancer (FIGO 2009 stage IA2–IB2) between 2012 and 2015 were identified using the National Cancer Data Base. The rates of SLN versus LND were evaluated, along with factors associated with the receipt of SLN. Kaplan-Meier survival curves were generated and compared using log rank tests to examine overall survival (OS) in patients diagnosed between 2012 and 2014 with at least 1 month of follow -up.

Results: A total of 6,835 patients met the inclusion criteria; 4.0% (276) had SLN performed. The use of SLN increased per year of diagnosis from 2.4% in 2012 to 5.9% in 2015. Patients who received SLN during the study period were more likely to undergo simple hysterectomy (45.2% vs 36.8%, $P = 0.008$). There were no differences in SLN and LND patients in race, FIGO stage, tumor size, presence of medical comorbid conditions, or rate of lymphovascular invasion. Significantly more patients

with SLN underwent a minimally invasive hysterectomy than patients with LND (84.3% SLN vs 60.3% LND, $P < 0.001$). The rate of positive lymph node detection was significantly higher in patients who underwent SLN (15.9% vs 12% in LND, $P = 0.047$). While there was no difference in positive node detection by FIGO stage, patients with tumors <2 cm had a higher rate of positive node identification with SLN (9.5%) compared to LND (4.2%) ($P = 0.01$). Patients in both groups had comparable rates of adjuvant therapy. SLN patients demonstrated shorter inpatient stays (median 1 vs 2 days, $P < 0.001$) and similar 90-day mortality (0.2% vs 0%, $P = 1.0$). There was no difference in OS between patients with SLN ($n = 176$) and LND (n = 4,959) ($P = 0.86$). Three-year OS rates were 92.8% and 93.4%, respectively.

Conclusion: Although the application of SLN remains low in early-stage cervical cancer, its use appears to be increasing. These data suggest SLN is associated with comparable outcomes to standard LND and may have improved detection rates in tumors <2 cm.

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Vulvar squamous cell carcinoma: Comprehensive genomic profiling of HPV(+) versus HPV(–) forms reveals a different set of potentially actionable biomarkers

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Objective: Vulvar squamous cell carcinoma (vSCC) is often associated with either detectable high-risk strains of human papillomavirus (HPV) or chronic dystrophic/inflammatory lesions of postmenopausal women. We sought to assess the genomics of a large cohort of aggressive vSCCs, with an aim to identify distinct mutational signatures based on the presence or absence of HPV genome reads.

Method: A total of 280 vSCCs were tested by hybridization capture of 406 cancer-related genes evaluated for base substitutions, small indels, amplification (amp), and rearrangements. HPV genome was detected by de novo assembly of nonhuman sequencing reads and BLASTn comparison against all viral sequences in the NCBI RefSeq database. Also analyzed were 864 hrHPV(+) cervical SCCs (cSCCs). Tumor mutational burden (TMB, mutations/Mb) was determined on ~1.1 Mbp of sequenced DNA. PD-L1 status was determined by immunohistochemistry (IHC) (Dako 22C3), with ≥50% tumor proportion score defined as high positive.

Results: Of 280 vSCCs, 102 contained HPV sequences. Of these, 90 were HPV-16, 7 HPV-18, 1 HPV-31, 3 HPV-33 (1 co-HPV-16), 1 HPV-58, and 1 HPV-67. Patients were significantly younger in the HPV(+) group (median 59 vs 64 years, $P = 0.001$). Compared with the HPV(–) cohort, HPV(+) patients showed significantly more pathogenic genomic alterations (GA) in *PIK3CA* (31% vs 17%, $P = 0.004$), *PTEN* (14% vs 2%, $P < 0.0001$), *EP300* (14% vs 1%, $P < 0.0001$), *STK11* (14% vs 1%, $P < 0.0001$), *AR* (5% vs 0%, $P = 0.006$), and *FBXW7* (10% vs 3%, $P = 0.03$). In contrast, HPV(–) patients showed significantly more alterations in *TP53* (82% vs 3%, $P < 0.0001$), *TERTp* (71% vs 8%, $P < 0.0001$), *CDKN2A* (55% vs 2%, $P < 0.0001$), *CCND1* (23% vs 2%, $P < 0.0001$), *FAT1* (25% vs 4%, $P < 0.0001$), *NOTCH1* (19% vs 6%, $P = 0.002$), and *EGFR* (amp, 12% vs 0%, $P < 0.0001$), as well as a higher frequency of 9p24.1 (*PDL1/PDL2)* amp (7% vs 1%) and PD-L1 IHC high-positive tumor staining (33% vs 9%, $P = 0.04$). HPV(+) vSCCs showed similar alterations to HPV(+) cSCCs. See **Figure 1**.

Conclusion: vSCCs show significant differences in molecular profile based on HPV status. Of all HPV(+) cases, 54% have a potentially actionable alteration in the PI3K/mTOR pathway, while 39% of HPV(–) cases have at least 1 potential predictive biomarker for response to immunotherapy (PD-L1 IHC high-positive tumor, *PDL1/PDL2* amp, or TMB > 10). Our findings provide a compelling rationale for comprehensive genomic profiling and HPV assessment of advanced vSCCs to more fully inform therapeutic options and stratification in clinical trials.

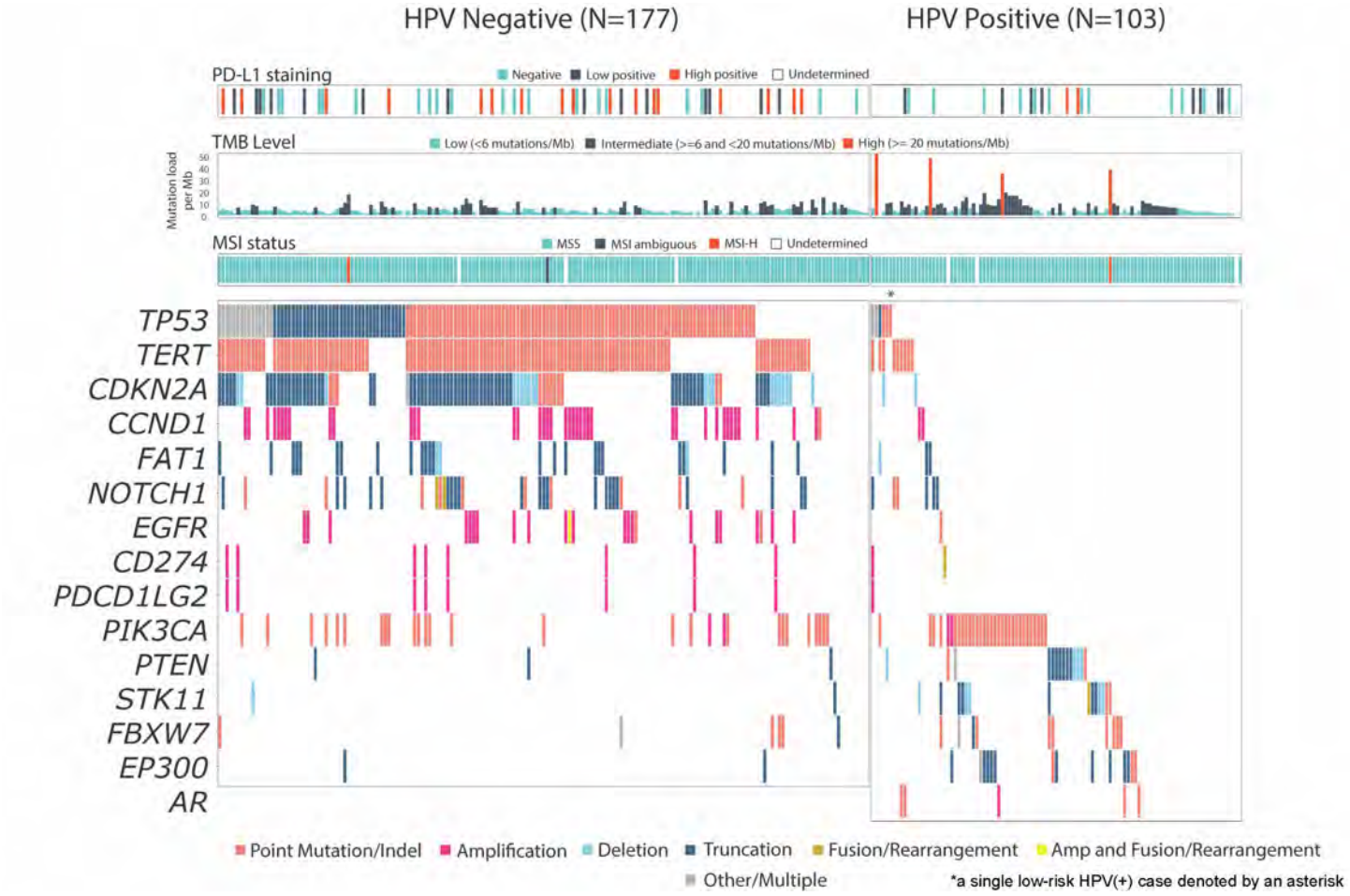

Fig. 1.

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118 - Featured Poster Session

Genetic heterogeneity of sertoli-leydig and juvenile-type granulosa cell tumors

S.H. Kim, A.D.C. Paula, P. Selenica, E.M. Da Silva, A. Stylianou, M. Vahdatinia, N.R. Abu-Rustum, R.A. Soslow, J. Reis-Filho and B. Weigelt. *Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Objective: Sertoli-Leydig and granulosa cell tumors are sex cord-stromal tumors of the ovary that primarily affect young women. Adult-type granulosa cell tumors (aGCTs) are characterized by pathognomonic somatic *FOXL2* mutations, and 30%–60% of Sertoli-Leydig cell tumors (SLCTs) harbor *DICER1* mutations. Here we sought to perform a comprehensive assessment of the repertoire of genomic alterations of juvenile (j)GCTs and SLCTs using whole-exome sequencing.

Method: Primary SLCTs (n = 2), jGCTs (n = 3), and 1 primary and matched mixed SLCT/aGCT recurrence were subjected to whole-exome sequencing. Somatic mutations, copy number alterations, and loss of heterozygosity (LOH) were defined using validated bioinformatics algorithms.

Results: The ovarian sex cord-stromal tumors included in this study displayed a low mutational burden, with a median of 14 (range, 7–57) nonsynonymous somatic mutations. Analysis of the primary and matched recurrent mixed SLCT/aGCT revealed similar patterns of copy number alterations (CNAs) and 32 shared mutations, including a*FOXL2*C134W hot spot mutation; 8 and 6 mutations were found to be restricted to the primary tumor and recurrence, respectively. Both pure SLCTs analyzed harbored somatic pathogenic *DICER1* mutations (p.D1810H hot spot; p.V311Gfs frame shift mutation), the only mutation shared between the 2 SLCTs. In addition, SLCTs were largely devoid of CNAs. In contrast, none of the 3 jGCTs analyzed harbored *FOXL2* or *DICER1* mutations, or any other recurrent somatic mutation or CNA. Of note, *SERPINB7* was mutated in 1 SLCT and 1 jGCT.

Conclusion: Our findings suggest that sex cord-stromal tumors are a genetically heterogeneous group of rare ovarian neoplasms. While SCLTs and aGCTs are characterized by the presence of *DICER1* and *FOXL2* mutations, respectively, no recurrent driver genetic alterations were identified in the jGCTs analyzed. Further studies to define the genetic and/or epigenetic underpinnings of jGCTs are warranted.

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Loss of X chromosome inactivation in monospermic complete hydatidiform moles with 46, XX karyotype

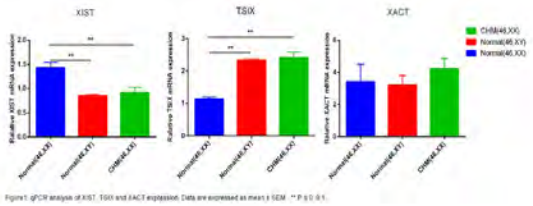
L. Wang, Y. Ma and X. Cheng. *Women's Hospital, Zhejiang University School of Medicine, Zhejiang, China*

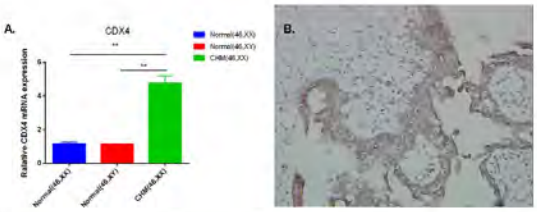
Objective: Most of complete hydatidiform moles (CHMs) present an androgenetic nature of the nuclear genome. In normal female embryo, one of two X chromosomes is inactive, but the status of X chromosome inactivation (XCI) in monospermic CHMs remains unknown.

Method: A total of 71 monospermic CHM tissues with 46, XX karyotype were collected; 74 normal female villi and 74 normal male villi were collected as controls. The expression of XCI markers (XIST, TSIX, and XACT) and a X-linked gene (CDX4) was detected by RT-PCR. Other XCI-associated genes were also examined, including the methylation status of human androgen receptor gene (HUMARA) by methylation-specific PCR (MSP), and the expression of H3K27me3, USP21, and Nanog by Western blot and immunofluorescence, respectively. In addition, 126 CHMs and 63 normal female villous samples were collected for CDX4 immmunohistochenmical staining.

Results: XIST RNA expression was significantly lower and TSIX RNA expression was significantly higher in monospermic CHMs than in normal female villi (both $P < 0.01$). The expressions of CDX4 mRNA in monospermic CHMs was elevated compared with normal (both $P < 0.01$), and CDX4 protein expression was also higher than that in normal female villous samples ($P < 0.01$). The expression of H3K27me3 was decreased in monospermic CHMs compared with normal female villi ($P < 0.01$). The methylation pattern of HUMARA lacked in monospermic CHMs. The expression of Nanog and UPS21 protein in monospermic CHMs was higher than in normal villi (both $P < 0.01$).

Conclusion: Both X chromosomes are active in monospermic CHMs with 46, XX karyotype, and the USP21-Nanog pathway may be involved in the disruption of XCI during this process.





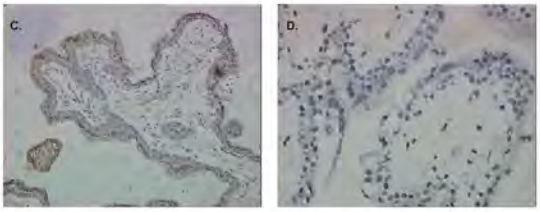


Figure 2. qPCR analysis and immunohistochemistry of CDX4 expression. A. qPCR analysis of CDX4 mRNA in CHMs, normal male villi and female villi. The expression of CDX4 mRNA in CHMs was significantly higher than that in normal female and male villi (both P < 0.05). B. Immunohistochemistry of CDX4 protein in CHM (400×). C.Immunohistochemistry of CDX4 protein in normal female villous (400×) D. negative control (400×).

Table 2. CDX4 immunostaining intensity in CHMs and normal villi

CDX4 expression	CHMs (n=126)	normal villi (n=63)
Low	0	7(11.1%)
Moderate	17(13.5%)	36(57.1%)
High	109(86.5%)*	20(31.7%)

* compared with normal villi (P=0.000)

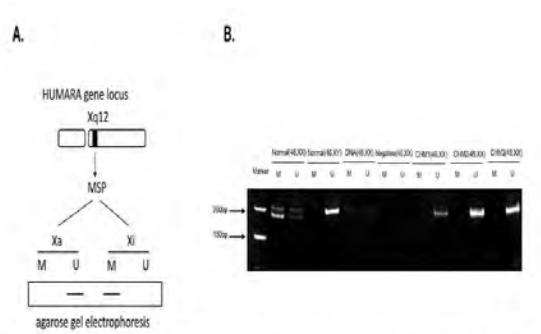


Figure4. A. Diagram of the X chromosomes containing the AR locus and the mechanism of using HUMARA-MSP to illustrate the XCI pattern. B. Electrophoretic separation of the HUMARA-MSP products in CHMs and normal villi. U, PCR products amplified with AR-U primers; M, PCR products amplified with AR-M primers.

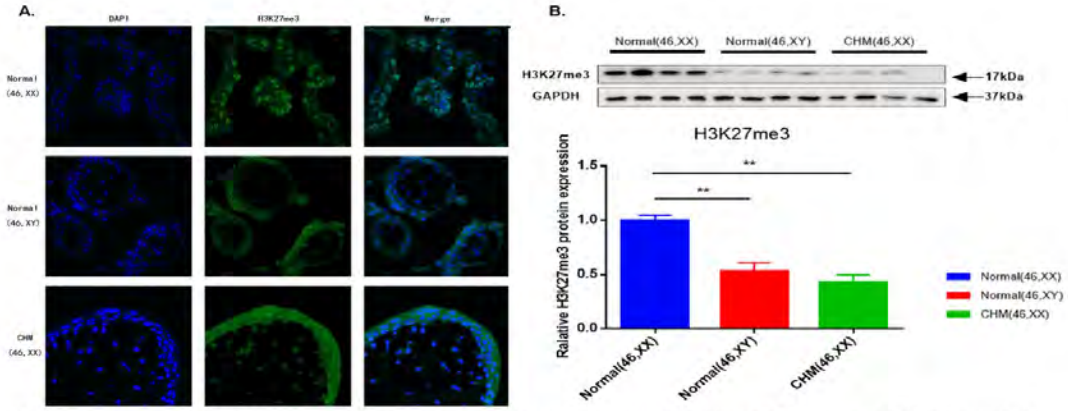


Figure3.The expression of H3k27me3 A.The expression of H3k27me3 measured by Immunofluorescence confocal microscopy.B.The expression of H3k27me3 measured by western blot, Quantity One soft ware (Bio -Rad Lab oratories , Inc , Hercules CA) was used to quantify the signal intensity of the bands . The H3k27me3 signal in each lane was normalized to GAPDH in the same lane before comparison. Data are expressed as mean ± SEM . **,P ≤ 0 .0 1

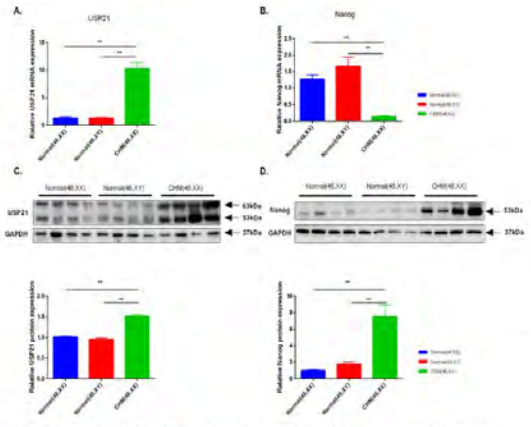


Figure5.The expression of USP21 and Nanog . A-B The RNA expression of USP21 and Nanog measured by qPCR.C-D The protein expression of USP21 and Nanog measured by western blot, Quantity One soft ware (Bio -Rad Lab oratories , Inc , Hercules CA) was used to quantify the signal intensity of the bands . The USP21 and Nanog signal in each lane were normalized to GAPDH in the same lane before comparison. Data are expressed as mean ± SEM . **,P ≤ 0 .0 1

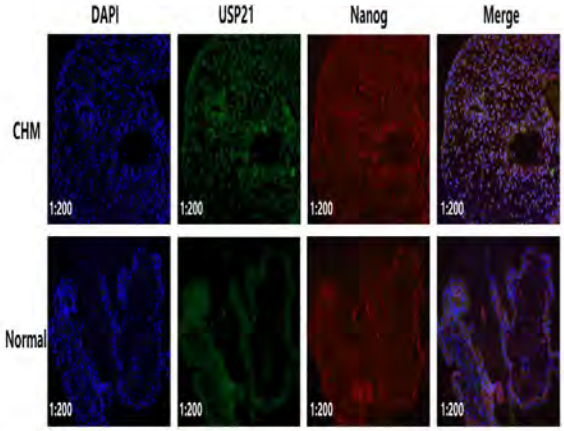


Figure6.Colocalization of USP21 and Nanog .A The colocalization of USP21 and Nanog was measured by Immunofluorescence confocal microscopy.

Fig. 1.

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Adjuvant HPV vaccination with surgical excision to prevent recurrent CIN2+: A systematic review and meta-analysis

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Objective: Our aim was to perform a systematic review and meta-analysis evaluating the efficacy of adjuvant human papillomavirus (HPV) vaccination in preventing recurrent CIN2+ after surgical excision.

Method: Electronic databases were searched for randomized controlled trials and prospective and retrospective cohort studies, comparing surgical excision alone to surgical excision with adjuvant HPV vaccination for CIN2+. Studies published from January 1, 1990, to January 1, 2019, were included. Outcomes evaluated include recurrence of CIN2+, CIN1+, and HPV strains 16/18-associated CIN within 6–48 months. Meta-analysis was performed using the random effects model of DerSimonian and Laird. Risk of bias and quality assessment were performed using the ROBINS-I and GRADE tools, respectively.

Results: Six studies met the inclusion criteria. Of the 2,984 women included in the studies, 1,360 (45.6%) received adjuvant HPV vaccination after surgical excision, and 1,624 (54.4%) received either placebo or surgical management alone for CIN2+. Recurrence of CIN2+ occurred within 6–48 months in 99 women (3.3%) overall; however, it was significantly lower for vaccinated women, 23 of 1,360 women (1.7%) versus 76 of 1,624 unvaccinated women (4.7%) (RR = 0.34, 95% CI 0.22–0.55). Similarly, the risk of CIN1+ was also significantly lower with adjuvant HPV vaccination, occurring in 86 of 1,360 vaccinated women (6.3%) versus 157 of 1,624 unvaccinated women (9.7%) (RR = 0.67, 95% CI 0.52–0.85). Four studies evaluated the recurrence of lesions specific to HPV strains 16/18. There were 35 women who developed recurrent HPV 16/18 CIN2+, 9 women who received adjuvant vaccination (0.9%), and 26 women who did not receive the vaccine (2.0%). In addition, 49 women developed HPV 16/18 associated CIN1+: 11 vaccinated women (1.1%) and 38 unvaccinated women (3.1%). Overall, there was a statistically significant reduction in the risk of HPV 16/18 associated CIN2+ lesions (RR = 0.41, 95% CI 0.20–0.85) and HPV 16/18 associated CIN1+ lesions (RR = 0.35, 95% CI 0.18-0.67).

Conclusion: Adjuvant HPV vaccination after surgical excision for CIN2+ significantly reduces the risk of both recurrent high-grade and low-grade cervical dysplasia. Furthermore, the risk of recurrent lesions caused by the most oncogenic strains (HPV 16/18) is also significantly reduced with adjuvant HPV vaccination. HPV vaccination should therefore be considered for adjuvant treatment to surgery in patients undergoing surgical excision for CIN2+.

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Circulating cell-free DNA in patients with newly diagnosed and recurrent cervical cancer

S.H. Kim, M. Wu, A. Stylianou, S. Ghafoor, Y. Lakhman, K.J. Park, M.M. Leitao Jr., Y. Sonoda, G.J. Gardner, V. Broach, E. Jewell, S. Cohen, W.P. Tew, O. Zivanovic, K. Long Roche, J.J. Mueller, D. Zamarin, N.R. Abu-Rustum, C. Aghajanian, K.A. Cadoo and B. Weigelt. *Memorial Sloan Kettering Cancer Center, New York, NY, USA*

Objective: Sequencing analysis of circulating cell-free DNA (cfDNA) has been shown to play a role in the diagnosis, prognosis, and disease-monitoring of cancer. Its potential in cervical cancer, however, has yet to be defined. We sought to determine whether the levels of cfDNA correlate with stage, histologic type, or both in cervical cancer patients.

Method: Newly diagnosed or recurrent cervical cancer patients were consented to an Institutional Review Board-approved protocol. cfDNA was extracted from peripheral blood collected prior to surgery or chemotherapy/radiation. Blood collections at 3- to 6-month intervals postsurgery/treatment are being performed, and DNA from the primary tumors and recurrences and cfDNA are being subjected to massively parallel sequencing.

Results: Of the 30 patients enrolled, 24 had newly diagnosed and 6 recurrent cervical cancer. Of those newly diagnosed, the majority presented with early-stage disease: 63% (15/24) stage IA1–IB3, 29% (7/24) stage II, 4% (1/24) stage III, and 4% (1/24) stage IV disease. Twenty-one patients had tumors visible on MRI, with a median tumor volume of 35.2 cm^3 (range 1.2–136.6). Most common histologic subtypes were adenocarcinoma (40%) and squamous cell carcinoma (40%), followed by adenosquamous (7%), small cell neuroendocrine (7%), gastric-type (3%), and glassy cell carcinoma (3%). Sixteen patients underwent primary surgery, while 14 received chemotherapy with or without radiation or immunotherapy. Median cfDNA concentration at diagnosis was 0.21 ng/μL (range 0.11–13.72 ng/μL). Surgical stage was significantly associated with cfDNA

concentration (P = 0.03): stage IA1–IB3 0.21 ng/μL (range 0.11–0.59 ng/ μL), stage II 0.15 ng/μL (range 0.14–0.23 ng/ μL), stage III 0.97 ng/μL, stage IV 0.73 ng/μL, and recurrent disease 0.67 ng/μL (range 0.20–13.72 ng/ μL). MRI-defined tumor volume was highly correlated with cfDNA concentration (P < 0.0001). No association between histologic subtype and cfDNA concentrations was found.

Conclusion: cfDNA in the plasma of cervical cancer patients is associated with tumor stage and tumor burden. Studies to assess whether the repertoire of genetic alterations in the cfDNA is representative of that of the primary tumors/recurrences, and whether mutation detection in cfDNA of cervical cancer patients can be employed for disease-monitoring, are currently being performed.

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Immune modeling analysis identifies ICOS and CTLA-4 as predictive biomarkers in serous epithelial ovarian cancer

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Objective: The goal of this study is to comprehensively determine the most clinically relevant immune checkpoint receptor in epithelial ovarian cancer (EOC).

Method: Stage III, grade III EOC formalin-fixed paraffin-embedded (FFPE) tumors from 10 patients were submitted to Cofactor Genomics to undergo RNA sequencing and machine learning analysis to determine immune cell content and levels of 10 well-established immunegenes. Patient samples were stratified by long progression-free survival (PFS) of 65 months or greater (n = 5) and short PFS of 7 months or less (n = 5). All patient tumors submitted were from primary debulking surgery and were naïve to chemotherapy. Immunohistochemistry (IHC) was employed to determine levels of ICOS in various T cell subpopulations. Levels of immunegenes were correlated to immune cell counts using Spearman rank test. Co-expression of ICOS and PD-1 in various T cell populations was visualized by flow cytometry.

Results: The two immune escape genes ICOS and CTLA-4 were found to be the most predictive biomarkers differentiating short and long PFS. ICOS median transcripts per million (TPM) were 418 and 1,621 in patients with short and long PFS, respectively (P < 0.03), while median TPM for CTLA-4 was 1,294 and 4,045 in patients with short and long PFS, respectively (P < 0.03). Higher percentages of CD4+ T cells, CD8+ T cells, CD19+ B cells, and T regulatory cells (Tregs) were detected in patients with a long PFS compared to short; however, these differences did not reach statistical significance. It was determined that patients with a long PFS had average higher levels of CD8+ and CD4+ ICOS+ cells but lower average levels of ICOS+ Tregs compared to patients with a short PFS. ICOS levels significantly (P < 0.05) correlated to CD8+ cells, Tregs, CD19+ B cells, and total immune content. Furthermore, ICOS and PD-1 levels significantly correlated, and this phenomenon was confirmed via flow cytometry.

Conclusion: Immune modeling analysis revealed ICOS and CTLA-4 as the most predictive immune biomarkers for PFS in EOC. Future directions include repeating this assay in a larger patient cohort to validate the predictive threshold determined for ICOS and CTLA-4, as well determining the efficacy of targeting these agents in combination in vivo.

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CD3+ tumor-associated lymphocytes as a novel prognostic biomarker in endometrial carcinoma

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Objective: Mismatch repair deficient (MMRd) endometrial cancers are associated with higher numbers of tumor-associated lymphocytes, but the clinical significance of this observation is unknown. Our objective was to quantify CD3+ and CD8+ lymphocytes in different regions of MMR intact (MMRi) and MMRd endometrioid-type endometrial carcinomas and determine whether these counts were associated with survival.

Method: MMR status was determined by immunohistochemistry. MMRd was defined as endometrial carcinomas with loss of MLH1 expression due to *MLH1* gene methylation. MMRi was defined as positive expression of *MLH1*, *MSH2*, *MSH6*, and *PMS2*. Immunohistochemistry followed by Aperio image-based quantification was used to assess CD3+ and CD8+ lymphocyte populations in different regions of the primary endometrial carcinomas, including tumor periphery (tumor-myometrial interface), tumor center (bounded on all sides by tumor), and tumor hotspot (area with highest number of lymphocytes). Recurrence-free survival was estimated using Kaplan-Meier and Cox regression. Median follow-up time was 44 months.

Results: A total of 180 endometrial cancer patients were analyzed, 48 MMRd and 132 MMRi. The MMRd group had significantly higher levels of CD3+ and CD8+ lymphocytes regardless of which tumor region was assessed (**Figure 1a**, $P < 0.001$). Lymphocyte counts in both MMRd and MMRi groups had wide standard deviations such that there was some overlap in counts between the groups (**Figure 1**). Both MMRd and higher CD3+ counts were associated with worse recurrence-free survival. However, quantification of CD3+ in the tumor periphery captured 21/23 recurrences (**Figure 1b**, HR = 8.04, 95% CI 1.88–34.31, $P = 0.005$); this included all of the MMRd cases that recurred and 7 MMRi cases with higher numbers of CD3+ lymphocytes that also recurred.

Conclusion: Patients with MMRd endometrial cancers have higher numbers of CD3+ lymphocytic infiltrates within the primary tumor. Regardless of tumor region, higher CD3+ infiltration is associated with greater risk of recurrence. In predicting tumor recurrence, lymphocytic quantification performed better than assessment of MMR. Thus, quantification of CD3+ lymphocytes should be explored as a clinically relevant biomarker.

Figure 1a. Box Plot of CD3+ & CD8+ Lymphocyte Distribution in MMR Deficient Cohort

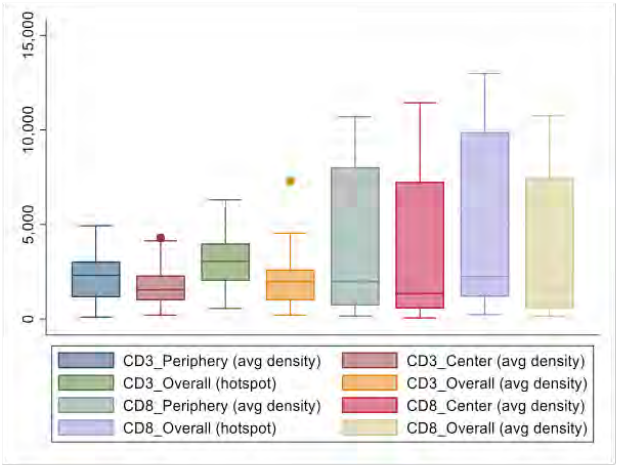

Figure 1b. Box Plot of CD3+ & CD8+ Lymphocyte Distribution in MMR Intact Cohort

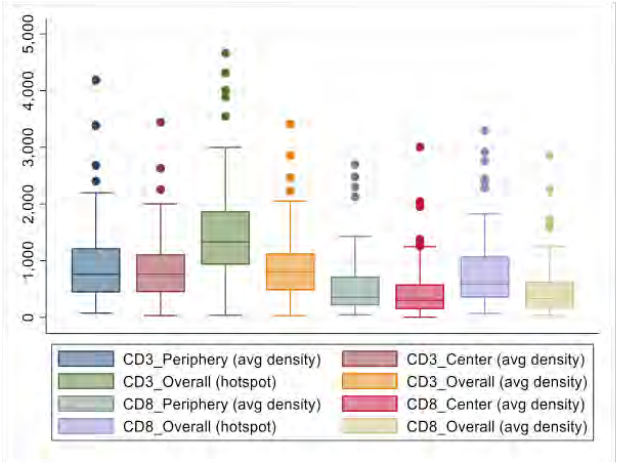

Fig. 1.

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The role of the microbiome in predicting development of uterine cancer

M. Frimer[a], W. Shan[b], L. Palette[b], A. Kapedani[b], B. Bustamante[a], A. Sakaris[a], L. dos Santos[a], K.K. Shih[a], A.W. Menzin[a], J.S. Whyte[a], A. Liew[c], G.L. Goldberg[b] and A. Lee[d]. *[a]Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, NY, USA, [b]Hofstra - North Shore Long Island Jewish School of Medicine, Manhasset, NY, USA, [c]Feinstein Institute, Long Island, NY, USA, [d]Feinstein Institute for Medical Research, Manhasset, NY, USA*

Objective: The human microbiome is thought to influence the inflammatory response and cancer development. This pilot study aimed to characterize the role of the gastrointestinal, cervico-vaginal, and endometrial microbiome in uterine cancer

development in postmenopausal women with benign conditions, grade 1 endometrioid adenocarcinoma (EC), and uterine serous carcinoma (USC).

Method: Postmenopausal women undergoing hysterectomy were prospectively recruited. Swabs were collected from the cervix/vagina and rectum prior to surgery and the endometrial cavity after completion of the hysterectomy. DNA was extracted and amplified, and high-throughput next generation sequencing (MiSeq) of the 16S rRNA V3-V5 conserved region was performed to identify the microbiota present. Species count data were normalized by cumulative sum sampling. Differential abundance of bacteria species between organ sites and histologies was assessed using alpha diversity indices and beta diversity comparisons.

Results: A total of 48 patients were recruited: 18 women with benign uterine conditions, 15 with EC, and 15 with USC. Alpha diversity indices suggested highly richer species diversity in the rectum compared to that in the cervix/vagina, and the least diversity was observed in uterine specimens (**Figure 1**). When species diversity was compared between histologic subtypes within each organ site, both rectal and uterine specimens exhibited decrease of richness from benign to EC and increase from EC to USC ($P < 0.05$), whereas no difference was observed in cervico-vaginal specimens. Beta diversity analyses showed that in the rectum, EC and USC exhibited significantly differential species abundance. In the uterus, statistically differential species abundance was noted between benign and EC ($P < 0.05$). Cervico-vaginal specimens did not demonstrate differences between the histologic subtypes.

Conclusion: Statistically significant differential abundance of bacterial species was observed between EC and USC in the rectal samples and between benign and EC in endometrial samples. Downstream studies will focus on elucidating the role of differentially abundant bacteria species in the development of EC and USC, and identify clinical variables that contribute to the evolvement of specific ecologic groups.

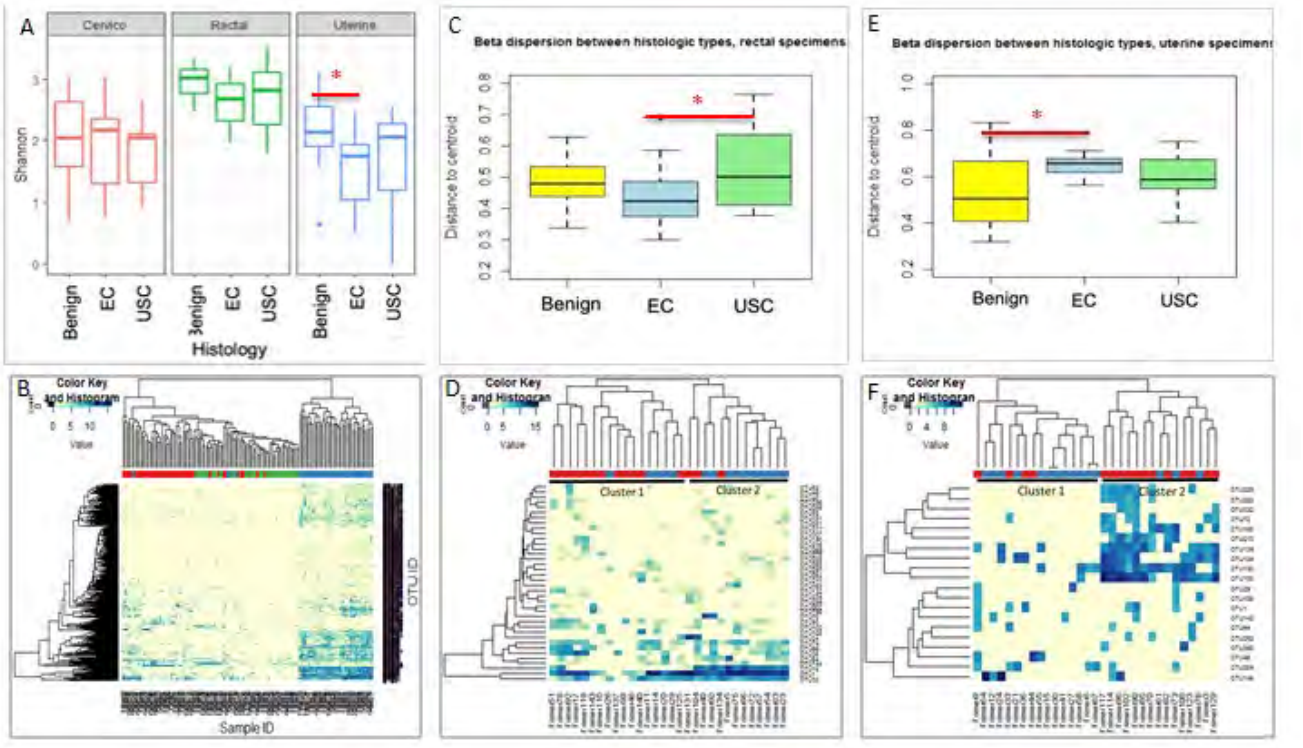

Fig. 1. A, comparison of Shannon diversity index between histologic subtypes in the cervix/vagina, rectum and uterine samples. B, clustering within organ sites by the 200 most differentially present species by heat-mapping. C, community dissimilarity between histotypes in the rectal specimens (represented by beta dispersion). D, clustering within EC and USC by 40 most differentially abundant species in the rectum. E, community dissimilarity between histotypes in the uterine specimens (represented by beta dispersion). F, clustering within benign and EC by 20 most differently abundant species in the uterus. Asterisk, difference groups with p-value <0.05.

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Compositional and temporal changes of the gut microbiome in women with cervical cancer undergoing chemoradiation: Does it predict response?

T.T. Sims[a], L.E. Colbert[a], T. Karpinets[a], G.W.G. Biegert[a], A.Y. Delgado[a], M.P. Mezzari[b], T. Solley[a], K. Yoshida-Court[a], A. Mitra[a], L.L. Lin[a], L.M. Ramondetta[a], A.A. Jazaeri[a], M. Frumovitz[a], A. Jhingran[a], K. Schmeler[a], J. Wargo[a] and A.H. Klopp[a]. [a]*The University of Texas MD Anderson Cancer Center, Houston, TX, USA,* [b]*Alkek Center for Metagenomics and Microbiome Research, Baylor College of Medicine, Houston, TX, USA*

Objective: The gut microbiome may influence response to various cancer therapeutics, and its application in cervix cancer (CC) is lacking. This study aimed to assess the effect of chemoradiation (CRT) on the gut microbiome and to examine the association between the gut microbiome and clinical outcomes in women with CC undergoing CRT.

Method: We longitudinally analyzed the 16S rDNA fecal microbiome of 55 CC patients undergoing definitive CRT at baseline, week 1, week 3, week 5, and week 12. Patients were classified as exceptional responders (ER), standard responders (SR), or poor responders (PR) based on clinical examination and imaging at week 5 and month 3. Inverse Simpson Diversity (ISD) was used to evaluate α (within sample) diversity. Relative abundance of specific taxa was compared using Linear Discriminant Analysis Effect Size (LEfSe). Overall survival (OS) and recurrence-free survival (RFS) were analyzed using log rank statistics and Kaplan-Meier curves.

Results: For all patients, α-diversity was stable from baseline to week 3, but declined at week 5, with a median ISD of 9.9 (IQR 6.29–15.12) at baseline and 8.01 (IQR 3.97–12.41) at week 5 ($P = 0.039$) (**Figure 1A**). At week 1, α-diversity of the gut microbiome was significantly higher for ER versus SR/PR (ISD 13.34 vs 9.49 and 8.41, respectively, $P = 0.023$) (**Figure 1B**). For all patients, multiple taxa significantly differed at baseline when compared to week 5 of CRT. *Clostridia, Ruminococcaceae,* and *Peptococcaceae* were significantly enriched in baseline samples, while *Staphylococcaceae, Corynebacterium,* and *Pasteurellaceae* were significantly enriched in week 5 samples ($P < 0.05$, LDA score > 4) (**Figure 1D** and **Figure 1E**). At baseline, only *Clostridia* was significantly enriched in ER versus SR/PR (**Figure 1C**). High gut diversity at week 1 suggests a trend toward prolonged RFS and OS when compared to those with low diversity ($P = 0.055$ and $P = 0.096$, respectively) (**Figure 1F** and **Figure 1G**). High relative abundance of *Clostridia* at baseline was associated with a longer RFS ($P = 0.041$) (**Figure 1H**).

Conclusion: The gut microbiome undergoes compositional and temporal changes during CRT. Gut diversity early in the course of CRT may predict response. *Clostridia* may have prognostic significance for predicting RFS in patients with CC. Additional studies are needed to validate these promising gut microbial signatures.

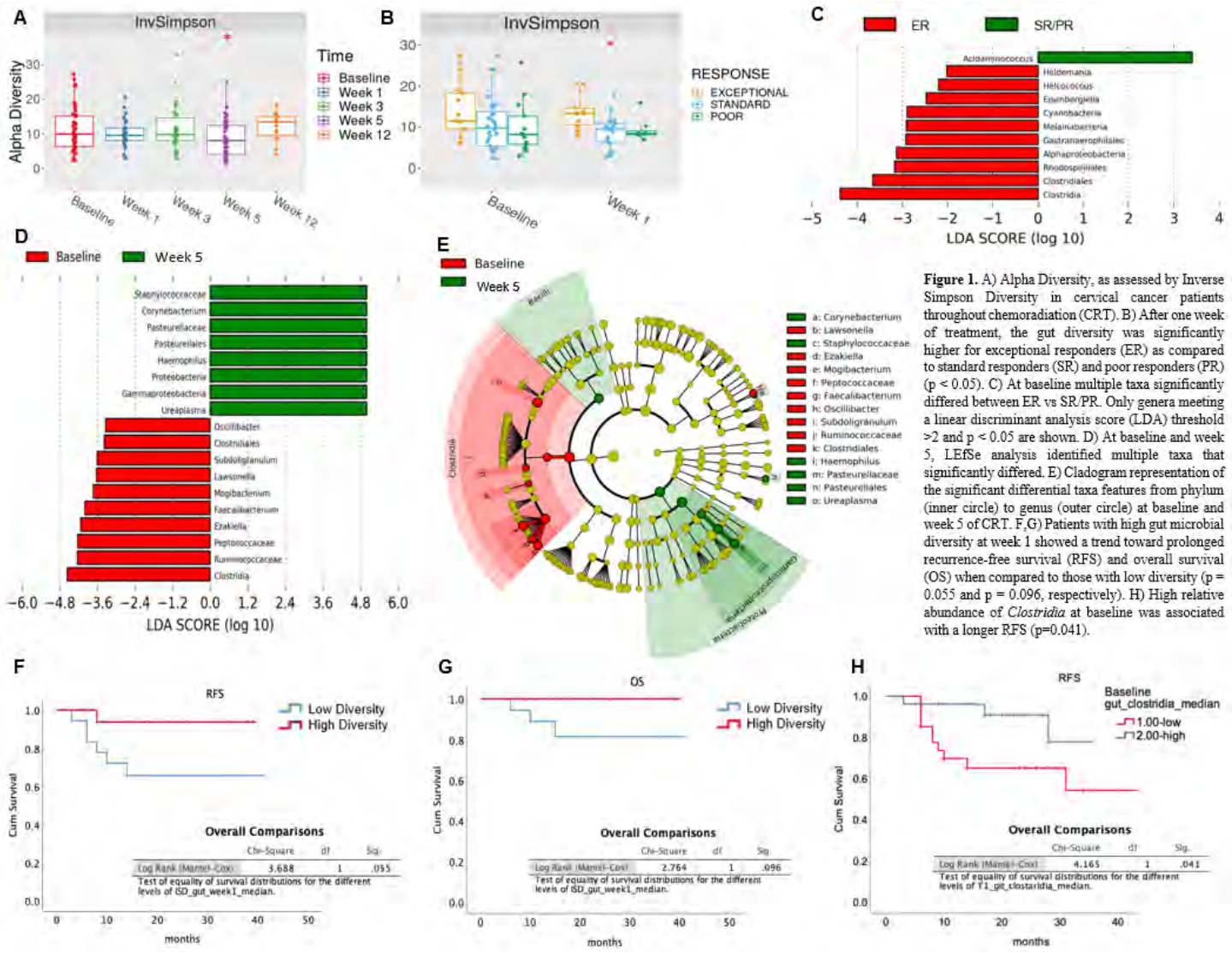

Figure 1. A) Alpha Diversity, as assessed by Inverse Simpson Diversity in cervical cancer patients throughout chemoradiation (CRT). B) After one week of treatment, the gut diversity was significantly higher for exceptional responders (ER) as compared to standard responders (SR) and poor responders (PR) ($p < 0.05$). C) At baseline multiple taxa significantly differed between ER vs SR/PR. Only genera meeting a linear discriminant analysis score (LDA) threshold >2 and $p < 0.05$ are shown. D) At baseline and week 5, LEfSe analysis identified multiple taxa that significantly differed. E) Cladogram representation of the significant differential taxa features from phylum (inner circle) to genus (outer circle) at baseline and week 5 of CRT. F,G) Patients with high gut microbial diversity at week 1 showed a trend toward prolonged recurrence-free survival (RFS) and overall survival (OS) when compared to those with low diversity ($p = 0.055$ and $p = 0.096$, respectively). H) High relative abundance of *Clostridia* at baseline was associated with a longer RFS ($p=0.041$).

Fig. 1.

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126 - Featured Poster Session

Development of a predictive signatures for immune therapy in ovarian cancer: Whom to treat and whom not to treat?

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Objective: To understand the immune landscape of the ovarian cancer (OC) microenvironment and to develop predictive biomarkers to select candidates for immune therapy, we have initiated a study to comprehensively analyze the unique molecular and histopathological characteristics of tumor samples taken during primary debulking and interval debulking and at recurrence.

Method: We have enrolled over 60 women and have completed single-cell RNA sequencing (scRNAseq), multiplex immunohistochemical assays, H&E scoring for tumor-infiltrating lymphocytes (TILs), and NanoString molecular subtyping in 30 women. ScRNAseq was performed using the 10X genomics platform. Gene expression patterns of costimulatory molecules, programmed cell death protein, and its ligand, PD-1 and PDL-1, were analyzed. TIL scoring was performed using the Salgado criteria, and PDL-1/PD-1 IHC staining was assessed based on Tumor Proportion Score (TPS) and Combined Proportion Score (CPS).

Results: ScRNAseq revealed PD-1 and PDL-1 gene expression in 23/30 (76%) patients when all cell types (range 1%–22%) were analyzed, while 20/30 (66%) showed expression both in immune and epithelial cells. Highest expression of both genes was noted in 4/30 (12%) patients. PDL-1 gene levels by ScRNAseq demonstrated robust linearity across high- and low-expression ranges noted on IHC assays. ScRNA-seq had an added advantage of being able to detect genes on tumor samples with absent PDL-1 IHC staining. Differential expression of PD-1/PDL-1 genes among 4 molecular subtypes showed highest expression in the immunoreactive group. Interestingly, 2 patients in this group did not have detectable expression of PD-1/PDL-1, indicating that molecular subtyping alone might not be predictive of immunotherapy response. Stromal TILs of 50%–90% and 20%–40% were observed in 4/30 (13%) and 10/30 patients (33%), respectively, although no correlation was noted between TIL scoring and level of PD-1/PDL-1 genes.

Conclusion: ScRNAseq is more reliable in identifying PD-1/PD-L1 across cells than IHC assays. Single biomarker alone might not be predictive of treatment response. Our study is ongoing, and we will categorize these patients into various subtypes based on presence or absence of multiple immune markers (PD-1/PDL-1, TILs, molecular subtypes, IHC assays) and will follow their disease course. This could help identify patients most likely to benefit from immunotherapy in the future and further our understanding of the mechanism of immune evasion in OC.

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127 - Featured Poster Session

Risk stratification using hotspot genotyping in low-grade serous ovarian cancer

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Objective: The goal of this study was to examine a large clinical dataset of low-grade serous ovarian carcinoma (LGSC) through the Ovarian Cancer Association Consortium, with the primary objective of identifying factors that have an impact on survival.

Method: We performed a clinical and genomic, retrospective, multicenter cohort analysis of women with LGSC. Cases were included if both clinical and genomic data from the OncoArray platform were available. Forty-seven relevant single-nucleotide polymorphisms (SNP) were selected and used for further analysis. Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method.

Results: A total of 380 patients were included in this study. Of those, 20.5% were stage I, 7.9% stage II, 61.1% stage III, 6.1% stage IV, and 4.5% an unknown stage. The median age at diagnosis was 54 years (range 20–85 years). Ethnicity was known in 324 patients: 90.1% white, 2.5% African-American, 5.2% Asian, and 2.2% other. Surgical outcome was known in 160 patients: 60% had optimal cytoreduction with no visible residual disease; 26.3% had optimal cytoreduction with residual disease <1.0 cm^3; and 13.8% had suboptimal cytoreduction. Chemotherapy status was known in 191 patients, and of these, 94.2% received primary chemotherapy. The median follow-up was 60.0 months (range 0–286.8 months). The median overall survival was 105.8 months (95% CI 86.6–125.1 months), and the 5- and 10-year overall survival rates were 63.5% and 45.5%, respectively. Information on disease progression was available for 212 patients, of which 60.4% experienced disease progression. Disease stage and surgical cytoreduction were significantly associated with OS ($P < 0.001$) and PFS ($P < 0.001$). The Rs17161747 G>C variant (a SNP of the *BRAF* gene) was found in 12.0% of patients and was associated with a lower PFS (23.3 vs 31.8 months) ($P = 0.041$).

Conclusion: Despite its histologic low-grade features, LGSC is associated with a poor long-term outcome. Stage at presentation and residual disease following surgical cytoreduction are significant predictors for PFS and OS. The association of variants in the *BRAF* gene with worse survival is an interesting finding and warrants further investigation.

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128 - Featured Poster Session

Predicting recurrence in endometrial cancer based on a combination of classical parameters and immunohistochemical markers

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Objective: The aim of this study was to establish a nomogram for predicting the recurrence of endometrial cancer (EC) by adding immunohistochemical markers to the traditional clinical and pathological parameters.

Method: The archived data of 537 patients with stage I–III endometrial cancer who received primary surgical treatment between October 2013 and May 2018 were retrieved and analyzed. Data of 473 included patients were randomly split into two sets: training and validation in a predefined ratio of 7:3. A univariate regression was performed to screen factors

associated with recurrence in EC in the training cohort (*n* = 332), and a Cox proportional hazards multivariate model of selected prognostic features was applied to develop a nomogram, which was further validated in the validation cohort (*n* = 141). The prediction capabilities of different combinations of parameters were also compared to confirm the capacity of this proposed model in clinical utility.

Results: There were 47 recurrent patients in the training cohort and 20 patients in the validation cohort. Screened by univariate Cox regression, FIGO stage, histological type, histological grade, myometrial invasion, cervical stromal invasion, postoperative adjuvant treatment, adequate treatment, and 4 immunohistochemical makers were the most related factors for recurrence in EC, among which FIGO stage, histological type, ER, and P53 were considered statistically and clinically correlated with recurrence in EC. Therefore, recurrence-free survival rate was best predicted by the proposed nomogram with a C-index of 0.88 (95% CI 0.84–0.92), and the validation set confirmed the findings with a C-index of 0.79 (95% CI 0.66–0.92).

Conclusion: Immunohistochemical markers in addition to traditional clinicopathological parameters can best predict recurrence in FIGO stage I–III EC. This nomogram model was demonstrated to be a robust tool for predicting recurrence-free survival rate.

Sunrise Session II: On the Horizon: A Glimpse of What's to Come for SGO 2025

LBA 1 - Sunrise Session

A first-in-human proof-of-concept trial of intravaginal artesunate to treat cervical intraepithelial neoplasia (CIN2/3)

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Objective: Most treatment options for cervical intraepithelial neoplasia 2/3 (CIN2/3) are either excisional or ablative, and require sequential visits to health care providers. Artesunate, a compound that is WHO-approved for treatment of acute malaria, also has cytotoxic effect on squamous cells transformed by human papillomavirus (HPV). We conducted a first-in-human proof-of-concept study to assess the safety and efficacy of self-administered artesunate vaginal inserts in biopsy-confirmed CIN2/3.

Method: Safety analyses were based on patients who received at least 1 dose and were assessed by the severity, frequency, and duration of reported adverse events. Tolerability was assessed as the percentage of subjects able to complete their designated dosing regimen. Modified intention-to-treat analyses for efficacy and viral clearance were based on patients who received at least 1 dose for whom endpoint data were available. Efficacy was defined as histologic regression to CIN1 or less. Viral clearance was defined as absence of HPV genotype(s) detected at baseline.

Results: A total of 28 patients received 1, 2, or 3 5-day treatment cycles at study weeks 0, 2, and 4, respectively, prior to a planned, standard-of-care resection after study week 15. Reported adverse events were mild and self-limited. In the modified intention-to-treat analysis, histologic regression was observed in 19/28 (67.9 %) subjects. Clearance of HPV genotypes detected at baseline occurred in 9 of the 19 (47.4%) subjects whose lesions underwent histologic regression.

Conclusion: Self-administered intravaginal artesunate inserts were safe and well-tolerated, at clinically effective doses to treat CIN2/3. These findings support proceeding with phase II clinical studies.

LBA 2 - Sunrise Session

Mutation detection in cell-free DNA using ultra-high depth sequencing in prospectively collected newly diagnosed endometrial cancer patients

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Objective: We sought to define whether mutations could be detected in cell-free DNA of newly diagnosed endometrial cancer patients, and whether mutation detection is associated with disease burden and/or tumor type.

Method: Following Institutional Review Board approval, cell-free DNA was extracted from prospectively collected peripheral blood at diagnosis and postsurgery of 44 newly diagnosed endometrial cancer patients. Disease burden at diagnosis was

quantified using magnetic resonance imaging (MRI). Primary endometrial cancers were subjected to an FDA-approved 468 cancer-related gene massively parallel sequencing assay, and the matched cell-free DNA of 29 patients to ultra-high depth sequencing using unique molecular identifiers (median depth 26,825x, range 14,767–66,300x) of 129 genes, a subset of the 468 genes. Sequencing analyses were performed using state-of-the-art bioinformatics tools.

Results: Of the 44 endometrial cancer patients accrued, 29 had sufficient preoperative cell-free DNA (≥10 ng) for ultra-high depth sequencing (15/29 stage IA, 2/2 stage IB, 10/11 stage III, 2/2 stage IV; 7/14 endometrioid grade 1, 9/12 endometrioid grades 2–3, 6/8 serous, 2/2 clear cell, 1/1 undifferentiated, 3/6 carcinosarcoma, 1/1 adenosarcoma). Sequencing analysis of the 29 primary endometrial cancers (restricted to the 129-gene cell-free DNA panel) revealed a median of 10 (range 2–101) nonsynonymous somatic mutations. At least 1 nonsynonymous somatic mutation present in the primary tumor was detected in the preoperative cell-free DNA of 3/15 (20%) stage IA, 0/2 (0%) stage IB, 6/10 (60%) stage III, and 2/2 (100%) stage IV endometrial cancers. Mutation detection in preoperative cell-free DNA was associated with higher tumor volume based on MRI (detectable mutations median 111 cm^3, range 8–2,608 cm^3, vs undetectable 1.9 cm^3, range 0–43 cm^3), and was less frequent in patients with endometrioid carcinomas (12.5% grade 1, 37.5% grades 2–3) than in other histologic types (64%). Of the 29 cases, 25 had postoperative cell-free DNA sequencing data, and in 5, mutations were identified (all stages III or IV); all 5 cases had residual disease after primary therapy or recurred within a year. By contrast, only 1/20 (5%) case without postsurgery cell-free DNA mutations progressed within 2 years.

Conclusion: Mutation detection in cell-free DNA of endometrial cancer patients varies according to disease burden and tumor type, and may portend a poor outcome for patients if identified postsurgically.

LBA 3 - Sunrise Session

Resveratrol inhibits the invasion and migration of endometrial cancer by reversing MTA1-ZEB2-induced epithelial-mesenchymal transition

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Objective: Resveratrol shows anticancer properties in many human cancers, but the specific mechanism in endometrial cancer is still unknown. Metastasis-associated protein 1 (MTA1) has been shown to promote tumorigenesis and progression of cancers, including endometrial cancer. In the process of cancer development, epithelial-mesenchymal transition (EMT) is crucial to promoting the invasion and migration of tumor cells. However, MTA1-induced EMT and the anti-invasion mechanism of resveratrol on endometrial cancer are not yet completely understood and need to be elucidated.

Method: In the present study, the role of resveratrol on MTA1-induced EMT and migration was investigated in endometrial cancer cells (Ishikawa, HEC-1B, RL-952) and a xenograft-bearing mouse model. CCK-8 assay, colony-formation assay, flow cytometry, cell scratch assay, and Transwell assay were performed to determine cell proliferation, apoptosis, migration, and invasion abilities, respectively. Western blotting and real-time PCR were used to assess the expression of target gene. Immunoprecipitation was preformed to investigate the relationship between MTA1 and ZEB2. In addition, the IC_{50} of resveratrol was determined by CCK-8 assay.

Results: In vitro, we found resveratrol inhibited endometrial cancer cell proliferation, migration invasion, and induced apoptosis, and meanwhile decreased MTA1 expression. Intriguingly, the inhibition of resveratrol on cell function could be abrogated partly by MTA1 over-expression. Next, it showed that ZEB2 was downregulated followed by MTA1 through RNA-sequencing analysis, and ZEB2 knockdown led to an inhibition of endometrial cancer cell migration and invasion, which could be reversed by MTA1 over-expression. MTA1 over-expression led to an increased expression of ZEB2 and Vimentin, and decreased E-cadherin expression, which could be blocked by resveratrol. In addition, there was a physical combination between MTA1 and ZEB2, which implied an interrelation between them. In vivo, resveratrol suppressed tumor growth as well as the expression of MTA1 and ZEB2, without marked changes in body weight. These results indicate that resveratrol inhibited the tumorigenesis and progression of endometrial cancer by reversing MTA1–ZEB2-induced EMT.

Conclusion: Our results suggest that resveratrol inhibits the development of endometrial cancer by reversing MTA1–ZEB2-induced EMT, and provide new insight of resveratrol in future therapeutic approaches.

LBA 4 - Sunrise Session

A DNA methylation test from pap smears with abnormal uterine bleeding for endometrial cancer detection: A

multicenter validating confirmatory study
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Objective: The increasing incidence and mortality of uterine cancer worldwide suggests a need for new strategies. DNA methylation assays from conventional Pap materials used as a triage test may allow women to avoid unnecessary endometrial biopsy. The present study intends to validate the performance of a DNA methylation test.

Method: We performed a multicenter confirmatory study to test the diagnostic accuracy of a standardized DNA methylation assay including *BHLHE22* and *CDO1* genes against results from invasive procedures. Women older than 40 years with abnormal uterine bleeding underwent a transvaginal ultrasound, the methylation test, and endometrial tissue biopsy by suction curettage, dilatation and curettage, or hysteroscopic biopsy. Sensitivity, specificity, and accuracy were calculated.

Results: In January 2018, we started to enroll patients from 5 centers around Taiwan. A preliminary analysis of 251 women as a training set revealed sensitivity of 90%, specificity of 75%, and accuracy of 90% for the detection of endometrial cancer, which is better than transvaginal ultrasonography with accuracy around 65%–70%.

Conclusion: The application of DNA methylation including *BHLHE22* and *CDO1* for endometrial cancer detection is promising. DNA methylation testing, used as a triage before an invasive endometrial biopsy, may substantially reduce the risks and cost of over-diagnosis. Further validations in different ethnic backgrounds are imperative.

LBA 5 - Sunrise Session
A2m – a novel diet related endometrial cancer biomarker
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Objective: We sought to determine whether transcriptomic changes induced by a high-fat diet (HFD) in an endometrial cancer rat model can be replicated in human endometrial cancer.

Method: Ninetten BDII/Han rats were included. Group A (n = 7) were given ad lib access to normal-calorie, normal-chow diet (NCD), while group B (n = 12) were given ad lib access to calorie-rich HFD for 15 months. RNA sequencing was performed on endometrial tumors from both groups. Top ranking genes were examined in a The Cancer Genome Atlas (TCGA) endometrial cancer dataset to determine their significance in human endometrial cancer.

Results: The weight gain in HFD rats was double the weight gain of NCD rats (50 g vs 25 g). Four rats in each group developed endometrial cancer. A total of 368 DEGs were identified between the tumors in the HFD group compared to the NCD group. Alpha-2 macroglobulin (A2m) was significantly downregulated in the HFD group. Kaplan-Meier analysis demonstrated increased levels of A2m were associated with improved OS (P = 0.02) in the TCGA cohort. Assessment of the relationship between A2m and clinicopathological variables demonstrated increased A2m expression was associated with low grade (P < 0.001), endometrioid tumors (P = 0.003). Increased A2m mRNA expression was associated with *PTEN* and *CTNNB1* mutations. There was a significant negative correlation between A2m mRNA expression levels and BMI in the TCGA cohort (Spearmans ρ = −0.263, P < 0.001), consistent with our findings in the rat model.

Conclusion: Diet and obesity can alter endometrial cancer transcriptomic profiles environment at a transcriptomic level. These findings demonstrate that the BDII/Han rat model can be used to identify clinically relevant biomarkers in human endometrial cancer.

Focused Plenary I: Opioid Reduction and ERAS in Gynecologic Oncologic Surgery

48 - Focused Plenary Session
Patient satisfaction of a restrictive opioid prescribing algorithm in gynecologic oncology patients undergoing surgery
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Objective: Our goal was to evaluate patient satisfaction in gynecologic oncology patients undergoing surgery managed with a restrictive opioid-prescribing algorithm (ROPA).

Method: This retrospective cohort study included gynecology oncology patients undergoing any surgical procedure from October 2018 to August 2019. A control group without restrictive prescribing practices was identified from October 2016 to September 2017. Patients were educated preoperatively about pain management goals, the ROPA, and disposal of leftover opioids. Standardized prescriptions were written on discharge based on surgical complexity (4-tiered system) and 24-hour postoperative opioid use. During the first 6 months of the study, patients were asked to complete a survey at their postoperative visit evaluating patient satisfaction, number of leftover pills, and disposal methods. Statistical analysis was performed using SPSS Statistics v.24.

Result: A total of 2,549 patients met inclusion criteria in the total cohort, 1,321 in the control group and 1,369 in the ROPA group. Patient demographics, including age, BMI, and surgical procedures, were similar between groups. The average number of pills prescribed at discharge was significantly lower in the ROPA group (30.5 pills vs 11.3 pills, $P < 0.001$). A total of 694 patients were asked to complete the survey. Completion rate was 58.5% (406 patients). Patients reported that 95.8% of the time they were "very satisfied" or "somewhat satisfied" with their postoperative pain control. Of these, 16.2% noted that they did not fill their opioid prescription at all, while 54.2% stated they had leftover pills (mean 5.8). Of those patients, 35.6% disposed of their leftover pills, the most common method being toilet-flushing (71.2%) and least common being a disposal center (6.8%). Of all patients, 11.1% needed a refill opioid prescription.

Conclusion: A restrictive prescribing practice allows for a significant reduction in the amount of opioids prescribed, maintaining high patient satisfaction with pain management. Even with restrictive practices, 16% of patients did not fill their opioid prescription due to adequate pain control with over-the-counter pain medications. Despite increased education, only 35% of patients disposed of leftover opioids. Further research is underway to address disposal methods for patients with leftover pills.

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49 - Focused Plenary Session

Preliminary prospective quality of life and clinical outcomes with an opiate restrictive enhanced recovery protocol in a gynecologic oncology population

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Objective: The impact of enhanced recovery after surgery (ERAS) protocols on quality of life (QOL) is not well defined. We describe initial clinical and QOL outcomes following an enhanced ERAS protocol that relies upon opiate-sparing anesthesia.

Method: After obtaining study consent, patients undergoing surgery by gynecologic oncology completed a validated QOL survey (SF36) preoperatively and 2-week and 6-week postoperatively to measure 8 domains of QOL. A departmental ERAS protocol involving opiate-sparing anesthesia was used for all patients**.** Clinical demographics were abstracted from medical records. QOL scores after minimally invasive surgery (MI) versus open approach (XL) were compared using Student *t* test or nonparametric Mann–Whitney 2-sample test. Primary outcome is a 10% difference in general health score of SF36. Clinical data were compared using Student *t* test, χ^2, Fischer exact test, or Wilcoxon rank sum test.

Results: To date, clinical data from 87 patients and QOL data from 63 patients have accrued. The 2 groups were comparable overall for patient characteristics and clinical outcomes. XL patients were more likely to have FIGO stage 2, 3, or 4 disease (0% vs 19.6%, $P = 0.015$) and to undergo paraaortic lymphadenectomy (LND) ($P = 0.01$), but less likely to undergo hysterectomy ($P = 0.002$) than to MI patients. The difference in blood loss was not clinically significant (22.5 cc MI vs 50 cc XL, $P = 0.02$). Median hospital stay was 0 days for MI and 1 day for XL. No differences were found in readmission rates ($P = 0.8$), surgical site infection ($P = 0.55$), or number of patient phone calls ($P = 0.74$). QOL outcomes are summarized in **Table 1**. Six-week scores for all categories were comparable to preoperative for both groups, except for physical health (XL 52.2 vs 27.5, $P \leq 0.05$). Compared to baseline, XL 6-week scores were higher for both emotional well-being (69.6 vs 75.9, $P \leq 0.05$) and health change (39.1 vs 59.6, $P \leq 0.05$). There were no differences between XL and MI QOL scores at the 6-week visit.

Conclusion: Our preliminary analyses indicate that QOL following XL versus MI is comparable following our enhanced ERAS protocol. Patients undergoing XL were safely discharged to home typically on the first postoperative day without increased rates of readmissions, infection, or phone calls.

Table 1. Quality of life scores for minimally invasive versus open.

	Preoperative		2-week Postoperative		6-week Postoperative	
SF-36 Measure	**Minimally invasive (*n* =17)**	**Open surgery (*n* = 46)**	**Minimally invasive (*n* = 16)**	**Open surgery (*n* = 45)**	**Minimally invasive (*n* – 15)**	**Open surgery (*n* = 40)**
Physical function	**82.3 (19.7)[b]**	**67.7 (27.5)[b]**	**52.5 (25.4)[a]**	**40.0 (26.9)[a]**	75.7 (20.3)	60.0 (31.2)
Role: Physical health	58.8 (48.4)	52.2 (44.4)	**21.9 (34.0)[a]**	**11.1 (23.6)[a]**	46.7 (35.2)	**27.5 (36.2)[a]**
Role: Emotional problems	58.3 *46.4)	64.5 (43.0)	58.3 (44.8)	66.7 (44.3)	68.9 (42.7)	65.0 (43.4)
Energy/fatigue	51.5 (24.7)	44.8 (21.5)	41.3 (23.6)	41.2 (18.3)	47.3 (25.8)	49.9 (21.1)
Emotional well-being	71.6 (13.7)	69.6 (20.6)	71.5 (16.7)	74.2 (17.2)	73.9 (16.8)	**75.9 (16.8)[a]**
Social Functioning	70.4 (30.9)	71.6 (25.3)	53.4 (23.5)	50.0 (25.3)[a]	71.9 (26.9)	64.5 (30.7)
Pain	65.8 (28.4)	56.2 (30.2)	**48.3 (22.6)[a]**	**36.2 (24.8)[a]**	61.9 (30.2)	62.2 (24.7)
General Health	60.7 (26.7)	64.2 (22.5)	60.0 (24.9)	67.0 (22.3)	61.7 (26.4)	67.2 (26.3)
Health Change	44.1 (28.7)	39.1 (25.1)	53.1 (20.2)	47.8 (26.0)	51.7 (27.5)	**59.6 (30.3)[a]**

Data presented as mean (standard deviation)
Preoperative vs. week 6: [a]$P < 0.05$. Minimally invasive vs. open: [b]$P < 0.05$
P value for between groups were obtained using the Student's t-test
P value for within groups were obtained using paired t-test

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50 - Focused Plenary Session

Factors associated with acute kidney injury (AKI) in patients undergoing surgery on an enhanced recovery after surgery pathway

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Objective: Goal-directed fluid therapy, a tenant of enhanced recovery after surgery (ERAS) programs aimed at reducing complications associated with restrictive or liberal IV fluid administration, has markedly reduced the total amount of IV fluids administered intra- and postoperatively. We aimed to describe the incidence of acute kidney injury as defined by the RIFLE criteria within an ERAS program.

Method: Patient demographics and clinical characteristics were summarized. χ^2 or Fisher exact test was used to compare categorical variables among groups, and Wilcoxon rank sum test was used to compare medians. Patients were classified as having acute kidney injury if they had acute kidney risk, injury, or failure by the RIFLE criteria. We estimated the proportion of patients with acute kidney injury using exact binomial proportions and a 95% confidence interval.

Results: Among 1,127 patients who underwent open gynecologic surgery in an ERAS pathway, 140 (12.4%) met RIFLE criteria for acute kidney injury. We are 95% confident that the proportion of patients who will experience acute kidney injury is between 10.5% and 14.5%. There were no significant differences in median preoperative creatinine clearance between those who experienced acute kidney injury and those who did not. There were no significant differences between the groups who did experience acute kidney injury and those who did not in terms of anesthesia technique, strict adherence to goal-directed fluid therapy monitoring techniques, or intraoperative urine output. Women with acute kidney injury were more likely to be older, 65 years (33–86 years) versus 57 years (18–87 years) ($P < 0.001$) and have more comorbid conditions (Charlson comorbidity index 3+) (73.6% vs 47.8%, $P < 0.001$). Specifically, women with acute kidney injury were more likely to be diabetic or have pre-existing hypertension. Women with acute kidney injury had a higher median estimated blood loss (400 ml vs 250 ml, $P < 0.001$) and were more likely to have hypotension in the postoperative setting (5.7% vs 1.8%, $P = 0.010$). Acute kidney injury was associated with an increased median length of stay (4 days vs 3 days, $P < 0.001$) and higher proportion of patients undergoing reoperation (5% vs 1.3%, $P < 0.001$) and readmission (20% vs 9.3%, $P < 0.001$). See **Table 1**.

Conclusion: The rate of acute kidney injury in patients undergoing surgery on an ERAS pathway is 12.4%. Future efforts should be aimed at identifying risk factors and implementing ERAS pathway interventions to ameliorate renal compromise.

Table 1. Patient demographics and clinic characteristics associated with AKI within ERAS patients

Variable	no AKI N = 987	AKI N = 140	P-value
Age [median (min, max)]	57.0 (18.0, 87.0)	65.0 (33.0, 86.0)	< 0.001
Charlson Comorbidity Index			< 0.001
0	115 (11.7%)	3 (2.1%)	
1-2	400 (40.5%)	34 (24.3%)	
3+	472 (47.8%)	103 (73.6%)	
OR Time (minutes) [median (min, max)]	211.0 (33.0, 1437.0)	263.0 (58.0, 686.0)	< 0.001
Ethnicity			0.548
Hispanic or Latino	156 (15.8%)	25 (17.9%)	
Not Hispanic or Latino	796 (80.6%)	108 (77.1%)	
Unknown	35 (3.5%)	7 (5.0%)	
Race			0.036
White or Caucasian	682 (69.1%)	93 (66.4%)	
Black or African American	106 (10.7%)	25 (17.9%)	
Asian	61 (6.2%)	2 (1.4%)	
Native Hawaiian or Other Pacific Islander	2 (0.2%)	0 (0%)	
American Indian or Alaskan Native	2 (0.2%)	1 (0.7%)	
Unknown	134 (13.6%)	19 (13.6%)	
Preop creatinine clearance [median (min, max)]	96.1 (8.5, 299.2)	89.3 (30.6, 217.6)	0.288
Comorbidity - Diabetes Mellitus (yes)	121 (12.3%)	30 (21.4%)	0.005
EBL [median (min, max)]	250.0 (5.0, 5550.0)	400.0 (20.0, 4000.0)	< 0.001
Urine Output [median (min, max)]	300.0 (0.0, 2070.0)	295.0 (10.0, 2000.0)	0.966
Goal-directed therapy (yes)	560 (56.8%)	89 (63.6%)	0.144
Crystalloids (mL) [median (min, max)]	1500.0 (0.0, 4510.0)	1700.0 (350.0, 6600.	< 0.001
Colloids (mL) [median (min, max)]	500.0 (25.0, 3000.0)	1000.0 (250.0, 2500.	< 0.001
Net Fluid Balance (mL) [median (min, max)]	1250.0 (-6420.0, 618	1515.0 (-936.0, 7170	< 0.001
Length of stay (days) [median (min, max)]	3.0 (1.0, 43.0)	4.0 (2.0, 57.0)	< 0.001
Readmission	92 (9.3%)	28 (20.0%)	< 0.001
Reoperation	13 (1.3%)	7 (5.0%)	0.008
Hypotension	18 (1.8%)	8 (5.7%)	0.010
Hypertension	16 (1.6%)	6 (4.3%)	0.045

Focused Plenary II: Tipping the hand of immunotherapy for gynecologic malignancies

51 - Focused Plenary Session

A phase I/II study of chemo-immunotherapy with durvalumab (durva) and pegylated liposomal doxorubicin (PLD) in platinum-resistant recurrent ovarian cancer (PROC): Genomic sequencing and updated efficacy results

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Objective: The objectives of this study, where durvalumab (durva, an anti-PD-L1 antibody) is added to pegylated liposomal doxorubin (PLD), standard therapy for platinum-resistant ovarian cancer (PROC), are to evaluate the efficacy and safety of the combination and to identify genomic characteristics associated with response and progression-free survival (PFS).

Method: This is a phase I/II, multicenter, single-arm, open-label study (NCT02431559). PLD is reported to have a 6-month PFS (PFS6) of 25%. The null hypothesis of PFS6 ≤ 25% was tested against the alternative hypothesis at 0.05 level using 90% 2-sided CI; the primary endpoint, PFS6, was reported at ESMO 2018. Exom sequencing was done on PBMCs and tumor samples at baseline. Updated efficacy and DNA sequencing results are provided.

Results: In phase II, 40 patients (median age 65 years [32–83] years) each received at least 1 dose of the study drug (PLD 40 mg/m^2 + durva 1,500 mg every 4 weeks IV). PFS6 by RECIST1.1 was 47.7% (per protocol *n* = 36, 90% CI 33.1–60.9) and 42.9% (ITT *n* = 40, 90% CI 27–57.8). Response rate (ORR) was 22.5% (90% CI 10.8–38.5, 4 CR, 5 PR); median PFS was 5.5 (0.3 to 28.8+) months; and median overall survival was 17.6 (1.7 to 32.5+) months. Treatment-related adverse events ≥ grade 3 in ≥2 patients were palmar-plantar erythrodysesthesia syndrome/rash (27.5%), stomatitis (10%), lymph count decrease (10%), lipase increase (5%), and anemia (5%). Exom sequencing data are available for 28 of 40 patients. No patient had *BRCA1*/*BRCA2* mutation; 3 patients had hypermutated non-MSI phenotypes. Analysis of copy numbers found multiple potential mechanisms for resistance to the PLD + durva combo. Deletions of LRP1B were previously shown to drive resistance to PLD. We also found that PFS (P = 0.0016) for patients on PLD + durva negatively correlated with LRP1B deletions. Patients with MYC amplifications had a lower response (P = 0.0005) and shorter PFS (P = 0.006, HR = 2.889) on the PLD + durva combination. In the TCGA ovarian cancer dataset, MYC amplification is linked to overexpression of IDO1, CXCL17, CXCL11, suggesting a unique immune suppressive microenvironment driven by MYC amplifications. Additional analyses including *BRCA* mutation are ongoing and will be presented.

Conclusion: The PLD + durva combination has a tolerable safety profile and promising efficacy. The study met its primary endpoint with improvement in PFS6. We confirm the negative impact of LRP1B deletions on PLD-based therapies. MYC amplification may be central in driving resistance to the combination and has not been previously linked to PLD efficacy.

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52 - Focused Plenary Session

Pembrolizumab window study: Illuminating the immunologic landscape in gynecologic cancers

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Objective: A "window of opportunity" study in newly diagnosed ovarian (OV) and endometrial (EM) carcinoma patients was conducted to assess changes in PD-L1 expression and immune cell recruitment in response to pembrolizumab, a PD-1 inhibitor.

Method: Patients with newly diagnosed OV or EM cancer were eligible. Participants underwent biopsy pre-pembrolizumab therapy (200 mg IV once) followed by repeat tumor acquisition >7 days later. Subsequent treatment was per standard of care (SOC), and after completion, participants were allowed optional pembrolizumab maintenance therapy every 3 weeks for 12 months. Primary objectives were to determine (1) feasibility and safety of pembrolizumab prior to SOC therapy (frequency and grade of immune-related events) and (2) changes in PD-L1 expression (by immunohistochemistry with monoclonal antibody clone 22C3 on FFPE specimens;l Qualtek, PA) scored using a quantitative modified proportion score (MPS) and qualitative assessment of immune presence at the stromal interface (SI). Exploratory objectives included assessment of cytokines (CXCL10, IFNg, IL10, IL12p70, IL-1b, IL-2ra, IL-6, TNFa) in EDTA plasma samples at baseline and during treatment. Descriptive statistics are provided.

Results: Fifteen patients enrolled and received pembrolizumab. Primary sites included OV 13, EM 2. One patient experienced fever as an immune-related toxicity after a single dose with no impact on SOC. Eleven patients had adequate pre- and post-treatment tissue samples for paired PD-L1 MPS and 9 for SI assessment. Baseline and post-treatment PD-L1 MPS ranged from 0 to 95 (median 1) and 0 to 85 (median 6), respectively. SI was negative at baseline in 6 of 9 assessable cases. PD-L1 MPS score

increased in 7 cases. SI switched from negative to positive in 3 cases. Combining both parameters, 8 of 10 assessable tumor specimens demonstrated either an increase in PD-L1 MPS or a switch from negative to positive SI. Five patients had pre- and post-treatment plasma samples. CXCL10, IFNg, IL10, IL-2ra, and TNFa levels all increased after pembrolizumab in responding patients (CR/PR), but decreased in the 1 patient who progressed on-treatment.

Conclusions: A single dose of pembrolizumab prior to SOC increased PD-L1 MPS and/or SI immune cells, suggesting potential for local tumor immunologic recruitment. In addition, increases in systemic inflammation after 1 dose of pembrolizumab were noted, but increases in cytokine production were limited to the responding patients.

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53 - Focused Plenary Session

Intraperitoneal or subcutaneously administered IL-15 superagonist (N-803) increases NK cell cytotoxicity in ovarian cancer

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Objective: Our goal was to determine the effect of an IL-15 superagonist (N-803) on the immune microenvironment in the peritoneal cavity and peripheral blood when administered weekly as maintenance therapy in a phase II clinical trial.

Method: Patients who received at least 3 cycles of intraperitoneal (IP) chemotherapy first line are randomized to IP versus subcutaneous (SC) administration of N-803 weekly for 4 weeks for cycle 1 followed by SC dosing weekly for 4 weeks every other month for 4 cycles as maintenance therapy. Peripheral blood mononuclear cells (PBMCs) and IP washings are collected at baseline and prior to delivery of each cycle of N-803. Ki67 levels by flow cytometry were examined for CD4+, CD8+, and CD4+Foxp3+. Cytotoxicity assays were performed against ovarian cancer cell lines. CyTOF (Fluidigm, mass cytometry) was performed to comprehensively evaluate immune evolution and checkpoint marker expression during weekly time points.

Results: To date there have been no grade 4 or 5 adverse events. The most frequent adverse events are injection site reaction (Gr 1), chills (Gr 2), and flu-like symptoms (Gr 3). Flow cytometric data of PBMCs from 6 patients to date indicate that N-803 treatment induces maximal proliferation (Ki-67) on peripheral blood NK cells by day 8 post-treatment and cytotoxicity by day 15, but activity wanes at later time points; CD8+ T cells follow a similar pattern (**Figure 1A**). NK cell cytotoxicity against ovarian cancer cell lines was maximal at day 15 following N-803. Cytof analysis of IP washings correlate with peripheral blood findings in that Ki67 is maximal at day 8 post-treatment for NK, CD8+, and CD4+ cells. NKG2D, an activating receptor for NK cytotoxicity, is maximal on peritoneal NK and CD8+ T cells at day 15. The decrease in proliferation at day 8 correlates with an increase and retention of PD-1 expression in both the NK and CD8+ T cell population (**Figure 1B**).

Conclusion: N-803 (IL-15) improves NK cell activation and ovarian cancer target killing initially. However, NK cell activation and killing are countered by inhibitory signaling provided by the PD-1/PD-L1 axis. These findings suggest checkpoint blockade, in combination with IL-15, may result in significant increase in patient-derived NK cell function against ovarian cancer.

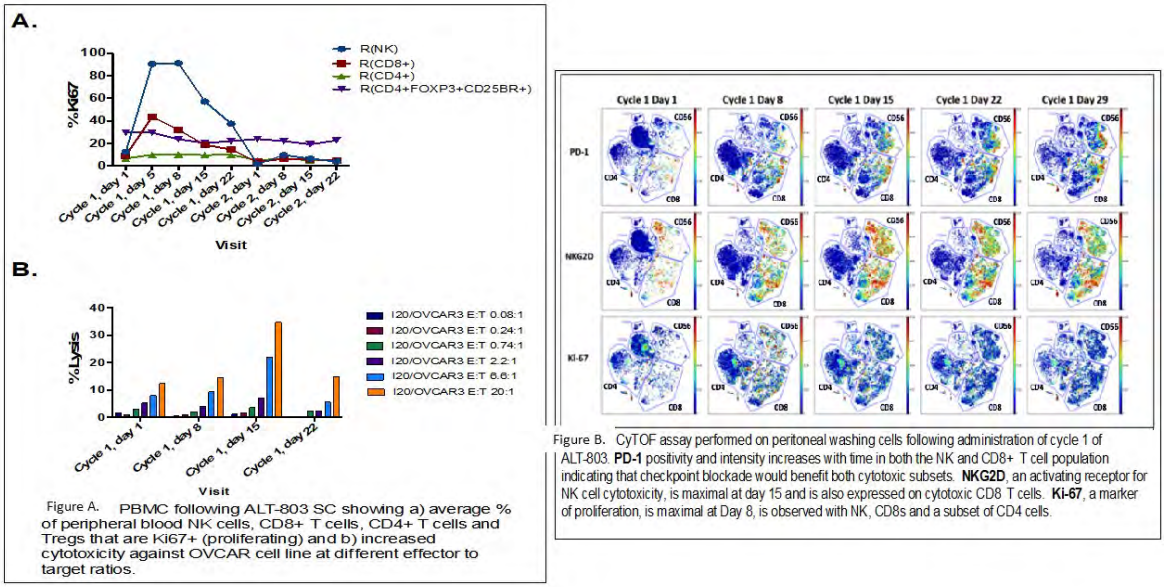

Figure A. PBMC following ALT-803 SC showing a) average % of peripheral blood NK cells, CD8+ T cells, CD4+ T cells and Tregs that are Ki67+ (proliferating) and b) increased cytotoxicity against OVCAR cell line at different effector to target ratios.

Figure B. CyTOF assay performed on peritoneal washing cells following administration of cycle 1 of ALT-803. **PD-1** positivity and intensity increases with time in both the NK and CD8+ T cell population indicating that checkpoint blockade would benefit both cytotoxic subsets. **NKG2D**, an activating receptor for NK cell cytotoxicity, is maximal at day 15 and is also expressed on cytotoxic CD8 T cells. **Ki-67**, a marker of proliferation, is maximal at Day 8, is observed with NK, CD8s and a subset of CD4 cells.

Fig. 1.

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54 - Focused Plenary Session

A phase I clinical trial of autologous chimeric antigen receptor (CAR) T cells genetically engineered to secrete IL-12 and to target the MUC16ecto antigen in patients (pts) with MUC16ecto+ recurrent high-grade serous ovarian cancer (HGSOC)

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Objective: Chimeric antigen receptor (CAR) T cell therapy has shown efficacy in leukemia. MUC16^{ecto} is a tumor-associated antigen that is highly expressed in certain solid tumors, including high-grade serous ovarian cancer. We conducted a first-in human phase I dose escalating trial testing the safety of autologous 4H11-28z/fIL-12/EFGRt^{+} CAR T cells in patients with recurrent MUC16^{ecto+} HGSOC (NCT02498912). We incorporated regional intraperitoneal (IP) and intravenous (IV) delivery of the cells.

Method: 4H11-28z/fIL-12/EFGRt^{+} CAR T cells were genetically modified to target MUC16^{ecto} antigen and to secrete IL-12. Given the concern for potential systemic toxicity, the vector included a gene for truncated epidermal growth factor receptor (EGFR). Patients with recurrent measurable MUC16^{ecto+} (confirmed by immunohistochemistry) HGSOC with 2–7 prior cytotoxics were eligible. Fifty percent of planned CAR T cell dose was given IV, and if tolerated, the remaining 50% IP 1–2 days later. The primary endpoint was safety using Common Terminology Criteria for Adverse Events (CTCAE) criteria. Secondary endpoints included response by Response Evaluation Criteria in Solid Tumors (RECIST)/irRECIST criteria. Standard dose escalation proceeded based on dose-lmiting toxicity (DLT) assessment at 4 dose levels (3×10^5 to highest treated dose of 1×10^7 CAR T cells/kg). An additional cohort was treated at dose level 3 (3×10^6 CAR T cells/kg) following pretreatment with cyclophosphamide/fludarabine. Correlative studies included serial measurement of cytokine levels and CAR T cell persistence in blood and ascites.

Results: Eighteen heavily pretreated patients with MUC16^{ecto+} HGSOC received CAR T cells. Intense monitoring for on-target, off-tumor toxicity by clinical (including cornea) and radiological examination found no significant toxicity in the cohorts of patients treated with CAR T cells alone. As expected, cytokine release syndrome was observed at all doses. No DLT occurred in cohorts I–IV. Best response seen was stable disease. In the cohort with lymphodepleting chemotherapy (cohort V) 2/3 patients experienced DLT (hemophagocytic lymphohistiocytosis/macrophage activation-like syndrome). No further patients were treated with that combination. **Figure 1** shows CAR T cells persistence in peripheral blood (1–12 weeks).

Conclusion: IV and IP IL-12 secreting MUC16^{ecto}-targeted CAR T cells were safely administered in the absence of chemotherapy. Toxicity was observed when the CAR T cells were given post-lymphodepleting chemotherapy. Dose escalation

of CAR T cells will continue to dose level 5 (3×10^7 CAR T cells/kg). Based on our preclinical data, we aim to enhance persistence of the CAR T cells by administering them combination with anti-PD-1 therapy.

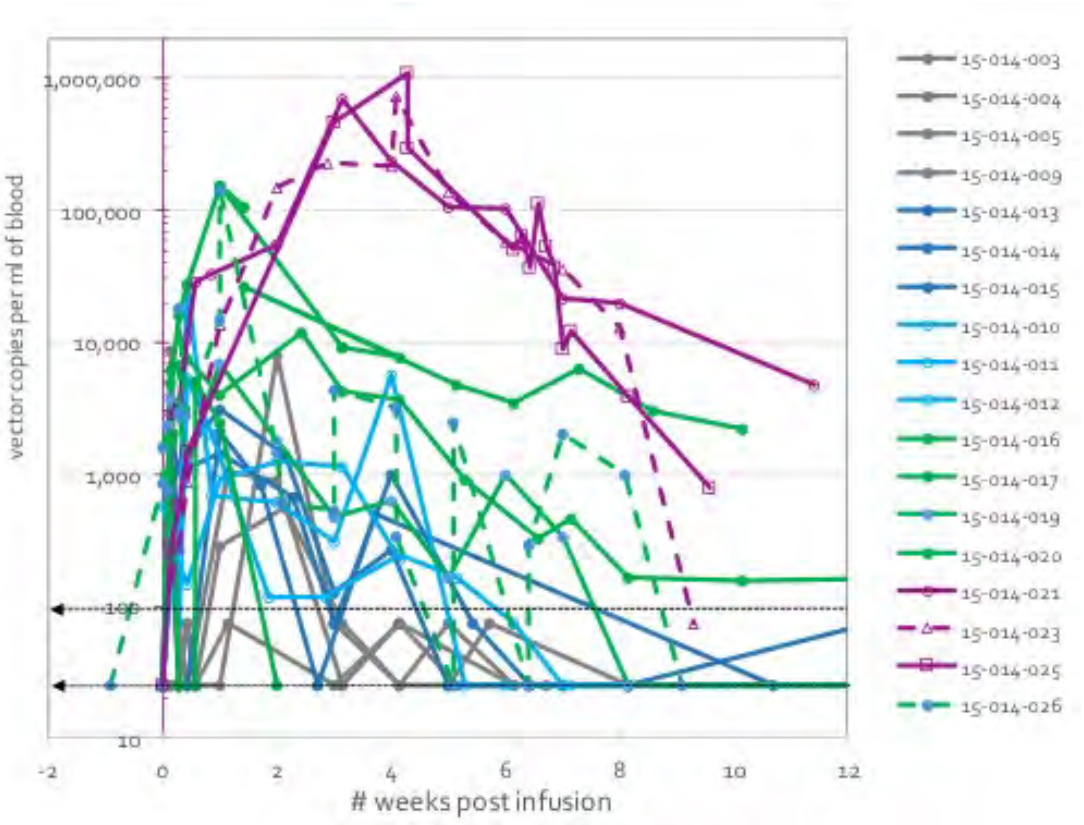

Fig. 1.

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55 - Focused Plenary Session

Apatinib plus camrelizumab in patients with advanced cervical cancer: A multicentre, open-label, single-arm, phase II trial

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Objective: Apatinib is a selective inhibitor of vascular endothelial growth factor receptor-2 (VEGFR2). We aimed to assess the efficacy and safety of apatinib plus camrelizumab, a fully humanized anti-PD-1 monoclonal antibody, in patients with advanced cervical cancer.

Method: In this open-label, single-arm, phase 2 study done at 4 centers in China, eligible patients were aged 18 years or older, had an Eastern Cooperative Oncology Group performance status of 0 or 1, progressed after at least 1 line of systemic chemotherapy for metastatic, recurrent, or persistent cervical cancer, and had measurable disease. Patients received oral apatinib 250 mg once daily and intravenous camrelizumab 200 mg every 2 weeks. Treatment continued until disease progression, unacceptable toxicity, and withdrawal of consent. The primary endpoint was the objective response rate (ORR) assessed by the Response Evaluation Criteria in Solid Tumor (RECIST, version 1.1). An optimal Simon 2-stage design was employed to test the null hypothesis of a 17% ORR versus 35% alternative (1-sided alpha 0.10, 80% power), if more than 3 responses out of the first 16 patients were observed, then the study will continue to enroll a total of 44 patients.

Results: Between January 21, 2019, and August 1, 2019, 45 patients were enrolled and received at least 1 dose of camrelizumab (safety population). The median age was 51 years (range 33–67 years). Median previous treatment lines was 2 (range 1–4). In the first stage, 8 responses were noted among 16 patients, which met the first-stage criteria; then the study continued to stage 2. As of October 25, 2019, the median follow-up was 6.7 months (range 1.7–9.23). Twenty-five (57.1%) of 42 patients who had at least 1 post-baseline tumor assessment (efficacy evaluable set) achieved an objective response, including 1 (2.2%) complete response and 24 (53.3%) partial response. The disease control rate was 88.1% (37/42). The

median duration of response has not yet been reached. Thirty-one (68.9%) patients had grade ≥3 treatment-related adverse events (TRAEs). Grade ≥3 TRAEs occurring in ≥5% of patients were hypertension (22.2%), fatigue (15.6%), anemia (13.3%), and thrombocytopenia (6.7%). See **Figure 1**.

Conclusion: Apatinib plus camrelizumab showed promising antitumor activity and tolerable toxicities in patients with advanced cervical cancer.

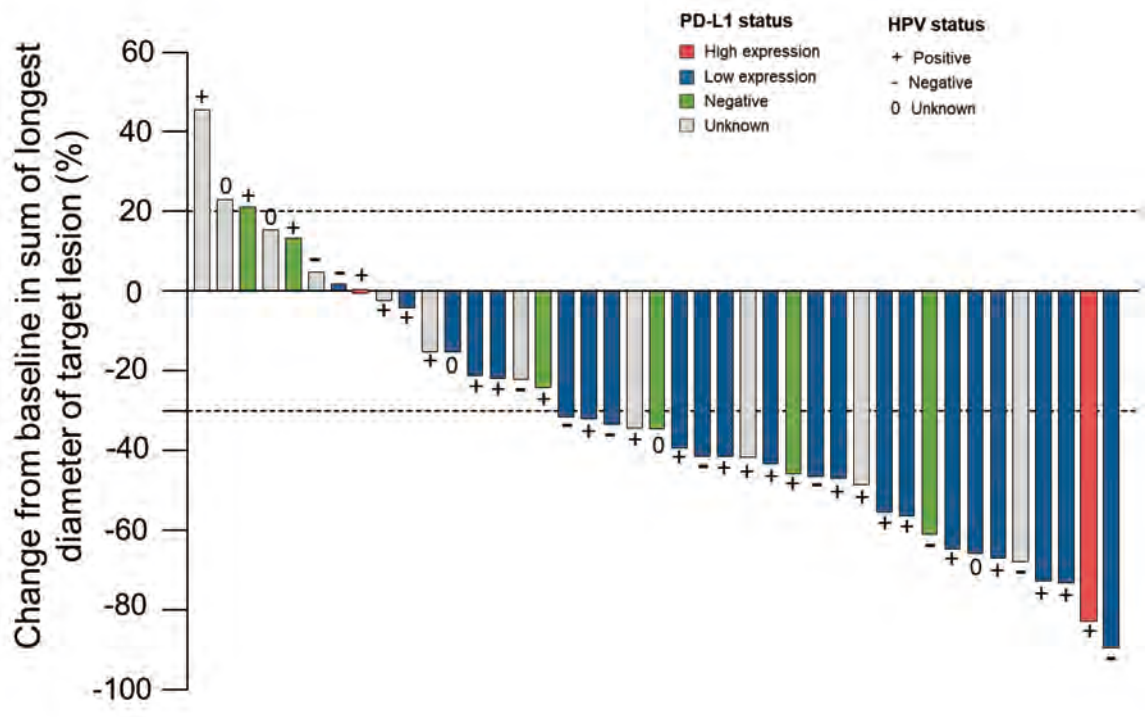

Fig. 1.

Focused Plenary III: Translational discoveries in ovarian cancer

56 - Focused Plenary Session
Histopathological characterization of the tubal fimbria reveals a subgroup of *BRCA1* mutation carriers with tumor-promoting gene-set enrichment
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Objective: Fallopian tube secretory epithelial cells have been implicated as the origin of high-grade serous ovarian cancer (HGSOC). Most ovarian cancers are diagnosed in postmenopausal women, although it is unclear how postmenopausal conditions contribute to cancer formation. Germline *BRCA1* mutations are associated with a 40% lifetime risk of ovarian cancer. This high-risk population is characterized by early onset of disease and predominant serous histology. The events that lead to secretory cell transformation are unknown. We aimed to identify potential precancerous niches in normal human fallopian tubes.

Method: Normal fallopian tube sections of 38 *BRCA* mutation carriers and 36 noncarriers were stained for PAX8, a marker for secretory cells and FOXJ1, a marker for ciliated cells. Digital image analysis was applied to determine secretory-to-ciliated cell ratios in the tubal fimbria. The same areas of interest were subjected to transcriptomic analysis.

Results: The PAX8/FOXJ1 cell ratio distinguishes two subgroups of *BRCA1* mutation carriers: ~70% resemble noncarriers and ~30% with a high PAX8/FOXJ1 cell ratio (**Figure 1A**). In postmenopausal patients, this segregation is maintained at the transcriptomic level (**Figure 1B** and **Figure 1C**). Strikingly, fimbriae of postmenopausal *BRCA1* mutation carriers with a high PAX8/FOXJ1 cell ratio are significantly enriched for ovarian cancer related pathways, mainly Ras, a known oncogene, its

effectors PI3K and AKT and Rap1, a Ras associated protein shown to promote ovarian cancer and metastasis. JAK/STAT3, a major signaling pathway associated with ovarian tumor progression and poor prognosis is also enriched (**Figure 1D**).

Conclusion: The PAX8/FOXJ1 cell ratio demarcates a unique population of postmenopausal *BRCA1* mutation carriers in which cancer-related gene sets emerge in healthy tubal fimbria. Further investigation is needed to determine whether these represent the earliest stages of cancerous transformation in hereditary ovarian cancer patients.

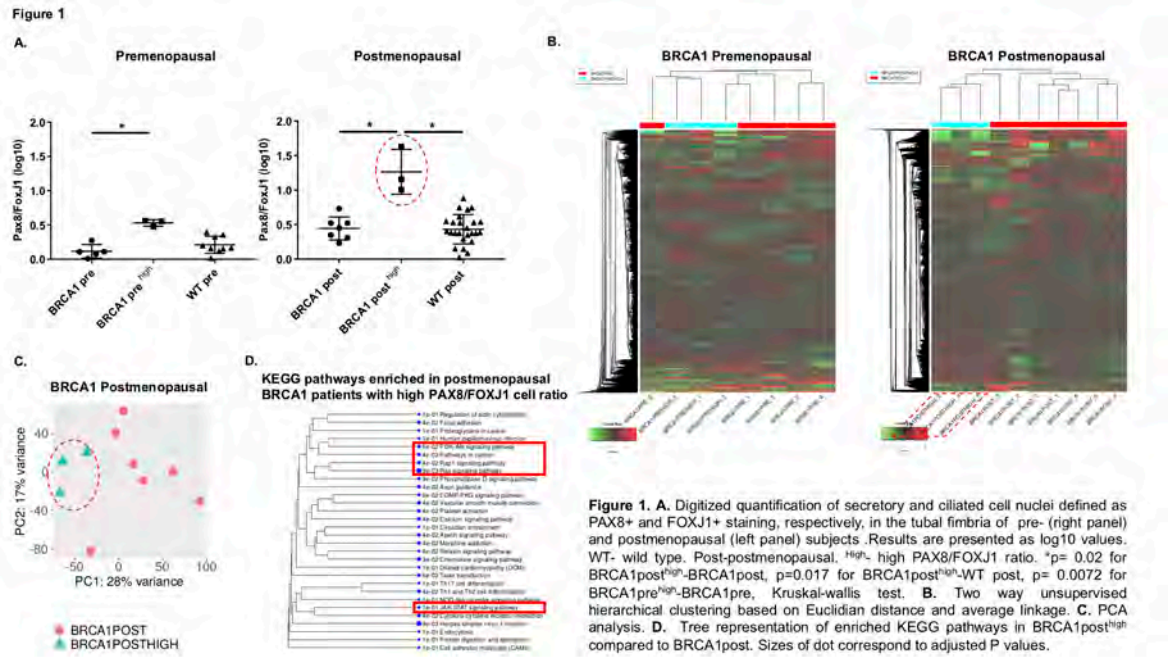

Figure 1. A. Digitized quantification of secretory and ciliated cell nuclei defined as PAX8+ and FOXJ1+ staining, respectively, in the tubal fimbria of pre- (right panel) and postmenopausal (left panel) subjects .Results are presented as log10 values. WT- wild type. Post-postmenopausal. ^{High}- high PAX8/FOXJ1 ratio. *p= 0.02 for BRCA1post^{high}-BRCA1post, p=0.017 for BRCA1post^{high}-WT post, p= 0.0072 for BRCA1pre^{high}-BRCA1pre, Kruskal-wallis test. **B.** Two way unsupervised hierarchical clustering based on Euclidian distance and average linkage. **C.** PCA analysis. **D.** Tree representation of enriched KEGG pathways in BRCA1post^{high} compared to BRCA1post. Sizes of dot correspond to adjusted P values.

Fig. 1.

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57 - Focused Plenary Session
Metabolomic and transcriptomic response to neoadjuvant chemotherapy in HGSOC
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Objective: Variability exists between genetic expression and metabolic profiles of primary tumor and ascites in patients with high-grade serous ovarian cancer (HGSOC). The objective of this study was to utilize primary patient samples to better characterize these differences and to analyze the effect of chemotherapy on gene expression and tumor metabolism.

Method: Tissue and ascites were collected from patients with suspected HGSOC. A subset of patients received neoadjuvant chemotherapy (NACT) and thus tumor was also collected at interval debulking. Full RNA sequencing was performed on 166 samples. Forty of these samples included tumor from patients (n = 20) pre- and post-NACT. Mass spectrometry-based metabolomics was performed on a subset (n = 26). RNA expression and metabolic profile differences between primary tumor and ascites were compared in 29 patients.

Results: Differences in gene expression pre- and post-NACT suggested changes in cell proliferation, cell cycle, and DNA damage response. The TCGA-based gene expression subtype changed in over half of patients following treatment. There was no statistically significant difference in immune signature post-NACT. In ascites, high lactose dehydrogenase was associated with malignant ascites. When comparing 29 matched tumor and ascites samples, the Cancer Genome Atlas (TCGA)-based subtype was the same in about 50% of patients. Differences between ascites and tumor from the same patient were significant for higher expression of genes associated with proliferation, cell migration, MAPK, and TGFb in the ascites. In a comparison of pre-NACT tumors from platinum-resistant and -sensitive patients, expression was significantly different in 84 genes. Platinum-resistant tumors were highly enriched for genes involved in nucleotide metabolism, redox, and oxidative phosphorylation. In a comparison of gene expression to metabolomic data, TCGA cycle metabolism was correlated with increased cellular proliferation in tumor tissue.

Conclusion: In this study, we demonstrate the importance of understanding the heterogeneity that exists in the transcriptomic and metabolomic profiles of the primary tumor, metastatic ascites, and changes induced by standard chemotherapy. Our data highlight the importance of understanding patients' initial response to treatment based not only on DNA-based next generation sequencing, but also on changes in RNA expression and metabolic profiles, which may help direct subsequent therapy.

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58 - Focused Plenary Session

Compositional and architectural characterization of high-grade serous ovarian carcinomas using single cell technologies and multiplex microscopy

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Objective: Therapy of high-grade serous ovarian carcinoma (HGSOC) remains challenging partly due to tumor heterogeneity and complex interactions with the tumor microenvironment (TME). The objective of the study was to determine whether immune cell states are related to their spatial localization within ovarian tumors.

Method: Patients with advanced ovarian cancer undergoing primary debulking surgery or diagnostic laparoscopy were prospectively identified. In order to analyze the interpatient ovarian cancer TME heterogeneity using orthogonal approaches, CD45− and CD45+ populations sorted from tumors were subjected to single cell RNA-sequencing (scRNAseq) analysis. Multiplex immunofluorescence (IF) analysis of the TME was performed on site-matched tumor samples. DNA from the primary site-matched tumors is being subjected to massively parallel sequencing.

Results: Ten patients undergoing primary debulking or diagnostic laparoscopy were included. Median age at diagnosis was 64 years (range 48–79 years). Nine of the 10 (90%) patients had HGSOC, and 1 (10%) had endometrioid ovarian cancer. scRNAseq data demonstrated quantitative and qualitative heterogeneity in tumor-infiltrating immune cell types among patients. The endometrioid ovarian cancer displayed a predominance of B cells compared to the HGSOCs. Multiplex IF analysis of the samples revealed an additional layer of information, demonstrating predominant localization of the CD8+ T cells and macrophages to the stromal rather than tumor compartment: CD8 tumor (median 0.15%, range 0.06–0.78%), CD8 stroma (median 0.56%, range 0.26–1.65%, $P = 0.009$), CD68 tumor (median 1.92%, range 1.18–5.55%), and CD68 stroma (median 11.96%, range 8.40–22.33%, $P < 0.001$). Confirming scRNAseq data, there was significant heterogeneity in the tumor-infiltrating CD8 cells, macrophages, and regulatory T cells among patients. See **Figure 1**.

Conclusion: Our findings highlight that broad characterization of the immune cell types and functional states in the ovarian cancer TME using scRNAseq fails to capture their geographic distribution (i.e., tumor vs stroma). Orthogonal datasets highlighting the TME composition as well as the functional state and distribution of T cells will be essential to understanding the mechanisms promoting tumor immune infiltration or exclusion and development of therapeutic approaches targeted to the specific TME phenotypes.

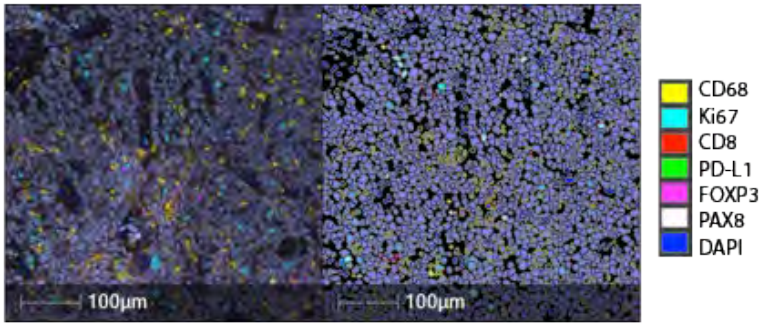

Fig. 1. Multiplex immunofluorescence imaging of omental sample acquired from a patient with HGSOC stained with select immune and tumor-specific markers (left). Segmentation masks demonstrating accurate recognition of individual cells, markers and colocalization (right).

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59 - Focused Plenary Session

***BRCA* tumor-testing in a tertiary referral center: Are we missing something or not?**

M. D'Indinosante[a], C. Marchetti[b], C. Caricato[a], M. Arcieri[c], M. Petrillo[d], R. Ergasti[a], A. Pietragalla[b], A. Minucci[b], A. Fagotti[b] and G.

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Objective: Investigating *BRCA* mutational status in ovarian cancer patients has a key role, both to identify hereditary cancer predisposition and to address therapeutic choices. Approximately 20–25% of patients with high-grade serous ovarian cancers (HGSOC) present with a germline *BRCA1/2* mutation, but a further 5–7% of patients will have a somatic *BRCA1/2* mutation, which might be missed if tumor genomic profile is not performed. The objective of this prospective study is to investigate the feasibility and reliability of a *BRCA* screening workflow based on tumor-tissue *BRCA* analysis and secondary germline screening, in a tertiary referral center.

Method: All newly diagnosed HGSOC patients with FIGO stage IIIC–IV treated from January 2017 to December 2018 underwent tumor *BRCA* testing and were recommended for blood *BRCA* analysis when a pathogenic variant was identified. Data concerning patients' clinical characteristics, treatments, outcomes, and genetic assessment were collected and analyzed.

Results: Overall, 305 patients with stage III–IV HGSOC were primarily treated at our institution and underwent tumor genomic profiling for assessing *BRCA* mutational status. In the whole population, 106 (35%) patients had a somatic pathogenic variant, specifically 66 patients with *sBRCA1*-PVs (62%) and 40 with *sBRCA2*-PVs (38%). Seven patients (2%) showed a variant of uncertain significance (s-VUS), and 192 (63%) a wildtype variant (s-WT). Among patients with s-PVs, 101 (95%) received the germline test, which confirmed the mutation in 89 (88%) patients and showed a wildtype variant in 12 patients (12%) (**Figure 1**). Also, a germline mutation was searched for in 71 (37%) of the s-WT patients; in 70 (98.5%) of them results were confirmed, while in 1 (1.5%) a germline-*BRCA2* VUS was identified.

Conclusion: In our experience, tumor-tissue sample has allowed the identification of 12% of patients potentially eligible for treatment with PARP-inhibitors (PARPi) that would have been missed if only germline testing had been performed. Waiting for results of PARPi trials in the first-line setting, tumor-tissue testing represents a reliable, feasible and cost-saving screening procedure for *BRCA* mutational status assessment.

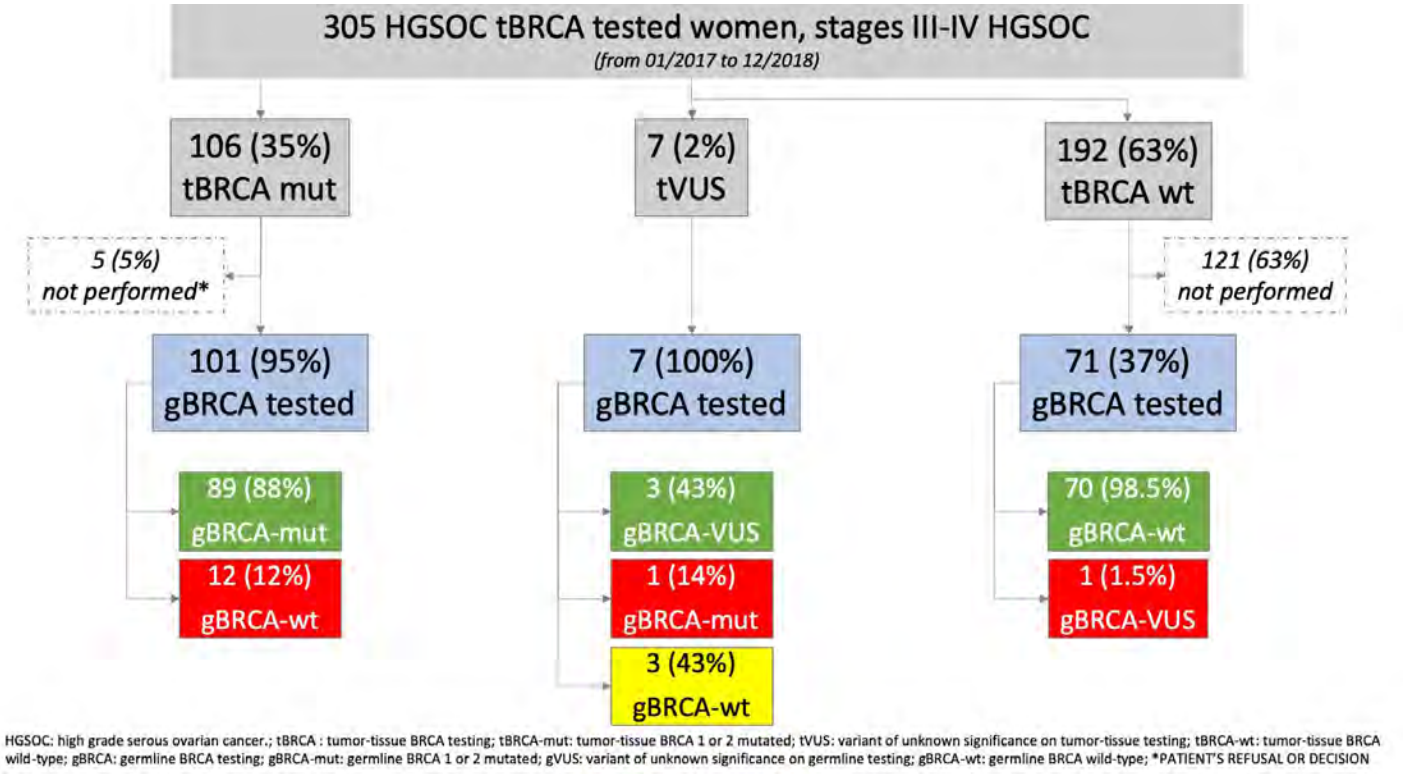

Fig. 1.

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60 - Focused Plenary Session
Clinical indication of *BRCA1* variation: Time for reassessment
L. Li[a], C. Zhu[b], D. Shao[b] and M. Wu[a]. [a]*Peking Union Medical College Hospital, Beijing, China,* [b]*BGI Genomics, Shenzhen, China*

Objective: Germline variation of *BRCA* genes provides preventive and therapeutic approach for patients with epithelial ovarian cancer (EOC). Patients bearing *BRCA* mutations show significant response to platinum-based regimen as well as PARP inhibitors. We showed limited benefit of platinum-based therapy for patients with *BRCA1* mutation, which is in line with limited survival advantage as reported. This study aims to decipher in detail an association of *BRCA1* mutation type with platinum sensitivity.

Method: A total of 1,060 EOC patients with informed consent were recruited from January 2017 to January 2019 from 18 medical centers in China. Peripheral blood samples were collected, and genomic DNA was isolated followed by targeted sequencing of hereditary cancer associated genes by MGI-seq 2000 platform.

Results: A total of 204 patients (19.2%) were carriers of germline *BRCA1* deleterious mutation. Frameshift and nonsense variation are predominant (n = 94, 46% and 72.35%. respectively); 6% *BRCA1* (n = 12) mutation are large-scale deletions. Distinct spectrum of *BRCA1* variation was explored between platinum-sensitive and -resistant patients. *BRCA1* splice variations enriched in platinum-sensitive patients. Large-scale deletion was significantly accumulated in platinum-resistant patients (4% vs 18% in platinum-sensitive vs -resistant group, $P < 0.05$). Detailed analysis revealed platinum sensitivity was associated with small-scale indel, of which single-base indel of *BRCA1* was associated with platinum resistance ($P = 0.046$), and multibase indel was associated with platinum sensitivity ($P = 0.07$). See **Figure 1**.

Conclusion: The complexity of *BCRA1*-mediated platinum response should be considered in detail. Further investigation on *BRCA1*-associated mechanism may be of importance in aiding clinical decision.

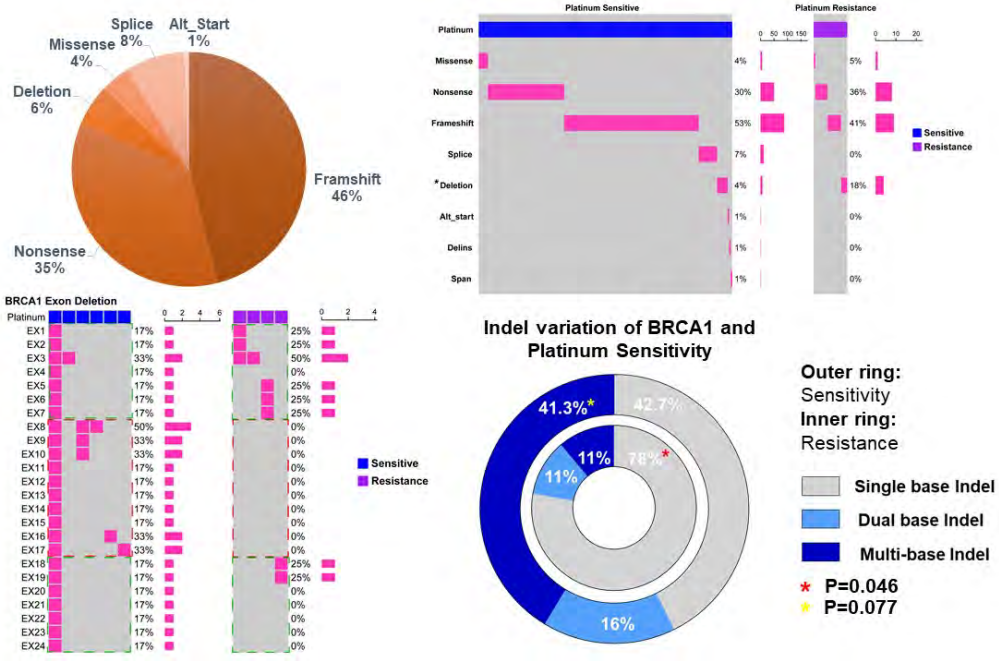

Fig. 1.

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61 - Focused Plenary Session

Comparing mutation frequencies for homologous recombination genes in uterine serous and high-grade serous ovarian carcinomas: A case for homologous recombination deficiency testing in uterine serous carcinoma

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Objective: Our goal was to compare the frequencies of somatic homologous recombination (HR) gene mutations identified in next-generation sequencing (NGS) genomic profiling of uterine serous carcinomas (USCs) and high-grade serous ovarian carcinomas (HGSOCs).

Method: Data for this analysis were obtained from AACR Project GENIE (*Cancer Discov.* 2017 Aug;7[8]:818-831), a multiinstitutional dataset of clinical-grade NGS genomic profiling results for many cancer sites and histologic subtypes,

through cBioPortal (http://genie.cbioportal.org). Patient/specimen groups used for analysis were USC and HGSOC. Eighteen HR genes were queried for each group with respect to mutation frequency. For each HR gene, the difference in mutation frequency between the 2 groups was evaluated using Fisher exact test. The threshold for statistical significance was $P < 0.05$.

Results: In the USC group, there were 340 samples from 336 patients. In the HGSOC group, there were 1,208 samples from 1,193 patients. There was no overlap of patients between the 2 groups. Median patient age was 67 years for USC versus 63 years for HGSOC ($P < 0.001$). See **Table 1** for HR gene mutation frequencies for USCs and HGSOCs. The most frequently mutated HR gene for USC was *BRCA2* (4.12%) and for HGSOC, *BRCA1* (7.20%). Mutation frequency was significantly different between USC and HGSOC for *BRCA1* ($P < 0.001$) and *BRCA2* ($P = 0.034$). For the 16 non-*BRCA* HR genes, mutation frequency was not significantly different between USCs and HGSOCs.

Conclusion*: BRCA2* was the most frequently mutated HR gene identified in NGS genomic profiling of USC. Mutation frequency for non-*BRCA* HR genes was not significantly different between USCs and HGSOCs. These data add to the growing rationale for HR deficiency tumor testing and targeting (e.g., with PARP inhibitors) in future clinical trial development for women with USC.

Table 1. Mutation frequencies for homologous recombination (HR) genes analyzed by clinical-grade NGS genomic profiling of uterine serous carcinomas (USCs) and high-grade serous ovarian carcinomas (HGSOCs). *P* values listed if significant (< 0.05).

HR gene	**USC** n = 340 (%)	**HGSOC** n= 1208 (%)	**p-value**
ATM	11 (3.24)	47 (3.89)	-
BARD1	1 (0.29)	6 (0.50)	-
BRCA1	6 (1.76)	87 (**7.20**)	< 0.001
BRCA2	14 (**4.12**)	84 (6.95)	0.034
BRIP1	2 (0.59)	19 (1.57)	-
CDK12	9 (2.65)	31 (2.57)	-
CHEK2	2 (0.59)	9 (0.75)	-
FAAP20	1 (0.29)	1 (0.08)	-
FAN1	1 (0.29)	2 (0.17)	-
FANCE	1 (0.29)	9 (0.75)	-
FANCM	2 (0.59)	3 (0.25)	-
MRE11	0	5 (0.41)	-
NBN	3 (0.88)	14 (1.16)	-
PALB2	6 (1.76)	12 (0.99)	-
POLQ	0	9 (0.75)	-
RAD51B	0	1 (0.08)	-
RAD51C	1 (0.29)	2 (0.17)	-
RAD51D	1 (0.29)	3 (0.25)	-

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62 - Focused Plenary Session

Inherited mutations in fallopian tube, ovarian, and primary peritoneal carcinoma: Changes in diagnoses and mutational frequency over 20 years

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Objective: Fallopian tube carcinoma (FTC) had a higher reported frequency of inherited *BRCA* mutations than ovarian carcinoma (OC) or primary peritoneal carcinoma (PPC). We hypothesized that the adoption of serial sectioning of the fallopian tube would lead to an increased proportion of cases designated as FTC and could change mutation fraction. We investigated the prevalence of inherited mutations in women with FTC compared with OC and PPC, and how the fraction of FTC and inherited mutations changed over time.

Method: Women diagnosed from 1998 to 2018 were enrolled at diagnosis into an institutional tissue bank. Germline DNA from 700 women with primary FTC (*n* = 124), OC (*n* = 511), and PPC (*n* = 65) was assessed using targeted capture and massively parallel sequencing for mutations in ovarian cancer susceptibility genes. To assess the fraction of FTC over time, cases were split between those prior to the adoption of serial sectioning (1998–2008) and those after (2009–2019).

Results: Inherited mutation frequency was similar among women with FTC (24/124, 19%), OC (106/511, 21%, *P* = 0.42), and PPC (16/65, 25%, *P* = 0.25). In FTC, 16 mutations were identified in *BRCA1* (13%), 2 in *BRCA2* (1.6%), and 6 in non-*BRCA* genes (4.8%). The proportion of carcinomas attributed as FTC after 2009 was 31.3% (107/342), significantly higher than prior to 2009 (4.7% (17/358, *P* < 0.0001, OR = 9.1, 95% CI 5.4–15.7). Germline mutation rates in FTC were lower after 2009, with 16/107 cases (15.0%) compared to 8/17 cases (47.1%) prior to 2009 (*P* = 0.005, OR = 0.20, 95% CI 0.06–0.64).

Conclusion: The prevalence of inherited mutations is similar in FTC compared to OC or PPC when using modern pathological assignment. The adoption of complete serial sectioning of fallopian tubes has significantly increased the diagnosis of FTC and subsequently decreased the frequency of inherited mutations. All women with FTC, OC, and PPC should be offered genetic testing for inherited mutations in cancer predisposition genes.

Scientific Plenary VI: The Farr Nezhat Surgical Innovation Session

63 - Scientific Plenary

Minimally invasive hysterectomy rates and surgical outcomes in uterine cancer: A Society of Gynecologic Oncology clinical outcomes registry analysis

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Objective: Minimally invasive surgery (MIS) is a quality measure for endometrial cancer (EC). However, studies suggest that the overall U.S. MIS rate is approximately 60%. Our study objective was to assess the proportion of EC cases performed by MIS at SGO Clinical Outcomes Registry (SGO-COR) centers and evaluate perioperative outcomes.

Method: The SGO-COR has undergone a recent validation process (described in a companion abstract). A retrospective cohort study of women with apparent stage I–III EC who underwent hysterectomy plus or minus staging (HYST) during 2012–2017 at a U.S. SGO-COR center was performed. Multivariate logistic regression models analyzed factors associated with failure to perform MIS and perioperative complications.

Results: In total, 3,730 women were included from 25 SCO-COR centers; 48.3% of centers were university and 51.7% were non-university-based. Overall, 83.2% of women had stage I, 4.7% had stage II, and 12.1% had stage III disease. The median age was 57 years; most were white (88.0%) and obese (67.1%), had endometrioid histology (80.4%), and had grade 1 or 2 disease (77.7%). Most (88.8%) underwent MIS HYST (robotic-assisted 73.9%, laparoscopic 13.4%, vaginal 1.6%). The proportion of patients undergoing MIS was significantly higher at non-university than at university hospitals (92.6% vs 82.7%, *P* < 0.0001), but there was no difference across U.S. geographic regions. On multivariate analysis, black race (aOR = 0.57, 95% CI 0.39–0.83), BMI > 35 (aOR = 1.40, 95% CI 1.00–1.96), stage II (aOR = 0.0.49, 95% CI 0.32–0.75) and III (aOR = 0.36, 95% CI 0.27–0.48) disease, carcinosarcoma/leiomyosarcoma (aOR = 0.58, 95% CI 0.35–0.95), and university hospital (aOR = 3.46, 95% CI 2.66–4.50) were factors most associated with failure to undergo MIS. Laparotomy was associated with more in-hospital complications, including unscheduled intensive care unit stays (*P* ≤ 0.001) and prolonged hospital stay (*P* = 0.0002) compared to MIS.

Conclusion: In this inaugural SGO-COR study, the MIS HYST rate in women with stage I–III EC was significantly higher than in previously published studies, with low perioperative complication rates. This occurred across a spectrum of high-EC-volume participating university and non-university hospitals. A proposed MIS HYST benchmark of >80% in EC care is feasible and should be recognized as a standard of care.

64 - Scientific Plenary

Does the presence of nodal micrometastases or isolated tumor cells increase the risk of recurrent endometrioid adenocarcinoma? A case control study.

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Objective: The purpose of this case control study was to explore whether the presence of micrometastases (MMs) or isolated tumor cells (ITCs) is associated with an increased the risk for recurrence in women with fully staged, stage I–II endometrioid endometrial cancer.

Method: From 2008 to 2018, women with recurrent stage I or II endometrioid endometrial cancer who also had a full staging lymphadenectomy were identified. The outcome of interest was the presence of recurrence. A control group of women without recurrence within 2 years was selected based on the frequency-matching approach, with group size double that of the case group. The exposure of interest was the presence of previously unseen MMs (>0.2 mm) or ITCs (≤0.2 mm) on original surgical pathology. Original nodal surgical slides were re-reviewed for both cases and controls by a gynecologic pathologist; both pankeratin and H&E stained slides were evaluated to determine the presence of MMs or ITCs in nodal tissue. The effect of ITCs on recurrence was modeled by using logistic regression.

Result: A total of 153 participants were included for analysis, 50 with recurrence and 103 without, at a minimum of 24 months. There was no significant difference in age (P = 0.46), race (P = 0.24), stage (P = 0.50), FIGO grade (P = 0.64), lymphovascular space invasion (LVSI) (P = 0.85), or meeting GOG 99 high-intermediate risk criteria (P = 0.43). Patients with recurrence had a significantly higher mean number of lymph nodes removed (21.9 vs 18.9, P = 0.03). At time of analysis, 120 pathologic cases were reviewed with the identification of 10 ITCs (8.3%) and no MMs. Finding of ITCs was not associated with higher number of lymph nodes removed (P = 0.33) or tumor grade (P = 0.55) but was marginally associated with the presence of LVSI (P = 0.07). After adjusting for total lymph nodes removed, the presence of ITCs was not significantly associated with recurrence (P = 0.93). See **Figure 1**.

Conclusion: In an early-stage, appropriately treated, endometrioid endometrial carcinoma population, the finding of previously undiagnosed MMs and ITCs is a rare occurrence and is most closely associated with the finding of LVSI. The presence of ITCs was not significantly associated with recurrence-free survival or overall survival in this population. Thus, adjusting staging or treatment planning should be avoided with the finding of ITCs in otherwise negative LNs.

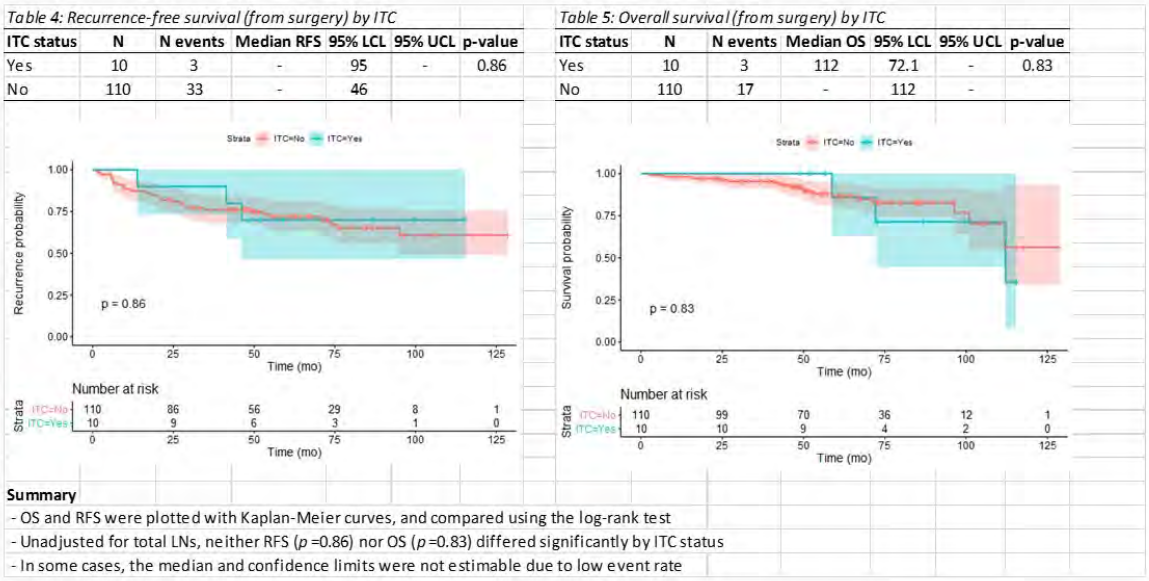

Table 4: Recurrence-free survival (from surgery) by ITC

ITC status	N	N events	Median RFS	95% LCL	95% UCL	p-value
Yes	10	3	-	95	-	0.86
No	110	33	-	46		

Table 5: Overall survival (from surgery) by ITC

ITC status	N	N events	Median OS	95% LCL	95% UCL	p-value
Yes	10	3	112	72.1	-	0.83
No	110	17	-	112	-	

Summary

- OS and RFS were plotted with Kaplan-Meier curves, and compared using the log-rank test
- Unadjusted for total LNs, neither RFS (p =0.86) nor OS (p =0.83) differed significantly by ITC status
- In some cases, the median and confidence limits were not estimable due to low event rate

Fig. 1.

65 - Scientific Plenary

Characterization of patients with isolated tumor cells and micrometastasis on sentinel lymph node biopsy performed for endometrial cancer staging

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Objective: Isolated tumor cells (ITC) are tumor deposits measuring ≤0.2 mm, whereas micrometastasis (MM) is defined as a metastatic deposit measuring >0.2 to ≤2 mm. While the characterization of these findings and their significance have been discussed in breast cancer literature, less is known about these results in endometrial cancer. We sought to determine whether patient and disease characteristics correlate with the finding of ITC or MM on sentinel lymph node (SLN) biopsy for endometrial cancer.

Method: We carried out an Institutional Review Board-approved retrospective chart review of all women with endometrial cancer who underwent SLN mapping and biopsy during surgical staging at two academic medical centers between 2013 and 2018. When available, follow-up data were included in the analysis. Statistical analysis was performed using a multiple logistic regression model.

Results: A total of 573 patient charts were identified and reviewed. Unilateral or bilateral SLNs were detected successfully in 92.7% (*n* = 531). Among women with identified SLN, 6% (*n* = 31) were found to have ITC or MM. Characteristics of women with ITC or MM can be found in **Table 1**. The median age of women with positive ITC or MM was 63 years (range 46–92 years), and median BMI was 33.8 (range 21–53). Neither was found to be related to the presence of ITC or MM. Tumors were most commonly FIGO grade 2 (45%, *n* = 13). Lymphovascular space invasion (LVSI) was present in 70% (*n* = 21). A small majority (55%, *n* = 17) had uterine disease confined to the inner 2/3 of the myometrium. ITC or MM was more likely to be seen in patients with LVSI (OR = 11.56, 95% CI 4.74–28.2) and with increasing tumor grade (OR = 1.93, 95% CI 1.13–3.31). In addition, the absolute depth of myometrial invasion had a weak effect on the presence of ITC or MM (OR = 1.13, 95% CI 1.07–1.19), as did percentage of myometrial invasion (OR = 1.03, 95% CI 1.02–1.04). Follow-up information was available for 272 patients in the cohort, including 14 patients with positive ITC or micrometastasis. Of these 14 patients, 1 had disease recurrence (7%). In patients with a negative SLN biopsy, the recurrent rate was 6.4%.

Conclusion: ITC or MM is a relatively rare diagnosis in women undergoing SLN biopsy for endometrial cancer staging. Additional data are needed to clarify risk factors for this finding and associated patient outcomes.

Table 1. Characteristics of patients with ITC or micrometastasis on SLN biopsy (n=31).

	***n* (%)**
Age	
< 50	11 (35)
50-69	13 (42)
≥ 70	7 (23)
BMI	
≤ 25	2 (7)
25-30	9 (29)
30-40	15 (48)
≥ 40	5 (16)
FIGO Grade[a]	
1	9 (31)
2	13 (45)
3	7 (24)
Lymphovascular space invasion[b]	
Present	21 (70)
Absent	9 (30)
Depth of myometrial invasion[c]	
Inner 1/3	6 (19)
Inner 2/3	17 (55)
Outer 1/3	14 (45)
Follow-up (*n* = 14)	
No evidence of disease	13
Recurrence	1

[a] Information not available for 2 patients, *n* = 29

[b] Information not available for 1 patient, $n = 30$
[c] Percentage does not total 100, because 'inner 2/3' also includes all patients with 1/3 myometrial depth of invasion

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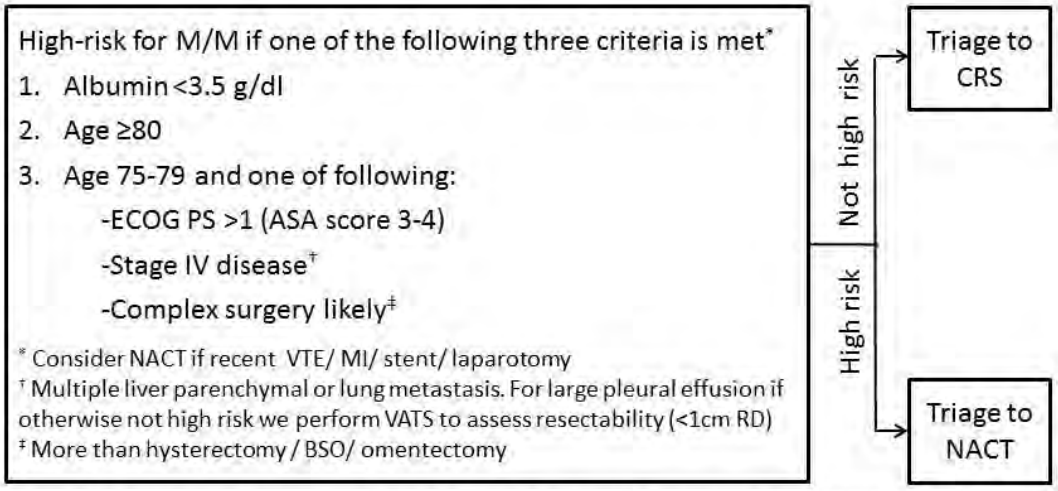
66 - Scientific Plenary
Less guessing, more evidence in the decision for neoadjuvant chemotherapy versus surgery: A validated triage algorithm to identify women at high risk of morbidity/mortality associated with ovarian cancer cytoreduction
D.M. Narasimhulu, A. Kumar, A.L. Weaver, M.E. McGree, C.L. Langstraat and W.A. Cliby. *Mayo Clinic, Rochester, MN, USA*

Objective: We previously reported a triage algorithm to identify women at high risk of poor operative outcomes to successfully improve surgical outcomes after cytoreductive surgery (CRS) for advanced epithelial ovarian cancer (EOC). This provides a sensible, evidence-based approach to triage between neoadjuvant chemotherapy (NACT) and CRS rather than subjective bias or institutional preference. We sought to independently validate the performance of our algorithm using national multiinstitutional data.

Method: Women who underwent CRS for stage IIIC–IV EOC between January 1, 2014, and December 31, 2017, were identified from the National Surgical Quality Improvement Program (NSQIP) database using hysterectomy-targeted participant use files. A surgical complexity score (SCS) was assigned using a previously published scoring system. Women were classified as either triage appropriate if they had no high-risk factors at the time of CRS or high risk if factors were present such that a priori use of the algorithm would have recommended NACT (**Figure 1**). Outcomes were compared between groups using the χ^2 test.

Results: A total of 1,777 women met inclusion criteria; the mean age was 62.6 years, and 81.9% had stage IIIC disease. Nationally, the SCSs were low (69.8% low, 25.2% intermediate, and 5.0% high). Compared to women identified as appropriate for CRS, those scored as high risk by our algorithm had worse outcomes. Specifically, high-risk women had a 2-fold higher rate of severe 30-day complications (6.2% vs 3.5%, $P = 0.01$) and a 3-fold higher rate of 30-day mortality (1.4% vs 0.5%, $P = 0.07$), and more patients had macroscopic residual disease (RD) (47.4% vs 37.2%, $P < 0.001$) including suboptimal RD (≥1 cm) (12.8% vs 6.2%, $P < 0.001$).

Conclusion: Using national data, we confirm the ability of our triage algorithm to identify women at increased risk of morbidity, mortality, and higher RD after CRS. Important differences in outcomes between triage appropriate and high-risk patients were observed even in this lower SCS setting and despite using 30-day (vs 90-day) mortality. We expect the differences to be larger when the SCS is higher and 90-day mortality is considered. Objective surgical risk assessment should be the standard of care in treatment planning for EOC and can be incorporated into practice using our evidence-based triage algorithm.



Abbreviations: ASA, American society of Anesthesiologists; BSO, Bilateral salpingo-oophorectomy; CRS, cytoreductive surgery; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EOC, Epithelial ovarian cancer; MI, Myocardial infarction; M/M, Morbidity and mortality; NACT, Neoadjuvant chemotherapy; RD, Residual disease; VATS, Video assisted thoracoscopic surgery; VTE, Venous thromboembolism.

Fig. 1. Triage algorithm to reduce surgical M/M after CRS for EOC.

67 - Scientific Plenary

Use of a dedicated radiologic assessment score to individualize the management of women with primary advanced epithelial ovarian cancer: A triage tool to optimize outcomes and minimize interventions

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Objective: Our goal was to evaluate the impact of a preoperative radiologic assessment tool in the primary management of patients with advanced epithelial ovarian cancer (EOC). This previously published resectability score (R score) was developed to estimate the likelihood of incomplete primary debulking surgery (PDS), i.e., any gross residual disease.

Method: All patients with primary, advanced EOC treated at our institution from May 2015 to August 2018 were identified; those with no contraindication to PDS were included and an R score was calculated. An R score of ≤6 was low risk (LR) for incomplete PDS, and an R score of ≥7 was high risk (HR). The R score was utilized to triage patients to laparotomy/PDS, diagnostic laparoscopy, or neoadjuvant chemotherapy (NACT). Futile laparotomy was defined as residual disease >1 cm.

Results: A total of 308 women were included and their R scores calculated: 234 (76%) were LR and 74 (24%) were HR (**Figure 1**). In the LR group, 181 (77%) underwent PDS, 5 (2%) received NACT, and 48 (21%) underwent diagnostic laparoscopy, of whom 31 (65%) proceeded to PDS and 17 (35%) to NACT. Of the 212 LR patients undergoing PDS, resection rates were as follows: 167 (79%) complete gross resection (CGR), 197 (93%) optimal resection (O), and 15 (7%) futile laparotomy. In the HR group, 9 patients (10%) underwent PDS, 17 (23%) received NACT (23%), and 48 (65%) underwent diagnostic laparoscopy, of whom 28 (58%) proceeded to PDS and 20 (42%) received NACT. Of the 37 HR patients undergoing PDS, resection rates were 20 (54%) CGR, 35 (95%) O, and 2 (5%) futile laparotomy. In total, 249 (81%) patients underwent PDS with a CGR rate of 75% (*n* = 187) and optimal rate of 93% (*n* = 232). Use of the R score led to an diagnostic laparoscopy utilization rate of 31% (*n* = 96) with only a 5.5% (*n* = 17) rate of futile laparotomy.

Conclusion: The use of a dedicated preoperative radiologic assessment tool in this cohort of patients with advanced EOC led to excellent surgical outcomes in the majority of patients with a modest utilization of diagnostic laparoscopy and a low rate of futile laparotomy. While universal diagnostic laparoscopy has been suggested as a triage tool, these data suggest that an individualized approach with multidisciplinary input is feasible without compromising outcomes. Further investigation into the impact of this tool as an alternative to universal diagnostic laparoscopy on patient morbidity and resource utilization is warranted.

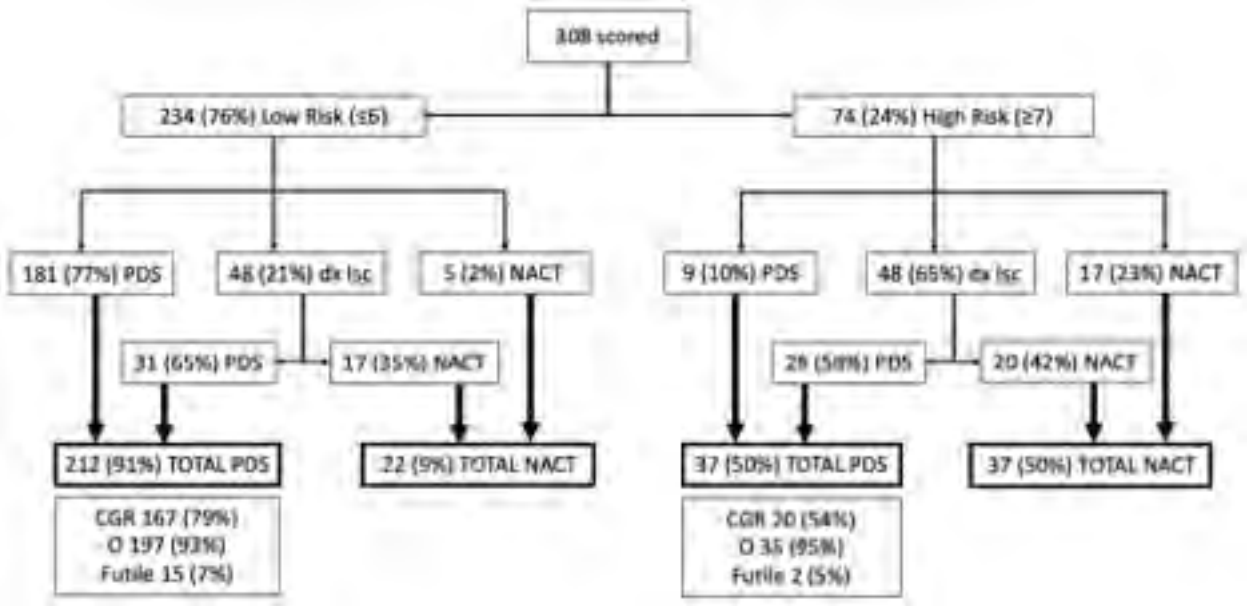

Fig. 1. Allocation of treatment after R-score.

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Natural language processing and machine learning to predict outcomes after ovarian cancer surgery

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Objective: Our goal was to determine whether natural language processing (NLP) of preoperative CT scans with machine learning techniques improves the ability to predict postoperative outcomes among women with ovarian cancer undergoing surgery when compared with discrete data alone.

Method: We identified women undergoing primary surgery for ovarian cancer at two institutions from 2012 to 2018 using ICD-9 and CPT codes. Outcomes evaluated included 30-day major surgical complications defined as a 3 or higher on the Clavien-Dindo scale and 30-day hospital readmission. Predictive factors included discrete data such as demographic (e.g., age, race) and clinical characteristics (e.g., stage, comorbid conditions) as well as features extracted using NLP methods (Bag of Words, PCA embeddings, and Word2Vec vectors) on the full text preoperative CT scans, which were performed within 30 days of surgery. We fitted several predictive models such as Random Forests, Extra trees classifier, Gradient Boosting Machines, XGBoost, and Stacking. Five-fold cross-validation was used to test generalizability. Discrimination was measured using the area under the receiver operator characteristic curve (AUROC).

Results: We identified 291 patients with ovarian cancer who underwent primary surgical treatment. Median age was 59 years (IQR 52–69 years), and median CA-125 was 358 (IQR 18–154). Using discrete data alone, the model was showed reasonable discrimination for postoperative 30-day major complication with an AUROC of 0.61 (95% CI 0.60–0.63). The addition of NLP of preoperative CT scans improved this to an AUROC of 0.68 ($P < 0.001$). Similarly for 30-day hospital readmission, discrete data alone provided an AUROC of 0.62 (95% CI 0.61–0.64), while the addition of NLP with machine learning improved this to 0.70 (95% CI 0.68–0.72, $P < 0.001$). Phrases predictive of both readmission and complication included large ascites, definite adenopathy, mesenteric stranding, and exophytic and omental metastases.

Conclusion: The addition of NLP to machine learning techniques for preoperative CT scans improves the ability to predict both postoperative complication and postoperative readmission among women with ovarian cancer undergoing primary surgery. Artificial intelligence using machine learning of electronic medical record data has application within gynecologic cancers.

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Laparoscopic interval debulking surgery for advanced ovarian cancer after neoadjuvant chemotherapy

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Objective: Neoadjuvant chemotherapy (NAC) for advanced ovarian cancer facilitates interval debulking via a minimally invasive surgery (MIS) technique without demonstrable survival disadvantage compared to laparotomy. Yet an earlier study from 2010 to 2012 suggested this was adopted only in 15% of cases. We aim to study a more contemporary population to clinical outcomes.

Method: We queried the National Cancer Data Base (NCDB) to identify patients with stage IIIC or IV epithelial ovarian cancer, between 2013 and 2016, who received NAC and interval debulking surgery. The primary outcome was overall survival at 3 years by intention to treat. Secondary outcomes were duration of hospitalization, unplanned readmission, and extent of surgery between MIS and laparotomy. We used the Kaplan-Meier method, log rank test, Cox regression model in addition to logistic and linear regression multivariate analysis.

Results: We identified 4,038 women meeting inclusion, of whom 971 (24%) underwent an MIS approach. There was no difference in 3-year survival between patients undergoing MIS (51.1%, 95% CI 46–56%) and laparotomy (51.8, 95% CI 49–54%, $P = 0.95$, adjusted $P = 0.61$). Interval MIS debulking was associated with shorter hospitalization (1.7 days less, $P = 0.00$), with no difference in unplanned readmissions within 30 days (2.37% MIS compared to 3.16% laparotomy, $P = 0.20$) and extent of surgery (21% MIS and 20.7% laparotomy, $P = 0.68$). Geographical differences exist in rates of MIS, with the highest in the Mountain (33%) and South Atlantic (30%) regions. Patients undergoing debulking at academic or comprehensive cancer centers were more likely to undergo MIS ($P = 0.01$). There was also a difference among racial groups, with Hispanic patients (30%) more likely to have MIS than non-Hispanic white (23%) and black patients (22%, $P = 0.003$), and a decreased rate of MIS among Medicaid and uninsured patients (2% compared to 21.9% private and Medicare patients, $P = 0.006$).

Conclusion: One-quarter of advanced ovarian cancer patients receiving NAC have interval debulking surgery initiated by MIS with comparable survival to open laparotomy. The rate of MIS is gradually increasing, suggesting that this approach is gaining acceptance among gynecologic oncologists; yet racial and geographic disparities exist and warrant further study.

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70 - Scientific Plenary
Modifying risk factors for anastomotic leak in gynecologic oncology surgery
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Objective: Anastomotic leak (AL) after bowel resection is a life-threatening complication. In gynecologic oncology surgery, the reported rate of AL after bowel resection varies from 1.7% to 7.9%. Diverting ileostomy has been proposed for patients who meet certain criteria, such as albumin <3.0 g/dL and/or multiple concurrent bowel resections. Our goal was to describe the rate of AL for gynecologic oncology patients at our institution and to identify risk factors associated with increased risk of AL to determine the utility of diverting ileostomy.

Method: Women who underwent gynecologic oncology surgery with bowel resection and anastomosis between January 1, 2006, and April 1, 2017, were identified. Data were abstracted from charts including demographics, surgical details, morbidity, and postoperative outcomes.

Result: A total of 317 patients were identified, and the majority had a diagnosis of ovarian cancer. There were 8 cases of AL identified for an overall AL rate of 2.5% (8/317). All AL were confirmed by contrast imaging or intraoperative findings. Fifty percent of patients were operated on immediately; 25% elected for comfort care; 12.5% had conservative management; and 12.5% had delayed operation. In univariate analysis, no individual patient or perioperative factor was significantly associated with an increased risk of AL (**Table 1**). Based on serum albumin, the AL rate was 4.4% for levels <3.0 g/dL and 2.4% for patients with albumin ≥3.0 g/dL (OR = 1.81, 95% CI 0.16–20.99, *P* = 0.63). The AL rate for patients who underwent more than 1 bowel resection was 11.1%, whereas it was 2.86% for patients with 1 bowel resection (OR = 4.25, 95% CI 0.66–27.4, *P* = 0.12). There was a low rate (4.1%, 13/317) of patients who underwent a protecting ileostomy, and none of these patients experienced an AL.

Conclusion: Over a 10-year period, our institutional AL rate was low at 2.5%. Although no individual factor was identified that significantly increased the risk of AL, diverting ileostomy could be considered for patients with low albumin (<3.0 g/dL) and more than than 1 bowel resection as these factors may be associated with increased AL risk.

Table 1.

Variable		No AL N (%)	AL N (%)	Odds Ratio	95% CI	P
ASA Class	1 or 2 3 or 4	27 (38.6%) 43 (61.4%)	2 (28.6%) 5 (71.4%)	1.57	0.28 – 8.67	0.61
Tobacco use	Yes No	21 (16%) 111 (84.1%)	1 (14.2%) 6 (85.7%)	0.88	0.10 – 7.70	0.91
Alcohol use	Yes No	41 (32.8%) 84 (67.2%)	4 (50%) 4 (50%)	2.05	0.49 – 8.6	0.32
Diabetes	Yes No	17 (12.5%) 119 (87.5%)	1 (12.5%) 7 (86.5%)	1.0	0.11 – 8.64	1.00
Preoperative hemoglobin	≥10 <10	122 (85.3%) 21 (14.7%)	5 (62.5%) 3 (37.5%)	3.48	0.77 - 15.7	0.10
Anastomosis oversewn	Yes No	99 (68.8%) 45 (31.2%)	7 (87.5%) 1 (12.5%)	0.31	0.04 – 2.63	0.28
Drain placed at time of surgery	Yes No	103 (74.6%) 35 (25.3%)	5 (83.3%) 1 (16.7%)	0.59	0.07 – 5.21	0.6
Operative time	<200mins ≥200mins	34 (44.7%) 42 (55.3%)	3 (42.9%) 4 (57.1%)	1.07	0.23 – 5.16	0.92
Intraop blood transfusion	Yes No	56 (40.9%) 81 (59.1%)	1 (12.5%) 7 (87.5%)	0.21	0.03 – 1.73	0.15
Postop ppx antiobiotics	Yes No	38 (39.2%) 59 (60.8%)	2 (25%) 6 (75%)	0.52	0.09 – 2.70	0.43
Postoperative NSAIDs	Yes No	69 (48.9%) 72 (51.1%)	2 (25%) 6 (75%)	0.34	0.07 – 1.78	0.21

71 - Scientific Plenary

Using near-infrared angiography to evaluate perfusion of rectal anastomosis in advanced epithelial ovarian cancer

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Objective: In patients with advanced epithelial ovarian cancer (EOC) undergoing debulking surgery, surgery of the intestinal tract is frequent. A method for evaluating rectosigmoid anastomotic perfusion that has had promising results in the colorectal literature is near-infrared angiography (NIR) with indocyanine green (ICG) via proctoscopy. The method has been reported as a feasible technique in identifying anastomosis at risk, thus decreasing leak rates and improving outcomes.

Method: In this film, patients with advanced EOC who have undergone a rectosigmoid resection at time of debulking surgery are used to illustrate the technique for performing NIR with ICG via proctoscopy. Normal and abnormal angiography are demonstrated. In addition, a 59-year-old patient with stage IVB clear cell carcinoma of the ovary undergoing interval debulking surgery is highlighted. The patient undergoes a rectosigmoid resection with end-to-end anastomosis, and this is evaluated with NIR with ICG.

Results: In the patient presented, the rectosigmoid anastomosis is noted to have abnormal profusion on NIR with ICG. Based upon the intraoperative findings, the anastomosis is revised. The patient was discharged home on postoperative day 10. After 30 days, the patient had no grade 3 or greater postoperative complications.

Conclusion: NIR with ICG via proctoscopy is a useful method for evaluating anastomotic blood flow. A randomized trial may determine whether NIR with ICG assessment of rectosigmoid anastomosis may lead to decreased postoperative complications and better outcomes in advanced EOC.

Late Breaking Abstract Session

LBA 6 – Late Breaking Abstract Session

Exploring the relationship between homologous recombination score and progression-free survival in *BRCA* wildtype ovarian carcinoma: Analysis of veliparib plus carboplatin/paclitaxel in the velia study

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Objective: The phase 3 VELIA trial demonstrated that veliparib dosed concurrently with carboplatin and paclitaxel and continued as maintenance monotherapy resulted in significantly better progression-free survival (PFS) compared to carboplatin and paclitaxel alone in patients with newly diagnosed advanced high-grade serous ovarian carcinoma (HGSC). VELIA enrolled patients without regard to germline or somatic *BRCA* mutations (*BRCA*m), homologous recombination deficiency (HRD), or platinum sensitivity, providing a unique opportunity to evaluate the prognostic and predictive role of the HRD assay.

Method: Patients with untreated stage III–IV HGSC received 6 cycles (21-day interval) of carboplatin and paclitaxel following primary cytoreduction or as neoadjuvant chemotherapy with interval cytoreduction. HRD score was determined by Myriad myChoice HRD CDx assay with cutoff ≥33 for HRD+ and <33 for non-HRD status. Randomization was stratified by disease stage, timing of surgery, residual disease post primary surgery, paclitaxel schedule, geographic region, and germline *BRCA* status (but not HRD). This analysis was restricted to patients randomized to carboplatin and paclitaxel with placebo then placebo maintenance (control), and carboplatin and paclitaxel with veliparib, and then veliparib maintenance (veliparib-throughout). Correlation of HRD score with outcome was limited to patients with *BRCA*wt HGSC to understand the predictive power of HRD score in *BRCA*wt HGSC using the PFS endpoint in veliparib-throughout versus control.

Result: A total of 532 patients from veliparib-throughout and control arms with HGSC confirmed *BRCA*wt and known HRD status were included in this exploratory analysis to evaluate HRD independent of *BRCA* status. Within the *BRCA*wt population, the HRD+ population had a PFS hazard ratio (HR) of 0.77 (95% CI 0.54–1.10) favoring use of veliparib, and the non-HRD

population had a similar PFS HR of 0.76 (95% CI 0.55–1.03), both upper confidence intervals crossing threshold of 1.00 in this post hoc analysis. Comparing HRD score versus observed HR between veliparib-throughout and control, no clear cutoff score could be identified to accurately determine who would benefit most from the veliparib-throughout regimen.

Conclusion: In patients with *BRCA*wt carcinomas, HRD score was not predictive of patient outcomes for veliparib-throughout versus control. Veliparib-throughout suggests veliparib benefit even at low HRD scores compared to carboplatin and paclitaxel. This analysis of *BRCA*wt HRD+ and non-HRD populations suggests veliparib benefit is similar in both groups.

LBA 7 – Late Breaking Abstract Session

Randomized double-blind placebo-controlled trial of primary maintenance vigil immunotherapy (VITAL study) in stage III/IV ovarian cancer: Efficacy assessment in BRCA1/2-wt patients

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Objective: Despite advances, overall prognosis for advanced epithelial ovarian cancer (EOC) remains poor. Considering elevated TGFβ expression correlates with poor prognosis in ovarian cancer, this study aims to determine whether a maintenance vigil could provide improvement in relapse-free survival. Vigil is an autologous tumor cell vaccine constructed from autologous harvested tumor tissue transfected with a DNA plasmid encoding GMCSF and bi-shRNA-furin, thereby creating TGFβ expression control.

Method: A randomized double-blind placebo-controlled trial of vigil versus placebo was performed in advanced-stage front-line ovarian cancer patients. Relapse-free survival (RFS), safety, and proportion of recurrences were endpoints. Patients who achieved complete clinical response were randomized (1:1 to placebo—control group—or vigil—vigil group) after completion of front-line surgery and chemotherapy. All patients received 1 × 10e7 cells/ml of vigil or placebo intradermally once a month for up to 12 doses.

Results: Ninety-one patients were randomized (vigil group $n = 46$; control group $n = 45$); 62 patients were tested for *BRCA1* or *BRCA2* status. The vigil group showed no added overall toxicity compared to the control group, and no grade 4/5 toxicities were observed. Grade 2/3 toxic events were observed in 18% of the control group patients (most common bone pain, fatigue) compared to 8% of the vigil group patients (most common nausea, musculoskeletal pain). From time of randomization, median RFS for all 91 patients was favorable in the vigil group (HR = 0.69, $P = 0.088$). Stratified by *BRCA* status, an advantage in RFS was seen in the *BRCA1* and *BRCA2*wt patients in the vigil group (19.4 months) compared to the control group (8 months) (HR = 0.51, 90% CI 0.26–1.01, one-sided $P = 0.050$) from time of randomization and HR of 0.49 (90% CI 0.25–0.97, one-sided $P = 0.038$) from time of surgery (**Figure 1**). Median time from surgery to randomization was 208.5 days (6.9 months) in the vigil group versus 200 days (6.6 months) in the control group. Of the *BRCA1* and *BRCA2*wt vigil-treated patients, 62.5% were relapse-free compared to 29% of placebo at time of analysis (September 17, 2019, median follow-up of 34.3 months for all $n = 91$ patients).

Conclusion: Front-line use of vigil immunotherapy as maintenance in stage III–IV ovarian cancer is well tolerated and showed trend in RFS clinical benefit. Specifically, *BRCA1* and *BRCA2*wt disease showed statistically significant benefit.

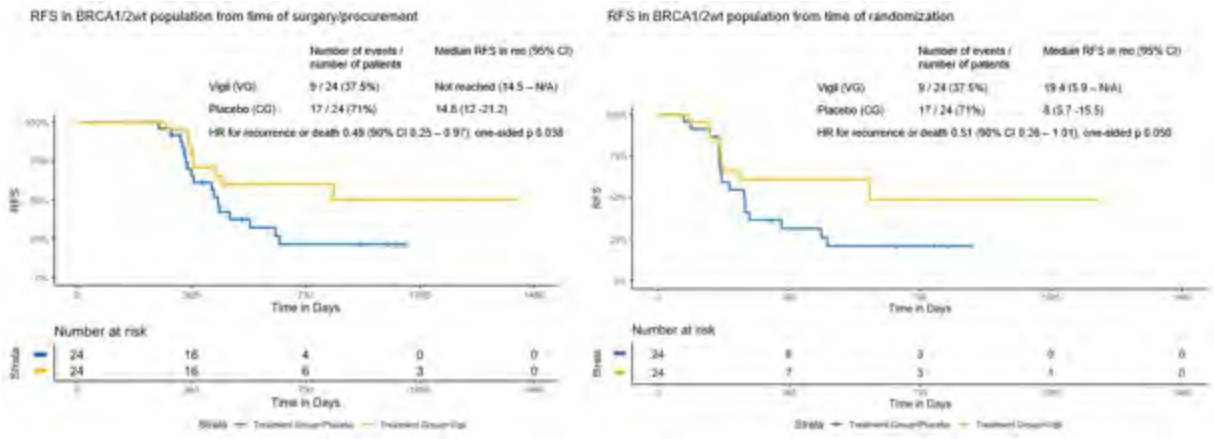

Fig. 1.

LBA 8 – Late Breaking Abstract Session

A phase 1 study of XMT-1536 in patients with solid tumors likely to express NaPi2b: A summary of dose escalation

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Objective: XMT-1536 is a first-in-class antibody-drug conjugate NaPi2B (SLC34A2), a transmembrane sodium-phosphate transporter that is expressed in ovarian carcinoma, non-small cell lung cancer (NSCLC), and other tumors. The purpose of this study was to determine the maximum tolerated dose (MTD) and/or the RP2D dose, and to evaluate the safety, tolerability, and preliminary efficacy of XMT-1536.

Method: Patients were enrolled in escalating dose cohorts of 3 mg/m^2 to 43 mg/m^2 (dose levels 1 to 7A, at q3w or q4w) and assessed for safety, pharmacokinetics, and response (via Response Evaluation Criteria in Solid Tumors v1.1). A safety review committee reviewed each cohort prior to escalation to the next higher dose level.

Results: To date, 59 patients have been enrolled (Table 1) including 37 patients with ovarian cancer and 11 patients with NSCLC. Most common treatment-related adverse events have been grade 1 and 2 transient AST elevations and fatigue. Three patients have experienced dose-limiting toxicity (DLT): grade 3 AST increased at dose level 6 (40 mg/m^2 q3w) and dose level 5A (30 mg/m^2 q4w) and treatment discontinuation following grade 2 AST increased and grade 1 ALT increased at dose level 6A (36 mg/m^2 q4w). There were no DLTs reported in the highest cohort completed (dose level 7A, 43 mg/m^2 q4w, n = 7). Thirty-two adverse events have been reported, of which 4 were determined to be possibly or probably related to XMT-1536 (congestive cardiac failure, 2 pyrexia, and vomiting).

Conclusion: XMT-1536 has been well tolerated with no DLTs reported in the highest dose level completed (dose level, 43 mg/m^2 q4w). Confirmed responses and prolonged stable disease have been observed. Dose expansion in high-grade serous ovarian carcinoma and NSCLC, adenocarcinoma subtype, is currently enrolling (NCT03319628). In addition, the safety review committee has recommended escalating to dose level 8A (52 mg/m^2 q4w), and enrollment in this cohort has been initiated. Complete safety data, confirmed response data, and biomarker expression for represented dose levels will be provided at the SGO 2020 meeting.

Table 1. Study MER-XMT-1536-1.

Dose Level	Dose (mg/m^2)	*n* (female/male)	Tumor Type (*n*)	DLTs (*n*)
1	3.0 (q3w)	1 (1/0)	Ovarian (*n* = 1)	---
2	6.0 (q3w)	1 (1/0)	Ovarian (*n* = 1)	---
3	12.0 (q3w)	7 (4/3)	Ovarian (*n* = 1) NSCLC (*n* = 2) Endometrial (*n* = 3) Papillary renal (*n* = 1)	---
4	20.0 (q3w)	6 (6/0)	Ovarian (*n* = 3) NSCLC (*n* = 1) Endometrial (*n* = 1) Salivary duct (*n* = 1)	---
5	30.0 (q3w)	4 (3/1)	Ovarian (*n* = 3) NSCLC (*n* = 1)	---
6	40.0 (q3w)	1 (1/0)	Ovarian (*n* = 1)	Grade 3 AST (*n* = 1)
4A	20.0 (q4w)	9 (8/1)	Ovarian (*n* = 8) Papillary renal (*n* = 1)	---
5A	30.0 (q4w)	15 (15/0)	Ovarian (*n* = 9) NSCLC (*n* = 2) Endometrial (*n* = 4)	Grade AST (*n* = 1)
6A	36.0 (q4w)	8 (7/1)	Ovarian (*n* = 7) NSCLC (*n* = 1)	Treatment discontinuation following grade 2 AST, grade 1 ALT (*n* = 1)
7A	43.0 (q4w)	7 (2/5)*	Ovarian (*n* = 3) NSCLC (*n* = 4)	---

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; DLT = dose-limiting toxicity; NSCLC = non-small cell lung cancer; q3w = every 3 weeks dosing; q4w = every 4 weeks dosing.
*One patient was not evaluable due to clinical disease progression not related to this study.

LBA 9 – Late Breaking Abstract Session

Anti-tumor activity of veliparib during combination phase with chemotherapy in velia study

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Objective: The VELIA study evaluated progression-free survival (PFS) with veliparib added to carboplatin and paclitaxel with and without veliparib maintenance in newly diagnosed high-grade serous ovarian carcinoma (HGSC) patients. As anticipated, few patients experienced PFS events during carboplatin and paclitaxel, and we evaluated other parameters to explore the impact of veliparib during carboplatin and paclitaxel.

Method: Patients with previously untreated stage III–IV HGSC received 6 cycles (21-day interval) of carboplatin and paclitaxel following primary cytoreduction or as neoadjuvant chemotherapy (NACT) with interval cytoreduction. Randomization was 1:1:1: veliparib-throughout, carboplatin and paclitaxel + veliparib then veliparib maintenance; veliparib-combo-only, carboplatin and paclitaxel + veliparib then placebo maintenance; and control, carboplatin and paclitaxel + placebo then placebo maintenance. These exploratory analyses evaluated responses during the combination phase, as assessed by CA-125 levels (response defined as ≥90% reduction from baseline or normalization) or Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.

Results: A total of 1,140 patients were enrolled, and 67% underwent primary cytoreduction (stratified prior to randomization). At baseline, the distribution of CA-125 levels was similar across each arm. By cycle 3, more patients receiving veliparib achieved a CA-125 response compared to control (**Figure 1**); a similar trend was seen among patients undergoing NACT. Among patients with measurable disease after primary surgery (*n* = 197), more patients in the veliparib-containing arms had complete response (CR) than those in the control arm.

Conclusion: Veliparib added to frontline carboplatin and paclitaxel during induction resulted in a modest increase in CA-125 responses and CRs in women with newly diagnosed HGSC. These exploratory analyses suggest that veliparib added to carboplatin and paclitaxel during combination phase may provide antitumor activity above carboplatin and paclitaxel alone.

	V-throughout (N=382)	V-combo-only (N=383)	Control (N=375)
Baseline CA-125 > ULN (all evaluable*)	323/377 (86%)	319/376 (85%)	323/369 (86%)
CA-125 response by cycle 3**	121/316 (38%)	101/323 (31%)	77/324 (24%)
CA-125 response by cycle 3 (NAC**)	49/86 (57%)	46/101 (46%)	38/100 (38%)
Complete responses+ (primary surgery with measurable disease)	25/98 (26%)	23/99 (23%)	17/93 (18%)
Stable disease+	8/98 (8%)	9/99 (9%)	18/93 (19%)

*Among those with documented values; missing values at baseline = 5, 7, 6 in each arm, respectively.
**Among those with documented values at baseline and cycle 3.
+RECIST v1.1

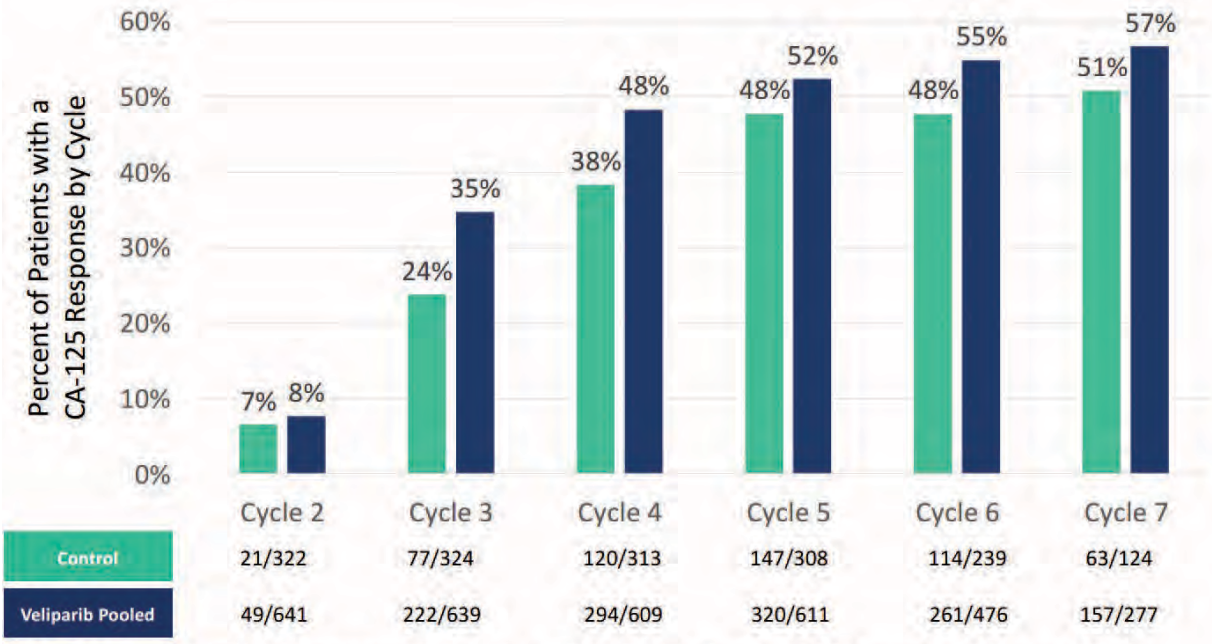

Fig. 1.

LBA 10 – Late Breaking Abstract Session

A phase 3 randomized controlled trial of preventive negative pressure wound therapy in postoperative incision management

M.M. Leitao Jr.[a], Q. Zhou[a], M.B. Schiavone[b], R.A. Cowan[a], E. Smith[a], A. Iasonos[a], M.W. Veith[a], M. Rafizadeh[a], K.G. Curran[a], B. Ramesh[a], K. Chang[a], D.S. Chi[a], Y. Sonoda[a], A.K. Brown[c], J.A. Cosin[d], N.R. Abu-Rustum[a], M.A. Martino[e], J.J. Mueller[a], K. Long Roche[a], E. Jewell[a], V. Broach[a], J.P. Diaz[f] and O. Zivanovic[a]. *[a]Memorial Sloan Kettering Cancer Center, New York, NY, USA, [b]Columbia University Medical Center, New York, NY, USA, [c]Hartford Hospital, Hartford, CT, USA, [d]Hartford Healthcare Cancer Institute at The Hospital of Central Connecticut, New Britain, CT, USA, [e]Lehigh Valley Health Network, Allentown, PA, USA, [f]South Miami Gynecologic Oncology Group, Miami, FL, USA*

Objective: The aim of this study was to test whether preventive negative pressure wound therapy decreases the incidence of wound complications in patients of any weight or in those with morbid obesity and benign disease undergoing laparotomy for gynecologic malignancy.

Method: Patients planned to undergo laparotomy were randomized 1:1 to either standard gauze (control) or an experimental arm using a negative pressure wound therapy device (Prevena™ Customizable™ Incision Management System, KCI USA, Inc, San Antonio, TX). All patients with presumed gynecologic malignancy were eligible. Patients with BMI ≥40 kg/m^2 with benign disease were also eligible. All procedures were performed through a vertical midline skin incision, and fascia closure was performed according to surgeon standard. Skin closure was required to be completed with surgical skin staples. Randomization, stratified by BMI, occurred only after skin closure with surgical staples was completed. Patients were followed for the development of a wound complication (primary outcome) for 30 days postoperatively. The trial enrolled the first patient in February 2016 and was closed to accrual in August 2019 after the second interim analysis because of futility.

Results: At the time of second interim analysis, 444 evaluable patients had been randomized (223 experimental, 221 control). The median age for the entire cohort was 60 years (range 21–88 years). Of all patients, 373 (84%) had malignant disease and underwent cytoreductive surgery; all had a vertical laparotomy incision. A wound complication occurred in 41 patients (18%) in the experimental arm (90% CI 14.1%–22.7%) compared to 38 (17%) in the control arm (90% CI 13.0%–21.4%). Given these rates/data, there was only a 3.9% chance that we would conclude with a positive result at the end of full enrollment; therefore, we stopped the trial early for futility. Updated data will be available for presentation.

Conclusion: Preventive negative pressure wound therapy for closed laparotomy wounds did not result in a decreased wound complication rate in our protocol-specified cohort.

Education Forum VII: HIPEC 2.0: Are we getting warmer?

72 - Education Forum

Heated intraperitoneal chemotherapy (HIPEC) use for ovarian cancer in the United States increases after publication of clinical trial and is associated with higher short-term cost and morbidity

L.M. Charo, J. Jou, P.S. Binder, C.C. Saenz, M.T. McHale, R.N. Eskander and S.C. Plaxe. *UCSD Rebecca and John Moores Cancer Center, La Jolla, CA, USA*

Objective: The goals of this study were (1) to determine whether trends in use of heated intraperitoneal chemotherapy (HIPEC) in ovarian cancer treatment increased after "HIPEC in Ovarian Cancer" was published in January 2018, and (2) to compare associated rates of hospital-based outcomes, including length of stay, intensive care unit (ICU) admission, complications, and costs, in ovarian cancer patients who underwent surgery with or without HIPEC.

Method: We queried Vizient®, an administrative claims database covering approximately 400 U.S. hospitals, for all ovarian cancer patients who had surgery from January 2016 to June 2019 using ICD-10 diagnosis and procedure codes. Sodium thiosulfate administration was used to identified HIPEC cases. Case mix index (CMI), a weighted metric of Medicare Severity-Diagnosis Related scores, reflects hospital clinical complexity. Student *t* tests and relative risk were used to compare continuous variables and complications, respectively.

Results: A total of 92 ovarian cancer patients had HIPEC at 31 unique hospitals, and 16,417 patients had surgery without HIPEC at 229 hospitals. Of the 96% HIPEC patients, 96% occurred after publication (**Figure 1**). During the index admission, HIPEC patients had a longer median length of stay (8.9 vs 4.9 days, $P < 0.001$) and a higher percentage of ICU admissions (63% vs 11.1%, $P < 0.001$), CMI (2.8 vs 2.2, $P = 0.002$), and complication rates (RR = 2.71, $P < 0.001$). Direct costs for the index admission (S22,256.96 vs S12,031.56, $P < 0.001$) and direct cost index (observed/expected costs) (1.88 vs 1.11, $P < 0.001$) were also greater in the HIPEC patients. No inpatient deaths or 30-day readmissions were identified after HIPEC in this cohort.

Conclusion: Use of HIPEC for ovarian cancer increased in the United States after publication of a prospective clinical trial, although the number of patients remains modest. Incorporation of HIPEC was associated with increased cost, hospital and ICU length of stay, and complication rates. Further studies are needed to evaluate long-term outcomes, including morbidity and survival.

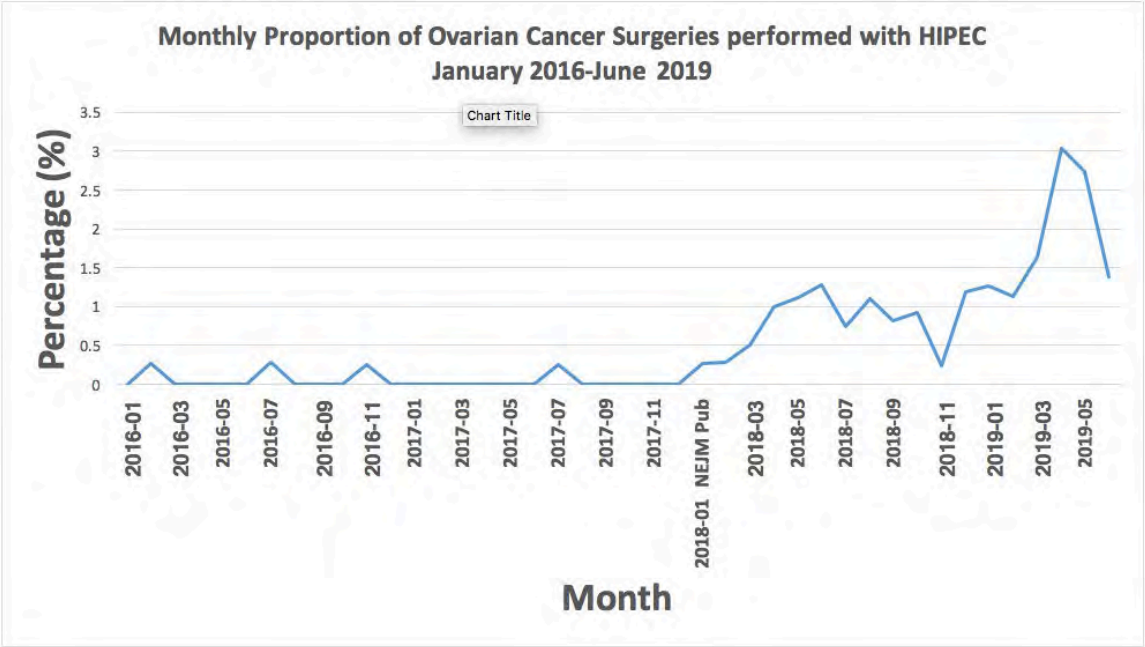

Fig. 1. Monthly rates of heated intraperitoneal chemotherapy (HIPEC) used in ovarian cancer surgery from January 2016 to June 2019. Rates of HIPEC use in ovarian cancer surgery increased after January 2018, the month that van Driel et al.'s "HIPEC in Ovarian Cancer" was published in the New England Journal publication (NEJM Pub).

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73 - Education Forum

Comparison of outcomes with utilization of hyperthermic intraperitoneal chemotherapy with paclitaxel and cisplatin versus cisplatin alone at interval debulking surgery in women with epithelial ovarian cancer

M.P. Horowitz[a], L. Moulton Chambers[a], M. Gruner[a], A.B. Costales[b], M. Morton[a], A.M. Chichura[c], P.G. Rose[a], C.M. Michener[c] and R. DeBernardo[c]. [a]*The Cleveland Clinic Foundation, Cleveland, OH, USA,* [b]*Baylor College of Medicine, Houston, TX, USA,* [c]*Cleveland Clinic, Cleveland, OH, USA*

Objective: The aim of this study was to investigate perioperative adverse outcomes in women with epithelial ovarian cancer (EOC) receiving interval debulking surgery (IDS) with hyperthermic intraperitoneal chemotherapy (HIPEC) with paclitaxel/cisplatin versus single-agent cisplatin.

Method: Women with primary EOC who underwent IDS with HIPEC with either paclitaxel/cisplatin or single-agent cisplatin were identified from a single-institution prospectively maintained HIPEC registry. Patient demographic and perioperative outcomes data were recorded. Univariate analysis was performed between the 2 cohorts.

Results: Among 39 women with EOC undergoing IDS with HIPEC, paclitaxel/cisplatin was administered in 24 patients (61.5%) and 15 (38.5%) received cisplatin alone. There were no differences in age (P = 0.10), ASA score (P = 0.61), stage (P = 0.99), disease location (P = 0.99), preoperative cycles of chemotherapy (P = 0.54), or days since last chemotherapy (P = 0.23). There was no difference in intensive care unit admission (20.8% vs 13.3%, P = 0.69), operative time (6.0 vs 6.0 hours, P = 0.61), or length of stay (5.0 vs 5.0 days, P = 0.28). Incidence of minor (25.0% vs 26.7%), moderate (8.3% vs 20.0%), and severe postoperative complications (12.5% vs 6.7%) (P = 0.74) were not different for those who received paclitaxel/cisplatin versus cisplatin alone. There was no significant difference in incidence of cellulitis (4.2% vs 6.7%, P = 0.99), ileus (8.3% vs 20.0%, P = 0.35), readmission (4.2% vs 13.3%, P = 0.55), reoperation (4.2% vs 6.7%, P = 0.99) or venous thromboembolism (4.2% vs 6.7%, P = 0.99). Median follow-up duration was significantly longer for paclitaxel/cisplatin versus cisplatin (16.1 vs 6.8 months, P = 0.003). However, 1-year recurrence-free survival (70.1% vs 66.5%, P = 0.99) and overall survival were not significantly different (90.2% vs 100.0%, P = 0.99).

Conclusion: Addition of paclitaxel does not significantly increase the incidence of adverse postoperative outcomes compared to cisplatin alone in women with advanced EOC undergoing IDS with HIPEC. Although disease outcomes from this prospective registry are immature, oncologic outcomes are no different at 1 year of follow-up. Data collection is ongoing to determine whether addition of paclitaxel to cisplatin will decrease recurrence and death women with EOC receiving IDS with HIPEC.

74 - Education Forum

Comparison of outcomes with utilization of hyperthermic intraperitoneal chemotherapy (HIPEC) at time of minimally invasive interval debulking surgery versus laparotomy

L. Moulton Chambers[a], M.P. Horowitz[a], A.B. Costales[b], M. Gruner[a], A.M. Chichura[c], M. Morton[a], M. Yao[c], P.G. Rose[a], R. DeBernardo[c] and C.M. Michener[c]. *[a]The Cleveland Clinic Foundation, Cleveland, OH, USA, [b]Baylor Scott & White Memorial Hospital, Temple, TX, USA, [c]Cleveland Clinic, Cleveland, OH, USA*

Objective: The aim of this study was to compare perioperative outcomes in women with advanced epithelial ovarian cancer (EOC) undergoing interval cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) via minimally invasive interval debulking surgery (MIIDS) or laparotomy.

Method: We performed a retrospective, single-institution study of women with advanced EOC who underwent IDS with HIPEC from 2017 to 2019. Univariate analysis was performed between the 2 cohorts.

Results: A total of 43 women were identified; 8 (18.6%) underwent MIIDS + HIPEC and 35 (81.3%) laparotomy + HIPEC. MIIDS included single-port (n = 6), robotic (n = 1), or multiport laparoscopy (n = 1). The majority of the patients had stage III disease (n = 27, 67.5%) and serous histology (n = 40, 93.0%). Median age of patients in the MIIDS group was 71.2 years versus 63.6 years in laparotomy (P = 0.03); there was no difference in ASA score or medical comorbid conditions (P > 0.05). The majority of patients in the MIIDS cohort underwent HIPEC with cisplatin alone (n = 6, 75.0%) versus the laparotomy cohort in which most received cisplatin with paclitaxel (62.9%, n = 22, P < 0.001). All patients who underwent MIIDS and laparotomy had optimal cytoreduction with no difference in rate of R0 resection (65.5% vs 71.9%, P = 0.25). There was no difference in intensive care unit admissions (25% vs 14.3%, P = 0.46), estimated blood loss (150 vs 275 cc, P = 0.13), or operative time (5.5 vs 6.0 hours, P = 0.58), but need for intraoperative pressor support was decreased for MIIDS versus laparotomy (37.5% vs 80.6%, P = 0.02). There was no difference in 30-day adverse major and minor events for MIIDS versus laparotomy, but length of stay was decreased for MIIDS (3 vs 4 days, P = 0.01) (**Table 1**). While time between chemotherapy cycles was significantly decreased for MIIDS versus laparotomy (44.5 days vs 60.5 days, P = 0.001), time to starting chemotherapy was not significantly affected (27 days, range 25–32 days, vs 32 days, range 27–42 days; P = 0.25)

Conclusion: Our data demonstrate that HIPEC with MIIDS is safe and effective and has a comparable incidence of adverse perioperative outcomes to laparotomy. Rate of achieving R0 cytoreduction was equivalent for both. MIIDS with HIPEC is associated with shorter hospitalization and decreased time between chemotherapy treatments than laparotomy. An MIIDS approach should not prevent surgeons from utilizing HIPEC where indicated for management of advanced EOC.

Table 1. Short-term perioperative outcomes in women with advanced epithelial ovarian cancer (EOC) undergoing interval cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) via minimally invasive interval debulking surgery (MIIDS) or Laparotomy (LAP).

	MIIDS (n = 8)	**LAP (n = 35)**	***P* value**
Major Adverse Events			
ICU admission	2 (25.0)	5 (14.3)	0.46
Reoperation	0 (0.0)	2 (5.7)	0.99
Venous Thromboembolism	0 (0.0)	2 (5.7)	0.99
Anastomotic Leak	0 (0.0)	3 (8.6)	0.99
Death	0 (0.0)	0 (0.0)	0.99
Minor Adverse Events			
Readmission	1 (12.5)	2 (5.7)	0.47
Ileus	1 (12.5)	4 (11.4)	0.99
Cellulitis	1 (12.5)	1 (2.9)	0.34
Pelvic Abscess	0 (0.0)	0 (0.0)	0.99
Blood Transfusion	4 (50.0)	11 (34.4)	0.41
Discharge Status			0.99
Home	6 (75.0)	22 (68.0)	
Home Health	1 (12.5)	3 (9.4)	
Home Therapy	0 (0.0)	1 (3.1)	
Skilled Nursing Facility	1 (12.5)	6 (18.8)	

Data presented as n(%)

Surgical Film - Education Forum

Hyperthermic intraperitoneal chemotherapy at the time of minimally invasive interval debulking surgery

M. Morton[a], A.M. Chichura[b], L. Moulton Chambers[a], M.P. Horowitz[a], A.B. Costales[b,c], P.G. Rose[a], R. DeBernardo[b] and C.M. Michener[b]. *[a]The Cleveland Clinic Foundation, Cleveland, OH, USA, [b]Cleveland Clinic, Cleveland, OH, USA, [c]The University of Texas Medical School at Houston, Houston, TX, USA*

Objective: Hyperthermic intraperitoneal chemotherapy (HIPEC) has been demonstrated to significantly increase overall survival in patients with advanced epithelial ovarian cancer. This video aims to demonstrate the utilization of HIPEC in the setting of minimally invasive surgery for interval debulking of ovarian cancers.

Method: After completion of optimal cytoreduction, inflow and outflow tubing is placed via the single port or umbilical port incision. The round outflow tubing is introduced into the abdomen and placed in the upper quadrants over the liver bed and along the diaphragm. The bifurcation of the inflow Y tubing is placed over the outflow tubing and introduced into the lower quadrants and pelvis. A 0 PDS on a CT-1 needle is then used to secure inflow and outflow tubing. This suture is continued in a running fashion to perform a temporary closure of the skin and fascia to achieve a seal during HIPEC to prevent spillage. If additional laparoscopic port sites are used, these are also temporarily closed. HIPEC is then performed in the standard fashion. The solution is circulated for 90 minutes with a goal outflow temperature of 42°C. After completion of HIPEC, the abdomen is irrigated via the tubing with normal saline. After evacuation of the fluid, the tubing is removed, and the incision is closed in the standard fashion.

Results: Optimal cytoreduction was achieved in all patients using a minimally invasive approach. There was no difference in overall complications, total estimated blood loss, or intensive care unit admissions for patients who underwent minimally invasive HIPEC compared to traditional HIPEC. Minimally invasive HIPEC patients had a significantly reduced length of hospital stay, with a median length of stay of 3 days.

Conclusion: HIPEC is feasible at the time of minimally invasive interval debulking and can decrease overall length of stay without an increase in complications.

Featured Poster Session II

129 - Featured Poster Session

Proactive inter-professional program to manage malignant bowel obstruction (MBO) in women with advanced gynecological cancer: Improving quality of care, education and awareness of malignant bowel obstruction among patients and health care providers

G. Bhat[a], N. Jivraj[a], A.M. Oza[b], N. Dhani[a], Y.C. Lee[c,d], A. Madariaga[a], L. Kasherman[a], M. McMullen[a], S. Liu[a], V. Bowering[a], S.E. Ferguson[a], J. Croke[a] and S. Lheureux[a]. *[a]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, [b]University Health Network, Princess Margaret Hospital, Toronto, ON, Canada, [c]Prince of Wales Hospital, Randwick, NSW, Australia, [d]NHMRC Clinical Trials Centre, Camperdown, NSW, Australia*

Objective: The aim of this study was to integrate and optimize the role of patient and health care provider education in the management of malignant bowel obstruction (MBO) in women with advanced gynecological cancers. The interprofessional MBO management program includes a clinical screening tool to identify patients at risk, a color-coded nurse-led symptom management algorithm, a standardized assessment tool, documentation template, bowel management regime, and education materials for patients and health care providers. The program was created to reduce unnecessary hospitalization and improve patient experience by providing coordinated care to allow patients to remain ambulatory and at home.

Method: We have developed educational resources for patients and health care providers on bowel function management for women with gynecologic cancers. Written education materials include a pamphlet on how to maintain good bowel function, full-fluid or low-fiber diet guidelines, and information on different laxatives to help manage bowel function. Our interdisciplinary and interprofessional team created a novel 5-part YouTube video series on MBO emphasizing early detection, self-care, and outpatient management, launched on May 24, 2019 (https://www.youtube.com/playlist?list=PLaLgrtXadEF8JI-TtwYcaaYM1DnxksUI8). Preprinted orders for inpatient management and education materials including a 3-part module on assessing and treating MBO for health care providers are currently in development. This nurse-led ambulatory symptom management algorithm, which is centered on symptom management through proactive calls, has been in place since July 2016.

Results: As of September 17, 2019, 404 patients were being managed under the MBO program. Based on the color-coding system, 282 are self-managing their bowel symptoms (green); 9 are at risk (yellow); 6 have an active bowel obstruction but are managed at home (orange); only 1 is currently admitted with bowel obstruction (red); and 106 have been transferred to palliative care (**Table 1**). Currently, 16 patients are being proactively followed in the MBO program. To date, nurses have made 2,445 proactive calls to manage symptoms at home.

Conclusion: A novel proactive program incorporating interprofessional care for ambulatory management of MBO optimizes the care of this vulnerable population with MBO. This patient-centered approach has empowered patients and families to improve self-management and effectively communicate their symptoms.

Table 1. Tool to direct management: Color code system.

Green	Yellow	Orange	Red	Blue
No MBO Patient may have ≥ 1 sign and symptom of MBO Patient may have ≥ 3 disease factors Patient has constipation Patient can self-manage	No MBO but at risk Patient has ≥ 2 signs and symptoms of MBO Patient has ≥ 3 disease factors RN to call the patient once a week or biweekly for a month	MBO diagnosis Outpatient management RN to call the patient once a week for a month	MBO diagnosis Inpatient management	No further treatment options Supported by Palliative Care Team

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130 - Featured Poster Session
Bone loss and osteoporosis risk in younger gynecologic cancer survivors
J. Sobecki-Rausch, B. Weigman, I. Anderson-Carter, T. Chandereng, M. Kliewer and E.M. Hartenbach. *University of Wisconsin School of Medicine and Public Health, Madison, WI, USA*

Objective: Women with cancer are at risk for treatment-related bone mineral density (BMD) changes. No long-term data exist among younger gynecologic cancer survivors who may have a higher lifetime risk of osteoporosis (OP). We sought to determine long-term BMD changes and OP risk in this population.

Method: We evaluated BMD in a retrospective cohort of women ≤65 years with uterine or ovarian cancer who underwent oophorectomy over a 5-year period (2010–2014). We performed CT-based L1 trabecular attenuation BMD measurements (Hounsfield units, HU) on previously performed CT scans at baseline and 1, 3, 5, and >5 years after cancer diagnosis. We categorized OP risk based on HU (<100 HU, concerning for OP; 100–150 HU, suggestive of osteopenia; >150 HU, normal). We used 1-sided *t* tests to compare baseline BMD to follow-up time points. Bivariate and multivariate analyses were performed to evaluate predictors of BMD (age, BMI, cancer type, chemotherapy, radiation, pretreatment BMD, smoking) at 1, 3, and 5 years.

Results: A total of 185 patients (median age 55 years, range 23–65; mean BMI 32) had a baseline CT scan and at least 1 additional follow-up CT scan. Of these, 78.1% had ovarian cancer; 78.1% received chemotherapy; 17.1% received external

beam radiation; and 63.6% remain alive in 2019. BMD significantly decreased between baseline and 1 year (179.4 vs 146.5 HU, $P < 0.001$), 3 years (176.0 vs 141.9 HU, $P < 0.001$), 5 years (179.1 vs 140.3 HU, $P < 0.001$) and >5 years (175.78 vs 123.63, $P < 0.001$). Half with normal BMD at baseline had risk for osteopenia or osteoporosis at 5 years. At baseline, 4.3% had OP risk compared to 7.4% at 1 year, 15.7% at 3 years, 18.0% at 5 years, and 23.3% at >5 years. Pretreatment BMD was a significant predictor at all time points (1 yr, $\beta = 0.7$, $P < 0.01$; 3 years, $\beta = 0.7$, $P = 0.02$; 5 years, $\beta = 0.8$, $P < 0.01$). Chemotherapy predicted bone loss at 1 year ($\beta = 10.9$, $P = 0.03$), and current smoking predicted bone loss at 5 years ($\beta = 52.4$, $P < 0.01$). See **Figure 1**.

Conclusion: Younger gynecologic cancer survivors experience a significant decrease in BMD and increased OP risk following treatment, especially in the first year. Our data suggest routine BMD assessments within 1 year following initiation of cancer treatment are warranted in this population. Opportunistic CT-based BMD measurements are a feasible OP screening tool in women with gynecologic cancer.

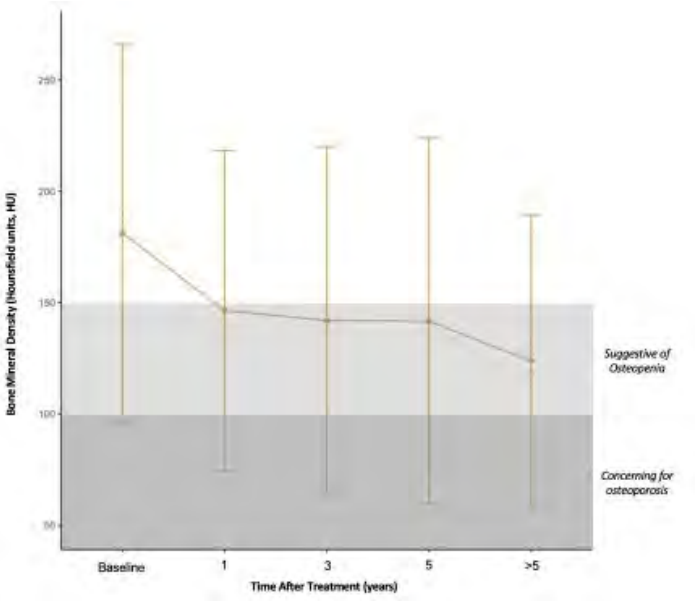

Fig. 1. Bone loss over time in younger women following treatment for gynecologic malignancies.

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131 - Featured Poster Session

Development of an online goals-of-care module for patients with gynecologic oncology malignancies

L.B. Turker[a], S. Eti[b], N.S. Nevadunsky[a] and G.M. Gressel[b]. [a]*Albert Einstein College of Medicine/Montefiore Medical Center, New York, NY, USA,* [b]*Montefiore Medical Center, New York, NY, USA*

Objective: The aim of this study was to create an online goals-of-care module for patients with gynecologic malignancies who qualify for hospice care.

Method: After Institutional Review Board approval, team members from the Divisions of Gynecologic Oncology and Palliative Care and "design thinkers" from the Parsons School of Design met to create an online platform for women with end-of-life gynecologic malignancies. After a prototype was created, semistructured interviews were performed with patients, caretakers, and gynecologic oncology providers. Interviews were recorded for qualitative analysis. Feedback from the interviews was then used to create the final online module.

Results: A prototype was created after collaboration with the design team. A total of 15 participants enrolled in the study: 5 patients, 2 caretakers, and 8 gynecologic oncology providers. All 15 participants found the online platform to be informative and potentially beneficial. All patient participants asked whether they could have the link to the online module for future use. An emerging theme from the semistructured interviews was that patients and caretakers use the internet to supplement information they receive from their treatment team. A participant stated, "I Google everything: medical websites, YouTube, you can find mostly everything." Patients appreciated that the online-based module is story-based, which helped them feel less alone. Patients stated, "it's good to read or listen to other patients' stories. It makes you think like it is not only you," and "people tend not to ask questions; people think they are the only ones going through this." Illustrative comments from participants are given in **Table 1**. Physician participants' feedback was focused on factual information and ensuring patients had a comprehensive understanding of their care team and their options going forward. After receiving feedback from all

study participants, a final prototype was created: https://drive.google.com/file/d/1xpZwvUx8dFn9Qj5Cku5FqOz-FJgzJbBV/view.

Conclusion: The goals-of-care module was well received among participants with patients having interest in using the module in the future. A randomized control trial comparing patient satisfaction after standard palliative care counseling versus standard counseling with addition on the online module is currently being performed.

Table 1. Illustrative quotes from participants.

Patient's understanding of their prognosis	Use of technology in regards to cancer	Reactions to online module	Feedback for the module
"Well I do understand that the ranking is 4 and it is usually terminal and that right now with the chemo it seems to be pretty good."	"I go on the computer and look up information about cancer and how to treat it and how to eat healthy and that sort of thing."	"I think it's helpful, especially the last part because unfortunately you have to think about it. You have to have the hard conversations. One thing we are very sure of is when you're born the next thing to come is death."	"I think there is a dearth of information regarding hospice. In my experience, the hardest part for the patient is to find out about the logistics and the details regarding making the transition to hospice care. Also very very important, the patients and their families always wonder, how much time does she have left?"
"Tell you the truth, I don't really understand. It is endometrial. I just started bleeding."	"I speak to the doctors, I look online. I put in the name of the cancer and find information. I think information there (online) is pretty standard."	"It is good to read or listen to other patients' stories, It makes you think like it is not only you. There are so many other people dealing with cancer."	"It should be available in Spanish."
"Well I know that the treatment is not going to be the cure. He (the doctor) explains to me what he is doing and going on all the time. I am well aware, although my family is not, that there is not going to be a cure."	"I google everything: medical websites, YouTube, you can find mostly everything. I can find out mostly everything. It is kind of depressing when I dig in sometimes really."	"I think it's good because I think… people tend to not ask questions; people are the only ones that are going through this and their questions are stupid so they tend to not ask question and I think that it might make it more comfortable and go to this app and see it is a common thing and feel more comfortable asking a question and getting to the proper person they need to get to."	"I would add one thing immediately. What do I do beforehand. Let's hit the cancer before it happens. I want to catch it."
"That it is just a disease and it can be fatal. I do not know other than that. I think it is serious."	"I was told listen to your doctors, don't go on the websites. So, I tend not to go on websites."	"I really like how it explains with the pictures so that you can know what is going on."	"I think it is good to be basic and clear and to the point and not too wordy."

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132 - Featured Poster Session
The prevalence of endometrial cancer symptoms in overweight and obese women presenting to a multidisciplinary weight management clinic

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Objective: Fifty percent of endometrial cancer (EC) cases are attributable to obesity, but most women are unaware of the relationship between their weight and EC risk. There is a dearth of data on the prevalence of endometrial hyperplasia (EH) and EC symptoms in obese women undergoing treatment for overweight/obesity. Our aim was to determine the prevalence of potential EH/EC symptoms among women presenting to a multidisciplinary weight management clinic.

Method: A menstrual history questionnaire was integrated into the intake form at an academic multidisciplinary weight management clinic in June 2018. We performed a cross-sectional study of all overweight or obese (BMI ≥ 25) women who presented to initiate care from June 2018 to May 2019. Heavy, irregular, and intermenstrual bleeding, as well as postmenopausal bleeding or discharge, were considered symptoms of EH/EC. Frequency of these symptoms and the prevalence of prior gynecologic work-up were calculated using descriptive statistics.

Results: A total of 76 women completed the intake questionnaire (100% of those to whom it was given); their median age was 47 years (range 23–72 years), and median BMI was 36 kg/m^2 (range 26–60 kg/m^2). Most women were white (65%, *n* = 49) or black race (19%, *n* = 15), were premenopausal (*n* = 41, 54%), and had not undergone a hysterectomy (*n* = 62, 82%). Five percent (*n* = 3) had a history of EH. Of the 62 women with an intact uterus, 34% (*n* = 26) reported ≥1 symptom of EH/EC. In the 42 premenopausal women, 42% (*n* = 18) reported heavy menstrual bleeding, 31% (*n* = 13) irregular periods, and 14% (*n* = 6) intermenstrual spotting or anovulatory cycles. In the 20 postmenopausal women, 15% (*n* = 3) reported postmenopausal bleeding or discharge. In all symptomatic women, 50% (*n* = 13) had discussed the symptoms with a gynecologist, and 31% (*n* = 8) had undergone an endometrial biopsy (EMB). Of 3 symptomatic postmenopausal women, only 1 (33%) reported a prior EMB.

Conclusion: In this at-risk overweight and obese female population, symptoms of potential EH/EC are quite prevalent, but only half of these women have ever sought gynecologic evaluation. Interventions to increase awareness of EH/EC symptoms in obese women are needed to increase rates of early detection of this disease.

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133 - Featured Poster Session

Association of treatment modality with sexual dysfunction in gynecologic cancer survivors: A secondary analysis of the gyne-GALS randomized controlled trial

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Objective: Sexual dysfunction is common in gynecologic cancer patients, but the extent to which it is associated with mode of therapy remains unclear and is rarely discussed with women prior to treatment. We aimed to evaluate the impact of treatment modality on the severity of psychosexual symptoms in gynecologic cancer survivors.

Methods: We performed a secondary analysis of baseline data from the GYNE-GALS randomized trial evaluating an online support group for cancer-related sexual problems at 5 centers in the United States and Canada (ClinicalTrials.gov, ID: NCT01654458). Gynecologic cancer survivors who met the cutoff score for sexual distress on the Female Sexual Distress Scale-Revised (FSDSR >11) at least 3 months after first-line therapy were enrolled. The primary outcome was sexual distress (FSDSR); secondary outcomes were sexual function (Sexual Function Questionnaire, SFQ) and body image (Sexual Adjustment and Body Image Scale, SABIS). We used multivariate linear regression models to assess the association of treatment modality with each outcome, adjusting for age, cancer site, time from diagnosis, stage, relationship status, pain, and depression/anxiety.

Results: We accrued 398 patients (cervix, 110; endometrium, 161; ovary, 94; vulva/vagina, 28) with mean age 50 (range 20–83) years. Surgery, chemotherapy, and radiation had been performed in 87%, 50%, and 44% of patients, respectively. Only 7% of women were being treated for sexual concerns despite documented distress. On multivariate analyses, neither chemotherapy (β = 0.74, *P* = 0.57), radiation (β = −0.63, *P* = 0.64), or surgery (β = −0.46, *P* = 0.82) were associated with FSDSR scores, or with SFQ and SABIS scores, and there was no significant interaction between surgery and radiation. Patients with increased symptoms of depression/anxiety had worse sexual function (*P* = 0.004), worse body image (*P* < 0.001), and increased sexual distress (*P* < 0.001). Older patients had worse sexual function (*P* = 0.021) but were not more distressed (*P* = 0.16).

Conclusion: Sexual concerns are undertreated in gynecologic cancer survivors with documented sexual distress. Modality of cancer therapy was not associated with severity of psychosexual symptoms. Women with existing mental health conditions are at risk of increased sexual dysfunction and distress, and should be counselled and treated appropriately.

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134 - Featured Poster Session
Sexual dysfunction in women with endometrial cancer and stress urinary incontinence
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Objective: Our aim was to determine characteristics associated with sexual function in women with endometrial cancer and stress urinary incontinence (SUI) at baseline and 12 months after treatment.

Method: This was a multicenter, prospective cohort study conducted at U.S. sites. Women with clinical stage I–II endometrial cancer or endometrial intraepithelial neoplasia and SUI with plan for hysterectomy were eligible. Sexual function data were collected preoperatively and 12 months postoperatively using the Female Sexual Function Index (FSFI). Sexual dysfunction, quality of life, SUI severity, demographics, and clinical measures were analyzed using χ^2 and Fisher exact tests or Wilcoxon rank sum tests.

Results: This is a secondary analysis describing sexual dysfunction in this cohort of 466 women. Prior to surgery, 31.1% of women (n = 145) were sexually active, and compared to women who were not sexually active, they were more likely to be younger (59 vs 63 years) and married (75.9% vs 49.8%), have private insurance (65.5% vs 52.0%), and lack medical comorbid conditions (16.6% vs 5.9%). Preoperatively, 61.4% (n = 89) of sexually active patients reported sexual dysfunction (FSFI score < 26). Patients with sexual dysfunction had lower quality of life scores on the Functional Assessment of Cancer Therapy-Endometrial index (125 vs 145, $P < 0.0001$) and more severe SUI ($P = 0.04$). Regardless of patients' preoperative sexual activity, patients were more likely to report sexual dysfunction/inactivity at their 12 month postoperative visit; 39.3% of patients with normal function preoperatively had new dysfunction or inactivity at their follow-up visit. Patients who underwent concomitant treatment of their SUI were found to have no difference in rates of sexual activity or dysfunction at 12 months on adjusted logistic regression testing whether they had surgical intervention (OR = 1.15, $P = 0.63$) or medical treatment of SUI (OR = 0.80, $P = 0.49$).

Conclusion: Sexual dysfunction is a widespread issue among patients with endometrial cancer and SUI and is more common with older, single, publicly insured, and medically complex patients. SUI treatment was not associated with improved sexual function in our study, with a significant proportion of women reporting worsening sexual function at 12-month follow-up regardless of SUI treatment. Early identification of these patients can help guide counseling and efforts to improve quality of life during endometrial cancer treatment and survivorship.

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135 - Featured Poster Session
Long-term oncologic outcomes after treatment of early-stage ovarian cancer: A 10-year follow-up study
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Objective: Conservative surgery is considered a valuable option for low-risk early-stage ovarian cancer. Here, we sought to assess long-term outcomes after surgery for apparent early-stage ovarian cancer, investigating the role of conservative surgery in high-risk (grade 3 or stage IC or more) disease.

Method: We conducted a retrospective study of women undergoing staging surgery for apparent early-stage ovarian cancer from January 1990 to December 2008. Patient demographics, pathology, and outcomes were recorded. Univariate and multivariate analyses as well as propensity-score matching were carried out in order to assess prognostic factors having an impact on survival outcomes. Survival outcomes were assessed using Kaplan-Meier and Cox models.

Results: Of the 233 charts reviewed, 182 (78.1%) patients were eligible and included having a follow-up longer than 10 years. The study population included 148 (83%) and 34 (17%) women undergoing radical or conservative procedures, respectively. Ten-year disease-free and overall survival was 83% and 88%, respectively. Ten-year cancer-specific survival was 93%. Median follow-up (for alive and nonrecurrent patients) was 175 (range 120–350) months. Patients submitted to conservative

or radical surgery had similar disease-free (P = 0.783, log rank test) and overall (P = 0.334, log rank test) survivals. These data were also confirmed after the application of propensity-score matching. High-risk features correlated with a nonsignificant slightly worse disease-free survival (P = 0.08). Furthermore, in the high-risk group, type of surgical approach (conservative vs radical) did not have an impact on survival (HR = 0.81, 95% CI 0.18–3.56, P = 0.78). Via multivariate analysis nonmucinous histology (HR = 0.27, 95% CI 0.08–0.91, P = 0.03) and increasing age (HR = 1.76, 95% CI 1.21–2.55, P = 0.003) had an impact on risk of recurrence and death, respectively.

Conclusion: Early-stage ovarian cancer patients experience excellent long-term survival. Presence of high-risk features has a detrimental effect on survival, regardless of the adoption of a conservative approach. High-risk disease should not be considered a contraindication, per se, to conservative surgery.

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Mobility-related basic and instrumental activities of daily living fluctuate over 2-3 cycles of chemotherapy for ovarian cancer in women over 70: An exploratory analysis

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Objective: The purpose of this exploratory secondary analysis was to describe trajectories of activities of daily living (ADLs) and instrumental ADL (iADLs) ability in older (age >70 years) ovarian cancer (OC) patients over the course of chemotherapy, to inform selection of activities to query in prospectively monitoring for supportive care needs to improve chemotherapy tolerance.

Method: This analysis of longitudinal data from an ongoing exercise feasibility pilot includes 17 women (mean 75.90 SD ± 4.53 years) with stage III–IV OC starting adjuvant (ADJ, n = 5) or neoadjuvant (NEO, n = 12) chemotherapy. We included 3 iADL and 10 physical function geriatric assessment (GA) items, and 9 mobility-related ADLs/iADLs with a 4-point ordinal scale: independent, modified, assist, and unable. Surveys were collected before chemotherapy cycles 1, 2, and 3 (and postoperatively for NEO). We used the Cumulative Link Mixed Model to test the time effect on 22 individual outcomes, and a likelihood ratio test to identify overall time effect, with significance level set at P = 0.05.

Results: We identified significant time effects on 2 GA outcomes in the NEO group: walk 1 block (P = 0.005) and bathe/dress (P = 0.026), and 4 outcomes in the ADJ group: walk several blocks (P = 0.045), and 4-point ordinal items of toilet transfers (P = 0.044), meal preparation (P = 0.032), and shopping (P = 0.005). Directional change (improve/worsen) differed by activity and group, while walk 1 block ability improved after cycle 2 in the NEO group; walk several blocks declined after cycle 2 in the ADJ group. Bathe/dress and shopping declined after cycle 1, but the decline partially reversed after cycle 2.

Conclusion: We identified 6 mobility-related ADL/iADLs of interest, differences by NEO/ADJ group, and unexpected trajectories of improvement or worsening across cycles. These results inform study design and supportive care referrals for OC patients over age 70 years.

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Frailty increases health care resource utilization after ovarian cancer surgery

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Objective: Frailty, defined as a state of vulnerability and decreased reserve following a stressor event, has been associated with postoperative complications and increased risk of short-term death following ovarian cancer surgery. We sought to determine the impact of frailty on health care resource utilization and outcomes in women with ovarian cancer who underwent surgery.

Method: Patients with ovarian cancer who underwent surgery between 2002 and 2014 were identified using the Nationwide Inpatient Sample. Frailty was identified using the Adjusted Clinical Groups frailty diagnoses indicators, which were designed and validated for research of frailty outcomes using administrative data. Univariate and multivariate log linear regression analyses were conducted to analyze the association between frailty and intensive care unit (ICU) admissions, nonroutine discharge, and inpatient mortality. A sensitivity analysis was performed adjusting for surgery-related complications and ICU diagnoses.

Results: We identified 44,010 hysterectomies in the database performed for ovarian cancer. Overall, 6.8% of the procedures were performed on frail patients. Nonroutine discharge occurred in 24.5% of patients (53.5% frail vs 22.4% nonfrail, $P < 0.0001$), and ICU admissions occurred in 18.6% of patients (45% frail vs 16.7% nonfrail, $P < 0.0001$). Inpatient mortality was 1.1% (5.5% frail vs 0.8% nonfrail, $P < 0.0001$). Frail patients were 1.6 times more likely to experience a nonroutine discharge (95% CI 1.56–1.65, $P < 0.01$), 1.94 times more likely to be admitted to the ICU (95% CI 1.88–2.0, $P < 0.01$), and 3.49 times more likely to die during their admission (95% CI 3.20–3.81, $P < 0.01$) than nonfrail patients. African-American race, age over 40 years, having 1 or more comorbid conditions, having public insurance, and having an extended procedure were significantly associated with all 3 outcomes. Sensitivity analyses adjusting for complications did not show a significant change in outcomes.

Conclusion: A significant number of women with ovarian cancer are frail at the time of diagnosis. Frail patients were significantly more likely to undergo nonroutine discharge, ICU admission, and also higher rates of inpatient mortality. Frailty should be considered when evaluating a patient for ovarian cancer debulking surgery.

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Stability of symptoms and symptom clusters over time for women with recurrent ovarian cancer on GOG-259: A GOG/NRG Oncology study

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Objective: Women with recurrent ovarian cancer experience a wide range of symptoms. Little is known about the stability of symptoms over time.The purposes of this analysis, in a sample of patients with recurrent ovarian cancer ($n = 294$) who participated in GOG-259 and completed 4 consecutive monthly symptom severity reports during long-term follow-up, were to (1) evaluate the stability of individual symptoms over time and (2) evaluate differences in the number and types of symptom clusters across time.

Method: At each assessment, the Symptom Representation Questionnaire was used to assess the occurrence and severity of 19 priority symptoms for women with ovarian cancer. Intraclass correlations and exploratory factor analyses at each time point were conducted.

Results: The most stable symptoms over time were lymphedema (intraclass correlation [ICC] = 0.938), peripheral neuropathy (ICC = 0.927), and sexuality concerns (ICC = 0.921). The least stable symptom was nausea (ICC = 0.761) Across the 4 assessments, 6 distinct symptom clusters were identified; however, only 3 of these clusters (emotional/cognitive, gastrointestinal distress, and peripheral pain/swelling) were relatively stable over time.

Conclusion: Findings provide insights into which symptoms are likely to remain stable versus change over time in women with recurrent ovarian cancer. The presence of 3 stable symptom clusters could provide insight into the mechanisms of common symptom clusters.

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Phase II VIRO-15 trial of olvimulogene nanivacirepvec (Olvi-Vec)-primed immunochemotherapy in platinum-resistant/refractory ovarian cancer (PRROC) (NCT02759588)

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Objective: A previous phase 1b trial with Olvi-Vec oncolytic viral immunotherapy (OVI) in platinum-resistant/refractory ovarian cancer (PRROC) established the recommended phase 2 dose of 3×10^9 pfu/day by intraperitoneal route. This trial evaluated the efficacy of OVI followed by carboplatin-doublet (CD) with and without bevacizumab (BEV) in PRROC.

Method: Patients who progressed on recent therapy received 2 consecutive days of Olvi-Vec followed by CD with and without BEV. Primary endpoints were progression-free survival (PFS) and overall response rate (ORR) by Response Evaluation Criteria in Solid Tumor (RECIST) and CA-125. Secondary endpoints were safety, overall survival, and translational analyses.

Results: A total of 26 heavily pretreated patients (median 4 prior regimens; 54% platinum refractory, 46% resistant; **Table 1**) enrolled, including 3 patients from phase 1b. At median 6 weeks after OVI, patients received mean 6 (±3) cycles of CD with and without BEV, and then BEV with and without single-agent nonplatinum as maintenance or continued therapy. Median PFS is 11.6 months (95% CI 9.6–NA). PFS at 6 months is 78%. ORR is 63% [95% CI 38%–84%; 1 (5%) complete response (CR), 11

(58%) partial response (PR)]; 32% (6) have stable disease (SD) by RECIST and ORR is 87% [95% CI 66%–97%; 8 (35%) CR, 12 (52%) PR]; and 13% (3) have SD by CA-125 in evaluable patients. There are no differences in PFS and ORR between resistant and refractory patients. Most frequent OVI adverse events were pyrexia (58%), abdominal pain (50%), nausea (50%), abdominal distension (46%), and fatigue (35%). Performance status (PS) was preserved or improved in 24 (92%) patients on subsequent CD with and without BEV. Multiplex IHC revealed OVI-induced infiltration of CD4+ and CD8+ lymphocytes penetrating the tumor islet. Activation of circulating tumor-specific T cells was shown by IFN-γ ELISPOT. NanoString RNA profiling in paired tumor biopsies showed OVI upregulated genes related to inflammation, T cell activation, and tumor regression. Overall, enhanced intratumoral infiltration of CD8+ T cells, upregulation of STAT1 expression (P = 0.008), and other OVI-induced changes to the tumor microenvironment may elucidate the apparent clinical reversal of PRROC.

Conclusion: Patients with PRROC treated with Olvi-Vec-primed immunochemotherapy produced PFS and ORR exceeding historical comparisons and patients' own last prior therapy. The majority of patients benefited from apparent reversal of platinum resistance with preserved or improved PS. Further clinical development in PRROC is warranted.

Table 1. Baseline characteristics.

Characteristic	**Patients (n = 26)**
Age, median (range)	63 (35-78)
Histology	
High grade serous	24 (92%)
Intermediate grade serous	1 (4%)
Mixed	1 (4%)
ECOG performance status	
0	16 (62%)
1	10 (38%)
Prior number of lines, median (range)	4 (2-9)
Prior platinum lines, median (range)	2 (1-5)
Platinum status at enrollment	
Platinum-resistant	12 (46%)
Platinum-refractory	14 (54%)
Prior antiangiogenic therapy with bevacizumab	
Yes	21 (81%)
No	5 (19%)
Prior PARP inhibitor therapy	
Yes	19 (73%)
No	7 (27%)
Baseline genetic profiles	
Tumor PD-L1 expression	
Positive	1 (4%)
Negative	24 (92%)
Unknown	1 (4%)
BRCA1/2 mutations	
Positive	7 (27%)
Negative	19 (73%)
Microsatellite instability status	
Stable	18 (69%)
Unknown	8 (31%)
Tumor mutational load	
Low	12 (46%)
Intermediate	4 (16%)
Unknown	10 (38%)
Response & PFS from last prior line before enrollment into VIRO-15 trial	
ORR by RECIST	3/26 (12%)
ORR by CA-125	5/24 (21%)
PFS (mos), median (95% CI)	4.6 (2.9 – 5.8)
PFS-6-month	30%

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Intraoperative capsule rupture, postoperative chemotherapy, and survival of women with stage I epithelial ovarian cancer: A JSOG-JSGO joint study

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Objective: The goal of this study is to examine the incidence and prognostic impact of intraoperative capsule rupture and to assess the effectiveness of postoperative chemotherapy for tumor rupture in stage I epithelial ovarian cancer.

Method: This is a society-based retrospective observational study in Japan examining 15,163 women with stage IA–IC1 epithelial ovarian cancer who underwent primary surgical treatment from 2002 to 2015. Associations between intraoperative capsule rupture and cause-specific survival (CSS) and between postoperative chemotherapy and CSS among intraoperatively ruptured cases were examined by histology type (clear cell n = 6,107; endometrioid n = 3,910; mucinous n = 3,382; and serous n = 1,764).

Results: Clear cell histology had the highest risk of intraoperative capsule rupture (57.3%) followed by endometrioid (48.8%), serous (41.8%), and mucinous (32.0%) histologies ($P < 0.001$). On multivariate analysis, clear cell type exhibited the largest impact of intraoperative capsule rupture on CSS (adjusted HR = 1.994, 95% CI 1.446–2.748) followed by serous (HR = 1.612, 95% CI 0.837–3.105), mucinous (HR = 1.281, 95% CI 0.786–2.087), and endometrioid (adjusted HR = 1.136, 95% CI 0.641–2.013) tumors. Postoperative chemotherapy for intraoperatively ruptured cases did not improve CSS in any histologic types in multivariate analysis: clear cell HR = 0.855, 95% CI 0.558–1.310; serous HR = 1.077, 95% CI 0.424–2.736; mucinous HR = 1.113, 95% CI 0.546–2.271; and endometrioid HR = 2.809, 95% CI 0.848–9.304 (all, $P > 0.05$). In the cohort-level analysis, postoperative chemotherapy utilization has significantly decreased in mucinous (16.3% relative decrease), endometrioid (13.1% relative decrease), and clear cell (9.3% relative decrease) (all, $P < 0.05$), but the cohort-level 5-year CSS rate did not change over time (all, $P > 0.05$). See **Figure 1**.

Conclusion: For stage I epithelial ovarian cancer, the clear cell type possesses a disproportionally high risk of capsule rupture during adnexectomy and carries the highest adverse impact on survival. A national decrease in the utilization of postoperative chemotherapy for intraoperatively ruptured cases is likely due to the absence of survival benefits.

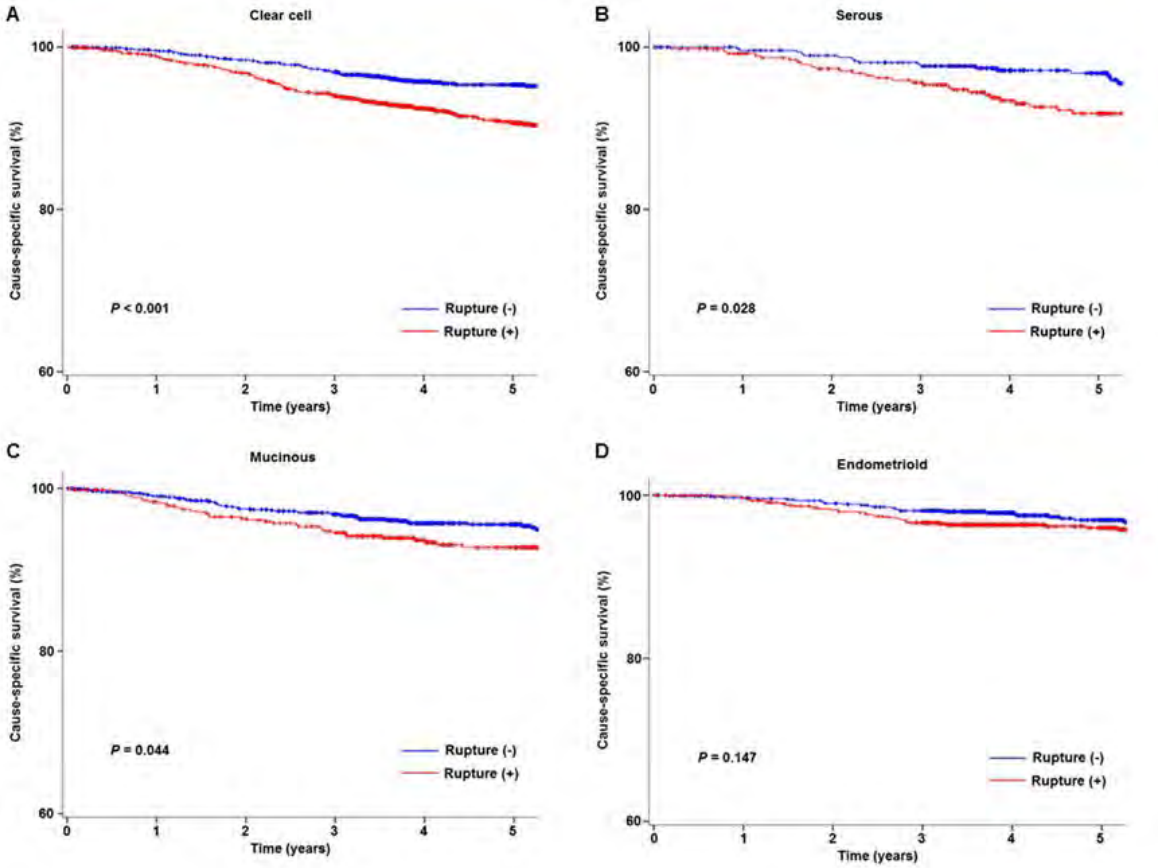

Fig. 1. Cause-specific survival related to intraoperative capsule rupture based on histology types.

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Use of adjuvant chemotherapy for early-stage low-grade serous ovarian carcinoma

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Objective: The aim of this study was to investigate patterns of use and the impact of adjuvant chemotherapy on overall survival (OS) of patients with stage IC and II low-grade serous ovarian carcinoma (LGSOC).

Method: Patients diagnosed with stage IC and II LGSOC between 2004 and 2015 were identified from the National Cancer Data Base. Survival data were collected from 2004 to 2014, capturing patients who had at least 1 month of follow-up. Factors associated with the receipt of chemotherapy were identified, and survival outcomes were assessed using Kaplan-Meier curves and compared with the log rank test. A multivariate Cox analysis was performed to control for confounders.

Results: A total of 545 patients met the inclusion criteria. Median patient age was 55 years, and the majority were white (88.8%), had stage IC disease (57.1%), and did not have medical comorbid conditions (81.3%). The overall rate of adjuvant chemotherapy (CT) use was 59.6%, whereas hormonal therapy was administered in 5.5% of this cohort (n = 30). CT use was more common in patients with stage II disease versus stage I disease (68.4% vs 53.1%, P < 0.001) and in those who underwent lymphadenectomy versus those who did not undergo lymphadenectomy (63.6% vs 50.9%, P = 0.005). No temporal trends in the use of CT were noted, and rates of CT use were comparable between academic and nonacademic facilities (62.3% vs 57.8%, P = 0.33). By univariate analysis, patients who received CT (n = 303) had improved OS compared to those who did not (n = 197) with 5-year OS of 92% and 82.4%, respectively (P = 0.026). After controlling for patient age, stage, performance of lymphadenectomy, presence of comorbid conditions, and type of insurance, CT was associated with better survival (HR = 0.59, 95% CI 0.37–0.92).

Conclusion: Adjuvant chemotherapy may be associated with a survival benefit for stage IC and II LGSOC.

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Cancer worry and decision making about risk reduction in women with *BRCA1* and *BRCA2* mutations

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Objective: Women with *BRCA1* and *BRCA2* mutations have high risks of breast and ovarian cancer. National guidelines recommend risk-reducing salpingo-oophorectomy (RRSO) but list risk-reducing mastectomy (RRM) as an option to discuss. We aimed to identify factors influencing uptake of RRM and RRSO for *BRCA* carriers, hypothesizing that higher cancer worry and depression would correlate with RRM but not with RRSO given guidelines dictating RRSO timing.

Method: This is a prospective, observational study of *BRCA* mutation carriers seen between 2004 and 2016. At enrollment, they had no history of breast or ovarian cancer, nor had undergone both RRSO and RRM. Initial surveys included the Cancer Worry Scale (CWS) and Patient Health Questionnaire (PHQ9). Analyses were completed in STATA IC 15.1.

Result: There were 248 women, 142 *BRCA1* and 106 *BRCA2* carriers. After enrollment, 95 women (38.3%) underwent RRM and 107 (43.1%) RRSO, at median ages of 39 (23–60) years and 41 (24–70) years, respectively. Median PHQ9 was 12 (range 0–26), with 184 (74.2%) participants meeting criteria for at least moderate depression (defined as PHQ9 of 10 or greater). Median CWS was 8 (range 4–16), with 237 (95.6%) having significant cancer worry (defined as CWS > 4). Fifty-seven (23.0%) women reported panic attack in the prior month. Women choosing RRM had higher PHQ9 (13.5 vs 12.7, $P = 0.16$) and CWS (8.6 vs 7.8, $P = 0.01$), and were significantly more likely to be parous (70.5% vs 49.3%, $P = 0.001$). In a multivariate model to predict RRM, being parous and having a higher CWS score remained independent predictors. RRSO was associated with higher PHQ9 (13.6 vs 12.3, $P = 0.01$) and CWS (8.7 vs 7.9, $P = 0.02$), and with being partnered (81.6% vs 36.3%, $P < 0.001$), parous (73.8% vs 36.3%, $P < 0.001$), and older at initial appointment (43 vs 30 years, $P < 0.001$); all but CWS remained independent predictors in multivariate modeling.

Conclusion: *BRCA* mutation carriers within this study had an overall high burden of depression, cancer worry, and panic. Having children was an independent predictor for both RRM and RRSO. Higher cancer worry scores were predictive of undergoing RRM but not RRSO, while higher depression scores predicted RRSO but not RRM. The burden of depression, cancer worry, and panic disorder in this population indicate a need to assess high-risk women for mental health comorbidity and provide appropriate support.

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Racial disparities in non-recommendation of adjuvant chemotherapy 'due to risk factors' in women with advanced ovarian cancer: A National Cancer Database study

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Objective: A recent National Cancer Data Base (NCDB) analysis demonstrated that black women with advanced ovarian cancer were less likely than white women to receive both surgery and chemotherapy. The current study sought to identify whether patient risk factors are, in certain populations, more likely to be cited in the NCDB as a reason for not administering adjuvant chemotherapy.

Method: This is a retrospective cohort study using NCDB data for advanced-stage ovarian cancer cases from 2004 to 2015. Women were included if they had stage II–III ovarian cancer, received primary surgery, and had complete data regarding adjuvant chemotherapy status and factors in our core model (age, race, Charlson-Deyo comorbidity score, insurance status, facility type). Multivariate logistic regression analyses evaluated factors associated with the NCDB code denoting that "chemotherapy was not recommended/administered because it was contraindicated due to patient risk factors (i.e., comorbid conditions, advanced age)."

Results: Of 45,036 women who met inclusion criteria, 522 (1.16%) did not receive adjuvant chemotherapy because it was determined to be contraindicated. Women who did not receive chemotherapy due to risk factors were more likely to be ≥70 years old (adjusted odds ratio [aOR] = 2.57, $P < 0.0001$) and more often had nonzero Charlson-Deyo comorbidity scores (score

1, aOR = 1.43, *P* = 0.001; score 2 or more, aOR = 2.64, *P* < 0.0001) (**Table 1**). Women who were not recommended for chemotherapy had greater odds of being black (OR = 2.02, *P* < 0.0001), and this trend persisted on multivariate analysis adjusting for age, comorbidity score, insurance status, and facility type (aOR = 2.13, *P* < 0.0001).

Conclusion: Advanced ovarian cancer patients who underwent primary debulking surgery but did not receive chemotherapy "because it was contraindicated due to patient risk factors" were more likely to be black, even when age, comorbid conditions, and level of treatment facility were similar. Determining eligibility for adjuvant chemotherapy requires an individualized approach, and the possibility of racial bias in individualized risk estimation should be considered.

Table 1. Univariate and multivariate logistic regression model for odds of not having chemotherapy recommended due to patient risk factors.

			Crude		Adjusted Model	
	N	Events (%)	OR (95% CI)	p	aOR (95% CI)	p
Age (years)						
18-<50	6,852	46 (0.67)	Ref		Ref	
50-<70	26,762	201 (0.75)	1.12 (0.81-1.54)	0.491	1.02 (0.73-1.41)	0.926
70 or older	11,422	275 (2.4)	3.65 (2.67-5.0)	<0.0001	2.57 (1.76-3.73)	<0.00
Race						
White	40,138	440 (1.1)	Ref		Ref	
Black	2,830	62 (2.2)	2.02 (1.55-2.65)	<0.0001	2.13 (1.62-2.80)	<0.00
Other	2,068	20 (0.97)	0.88 (0.56-1.38)	0.582	1.12 (0.71-1.76)	0.628
Insurance status						
Private	23,817	160 (0.67)	Ref		Ref	
Medicare/Other Govt. Insurance	17,279	324 (1.9)	2.83 (2.34-3.42)	<0.0001	1.47 (1.15-1.89)	0.002
Medicaid/Uninsured	3,940	38 (0.96)	1.44 (1.01-2.05)	0.044	1.36 (0.95-1.94)	0.096
Facility type						
Community program (CP)	1,611	23 (1.4)	Ref		Ref	
Comprehensive CP	16,623	234 (1.4)	0.99 (0.64-1.52)	0.948	1.01 (0.65-1.56)	0.966
Academic/Research program	20,070	169 (0.84)	0.59 (0.38-0.91)	0.017	0.63 (0.40-0.98)	0.039
Integrated Network Cancer	6,732	96 (1.4)	1.0 (0.63-1.58)	0.996	1.0 (0.63-1.59)	0.985
Charlson-Deyo score						
0	36,733	359 (0.98)	Ref		Ref	
1	6,814	113 (1.7)	1.71 (1.38-2.11)	<0.0001	1.43 (1.15-1.77)	0.001
2 or more	1,489	50 (3.4)	3.52 (2.61-4.76)	<0.0001	2.64 (1.94-3.58)	<0.00

Abbreviations: OR= ratio; aOR = adjusted odds ratio; CI= confidence interval; Ref = referent.
Adjusted model includes age, race, insurance status, facility type and Charlson-Deyo score.

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Risk factors for financial toxicity in gynecologic cancer patients receiving treatment

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Objective: Our goal was to measure the prevalence and identify the risk factors for financial toxicity in actively treated gynecologic cancer patients at a large cancer center.

Method: Institutional data were queried to identify gynecologic cancer patients treated between January 2016 and December 2018. Patients with preinvasive disease were excluded. Financial toxicity was defined based on available institutionally derived metrics, as the presence of 1 or more of the following: ≥2 bills sent to collections, application for and granting of a time payment plan, settlement, bankruptcy, enrollment into financial assistance programs, or documentation of a finance-related social work visit. Clinical characteristics were gathered using a 2-year look-back from time of the first financial toxicity event

or a randomly selected treatment date for those not experiencing toxicity. Risk factors were assessed using χ^2 tests. All significant variables on univariate analysis were included in the logistic regression model.

Results: Of the 5,188 patients undergoing treatment for gynecologic cancers, 22% (1,155) experienced financial toxicity. In the univariate analysis, cervical cancer (31%), stage 3 or 4 disease (29% and 27%), younger age (32% for age <30 years), nonpartnered marital status (28%), black (38%) or Hispanic (33%) race/ethnicity, self-pay (42%) or commercial insurance (26%), clinical trial participation (27%), more imaging studies (33% for ≥9), 1 or more emergency room visit (31%), longer inpatient stays (35% for ≥20 days), and more outpatient clinician visits (35% for ≥20 visits) were significantly associated with financial toxicity ($P < 0.01$). In multivariate analysis, younger age, nonpartnered marital status, black and Hispanic race/ethnicity, commercial insurance, more imaging studies, and more outpatient physician visits were significantly associated with financial toxicity (**Table 1**).

Conclusion: Financial toxicity is an increasingly recognized problem for gynecologic cancer patients. Our analysis suggests that demographic factors and health care utilization metrics may be used to proactively identify patients at greater risk of financial burden. Future work should focus on developing an intervention to minimize financial toxicity in at-risk patients.

Table 1. Univariate and multivariate analysis of variables associated with financial toxicity.

Characteristics	Financial Toxicity %(N)	No Toxicity %(N)	Univariate P-value	Multivariate Odds Ratios	Multivariate 95% CI
Baseline (N=5,188)	22.3 (1155)	77.7 (4033)	-	-	-
Disease Type			<0.001		
Uterine	19.5 (458)	80.5 (1886)		Referent	Referent
Cervical	30.9 (133)	69.1 (298)		1.27	0.97, 1.65
Ovarian	24.2 (444)	75.8 (1392)		0.92	0.76, 1.11
Other Female Genital	20.8 (120)	79.2 (457)		1.08	0.84, 1.38
Disease Stage			<0.001		
1	18.1 (359)	81.9 (1626)		Referent	Referent
2	20.9 (160)	79.1 (605)		0.86	0.67, 1.09
3	29.2 (224)	70.8 (544)		1.08	0.85, 1.37
4	26.6 (376)	73.4 (1039)		1.14	0.92, 1.41
Unknown	14.1 (36)	85.9 (219)		0.62	0.41, 0.92*
Age			<0.001		
<30	31.5 (35)	68.5 (76)		Referent	Referent
30-39	29.4 (83)	70.6 (199)		1.03	0.62, 1.73
40-49	27.8 (143)	72.2 (371)		0.93	0.58, 1.53
50-59	29.4 (347)	70.6 (833)		0.94	0.59, 1.51
60-69	21.2 (347)	78.8 (1292)		0.66	0.41, 1.06
70-79	14.5 (162)	85.5 (953)		0.47	0.28, 0.79*
≥80	11.0 (38)	89.0 (309)		0.34	0.19, 0.62*
Marital Status			<0.001		
Partnered	18.7 (581)	81.3 (2520)		Referent	Referent
Single/Widow/Divorce	27.5 (568)	72.5 (1501)		1.83	1.57, 2.13*
Race/Ethnicity			<0.001		
White (non-Hispanic)	19.3 (737)	80.7 (3089)		Referent	Referent
Black (non-Hispanic)	38.3 (158)	61.7 (255)		2.18	1.71, 2.76*
Hispanic	33.0 (105)	67.0 (213)		1.93	1.47, 2.52*
Asian	23.9 (91)	76.1 (289)		1.20	0.91, 1.56
Insurance Type			<0.001		
Commercial	26.3 (655)	73.7 (1834)		Referent	Referent
Medicaid	23.8 (87)	76.2 (279)		0.53	0.40, 0.71*
Medicare	15.1 (320)	84.9 (1793)		0.60	0.48, 0.74*
Self-pay	42.0 (87)	58.0 (120)		1.78	1.28, 2.45*
Clinical Trial Participation			<0.001		
No	21.4 (948)	78.6 (3472)		Referent	Referent
Yes	27.0 (207)	73.0 (561)		0.84	0.69, 1.02
Imaging Studies (MRI/PET/CT)			<0.001		
0	7.76 (34)	92.2 (404)		Referent	Referent
1-2	12.1 (153)	87.9 (1116)		1.64	1.11, 2.50*
3-4	19.7 (191)	80.3 (777)		2.59	1.72, 4.00*

Characteristics	Financial Toxicity %(N)	No Toxicity %(N)	Univariate P-value	Multivariate Odds Ratios	Multivariate 95% CI
5-8	28.2 (334)	71.8 (851)		3.43	2.25, 5.35*
≥9	33.4 (443)	66.6 (885)		3.46	2.21, 5.53*
Emergency Room Visits			<0.001		
0	18.9 (700)	81.1 (2997)		Referent	Referent
≥1	30.5 (455)	69.5 (1036)		1.08	0.90, 1.30
Inpatient Days			<0.001		
0	18.9 (560)	81.1 (2410)		Referent	Referent
1-10	25.5 (433)	74.5 (1265)		1.00	0.82, 1.21
11-20	30.4 (96)	69.6 (220)		0.90	0.64, 1.24
≥20	32.4 (66)	67.6 (138)		0.85	0.58, 1.26
Outpatient Clinician Visits			<0.001		
1-10	13.8 (383)	86.2 (2401)		Referent	Referent
11-20	28.4 (294)	71.6 (743)		1.95	1.56, 2.43*
≥20	35.0 (478)	65.0 (889)		2.43	1.88, 3.14*

CI = Confidence Interval; Treatment type, Other/Unknown Race/Ethnicity, Unknown Marital Status were included in the model and not significant; *=statistically significant p<0.05

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Impact of histology on disparities in survival between non-Hispanic black and non-Hispanic white women with epithelial ovarian cancer in Commission on Cancer®-accredited facilities

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Objective: The aim of this study was to investigate racial disparities in survival between non-Hispanic black and non-Hispanic white women with high-grade serous carcinoma (HGSC), endometrioid carcinoma (EC), mucinous carcinoma (MC), or clear cell carcinoma (CCC) of the ovary.

Method: Non-Hispanic black and non-Hispanic white women diagnosed with stage I–IV HGSC, EC, MC, or CCC of the ovary between 2004 and 2014 in the National Cancer Data Base were eligible. A propensity score approach was applied to sequentially balance the population within these 4 histologic subtypes. The following 7 characteristics were included: demographics, neighborhood income, insurance, comorbidity score, grade, stage, and treatment. Hazard ratio (HR) was calculated from weighted Cox modeling, and excess relative risk of death (ERR) was expressed as a proportion of the individual contribution of each factor.

Results: Racial disparity in survival was evident in all 4 histologic subtypes. The largest disparity was seen in MC followed by CCC, HGSC, and EC (**Figure 1A-1D**). After sequentially balancing for the 7 sets of explanatory variables, the HR dropped from 1.31 to 1.18 for HGSC, 1.31 to 1.04 for EC, 1.91 to 1.20 for MC, and 1.49 to 1.07 for CCC (**Figure 1A-1D**, respectively). The individual contribution to the ERR of death in non-Hispanic black women versus non-Hispanic white women varied by histology (**Figure 1E-1H**). The largest contributors to racial disparity in survival for HGSC were unexplained factors (58.1%), neighborhood income (12.9%), stage (12.9%), and treatment (9.6%) (**Figure 1E**) compared with neighborhood income (41.9%) and insurance (6.5%) for EC (**Figure 1F**). Stage, unexplained factors, and insurance accounted for 70.3%, 22%%, and 7.7%% of the ERR of death in MC (**Figure 1G**), whereas stage, insurance, and unexplained factors accounted for 61.2%, 24.5%, and 14.3% of racial disparity in survival in CCC (**Figure 1H**), respectively.

Conclusion: The largest disparity in survival between non-Hispanic black and non-Hispanic white women diagnosed between 2004 and 2014 was observed in MC, followed by CCC, HGSC, and EC. Neighborhood income and insurance represent potentially actionable factors to mitigate survival disparities between non-Hispanic black and non-Hispanic white women. Additional research is needed to investigate and mitigate disparities in MC, CCC, HGSC, and EC of the ovary.

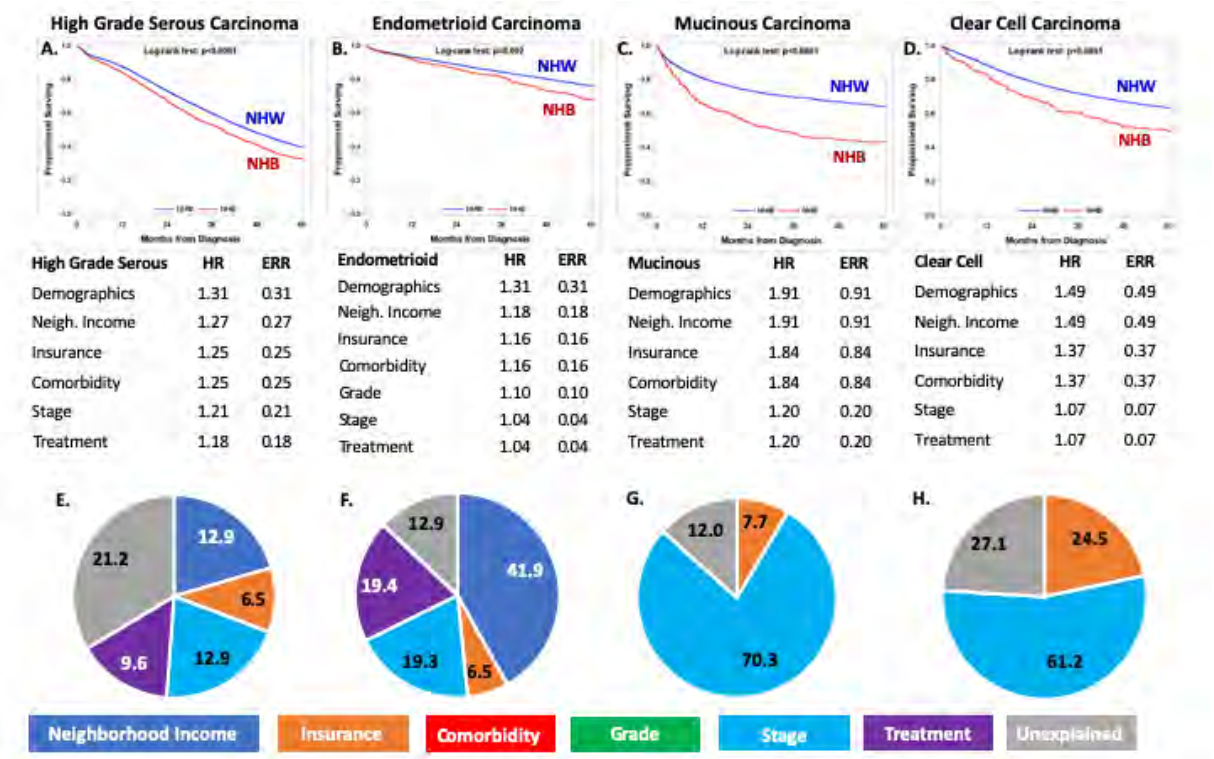

Fig. 1. Racial disparity in survival between non-Hispanic Black (NHB) and non-Hispanic White (NHW) women with high grade serous carcinoma (A), endometroid carcinoma (B), mucinous carcinoma (C) or clear cell carcinoma (D) with hazard ratio (HR) and the excess relative risk (ERR = 1 minus the HR) from the sequential weighted Cox models inserted into the underlying table. The pie chart displays the individual contribution to the ERR (%) for the NHB versus NHW women with high grade serous carcinoma (E), endometrioid carcinoma (F), mucinous carcinoma (G) or clear cell carcinoma (H). Grade was included in the analysis of women with endometrioid carcinoma, but not in patients with serous, mucinous or clear cell carcinoma.

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Does improved quality of care mitigate racial disparities in survival for endometrial cancer?

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Objective: Black women experience poorer survival than white women across all endometrial cancer stages and histologies. Differences in adherence to evidence-based guidelines have been proposed to be major contributors to this disparity. We examined whether adherence to evidence-based treatment recommendations for endometrial cancer could mitigate survival disparities between black and white women.

Method: The National Cancer Data Base was used to identify women with endometrial cancer treated from 2004 to 2016. We established 5 evidence-based quality metrics: surgical treatment within 6 weeks of diagnosis (Q1), use of minimally invasive surgery (stage I–IIIC) (Q2), pelvic nodal assessment (high-risk tumors) (Q3), adjuvant radiation (high intermediate risk) (Q4), and systemic chemotherapy (stage III–IV) (Q5). The rates of 30- and 90-day mortality and 5-year survival were compared between black and white women. To determine the influence of quality on outcomes, we compared outcomes among perfectly adherent black and white women with stage I and III endometrial cancer.

Results: We identified 310,208 women including 35,035 (11.3%) black women and 275,173 (88.3%) white women. Black women were less likely than white women to receive Q1 (65.8 vs 75.6%), Q2 (58.5 vs 72.9%), Q3 (71.3 vs74.2%), and Q5 (72.7 vs 73.2%) ($P < 0.05$ for all). Adherence to each quality metric was associated with improved survival. Among women with stage I disease, perfect adherence to the relative quality metrics was seen in 53.1% of white and 41.5% of black women. Among perfectly adherent stage I patients, outcomes in black women improved; however, they still experienced higher risk of 30-day (aRR = 2.25, 95% CI 1.30–3.90), 90-day (aRR = 1.84, 95% CI 1.23–2.76), and 5-year mortality (aHR = 1.42, 95% CI 1.26–1.59) than similar white women (**Table 1**). Among women with stage III tumors, perfect adherence to the relative quality

metrics was seen in 56.6% of white and 44.1% of black women. Perfectly adherent black women with stage III disease had improved outcomes, but remained at increased risk of 30-day (aRR = 1.86, 95% CI 1.01–3.44) and 5-year mortality (aHR = 1.35, 95% CI 1.22–1.50) compared to white women.

Conclusion: Black women are less likely than white women with endometrial cancer to receive evidence-based care. However, receipt of evidence-based care mitigates but does not eliminate racial disparities in outcomes, and black women remain at greater risk of death from endometrial cancer.

Table 1. Outcomes in black and white patients with stage I and III endometrial cancers.

	Stage I					
	Overall Study Population			*Perfectly Adherent*		
	Black	*White (reference)*	*aRR/aHR (95% CI)*	*Black*	*White (reference)*	*aRR/aHR (95% CI)*
30-day mortality	0.5%	0.3%	1.66 (1.22-2.26)	0.4%	0.2%	2.25 (1.30-3.90)
90-day mortality	0.8%	0.5%	1.60 (1.28-1.99)	0.6%	0.3%	1.84 (1.23-2.76)
5-year mortality	9.3%	6.8%	1.22 (1.15-1.30)	8.1%	5.1%	1.42 (1.26-1.59)
	Stage III					
	Overall Study Population			*Perfectly Adherent*		
	Black	*White (reference)*	*aRR/aHR (95% CI)*	*Black*	*White (reference)*	*aRR/aHR (95% CI)*
30-day mortality	1.6%	0.8%	1.84 (1.22-2.76)	1.4%	0.5%	1.86 (1.01-3.44)
90-day mortality	3.2%	2.0%	1.27 (0.97-1.68)	2.5%	1.4%	1.37 (0.89-2.11)
5-year mortality	45.9%	31.5%	1.19 (1.11-1.28)	45.9%	29.7%	1.35 (1.22-1.50)
aRR = adjusted risk ratio for 30- and 90- day mortality, aHR = adjusted hazard ratio for 5-year mortality. White women were treated as the referent group in the multivariable models.						

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Years of potential life lost due to cervical and uterine cancer deaths in 2015: Regional and country differences

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Objective: Our goal was to estimate and compare the years of potential life lost due to cervical and uterine cancer in 16 geographically distributed countries.

Method: Years of potential life lost due to cervical and uterine cancer were estimated for countries in South America (Brazil, Colombia), the Middle East (Iran, Israel), North Africa (Egypt, Morocco), Europe (France, Germany, Italy, Spain, Turkey, United Kingdom [U.K.]), Asia-Pacific (Japan, Thailand), Africa (South Africa), and North America (United States [U.S.]). Years of potential life lost at the country level was calculated by summing, for each death, the remaining gender and country-specific life expectancy at the age of death. The number of deaths by age due to each cancer type and remaining life expectancy by age were obtained from the World Health Organization (WHO) Mortality Database and Life Tables, respectively. The year 2015 was the most recent year with death data available for all countries, and thus was selected as the reference year. Years of potential life lost is presented as the sum of all deaths due to cervical or uterine cancer in the country in 2015, and as the average years of potential life lost per death, calculated as the total years of potential life lost divided by the number of deaths. Results by country and region were compared qualitatively to each other and against overall life expectancy and age at cancer death to identify trends.

Results: In 2015, a total of 25,392 deaths due to cervical cancer and 32,889 due to uterine cancer occurred in the 16 study countries. Years of potential life lost totaled 678,901 and 624,365 due to cervical and uterine cancer, respectively. Average years of potential life lost per death ranged from 20.8 years (Egypt) to 28.6 years (Brazil) for cervical cancer and 15.3 years (Germany) to 24.2 years (Thailand) for uterine cancer (**Figure 1**). Cervical cancer years of potential life lost per death trended similarly to life expectancy at birth, with countries with higher life expectancy tending to have more years of potential life lost per death. For uterine cancer, European countries were among the lowest in years of potential life lost per death, but highest in life expectancy, reflecting later age at death.

Conclusion: Years of potential life lost is a measure of the societal burden of early death and is a key component of the global burden of cancer. Regional differences in years of potential life lost per cervical and uterine cancer death generally mirror life expectancy for cervical cancer and age at death for uterine cancer.

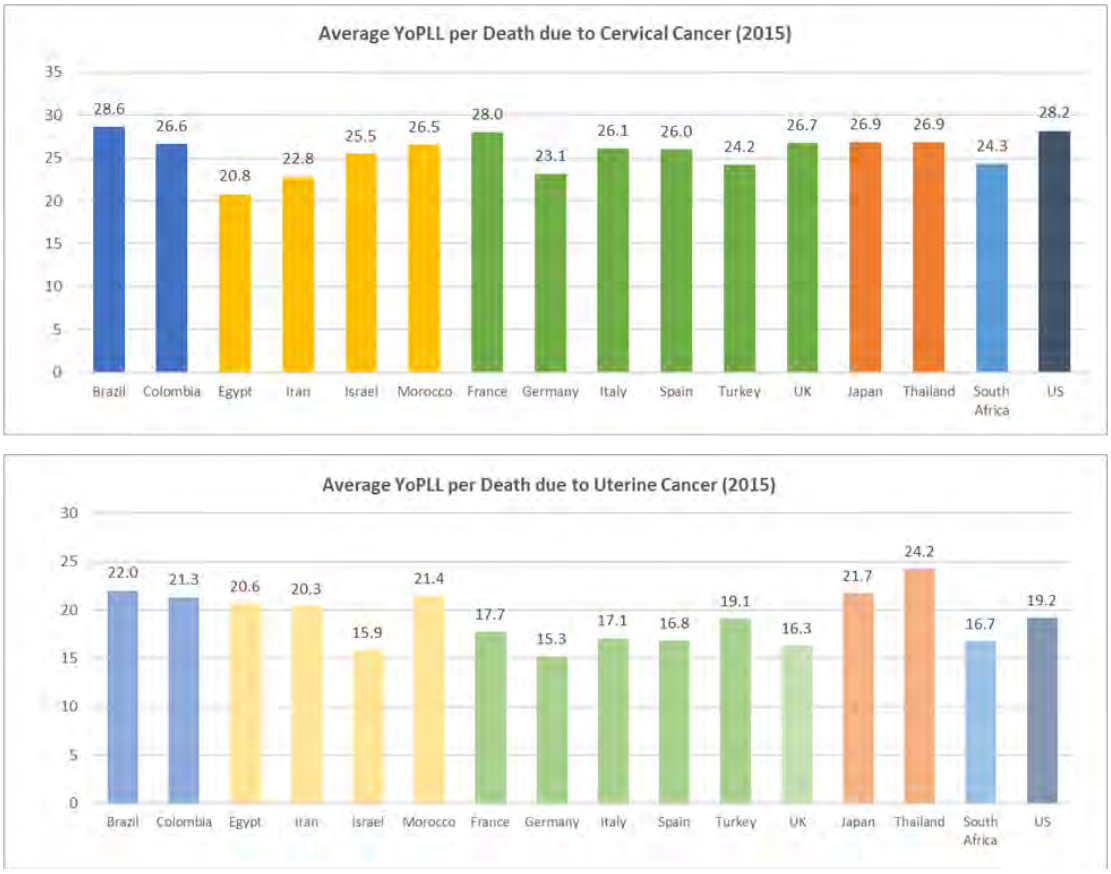

Fig. 1. Average years of potential life lost by country.

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Not immune from disparity: Two decades of racial minority participation in immunotherapy trials for breast and gynecologic cancers

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Objective: It is well established that cancer health disparities exist among minority women. While the causes are multifaceted, one theory focuses on lack of minority participation in clinical trials. Although prior studies have suggested that differences in tumor biology do exist in minority women, current enrollment protocols do not take this into consideration. Our objective is to evaluate minority participation in immunotherapy trials for gynecologic and breast cancers.

Method: Current and past clinical trials involving immunotherapy for breast and gynecologic cancers were reviewed. Completed trials were cross-referenced with publications to account for patients who did not complete the protocol. Minority enrollment was stratified by tumor site (ovary, endometrial, cervix, breast, general gynecological) and year published. Based on Centers for Disease Control and Prevention (CDC) age-adjusted incidence for race, expected and observed ratios of racial participation were calculated.

Results: A total of 131 clinical trials involving 29,478 patients were reviewed. Racial breakdown was provided in 16 studies (12%) for a total of 12,353 patients. Of these trials, 52% were breast (n = 69), 28% ovary (n = 37), 13% endometrial (n = 17), and 5% cervix (n = 7). Of the patients enrolled, 72% were white (n = 9,133), 2% black (n = 211), 22% Asian (n = 2,789), and 4% other (n = 506). Asian and other races exceeded age-adjusted enrollment in 12 (75%) and 6 (38%) of these trials, respectively. Utilizing CDC age-adjusted incidence, observed enrollment of black patients into immunotherapy trials was significantly less than expected if accrual rates were equal across all races. Observed enrollment was 23-fold lower for ovarian ($P < 0.001$), 14-fold lower for endometrial ($P < 0.001$), and 44-fold lower for breast ($P < 0.001$), and could not be calculated for cervical cancer as no black patients were enrolled ($P < 0.001$). Individually, none of the immunotherapy trials met expected enrollment for black patients by these methods.

Conclusion: A significant racial disparity is present in clinical trials evaluating the safety and efficacy of immunologic agents for breast and gynecologic cancers. Enrollment among black women is especially low. In order to better address the racial disparity in outcomes for these cancers, it is crucial that better efforts be made to involve these patients in clinical trials.

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149 - Featured Poster Session
Social determinants of health in uterine cancer patients in Ontario: Association with disease presentation and outcomes
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Objective: Delay in diagnosis and treatment of endometrial cancer may be associated with disease progression and impact management and outcomes. Social and cultural barriers influence recognition of symptoms and self-advocacy in seeking care. Associations between social determinants of health (SDH) and disease presentation, treatment, and prognosis have been shown in some health care systems. Our objective was to investigate these in Ontario's universal access system.

Method: Endometrial cancer patients in Ontario diagnosed 2009–2017 were identified, and clinical, social, and demographic information extracted from administrative databases using Institute of Evaluative Sciences (ICES) algorithms. SDH were quantified using previously validated marginalization quintiles (dependency, deprivation, instability, and ethnic concentration). Associations between SDH, disease stage, treatment, and outcome were explored using χ^2, log rank, and logistic regression.

Results: A total of 19,530 patients were identified; 73% of cancers were confined to the uterus. Stage distribution differed across marginalization quintiles ($P < 0.0001$) with advanced disease found more frequently in marginalized patients: deprivation, OR = 1.28 (95% CI 1.14–1.45); instability, OR=1.2 (95% CI 1.06–1.35); and ethnic concentration, OR = 1.3 (95% CI 1.15–1.46) ($P < 0.0001$). Median time from biopsy to surgery was also longer ($P < 0.0001$) in highly marginalized patients. Overall survival was shorter in patients in high deprivation and instability quintiles (log rank $P < 0.0001$) but not in high ethnic concentration quintiles, with HR = 1.4 for deprivation ($P < 0.0001$) and HR = 1.53 for instability ($P < 0.0001$). Survival differences persisted in more uniform cohorts of early (stage I) disease and endometrioid tumors. See **Figure 1**.

Conclusion: Marginalized populations diagnosed with uterine cancer present at more advanced stages, wait longer for surgery, and have shorter overall survival. Associations of SDH with uterine cancer presentation and management in Ontario could shed light on the impact of these factors on disease trajectory, drive policies for patient advocacy and redistribution of resources, and promote health care equity in this population.

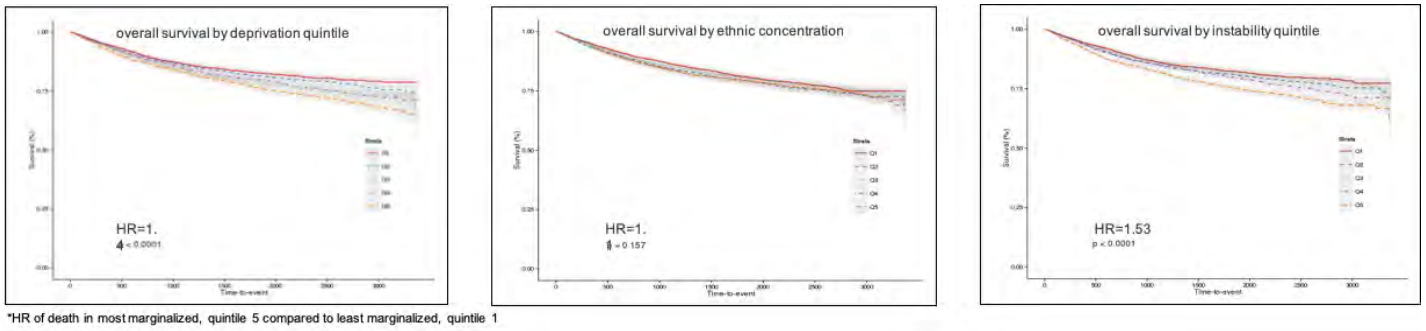

Fig. 1.

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150 - Featured Poster Session
State standards for insurance access to gynecologic oncologists
C.J. Moore and D.I. Shalowitz. *Wake Forest School of Medicine, Winston-Salem, NC, USA*

Objective: Health insurers may restrict provider networks as a cost-control measure. "Network adequacy standards" are regulations governing the minimum coverage needed for accreditation of an insurance plan. Unfortunately, in 2017, 114/428 (27%) silver plans offered on exchanges nationally did not include a gynecologic oncologist in network. In October 2018, the Centers for Medicare and Medicaid Services (CMS) released guidance intended to allow states additional autonomy in setting

network adequacy standards. Our objective was to review state and federal standards currently used for access to oncology providers to determine gaps in regulations that lead to inconsistent insurance coverage, as well as to identify opportunities to advocate for required access to a gynecologic oncologist.

Method: Representatives from the department of health or insurance (or equivalent) from 50 states and the District of Columbia were contacted by email at least twice, with phone calls as needed for clarification. In addition, official websites of the departments of health and insurance and CMS were searched for regulations and legislation on “network adequacy” or “provider network” standards. Standards were classified as including quantitative (e.g., oncologist required within a given travel time or distance of plan enrollees) and/or qualitative elements (e.g., enrollees must have "reasonable access" to an oncologist), as well as whether gynecologic oncologists were included as a required specialty.

Results: The reference network adequacy standard outlined by CMS includes qualitative and quantitative elements, but does not require access to a gynecologic oncologist. We received responses from representatives of 19/51 states. The remainder of the data were obtained from state websites. A total of 29 states had qualitative and quantitative standards for access to an oncologist, while 15 states had qualitative elements only. Standards from 7 states were not available. Only Pennsylvania appeared to require coverage of a gynecologic oncologist.

Conclusion: Insurance coverage of a gynecologic oncologist is not guaranteed by current federal and most state regulations, and many exchange plans do not currently include a gynecologic oncologist in network. As regulatory standards evolve, continued advocacy at the state and federal levels is needed to ensure that lack of insurance coverage is not a barrier to high-quality gynecologic cancer care.

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151 - Featured Poster Session

Inclusion of gynecologic oncology in cancer center leadership: Is representation equitable?

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Objective: Gynecologic cancers represented 6% of total cancer incidence and 5.5% of cancer mortality in the United States in 2019. This study sought to understand representation of gynecologic oncologists among cancer center leadership within U.S. academic institutions.

Method: The American Association of Medical College's list of accredited schools of medicine was used to identify academic institutions. Publicly available data were searched to identify whether a clinical cancer center affiliated with a medical school was present. The disease site focus of the cancer center director was identified. Ratios of disease site incidence and mortality to leadership were calculated.

Results: Of 154 accredited medical schools, 101 are affiliated with a clinical cancer center, and 98 have a cancer center director. Most cancer center directors were trained as medical oncologists (n = 58, 59.2%); 14 had PhDs; 10 were surgical oncologists; 5 were pediatric oncologists; 2 were gynecologic oncologists; and 9 had other training. Ninety cancer center directors had a specific disease site focus. Hematologic (n = 22, 24.4%), gastrointestinal (21, 23.3%), breast (16, 17.8%), thoracic (9, 10%), genitourinary (6, 6.7%), pediatrics (5, 5.6%), head and neck (4, 4.4%), sarcoma (3, 3.3%), and melanoma (1, 1.1%) were identified as nongynecologic cancer disease site focuses. Directors with a central nervous system focus were not identified. Medical oncologists focused on hematologic malignancies are most prevalent as cancer center directors (n = 18, 20%). Only 2 gynecologic oncologists are directors; 1 is at a National Cancer Institute-designated cancer center and 1 holds an interim position. In addition, one cancer center director is a radiation oncologist with a clinical focus on gynecologic cancer, leading to a total of 3.3% of cancer center directors with a gynecologic focus. No medical oncologist with a gynecologic cancer focus directs a cancer center. When incidence to leadership ratios were examined, gynecologic cancers rank ninth of 11 disease site categories. Gynecologic cancer is ninth in mortality to leadership ratio (**Figure 1**). These leadership ratios are below expected rates ($P < 0.01$, $P < 0.01$).

Conclusion: A bias in leadership within cancer centers toward common malignancies (hematologic and breast) is demonstrated. Representation of gynecologic oncologists in cancer center leadership is low despite the unique qualifications for cancer center leadership due to an expertise in both medical and surgical care. Future inclusion of gynecologic oncologists in cancer center activities, committees, and leadership should be prioritized.

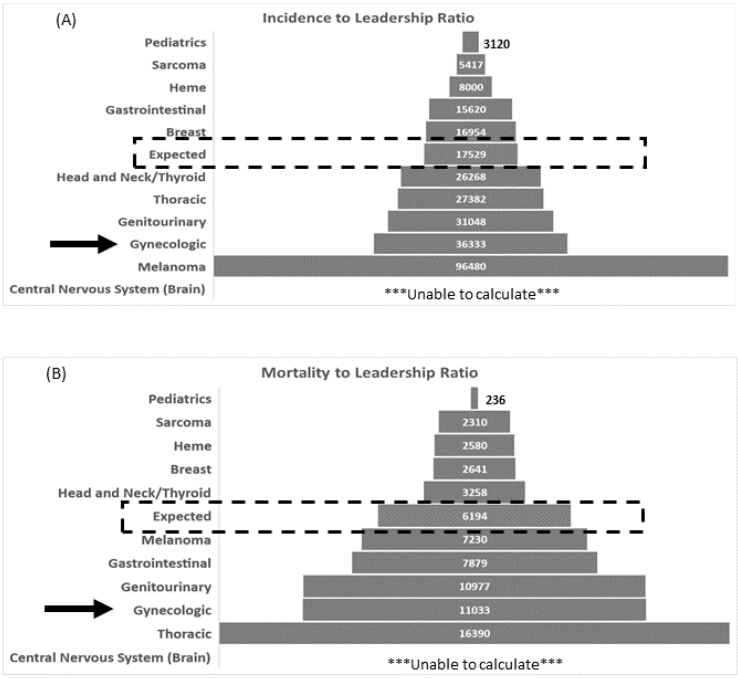

Fig. 1. (A) Incidence to leadership ratios of major cancer disease sites calculated using published publicly available data sources; (B) Mortality to leadership ratios of major cancer disease sites calculated using published publicly available data sources.

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Where are the women? Gynecologic oncology, gender and leadership in academic medicine.

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Objective: Gynecologic oncology includes increasing percentages of women surgeons. This study characterizes representation of faculty by gender and subspecialty in academic department leadership roles relevant to gynecologic oncology.

Method: By using the American Association of Medical Colleges list of accredited schools of medicine, academic institutions were identified. Observational data were obtained through institutional websites in July 2019.

Results: Of 154 accredited medical schools, 144 contain an obstetrics gynecology (OBG) department with a chair; 103 a gynecologic oncology division with a director; and 98 a clinical cancer center with a director. Women were overrepresented in academic faculty roles compared to the United States (66% vs 57%, $P < 0.01$) but not within gynecologic oncology divisions (55% vs 57%). Women were significantly ($P < 0.01$) underrepresented in all leadership roles (**Figure 1**). OBG departments with women chairs were more likely to have >50% women faculty (90.2% vs 9.8%, $P < 0.01$) and to have larger faculties (80.4% vs 19.6% >20 faculty, $P = 0.02$). The cancer center director gender did not correlate to OBG or gynecologic oncology faculty or leadership characteristics. The OBG chair subspecialty was more commonly reproductive-health focused (70.8%) including MFM (39.6%), generalist in OBG (20.1%), and REI (11.1%), compared to surgically focused gynecologic surgeons (13.9%) or GO (15.3%). A surgically focused chair was associated with >50% women faculty (85.7% vs 68.3%, $P = 0.03$) and faculty size >20 (85.7% vs 61.4%, $P < 0.01$). OBG departments with a surgically focused chair or gynecologic oncology chair were more likely to have a woman gynecologic oncology director (57.6% vs 29.4%, $P < 0.01$; 68.4% vs 31.7%, $P < 0.01$), and gynecologic oncology fellowship (50% vs 30.4%, $P < 0.01$; 59.1% vs 32%, $P < 0.01$). Women gynecologic oncologists represent 8 of 144 OBG department chairs (5.6%) and 9.9% of gynecologic oncology faculty (11.6% of women gynecologic oncology faculty) report to women gynecologic oncologists at the chair level.

Conclusion: Inclusion alone has been insufficient for women to attain leadership roles in gynecologic oncology or OBG. Within academic medical schools, women remain underrepresented in OBG and cancer center leadership. Gender equity in gynecologic oncology correlates to women and surgically focused leadership within OBG departments. Given the complexities

of gynecologic oncology, a surgical OBG chair may be better equipped to allocate resources and provide mentorship to gynecologic oncology compared with other subspecialists. Policies actively supporting women in gynecologic oncology and surgeons in OBG are needed to improve gender diversity in leadership.

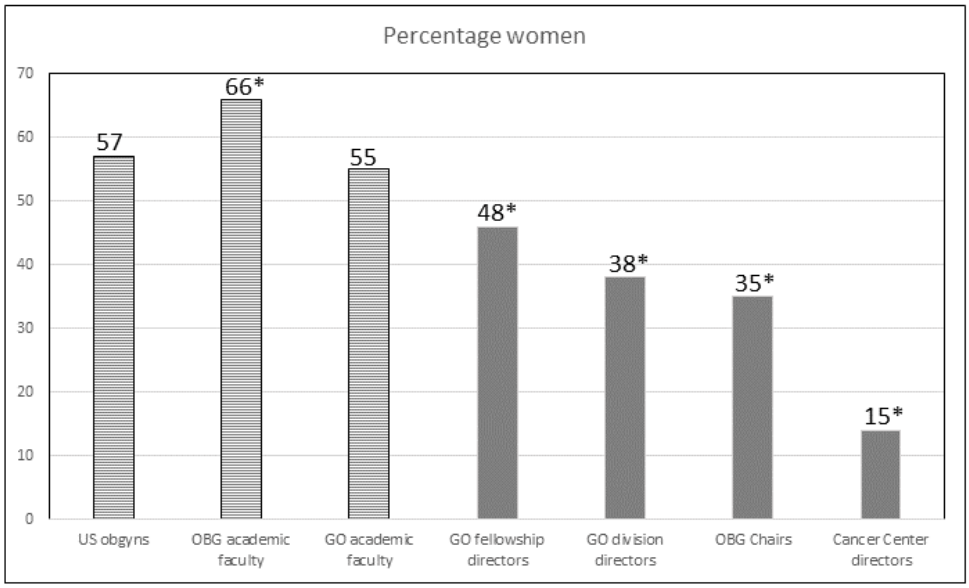

Fig. 1. Percentage of women in leadership positions compared to US OBGs, academic faculty OBGs and academic GO faculty.

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The society of gynecologic oncology's clinical outcome registry database validation process

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Objective: Our aim was to audit the accuracy of data in the Society of Gynecologic Oncology (SGO) Clinical Outcomes Registry (COR) database.

Method: The SGO undertook an initiative to collect clinical outcomes data relating to gynecologic cancers in 2013 by creating a registry. The COR was activated in January 2014 and accrued patients through January 2018. Recently, an effort to audit and validate the collected data was undertaken. The top 12 accruing sites were approached for participation in the validation audit, and 9 sites agreed. Eighteen validation data points were selected across 3 cancers, including ovary, cervix, and endometrial. Sites were asked to audit 10% of randomly selected charts for these data points. The data were then evaluated using percentage agreement and kappa coefficient statistic for both initial COR data and reentered validation data. Two data points were found to be erroneously mapped in the validation system and were excluded from the analysis, leaving 16 for analysis. Data with blank entries in the COR were excluded from this analysis.

Results: The majority of the sites (8/9) had a 100% completion rate for data entry, with a total 94% completion rate. There were 804 forms reviewed and audited: 613 endometrial, 133 ovarian, and 58 cervical cancers, compromising approximately 10% of the cases that are in COR. Endometrial cancer had 6 data points evaluated, with an average of 88.4% agreement, and kappa coefficients ranging from 0.30 fair agreement to 0.85 almost perfect. The average ovarian cancer percentage agreement over 7 data points was 79.7% and had a kappa coefficient ranging from 0.03 to 0.82 (slight agreement to almost perfect agreement); 2/7 data points had slight agreement. We evaluated 3 cervical cancer data points, with an average percentage agreement of 79.9% and kappa coefficients ranging from 0.57 to 0.73 (moderate to substantial agreement).

Conclusion: Statistical analysis for validation of the SGO COR confirmed high percentage rates of correlation and kappa coefficients. Although this validation study examined a small percentage of the overall data points, this audit is reassuring. This data should be considered valid for future clinical research.

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U.S. hospitals treating >100 ovarian cancer cases annually demonstrate best survival outcomes

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Objective: A goal volume of 20 surgical cases annually per hospital has been proposed as a standard in ovarian cancer care. Our goal was to assess the relationship between hospital case volume and ovarian cancer survival outcome at high-volume hospitals.

Method: We used the National Cancer Data Base to perform a retrospective cohort study of women with stage II–IV ovarian cancer from 2004 to 2015. Hospitals were stratified by annual overall volume and cytoreductive surgical (CRS) volume. We examined the association of overall hospital and CRS volume using Cox proportional hazard models adjusted for age, race, insurance status, income, education, distance traveled for care, stage, any comorbid conditions, location, and treatment at an academic center.

Results: A total of 96,521 women at 1,325 hospitals were identified. The mean overall hospital volume was 42 (95% CI 41–42). One-quarter of hospitals cared for ≤16 women per year. Survival was lowest among women cared for at hospitals with ≤20 ovarian cancer cases annually (**Table 1**). Survival was then relatively stable for hospitals with volumes of 21–140 and then improved significantly at hospitals treating >140 cases of ovarian cancer annually. Similarly, one-quarter of hospitals performed ≤21 CRS procedures per year, and the mean number was 45 (95% CI 45–46). Worse outcomes were seen at hospitals performing CRS procedures on ≤20 women. Significant survival improvement was observed at hospitals performing CRS procedures on >40 women and then increased further at hospitals performing >100 CRS procedures annually when compared to those performing fewer. There was a 5-month difference (95% CI 4.9-5.6) in mean survival between hospitals caring for ≤20 patients and hospitals caring for ≥20 patients. For surgical volume, there was a 3-month difference (95% CI 2.7–3.2) in mean survival between hospitals with ≤20 CRS procedues and hospitals performing more surgeries. Finally, there was a 6-month difference (95% CI 4.2–7.1) in mean survival between hospitals performing ≤20 and hospitals performing more than 100 surgeries.

Conclusion: Implementation of minimum-volume standards in hospitals and surgical volume for ovarian cancer care requires higher than previously published numbers of patients to improve survival. When possible, ovarian cancer care, and especially CRS procedures, should be concentrated at high-volume cancer centers.

Table 1.

	Hazard ratio of Ovarian Cancer Survival and Hospital Volume
	95% CI
1-20 women	1.07 (1.05-1.09)
21-40 women	1.00 (0.98-1.02)
41-60 women	0.97 (0.95-1.01)
61-80 women	1.02 (0.98-1.05)
81-100 women	1.02 (0.98-1.07)
101-120 women	0.95 (0.90-1.00)
120-140 women	1.00 (0.92-1.07)
140+ women	0.74 (0.68-0.81)
	Cytoreductive Surgeries performed per year
1-20 women	1.06 (1.02-1.09)
21-40 women	1.02(0.99-1.05)
41-60 women	0.95 (0.92-0.99)
61-80 women	1.06 (1.00-1.10)
81-100 women	1.02 (0.96-1.08)
101-120 women	0.91 (0.85-0.97)
120-140 women	1.07 (0.96-1.19)
140+ women	0.72 (0.64-0.81)
Women with Stage II-IV ovarian cancer Adjusted for age, race, insurance status, income, education, distance traveled for care, stage, any comorbidities, location, and treatment at an academic center.	

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Lymphadenectomy for high-risk endometrial cancer: Does it impact lymph node recurrence?

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Objective: The goal of this study was to assess factors associated with nodal recurrence to evaluate the therapeutic role of lymphadenectomy in high-risk endometrial cancer.

Method: Patients with high-risk histotypes of endometrial cancer treated with surgery between 2000 and 2010 at two tertiary care centers were identified and charts reviewed. Patients were followed until 2018 for recurrence. In those who recurred, factors predicting nodal recurrence were explored. In patients with at least 1 positive lymph node at the time of surgical staging, the effect of the number of lymph nodes removed on recurrence-free survival was analyzed. Kaplan-Meier curves were compared by log rank test, and a multivariate Cox proportional hazards model was performed using SAS version 9.4.

Results: Among 714 women treated with high-risk endometrial cancer, 167 were identified to have disease recurrence on imaging, with 98 women (58.7%) having a nodal recurrence and 69 women (41.3%) recurring at other sites. The median follow-up was 23.6 (5.3–144.2) months, and the median time to recurrence was 13.6 (3.0–120.0) months. In a multivariate analysis, presence of positive lymph nodes at surgical staging predicted nodal recurrence (HR = 4.0, 95% CI 1.5–10.6) significantly, while age, stage, adjuvant chemotherapy, and adjuvant radiation were not significant. As shown on the Kaplan-Meier curves in **Figure 1**, the nodal recurrence-free survival was lowest with positive lymph nodes (red), followed by no lymphadenectomy (purple), and highest with negative pelvic lymph nodes (blue) at surgical staging. There were 334 patients who underwent lymphadenectomy at surgical staging, with 74 patients having at least 1 positive lymph node. In patients with at least 1 positive node, the median (95% CI) recurrence-free survival was 87.1 (≥14.3) months when more than 15 lymph nodes were removed at lymphadenectomy, compared to 16.9 (13.6–35.6) months and 17.7 (8.5–39.8) months when 5–15 and less than 5 lymph nodes were removed, respectively (P = 0.02).

Conclusion: In high-risk endometrial cancer, positive lymph nodes at surgical staging predict nodal recurrence. In women with lymph node positivity, a more extensive lymph node dissection was associated with longer recurrence-free survival. The therapeutic role of lymphadenectomy in high-risk endometrial cancer should be further explored.

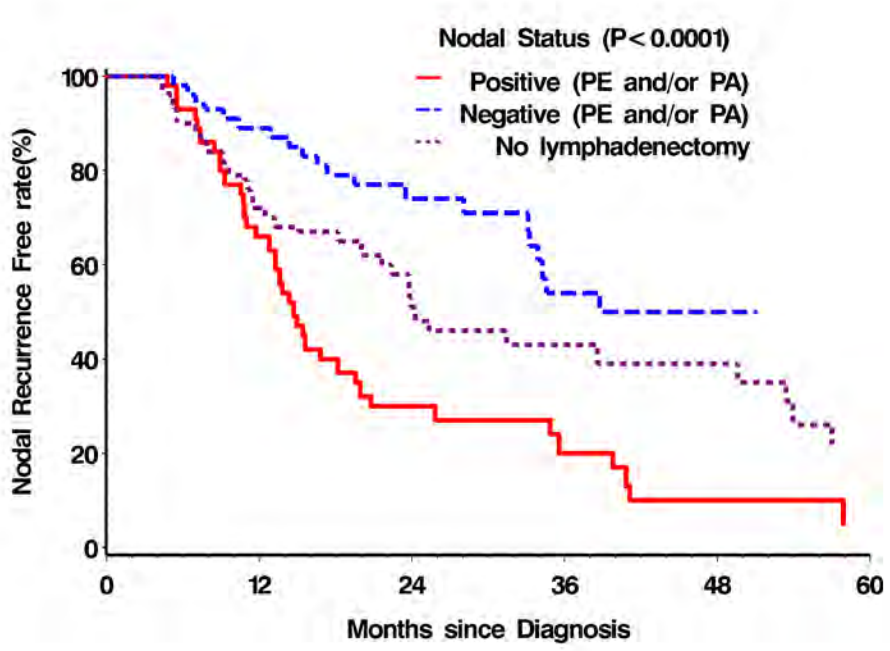

Fig. 1.

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Heterogeneity of patients with high-intermediate and high-risk endometrial cancer included in prospective trials

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Objective: Adjuvant therapy for endometrial cancer remains controversial. Clinical and pathologic characteristics have been used to stratify women based on risk of recurrence. Recently, several prospective trials have examined the use of various combinations of adjuvant chemotherapy and radiation for women classified as high-intermediate and high risk. These trials included a wide spectrum of tumor types and stages. We assessed the long-term survival of women with high-intermediate and high-risk endometrial cancer as classified by GOG 249 and PORTEC-3.

Method: The National Cancer Data Base (NCDB) was utilized to identify women with endometrial cancer who underwent hysterectomy from 2004 to 2016. The reported entry criteria for GOG 249 (pelvic radiotherapy vs vaginal brachytherapy and chemotherapy) and PORTEC-3 (pelvic radiation vs pelvic radiation and chemotherapy) were used to select the cohort (**Table 1**). We analyzed 5-year overall survival for the population of women who met the inclusion criteria for GOG 249 and PORTEC-3.

Results: A total of 82,128 patients were identified who would have fulfilled the entry criteria to GOG 249 or PORTEC-3. Five-year survival ranged from 56.7% to 86.8% for the various stage/histologic groups for women with GOG 249 criteria and from 36.5% to 80.1% for the stage/histologic groups of women with PORTEC-3 criteria. The highest 5-year survival, 86.8%, was noted for women age 18–49 years, with stage I tumors and 3 risk factors. In contrast, the lowest survival, 36.5%, was seen in those with stage III serous cancers. Survival for serous and clear cell tumors was significantly lower than that seen for endometrioid tumors.

Conclusion: Recent prospective trials of adjuvant therapy for high-intermediate and high-risk uterine cancer have included a heterogenous group of patients with widely varying prognoses. The variable risk of included patients may result in insufficient power to detect clinical benefit or alternatively, result in overestimation of benefit for lower risk patients.

Table 1. Five-year survival estimates for patients by inclusion criteria for GOG 249 and PORTEC-3 prospective trials.

	Clinical trial inclusion		NCDB survival estimate	
	GOG 249	**PORTEC-3**	**N**	**5-year survival (95% CI)**
Endometrioid				
Stage I, >70yo with 1 risk factor	x		14,639	78.3% (77.5-79.1)
Stage I, 50-69yo with 2 risk factors	x		11,313	86.3% (85.5-87.0)
Stage I, 18-49yo with 3 risk factors	x		122	86.8% (77.6-92.4)
Stage IA, grade 3, with LVSI		x	843	76.1% (72.0-79.7)
Stage IB, grade 3		x	5,528	70.8% (69.4-72.2)
Stage II		x	14,107	80.1% (79.4-80.9)
Stage IIIA		x	3,685	71.2% (69.3-73.0)
Stage IIIB		x	1,337	55.2% (52.0-58.3)
Stage IIIC		x	12,807	66.2% (65.3-67.2)
Serous				
Stage IA	x		6,440	77.4% (76.1-78.6)
Stage IB	x	x	1,523	58.5% (55.4-61.4)
Stage II	x	x	1,553	56.7% (53.8-59.5)
Stage III		x	4,944	36.5% (34.9-38.1)
Clear cell				
Stage IA	x		1,539	77.8% (75.3-80.1)
Stage IB	x	x	305	64.3% (57.6-70.2)
Stage II	x	x	477	66.2% (61.2-70.8)
Stage III		x	966	41.8% (38.2-45.3)
*Risk factors: grade 2 or 3, >50% myoinvasion, LVSI				

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The impact of frailty on health care resource utilization after endometrial cancer surgery

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Objective: Frailty has previously been associated with severe postoperative complications as well as non-home discharge after cancer surgery. It is defined as decreased reserve and ability to adapt after a stressor event. We sought to determine the association between frailty and adverse outcomes for women who underwent surgery for endometrial cancer.

Method: Patients with endometrial cancer who underwent hysterectomy between 2002 and 2014 were identified using the Nationwide Inpatient Sample. Frailty was identified using the Adjusted Clinical Groups frailty diagnoses indicators, which were designed and validated for research of frailty outcomes using administrative data. Univariate and multivariate log linear regression analyses were conducted to analyze the association between frailty and intensive care unit (ICU) admissions, nonroutine discharge, and inpatient mortality. A sensitivity analysis was performed adjusting for surgery-related complications and ICU diagnoses (sepsis, acute pulmonary collapse, and mechanical intubation, among others).

Results: We identified 77,930 women who underwent hysterectomy for endometrial cancer. Frailty was identified in 2.3% of the women. Nonroutine discharge occurred in 15.5% of patients (61.2% frail vs 14.4% nonfrail, $P < 0.0001$), and ICU admissions occurred in 8.5% of patients (41.1% frail vs 7.8% nonfrail, $P < 0.0001$). Inpatient mortality was noted in 0.4% of patients (5.1% frail vs 0.3% nonfrail, $P < 0.0001$). Frail patients were 2.17 times more likely to experience a nonroutine discharge (95% CI 2.10–2.25, $P < 0.01$), 2.78 times more likely to be admitted to the ICU (95% CI 2.66–2.90, $P < 0.01$), and 6.11 times more likely to die during their admission (95% CI 5.39–6.92, $P < 0.01$) than nonfrail patients. After adjusting for surgery-related complications and ICU diagnoses, sensitivity analyses did not show a significant change in outcomes. African-American race, age over 70 years, 2 or more medical comorbid conditions, public insurance, and being in the bottom half of income quartile were also associated with these outcomes.

Conclusion: A significant number of women with endometrial cancer are frail at the time of diagnosis. Frail patients who underwent endometrial cancer surgery were significantly more likely to undergo nonroutine discharge, ICU admission, and also higher rates of inpatient mortality.

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158 - Featured Poster Session

Long-term survival results of minimally invasive surgery in patients with uterine serous carcinoma

D. Basaran, D. Sassine, B. Brandt, J.J. Mueller, V. Broach, K.A. Cadoo, R.A. Soslow, K. Alektiar, N.R. Abu-Rustum and M.M. Leitao Jr. *Memorial Sloan Kettering Cancer Center, New York, NY, USA*

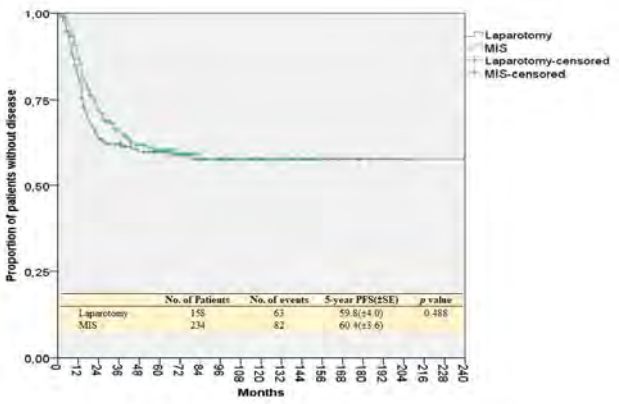
Objective: We sought to compare survival outcomes in women with uterine serous carcinoma (USC) who underwent surgical staging via minimally invasive surgery (MIS) versus laparotomy.

Method: Patients who underwent primary staging surgery for newly diagnosed USC at our institution between January 1, 1996, and December 31, 2017, were retrospectively reviewed. Patients were allocated to 2 cohorts: those who underwent surgical staging by MIS and those who had laparotomy. Demographic, surgical variables, and survival were analyzed.

Results: A total of 392 patients met the study criteria: 234 underwent MIS (32% laparoscopy, 68% robotic), and 158 underwent laparotomy. Both patient cohorts were comparable for age (median, 67 years), BMI, stage, depth of myometrial invasion, peritoneal washings, nodal metastasis rates, and adjuvant therapies. More patients had tumors with lymphovascular space invasion (LVSI) in the laparotomy cohort (33.8% vs 49.4%, $P = 0.001$). The MIS cohort had a higher percentage of patients who had sentinel lymph node mapping (79.1% vs 25.3%, $P \leq 0.001$), lower median lymph node count (9.8 vs 15, $P < 0.001$), and fewer patients with a paraaortic nodal dissection (44% vs 64.6%, $P < 0.001$). With a median follow-up of 52 months, progression-free survival (PFS) and overall survival (OS) were not significantly different between surgical cohorts. On multivariate analysis, stage, age, presence of LVSI, and positive peritoneal washings were associated with OS. See **Figure 1**.

Conclusion: Surgical staging of USCs with laparoscopic or robotic surgery had long-term oncologic outcomes similar to those of surgical staging with laparotomy.

Progression-free survival for all patients with USC



Overall survival for all patients with USC

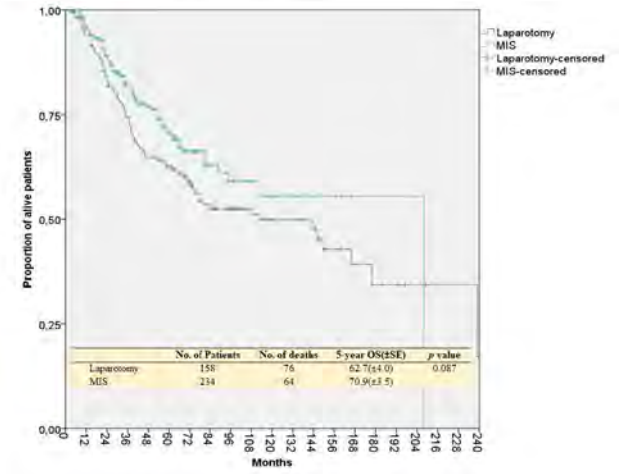


Fig.1.

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159 - Featured Poster Session

Is more better? Three versus six cycles of chemotherapy with and without radiation in early stage type II endometrial cancer

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Objective: The optimal adjuvant therapy for early-stage type II endometrial cancers (EC) is not known. Data from randomized trials suggest that chemotherapy with or without vaginal brachytherapy (VBT) and external beam pelvic radiotherapy (EBRT) are appropriate options. We sought to assess usage of adjuvant chemotherapy and radiation therapy in early-stage type II EC and its impact on overall survival.

Method: Patient data from the combined NCI's Surveillance, Epidemiology and End Results (SEER) registry-Medicare database from 1991 to 2015 were collected. The population included 1,689 patients with stage I–II EC of type II histologies. Patients were categorized by mode of adjuvant treatment: hysterectomy (HYS) alone, HYS with EBRT, HYS with chemotherapy, HYS with VBT, and combinations of adjuvant treatments. Patients who received chemotherapy were further subcategorized by number of cycles, 3 versus 6. Multivariate Cox regression was used to identify sociodemographic, comorbidity, and treatment factors associated with overall survival.

Results: There were 1,115, 299, and 275 patients with serous, carcinosarcoma, and clear cell histologies, respectively. Thirty-four percent underwent HYS alone; 18% had adjuvant chemotherapy; 20% had adjuvant radiation; and 28% had both. Of those who received radiation, 40% received VBT. Of those who received adjuvant chemotherapy, 45% had 3 cycles and 55% received 6 cycles. In all type II cancers, chemotherapy with VBT was associated with improved survival when compared with no treatment (HR = 0.69, 95% CI 0.51–0.95, *P* = 0.02). EBRT had worse survival when compared with chemotherapy with VBT (HR = 1.61, 95% CI 1.14–2.28, *P* = 0.007). These results were more dramatic in the serous subgroup: chemotherapy with VBT versus no treatment (HR = 0.53, 95% CI 0.36–0.79, *P* = 0.002) and EBRT versus chemotherapy with VBT (HR = 2.10, 95% CI 1.35–3.27, *P* = 0.001). The administration of 6 cycles of chemotherapy did not improve survival when compared with 3 cycles (HR = 0.98, 95% CI 0.71–1.37, *P* = 0.92). When analyzed individually by subtype, clear cell carcinoma showed similar benefits, whereas there was no benefit with either EBRT or chemotherapy with VBT in the carcinosarcoma population.

Conclusion: The administration of chemotherapy with VBT improves survival in early-stage type II EC, specifically in serous and clear cell carcinomas. While 6 cycles of CT did not appear to improve outcomes over 3 cycles, the optimal number of cycles remains undefined.

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160 - Featured Poster Session

Association of CD8+ T cell gene expression signatures with outcomes in the distinct molecular subtypes of endometrial cancer

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Objective: Increased numbers of tumor-infiltrating lymphocytes in endometrial cancer (EC) are associated with improved survival, but their association with EC molecular subtypes is not well defined. We sought to define the CD8+ tumor-infiltrating immune population present in ECs of distinct molecular subtypes and the association with patient outcomes.

Method: RNA-sequencing data of 232 ECs were obtained from The Cancer Genome Atlas and reanalyzed. Deconvolution of bulk gene expression data was performed using single-sample gene set enrichment analysis (ssGSEA). Median CD8+ ssGSEA enrichment scores were calculated and ECs classified into highly enriched for CD8+ gene signatures (CD8-high) and less enriched for CD8+ gene signatures (CD8-low) relative to the entire population. Patient characteristics and survival were compared using the appropriate statistics.

Results: The CD8+ ssGSEA enrichment scores showed little variation in ECs of POLE (ultramutated), MSI (hypermutated), or copy-number (CN)-low (endometrioid) subtypes. In contrast, of the 60 ECs classified as CN-high (serous-like) subtype, 19 ECs (32%) were CD8-high and 41 (68%) were CD8-low. There were no statistically significant differences in baseline patient characteristics including FIGO 2009 stage (*P* = 0.853) and histologic grade (*P* = 0.498). Of interest, CD8-high CN-high ECs were also significantly enriched for PDL-1 gene expression by ssGSEA (*P* = 0.017). There was a statistically significant difference in overall survival (OS) (*P* = 0.01) and progression-free survival (PFS) (*P* = 0.045). The 2-year PFS rate for the CD8-high and CD8-low CN-high ECs was 85% and 65%, respectively, and the OS rate was 100% and 83%, respectively. There were no statistically significant differences in OS between the CD8-high and CD8-low groups for the MSI (*P* = 0.646) and CN-low EC molecular subtypes (*P* = 0.793).

Conclusion: Deconvolution of bulk gene expression data revealed the existence of a CD8-high subset of CN-high ECs, which were found to display significantly longer PFS and OS than those with low CD8 expression, while CD8 signature had no prognostic significance in other genomic subtypes of EC. These findings highlight that mechanisms of immune escape may be different among the CN-high and CN-low tumors, which bears implications for development of biomarkers and combination immunotherapies for EC patients.

Scientific Plenary VII: Health Systems

75 - Scientific Plenary

Same-day hospital discharge for gynecologic oncology patients undergoing minimally invasive hysterectomy: Feasibility, barriers to discharge and risk factors for readmission

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Objective: Same-day hospital discharge (SDHD) following minimally invasive hysterectomy (MIH) has been reported as feasible but is not routine practice. We aim to reaffirm feasibility of SDHD in a gynecologic oncology cohort, describe barriers to SDHD, and explore readmission risk factors.

Method: A retrospective chart review was conducted of gynecologic oncology patients undergoing MIH from January 2017 to June 2019 at a single institution. Demographics, operative details, comorbid conditions, and 30-day readmissions were extracted. Statistical analyses included χ^2, *t* test, and logistic regression.

Results: A total of 1,058 patients were included. Final pathology was 672 (63.5%) cancer, 148 (14%) precancer, and 238 (22.5%) benign. Of cancers, 89.3% were endometrial, 5.7% cervical, and 2.1% ovarian. Most patients (736, 69.6%) had SDHD. Univariate analysis of 39 demographic, comorbid, and surgical variables revealed 23 factors associated with postoperative admission. On multivariate analysis, age, procedure length, start after 2 p.m., radical hysterectomy, cystoscopy, surgical complications, opioid use, and CHF remained significant. SDHD was feasible for procedures often thought to require admission: radical hysterectomy (35.1%), lymphadenectomy (53.8% full, 77.8% sentinel) and minilaparotomy (51.9%). Admission indications were failure to meet PACU milestones (26%), chronic condition (24%), perioperative medical event (13%), surgical factor (10%), late surgery time (3%), social circumstance (3%), or not specified (21%). The 30-day readmission was low (36 patients, 3.4%) and not statistically different between admission and SDHD (4.7% vs 2.9%, $P = 0.14$). **Figure 1** shows postoperative disposition of readmitted patients. On univariate analysis, age, procedure length, estimated blood loss, minilaparotomy, hernia repair, postoperative length of stay, and CAD were associated with readmission. Procedure length and CAD retained statistical significance on multivariate analysis. Common readmission indications were infection (6, 17%), bleeding (8, 22%), and gastrointestinal complications (10, 28%).

Conclusion: In a large cohort of gynecologic oncology patients undergoing MIH, SDHD was feasible with few 30-day readmissions. Identifying groups at high risk for admission and readmission provides targets for perioperative strategies to improve patient care and reduce health care costs.

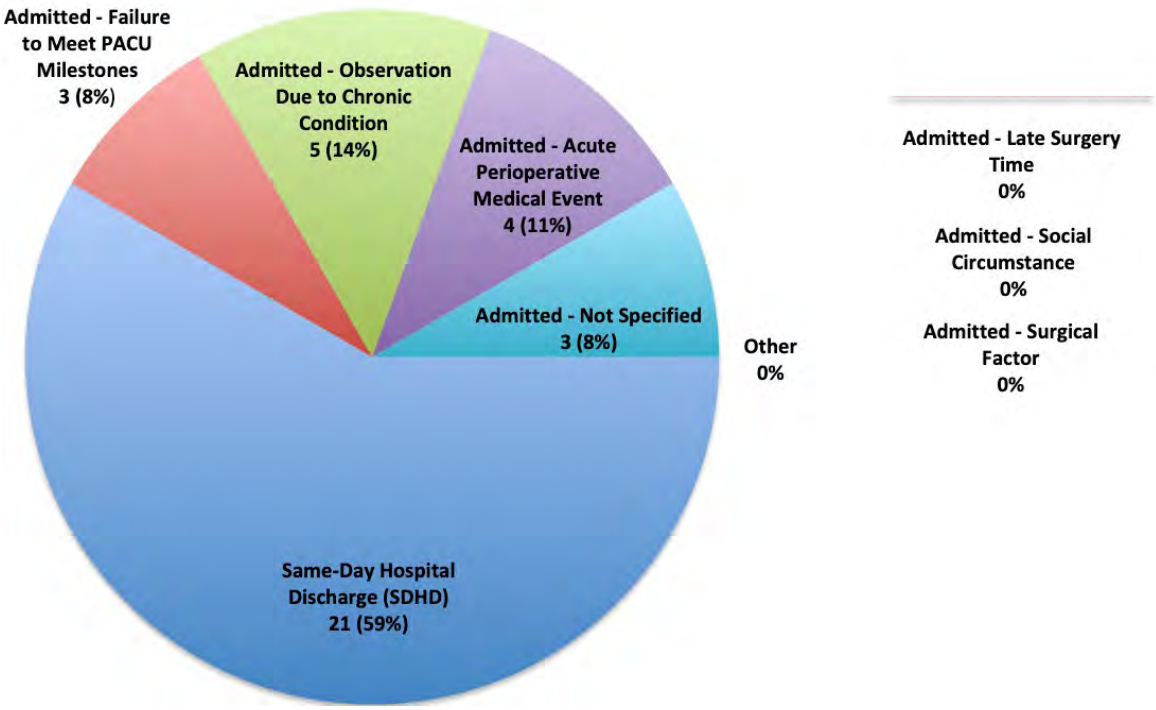

Fig. 1. Post-operative disposition of patients readmitted within 30 days of surgery.

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76 - Scientific Plenary

Risk factors for unplanned readmission due to uncontrolled symptoms or minor complications after surgery for gynecologic cancer

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Objective: Our goal is to determine the incidence of unplanned readmissions due to uncontrolled symptoms or minor complications after surgery for gynecologic cancers and to identify factors associated with unplanned readmissions.

Method: Women with unplanned readmissions within 30 days of abdominal surgery for a gynecologic cancer between 2015 and 2017 were identified from the National Surgical Quality Improvement Program (NSQIP) targeted hysterectomy dataset. NSQIP defined unplanned readmission indications were categorized into major or minor complications based on a modified Claviden-Dindo scale. Three independent reviewers categorized the reason for non-NSQIP defined unplanned readmissions as major surgical complication, minor complication, and medical-, cancer-, or symptom-related issues. Demographic, clinical, and operative factors were evaluated to determine their association with minor and symptom-related unplanned readmissions using bivariable and multivariable tests.

Results: A total of 19,222 women (60.5% uterine, 11.0% cervical, 28.5% ovarian) were identified. Of these, 1,141 (5.9%) women experienced an unplanned readmission (55.2% uterine, 15.5% cervical, 29.3% ovarian). Among those with an unplanned readmission, the reason was major surgical complication (62.8%), minor surgical complication (14.5%), and medical (10.8%), cancer (4.3%), or (7.6%) symptom-related issues (7.6%). Compared to those readmitted for major complications or medical/cancer-related issues, women readmitted for uncontrolled symptoms or minor complications were more likely to have cervical cancer (15.5% vs 9.7%), open surgery (68.4% vs 55.1%), and BMI > 35 (44.7% vs 36.0%) (all $P < 0.05$). They also had shorter operative times but more complex procedures (178 minutes, 32.1 RVU vs 186 minutes, 31.6 RVU; $P < 0.001$) and longer length of stay in the index hospitalization (4 [IQR 2–6] vs 3 [IQR 1–6] days, $P = 0.01$).

Conclusion: Among women with gynecologic cancer, 22.2% of unplanned readmissions were attributed to uncontrolled symptoms or minor complications that could potentially be managed in the outpatient setting. Women with obesity, cervical cancer, and open surgery were more likely to be readmitted for these reasons. Efforts to improve postoperative resource allocation and patient-monitoring programs are needed to help prevent these potentially avoidable unplanned readmissions.

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77 - Scientific Plenary

Utilization of the emergency department by gynecologic oncology patients: High rates and high needs in a medically vulnerable population

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Objective: Our goal is to characterize emergency department utilization by gynecologic oncology patients in a large academic cancer center in order to identify opportunities to decrease preventable emergency department visits.

Method: Institutional data were captured from the electronic medical record for July 2018–May 2019 for three major hospitals within an urban academic health system. Patients were identified as those with a gynecologic cancer diagnosis with any active treatment (chemotherapy and/or radiation) within the prior 180 days of emergency department encounter with an additional outpatient oncology visit within the last 90 days. Data including total number and hospital location of emergency department visits, cancer type, primary ICD-10 emergency department diagnosis, payer type, and zip codes were collected. The Community Needs Index (CNI) Score (range 1.0–5.0), publicly available data that aggregate five socioeconomic indicators/barriers that contribute to health care disparities (5.0 for greatest need), was linked to zip codes. Descriptive statistics were performed.

Results: There were 940 discrete emergency department visits by 305 gynecologic cancer patients. Of these encounters, 48.5% ($n = 456$) were treated and released. Admitted patient encounters ($n = 484$) had a mean length of stay (LOS) of 3.4 days (SD 6.4 days, range 1—85 days); 25.8% ($n = 125$) had a LOS of <2 days; and 27.9% had commercial insurance. Cancer types included 36% uterine, 28.3% ovary, 27.3% cervical, and 8.4% vulva/other. **Figure 1** depicts the frequency of all emergency department primary diagnoses. The most common categories with potential for outpatient or oncologic urgent care center intervention includeof pain (9.8%) and headache/nausea/vomiting/diarrhea (4.8%). Emergency department encounters by patients living in the 10 most frequent zip codes ($n = 384$, 41%) represented a median CNI of 4.0 (range 3–4.8).

Conclusion: Gynecologic cancer patients at an urban cancer center, including those from communities with significant health care disparities, have high emergency department utilization. Almost half of patients were treated and released. Of those admitted, 25% had an LOS of less than 2 days. Further analysis may reveal opportunities for changes in medical outreach to patients at risk for cancer health care disparities and for increasing triage and utilization of outpatient symptom management.

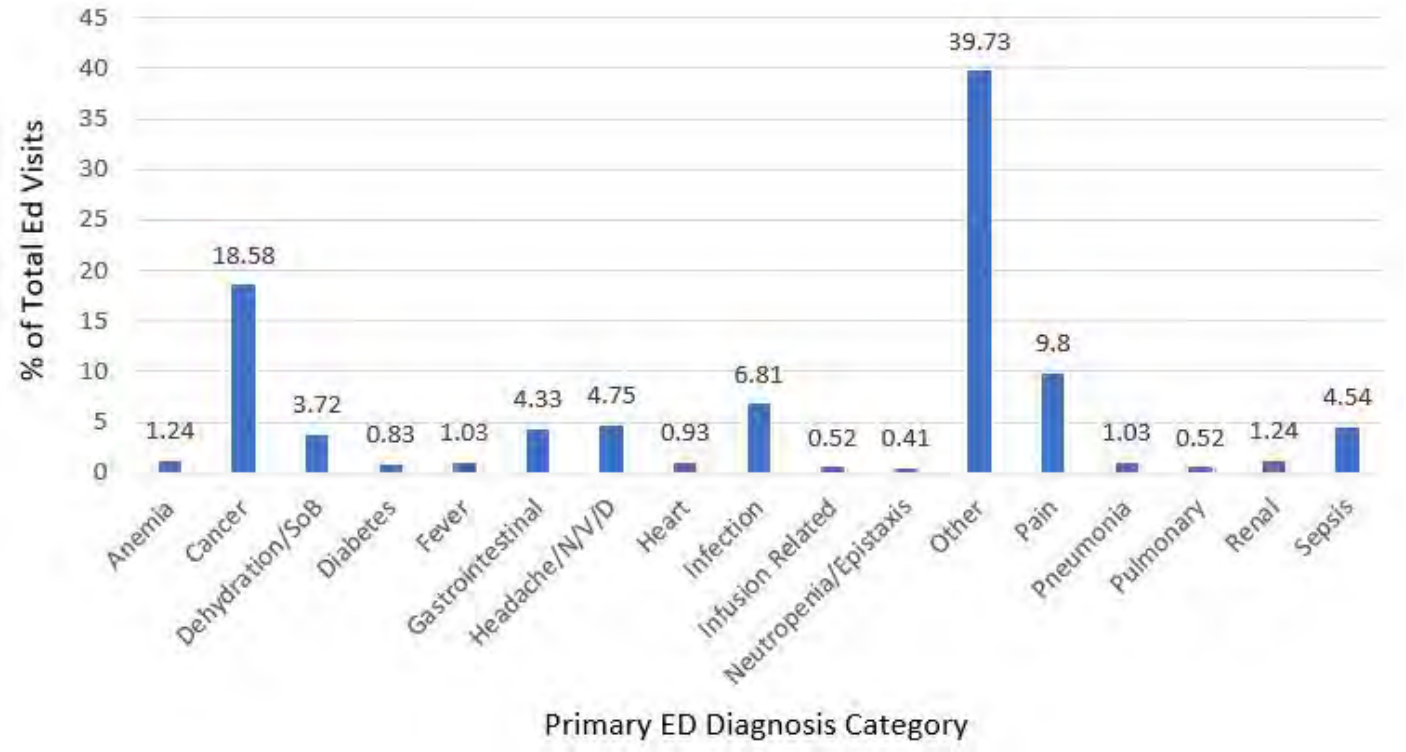

Fig. 1. Percent of total ED visits by diagnosis category.

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78 - Scientific Plenary

The impact of frailty on readmission morbidity and mortality after surgery for endometrial cancer

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Objective: Frailty is defined by vulnerability and decreased adaptive capabilities following a stressor. It has been associated with postoperative complications, nonroutine discharge, and intolerance to treatment in cancer patients. As the population of patients with endometrial cancer patient ages, the proportion of frail patients undergoing surgical therapy also increases. We sought to determine the impact of frailty on short-term readmissions and mortality in patients undergoing surgery for endometrial cancer.

Method: Patients with endometrial cancer who underwent surgery between 2010 and 2014 were identified using the Nationwide Readmissions Database. Frailty was identified using the Johns Hopkins Adjusted Clinical Groups Frailty Diagnoses Indicators, which has been validated for frailty outcomes using administrative data. In this index, frailty is defined as the occurrence of 1 of 10 frailty defining diagnoses. Univariate and multivariate log linear regression analyses were conducted to analyze the association between frailty and 30- and 90-day all cause readmission and mortality during those readmissions. Models were adjusted by patient, hospital, and clinical factors. Sensitivity analyses excluding readmissions for chemotherapy were also performed.

Results: We identified 148,154 patients. Frailty was documented in 2,698 (1.8%) patients. Frailty was associated with an increased risk of 30-day readmission (adjusted recurrence rate [aRR] = 1.28, 95% CI 1.17–1.40), 90-day readmission (aRR = 1.21, 95% CI 1.12–1.30), and mortality among women admitted at 30 days (aRR = 1.61, 95% CI 1.19–2.18). Both 30- and 90-day readmission and mortality rates were increased by discharge to skilled nursing facility or intermediate care facility, postoperative blood transfusion, and development of a medical or surgical complication. Minimally invasive surgical techniques decreased the risk of short-term readmission and mortality. Medicaid insurance coverage increased readmission rates but had no significant effect on mortality. Excluding patients who underwent readmissions for chemotherapy did not have an impact on frailty outcomes.

Conclusion: Frailty affects postoperative outcomes in endometrial cancer patients and is associated with an increased rate of readmission and mortality among those who are readmitted. Gynecologic cancer providers should screen for frailty and consider outcomes in frail patients when counseling them for surgery.

79 - Scientific Plenary

Prehabilitation is a cost-saving method with improved outcomes for medically frail patients undergoing surgery for epithelial ovarian cancer: A cost-effectiveness analysis

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Objective: To assess the potential cost-effectiveness of pre-habilitation —pre-operative interventions to improve peri-operative outcomes – in medically frail patients undergoing surgery for epithelial ovarian cancer.

Method: We created a cost-effectiveness model evaluating the impact of pre-habilitation on a cohort of medically frail women undergoing primary surgical intervention for epithelial ovarian cancer annually. Cost was assessed from the healthcare system perspective via 2 significant peri-operative costs: (1) inpatient charges derived from 2018-2019 institutional DRG data for surgeries with and without major complications; (2) nursing facility costs from published market surveys. Major complication and non-home discharge rates were estimated from the literature. Based on published pilot studies, pre-habilitation was determined to decrease these rates. Incremental cost-effectiveness ratio (ICER) for cost per life year saved was calculated using a willingness-to-pay threshold of $100,000/life year. Modeling was performed with TreeAge software.

Results: In a cohort of 4415 women, pre-habilitation would cost $371.1 Million (M) versus $404.9 M for usual care, a cost saving of $33.8 M/year. Per patient, the cost of care with pre-habilitation was $84,053; usual care was $91,713. When analyzed for cost-effectiveness, usual care was dominated by pre-habilitation, indicating both decreased cost and increased effectiveness of pre-habilitation. Sensitivity analysis showed cost-effectiveness of pre-habilitation compared to usual care up to a cost of $9,418/patient.

Conclusion: Pre-habilitation appears to be a cost-saving method to decrease healthcare system costs via improved patient outcomes. This may represent a novel way to optimize healthcare efficiency. Prospective studies should be performed to better characterize these interventions on medically frail patients with epithelial ovarian cancer.

Scientific Plenary VIII: Maintenance Therapy and Patient-reported outcomes (PRO)

80 - Scientific Plenary

Postprogression outcomes in patients with ovarian carcinoma associated with a mutation in a non-*BRCA* homologous recombination repair gene receiving rucaparib maintenance treatment: Results from the phase III study ARIEL3

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Objective: In the ARIEL3 study (NCT01968213), rucaparib maintenance treatment significantly improved progression-free survival (PFS) versus placebo in all predefined, nested cohorts (*BRCA* mutant; *BRCA* mutant + wildtype *BRCA*/high loss of heterozygosity; and intent-to-treat population). Here we analyzed postprogression outcomes to evaluate the durability of the clinical benefit of rucaparib maintenance treatment following disease progression in the subgroup of patients with tumors associated with a mutation in a prespecified, non-*BRCA*, homologous recombination repair (HRR) gene.

Method: Archival specimens from all patients in ARIEL3 (n = 564) were sequenced to identify deleterious mutations in a prespecified list of 30 HRR genes. Patients were randomized 2:1 to receive oral rucaparib 600 mg BID or placebo. Exploratory

postprogression endpoints of chemotherapy-free interval (CFI), time to first subsequent therapy (TFST), time to disease progression on subsequent line of therapy or death (PFS2), and time to second subsequent therapy (TSST) were assessed in patients with a non-*BRCA* HRR gene mutation.

Results: In the rucaparib group, 28 patients (7.5%) had a mutation in a non-*BRCA* HRR gene, most commonly in *RAD51C* or *RAD51D* (*RAD51C/D, n* = 10). In the placebo group, 15 patients (7.9%) had a non-*BRCA* HRR gene mutation, most commonly in *BRIP1* (*n* = 5) and *RAD51C/D* (*n* = 3). Among patients with a tumor associated with a *RAD51C/D* mutation, there was significantly longer PFS in those receiving rucaparib than in those receiving placebo (log rank *P* value, 0.0184); 9/10 rucaparib versus 0/3 placebo patients were progression-free at 12 months. Treatment with rucaparib versus placebo was associated with improvements in all the postprogression efficacy endpoints examined in patients with tumors associated with a non-*BRCA* HRR gene mutation (**Table 1**). Safety in this subgroup was consistent with that in the overall ARIEL3 safety population.

Conclusion: Although the number of patients in this subgroup was small, rucaparib improved the clinically meaningful endpoints CFI, TFST, PFS2, and TSST versus placebo in patients with platinum-sensitive, recurrent ovarian cancer harboring a non-*BRCA* HRR gene mutation. Mutations in a subset of HRR genes, such as *RAD51C/D*, may confer greater sensitivity to PARP inhibitor treatment.

Table 1. Postprogression outcomes for paitents with a Non-*BRCA* HRR mutation.

	Median, mo		
	Rucaparib (n=28)	**Placebo (n=15)**	**HR (95% CI)**
PFS[a]	11.1	5.5	0.21 (0.09-0.50)
CFI	18.2	7.7	0.21 (0.09-0.52)
TFST	16.9	6.3	0.16 (0.06-0.40)
PFS2	21.1	17.3	0.30 (0.12-0.72)
TSST	24.2	17.9	0.43 (0.18-1.04)

Visit cutoff December 31, 2017, unless otherwise noted.
HRs estimated with a Cox proportional hazards model.
[a]Visit cutoff April 15, 2017 (date of unblinding for primary efficacy analysis). Previously reported in O'Malley et al. *Mol Cancer Ther*. 2018;17(suppl 1):abst LB-A12.
CI, confidence interval; HR, hazard ratio

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81 - Scientific Plenary
Patient preferences for side effects and decision-making factors associated with maintenance therapy for ovarian cancer
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Objective: Women with ovarian cancer now have different options for maintenance therapy. Given the extended time over which maintenance therapy is given, we assessed patient preferences for potential side effects and decision-making factors.

Method: As part of a larger study of shared decision making for maintenance therapy, we assessed preferences of patients with advanced-stage ovarian cancer using the visual analog scale (VAS) during in-person, structured interviews. Patients were asked to rate descriptions of side effects associated with chemotherapy and maintenance therapy (0 = most bothersome, 100 = least bothersome). Patients were also asked to evaluate decision-making factors associated with consideration of maintenance therapy (0 = least important, 100 = most important). Differences in VAS scores were assessed based on clinical and demographic factors.

Results: A total of 34 patients with a median age of 64 years (range 37–76 years) completed interviews; 53% had recurrent ovarian cancer; 71% had a college degree; 62% had maintenance therapy; and 77% were married/partnered. **Table 1** lists median overall VAS scores. Patients with prior bevacizumab (BEV) treatment were less bothered by hypertension and anemia than patients without prior BEV (VAS = 65 vs 30, *P* = 0.03; 52 vs 14, *P* = 0.001, respectively). Patients with prior PARPi treatment were less bothered by pneumonitis than patients without prior PARPi (70 vs 36, *P* = 0.03, respectively). Patients with a college education or more were less bothered by all side effects than patients with lower educational levels, notably for fatigue (32 vs 6, *P* = 0.002), skin rash (70 vs 18, *P* = 0.02), and changes in taste (70 vs 30, *P* = 0.02). For decision-making factors, there were no differences based on prior BEV or PARPi; however, patients with prior exposure to maintenance

therapy viewed the need for additional medications as more important than patients who had never received maintenance therapy (82 vs 50, *P* = 0.03). Patients with lower education levels viewed all decision-making factors as more important than patients with a college education or more, specifically the need for additional medication (88 vs 60, *P* = 0.009), out-of-pocket costs (92 vs 59, *P* = 0.03), other costs (83 vs 47, *P* = 0.001), and treatment modality (85 vs 58, *P* = 0.02). Unmarried/nonpartnered patients viewed the treatment schedule as more important than patients who were married/partnered (97 vs 71, *P* = 0.009). This was also observed for patients with household incomes of <$75,000 compared to patients with household incomes of ≥$75,000 (99 vs 62, *P* = 0.001).

Conclusion: Prior treatment appears to influence preferences for different side effects. Demographic factors, particularly education level, are just as influential in the way patients perceive side effects and decision-making factors.

Table 1. Median overall VAS scores (N = 34 pts).

Side effects (0=least bothersome, 0=most bothersome	**VAS score**
Thyroid problems	67.5
Skin rash	61.0
Peripheral neuropathy	56.5
Concentration	50.0
Changes in how food tastes	50.0
Alopecia	47.0
Leg cramps	45.0
Hypertension	41.5
Nausea	41.0
Pneumonitis	40.0
Diarrhea	31.0
Thrombocytopenia	30.0
Anemia	27.5
Fatigue	27.0
Stomatitis	25.0
Chronic wound	24.5
Vomiting	21.0
Severe nausea/vomiting	1.5
Bowel perforation	0.5

Decision Factors (100=most important, 0=least important)	**VAS Score**
Physician's recommendation	100.0
Treatment efficacy	100.0
Potential side effects	88.5
Need for routine monitoring	84.0
Treatment modality	78.5
Length of treatment visits	75.0
Other issues [1]	75.0
Treatment schedule	75.0
Need to additional medications [2]	74.0
Out of pocket costs	70.0
Indirect costs [3]	61.5

[1] Time away from work or regular household activities due to treatment

[2] Medications needed to manage side effects associated with treatment

[3] Costs associated with receiving treatment such as parking fees, meals at clinic or hospital, gasoline/transportation costs

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82 - Scientific Plenary

Patient preferences for maintenance therapy versus routine surveillance: Gain in progression-free survival and risks of adverse effects

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Objective: Maintenance therapy offers improved progression-free survival (PFS) for women with ovarian cancer. Patients face a tradeoff between potential gain in PFS and the risk of experiencing adverse effects. We assessed patient preferences for maintenance therapy using direct elicitation methods.

Method: As part of a larger study of shared decision making for maintenance therapy, we conducted in-person structured interviews with ovarian cancer patients using modified time tradeoff (TTO) and standard gamble (SG) instruments. The TTO instrument asked patients to choose between maintenance therapy and routine surveillance in 4 separate hypothetical scenarios. The scenarios included the main maintenance therapy agent and progression-free survival (PFS) outcomes adapted from SOLO1, SOLO2, GOG 213, and GOG 218. PFS outcomes for routine surveillance were taken from the control arms of each trial. The PFS for maintenance therapy was varied until patients considered maintenance therapy equivalent to routine surveillance. In the SG instrument, patients evaluated 3 separate hypothetical scenarios of maintenance therapy versus routine surveillance. Each scenario described a maintenance therapy agent with a chance of developing routine surveillance adverse effects: (1) secondary leukemia, (2) ruptured bowel, or (3) adrenal insufficiency. The risk of developing each adverse effect was varied until patients were indifferent between maintenance therapy and routine surveillance. All patients completed the EQ-5D-5L health-related quality-of-life instrument.

Results: A total of 34 patients with a median age of 64 years (range 37–76 years) participated. Of these, 53% had recurrent disease. The median EQ-5D-5L VAS health status was 0.80; the median health utility index was 0.86. In the 3 SG scenarios, patients opted for routine surveillance if the median risks of developing secondary leukemia, ruptured bowel, or adrenal insufficiency exceeded 30%, 20%, or 40%, respectively. **Table 1** shows the TTO results. In the SOLO1 and SOLO2 scenarios more patients were willing to choose maintenance therapy over routine surveillance, citing the need to "do something for extra time" without disease. In the GOG 218 and GOG 213 scenarios, more patients opted for routine surveillance over maintenance therapy, citing insufficient gain in PFS given adverse effects and treatment modality.

Conclusion: In the SG, patients were willing to risk a 20%–40% chance of developing adverse effects before opting for routine surveillance. In the TTO, patients were more likely to select maintenance therapy in the SOLO1 and SOLO2 scenarios, while more patients would forgo maintenance therapy in the GOG 218 and GOG 213 scenarios. Patients weighed the gain in PFS against side effects and treatment modality. Future efforts should examine the role of disease setting, patients' prior experience with adverse effects, and patients' health numeracy skills in the context of medical decision making.

Table 1. TTO results.

Scenario (PFS MT vs. RS)	Disease setting	MT agent (side effects)	Always chose MT	Never chose MT	# pts who initially chose MT but switched to RS if median PFS dropped below X[1] mos
SOLO 1 (50 mos vs 14 mos)	Primary	Olaparib (fatigue, nausea, abdominal pain, low platelets, and very rare chance of 2^0 leukemia)	18	1	15 pts (24 mos)
GOG 218 (14 mos vs 10 mos)	Primary	Bevacizumab (hypertension, kidney problems, and very rare chance of bowel perforation)	12	19	3 pts (12 mos)
SOLO 2 (20 mos vs. 6 mos)	Recurrent	Olaparib (fatigue, nausea, abdominal pain, low platelets, and very rare chance of 2^0 leukemia)	17	4	13 pts (12 mos)
GOG 213 (14 mos vs. 10 mos)	Recurrent	Bevacizumab (hypertension, kidney problems, and very rare chance of bowel perforation)	13	18	3 pts (12 mos)

[1] X = threshold for median PFS of MT
MT=maintenance therapy; RS=routine surveillance

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83 - Scientific Plenary

Patient-reported outcomes (PRO) in patients receiving niraparib in the PRIMA/ENGOT-OV26/GOG-3012 trial

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Objective: Niraparib improves progression-free survival (PFS) in patients with newly diagnosed advanced ovarian cancer after responding to first-line platinum-based chemotherapy (CT). Here we report patient-reported outcomes (PROs) in patients receiving niraparib and placebo (PBO) in the PRIMA/ENGOT-OV26/GOG-3012 trial.

Method: This double-blind, PBO-controlled, phase 3 study randomized 733 patients with newly diagnosed advanced ovarian, primary peritoneal, or fallopian tube cancer with a complete or partial response (CR or PR) to first-line platinum-based CT. Patients received niraparib or PBO once daily for 36 months or until disease progression. The primary endpoint was PFS assessed by blinded independent central review. PROs, a secondary endpoint, were collected every 8 weeks for 56 weeks and then every 12 weeks thereafter while a patient was receiving treatment. Once a patient discontinued treatment, PRO evaluations were performed at the time of treatment discontinuation and then at 4, 8, 12, and 24 weeks (±1 week for each timepoint) after the end of treatment, regardless of the status of subsequent treatment. The validated PRO instruments utilized were FOSI, EQ-5D-5L, EORTC-QLQ-C30, and EORTC-QLQ-OV28.

Results: PRO analysis of the EORTC-QLQ-C30 and EORTC-QLQ-OV28 did not indicate a between-group difference in health-related quality of life scores of niraparib-treated patients versus placebo. Mean scores between niraparib and placebo arms were similar at each timepoint. Additional data for other PRO measures will be reported at the meeting.

Conclusion: PRO analysis indicated that niraparib was well tolerated by patients and was rated similarly to placebo. These data suggest that niraparib treatment has no detrimental effect on quality of life in this patient population.

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84 - Scientific Plenary

A prospective, large-scale patient-reported outcomes program in patients with gynecologic malignancy

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Objective: Collecting patient-reported outcomes (PROs) in patients with cancer is associated with improved overall survival. Despite this, routine collection of PROs is not widespread. This study describes the initial findings from a large-scale PRO program in patients with gynecologic malignancy.

Method: Our practice implemented routine, periodic collection of PROs for all medical and surgical patients with gynecologic malignancy. All patients received the European Organization for the Research and Treatment of Cancer (EORTC) QLQ-C30 and the Patient Reported Outcome Measurement Information System (PROMIS) Emotional and Instrumental Support Questionnaires. Patients also received a disease- specific patient-reported outcome measure (PROM): the EORTC Ov-28 (ovary), the EORTC-Cx 24 (cervix), the EORTC En-24 (uterus), or the FACT-V (vulva). PROMs were available online prior to appointment and on tablets in clinic. Results were immediately available to providers in the electronic health record (EHR, Epic Systems). Only the English language was supported by the EHR, so other spoken languages required an interpreter to complete. Relevant statistics were performed.

Results: A total of 1,811 patients were assigned PROMS between January 2018 and May 2019. Of these patients, 84% were white (n = 1518); 57.59% (n = 1043) had private insurance. Most patients had disease of the ovary (30.85%, n = 397), followed by uterus (24.6%, n = 316), cervix (22.7%, n = 293) and vulva (6.2%, n = 80). PROMs were completed 77% (n = 1,393) of the time. There was no difference in response rates by age or disease site or between black, white, and Asian patients. Hispanic patients were less likely (P = 0.003) to complete PROMs. Preoperative emotional/instrumental support scores did not predict postoperative complications. Patients reported no difference in the EORTC QLQ-C30 question, "Overall quality of life in the past week" between the pre- and postoperative periods.

Conclusion: Prospective collection of digital PROs can be seamless, but widespread dissemination requires clear algorithims and technology. All age groups had high response rates. Women speaking Spanish were less likely to complete PROMs, suggesting PROMs need to be administered in a patient's spoken language. Level of preoperative social infrastructure did not predict complications. Most importantly, patients with gynecologic malignancy do not report worsened quality of life after surgery.

Scientific Plenary IX: The Triple B: Bench to Bedside and Back Again

85 - Scientific Plenary

Anti-tumorigenic effect of combination treatment with ONC201 and TRAIL in endometrial cancer *in vitro* and *in vivo*

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Objective: ONC201 is a well-tolerated, orally active small molecule that demonstrated promising activity in patients with advanced endometrial cancer in a phase I clinical trial and is now being tested as a single agent in phase II trials. ONC201 activates the integrated stress response (ISR) and upregulates TRAIL and its receptor DR5. We hypothesized that ONC201 upregulation of DR5 could sensitize tumor cells to TRAIL and that the combination of ONC201 and TRAIL would lead to enhanced cell death in endometrial cancer models

Method: Five endometrial cancer cell lines, *AN3CA*, *HEC1A*, *Ishikawa*, *RL952*, and *KLE* , as well as a murine xenograft model, were treated with ONC201 alone or in combination with TRAIL. Effects on cell viability were assessed by the Cell Titer-Glo viability assay, colony formation assay, and cell cycle analysis by propidium iodide staining. QPCR and Western blot analysis

were used to evaluate mRNA and protein expression, respectively. Tumor volume and mouse weights were measured over time. Statistical analysis was performed using ANOVA, and Kaplan-Meier curves were used for survival analysis

Results: ONC201 decreased the cell viability of all 5 endometrial cancer cell lines at clinically achievable low micro-molar concentrations. ONC201 activated the ISR and induced protein expression of TRAIL and DR5 at the cell surface. Pretreatment with ONC201 sensitized endometrial cancer cell lines to TRAIL, leading to increased cell death induction compared to either agent alone. Tumor growth was reduced in vivo by the ONC201/TRAIL combination treatment in the xenograft model (P = 0.014). Mice treated with combination treatment survived significantly longer than mice from the 3 control groups (P = 0.018).

Conclusion: ONC201 decreased cell viability in endometrial cancer cells lines primarily through growth arrest, while the combination of ONC201 and TRAIL promoted cell death in vitro and in vivo. Our results suggest a novel cancer therapeutic strategy that can be exploited in the clinic.

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86 - Scientific Plenary

AVB500, a receptor tyrosine kinase AXL inhibitor, has improved therapeutic efficacy in combination with bevacizumab compared to bevacizumab alone in uterine serous cancer mouse model

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Objective: Our goal was to identify a targeted therapy to improve response to bevacizumab (BEV) using AVB500, a receptor tyrosine kinase AXL inhibitor, in a uterine serous cancer (USC) mouse model.

Method: A USC (ARK1) cell line was treated with AVB500 (Aravive Biologics, Houston, TX) in combination with BEV, which is a monoclonal antibody that blocks angiogenesis by inhibiting vascular endothelial growth factor A (VEGF-A). In vivo studies were performed using NOD-SCID mice injected with 1×10^7 ARK1 cells intraperitoneally followed by treatment q3 days for a 14-day treatment period. Treatment groups were vehicle control, AVB500 alone, BEV alone, and combination treatment (AVB500 + BEV). Differences in tumor nodules, tumor weight, and tumor volume were calculated using Graph Pad Prism.

Results: We found that the AVB500 + BEV group had a significantly fewer number of tumor nodules measuring >1 mm than the BEV only group (2.80 vs 6.60, P = 0.0039) and the AVB500 only group (2.80 vs 10.00, P < 0.0001). Similarly, the AVB500 + BEV group had significantly fewer number of tumor nodules <1 mm in comparison to the BEV only group (13 vs 53, P = 0.0003) and the vehicle control group (13 vs 40, P = 0.0019). There was a trend for lower tumor weight in the AVB500 + BEV group compared to BEV alone (0.05 g vs 0.15 g, P = 0.099). Last, the AVB500 + BEV group had less tumor volume than the BEV only group (14.8 mm^3 vs 102.60 mm^3, P = 0.013).

Conclusion: AVB500 in combination with BEV demonstrates an improved response over BEV alone in number of large (>1 mm) and small (< 1mm) tumor nodules, tumor weight, and tumor volume in vivo for a USC cancer cell line. Additional experiments with primary USC cancer cells extracted from metastatic USC patients and mechanistic angiogenesis assays are ongoing.

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87 - Scientific Plenary

A high-depth multi-omics analysis of clinically defined subsets of high-grade serous ovarian cancer

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Objective: To identify biological differences between clinically defined high-grade serous ovarian cancer (HGSOC) groups, we obtained pretreatment samples via a laparoscopic triage algorithm.

Method: Samples (primary and 2-3 metastatic sites) were obtained pretreatment based on a laparoscopic triage algorithm from patients who underwent R0 tumor debulking surgery (R0, n = 10) or received neoadjuvant chemotherapy (NACT) with excellent (NACT-ER, n = 10) or poor response (NACT-PR, n = 10). These samples were subjected to high-pass whole-genome and targeted deep DNA sequencing, RNA sequencing, reverse-phase protein arrays, LC-MS proteomics, and immune profiling.

Results: A total of 90 samples were analyzed. We identified significant genomic, transcriptomic, proteomic, phosphoproteomic, and immune cell repertoire variations between the groups. Importantly, we found a higher loss of *NF1*

copy number, and NF1 RNA and NF1 protein product copies, reduced chromothripsis-like patterns (CTLPs), significantly higher levels of strong-binding neoantigens in the R0 compared to the NACT groups. Interestingly, nonsense mutations in *TP53* were exclusively identified in the NACT groups, while most *TP53* mutations were missense mutations in the R0 group. Nonsense mutations in *CSMD3* and *PIK3CA* were exclusively identified in the NACT-PR group. Next, we identified 67 curated protein-coding transcripts including *POU3F3*, *NKX6-1,* and *PROK1*, and noncoding RNA-*miR7-2* were significantly upregulated in the R0 group compared with the NACT group. In addition, we observed significantly increased T cell infiltration and decreased numbers of macrophages in the R0 group versus the NACT-ER/PR groups, and identified significant differences in transcriptomes and proteomes in this group.

Conclusions: Our findings identify distinct molecular abnormalities and cellular changes in clinically defined HGSOC subgroups, and could have prognostic and therapeutic implications.

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88 - Scientific Plenary

Gene-specific management of gynecologic cancer risk in Lynch syndrome carriers: A decision analysis

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Objective: Women with Lynch syndrome (LS) have an estimated lifetime risk of developing endometrial and ovarian cancer as high as 53% and 17%, respectively. Thus, LS carriers are recommended to undergo hysterectomy with bilateral salpingo-oophorectomy (Hyst-BSO) between ages 35 and 40 years or after childbearing. However, cancer risks vary by pathogenic mismatch repair (*MMR)* gene variant (*MLH1, MSH2, MSH6, PMS2*). We evaluated gene-specific strategies for gynecological cancer prevention in LS such as surveillance and Hyst-BSO. We explored a novel strategy of bilateral hysterectomy and salpingectomy (Hyst-BS) with delayed oophorectomy to minimize adverse effects of surgical menopause.

Method: We developed a computer-based cohort state transition (Markov) model to simulate gene-specific outcomes. We modeled current strategies including Hyst-BSO at age 35 and 40 years with or without annual surveillance beginning at age 30 and 35 years, and explored novel strategies including surveillance beginning at age 30 and 35 years without Hyst-BSO, Hyst-BS at age 40 years with delayed oophorectomy at age 50 years, and Hyst-BSO at age 50 years with or without surveillance beginning at age 30 and 35 years. Eleven total strategies were assessed for each *MMR* gene. The primary endpoint was quality-adjusted life-years (QALYs) gained from ages 25–70 years. Secondary endpoints included cancer incidence, cancer mortality, and unadjusted life-years (survival).

Results: The strategies yielding the greatest QALYs varied by *MMR* gene (**Table 1**): Hyst-BS at age 40 years with delayed oophorectomy at age 50 years was optimal for *MLH1* and *MSH6* carriers; Hyst-BSO at age 40 years was optimal for *MSH2* carriers; and Hyst-BSO at age 50 years was optimal for *PMS2* carriers.

Conclusion: Our findings support gene-specific recommendations for risk-reducing surgery for the prevention of LS-associated gynecologic cancers. Hyst-BS with delayed oophorectomy may be a viable strategy for future clinical study, particularly for *MLH1* and *MSH6* carriers. While current recommendations are supported for *MSH2* carriers, *PMS2* carriers may benefit from delayed Hyst-BSO. Our analysis finds that tailoring management by *MMR* gene variant can optimize QALYs while mitigating cancer risk and can inform decision-making that incorporates individual patient preferences.

Table 1. QALYs and secondary outcomes by selected strategies and gene. Bold indicates optimal strategy. Hyst-BS: Hysterectomy with bilateral salpingectomy; Hyst-BSO: Hysterectomy with bilateral salpingo-oophorectomy; Ooph: Oophorectomy; QALYs: Quality-adjusted life-years.

	QALYs	**Life-years**	**Ovarian cancer incidence**	**Endometrial cancer incidence**
MLH1				
Hyst-BS at age 40, Ooph. at age 50	**21.86**	**46.27**	**5%**	**3%**
Hyst-BSO at age 40	21.78	46.61	2%	3%
Hyst-BSO at age 40 with surveillance at age 35	21.71	46.65	2%	3%
MSH2				
Hyst-BSO at age 40	**21.89**	**46.88**	**2%**	**1%**
Hyst-BS at age 40, Ooph. at age 50	21.87	46.23	7%	1%

Hyst-BSO at age 40 with surveillance at age 35	21.83	46.90	2%	1%
MSH6				
Hyst-BS at age 40, Ooph. at age 50	**21.91**	**46.35**	**6%**	**0%**
Hyst-BSO at age 40	21.79	46.62	4%	0%
Hyst-BSO at age 40 with surveillance at age 35	21.72	46.64	4%	0%
PMS2				
Hyst-BSO at age 50	**22.60**	**47.37**	**0%**	**1%**
Hyst-BSO at age 40	22.13	47.39	0%	0%
Hyst-BSO at age 40 with surveillance at age 35	22.05	47.39	0%	0%