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Conference Report

The American Society of Clinical Oncology 2019 annual meeting: A review and summary of selected abstracts☆

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1. Introduction

The 2019 55th annual meeting of the American Society of Clinical Oncology (ASCO) was held in Chicago, Illinois, led by ASCO president Monica Bertagnolli, the division director of surgical oncology at the Brigham and Women's Hospital in Boston. The theme of the meeting, and the title of her Presidential Address, was "Caring for Every Patient, Learning from Every Patient." In her address, Dr. Bertagnolli explained that the theme of the meeting represents a lofty goal: "that ***every*** person with cancer will have access to high-quality care, and also will have the opportunity to participate in clinical research." In line with the meeting's theme, the main plenary session included a diversion from the usual clinical trial paradigm: Dr. Davidoff delivered an abstract about the Affordable Care Act Medicaid expansion's impact on racial disparities, specifically with respect to time to cancer treatment (**LBA1**[1]). The study found that implementation of Medicaid expansion differentially improved African American cancer patients timely receipt of treatment, thereby reducing racial disparities in access to care.

In Gynecologic Oncology, the focus continued this year on poly (ADP-ribose) polymerase inhibitors (PARPi) and immunotherapy, with multiple options and combinations, in all the gynecologic malignancies. The presentations included many therapeutic trials, with the oral gynecologic plenary led by the long-anticipated presentation of Gynecology Oncology Group/NRG Oncology Group study 261 presented by Dr. Powell (**5500**). The trial demonstrates the feasibility of completing a randomized phase 3 study in a rare tumor subtype within the cooperative group framework, and definitively confirms paclitaxel and carboplatin as the standard of care for advanced or recurrent uterine carcinosarcoma.

This year's review will condense selected gynecologic cancer studies presented at the meeting and include data in table form for phase II studies included in the meeting program. (Tables 1 and 2). We highlight below chosen presentations from the Gynecology Oral Plenary session and Poster Discussion session, as well as a few relevant abstracts from other tracks.

2. Cervical cancer

2.1. Surgery in early cervical cancer: is there still a debate?

Ever since the presentation of the Laparoscopic Approach to Cervical Cancer (LACC) trial by Dr. Ramirez at the 2018 Society of Gynecologic Oncology (SGO) meeting, the results have been discussed, debated, and challenged. This year at ASCO, Dr. Uppal presented the anticipated large retrospective dataset collected from 8 "high-volume" institutions of patients undergoing radical hysterectomy for early stage cervical cancer from 2010 to 2017 (**5504**). Of the 704 cases that met inclusion criteria, 185 (26.3%) and 519 (73.7%) underwent open and minimally invasive surgery (MIS) respectively; the majority (91%) of the MIS cases were performed robotically. On multivariate analysis, after controlling for race, comorbidities, preoperative tumor size, histology, grade and smoking status, MIS had higher odds of recurrence (OR 2.24, 95% CI 1.04–4.87, $p = 0.04$). When also including lymphovascular space invasion, receipt of adjuvant therapy and vaginal margin status in the model, undergoing MIS remained associated with higher odds of recurrence (OR 2.37, 95% CI 1.1–5.1, $p = 0.031$). There was no difference in overall survival (OS) between the 2 groups: the authors suggest this

☆ The views expressed in this manuscript are those of the author(s) and do not reflect the official policy or position of the Department of Defense or the Uniformed Services University

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[1] The bolded numbers in parentheses represent the ASCO meeting abstract number.

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Table 1
Phase II trials of novel drug and cytotoxic treatment strategies in ovarian, fallopian tube, and primary peritoneal carcinomas.

Type	Abs no.	Agents/dose	Mechanism	Type of patients	Results	HR	*P*-value	Major toxicities
Phase II single agent	5538	Oral tivozanib (1.5 mg) once daily, 3 weeks on/1 week off	Potent, selective pan-VEGFR tyrosine kinase inhibitor with a long half-life	Recurrent, platinum-resistant OC/FTC/PPC, ECOG PS 0–1, normal end organ function, measurable disease (n = 30)	Median PFS 4 months Median OS 8 months PFS >6 months 7 (23.3%) PR 4 (13.3%) SD 12 (40%) CBR 53%	–	–	Gr3–4 AEs in ≥2 pts.: HTN (26.7%), f (10%), fistula (6.7%), hyponatremia (6.7%); Gr1–2 AEs in ≥10 pts.: f (63.3%), HTN (43.3%), anorexia (40%), arthralgia (36.6%), d (36.6%), and weight loss (33.3%)
Phase II combination	3030	NUC-1031[h] + carboplatin[h]	Cytotoxic agents	Recurrent OC, exhausted all other therapy options (n = 17)	ORR 29%, PR 5 (29%) SD 11 (65%) DCR 94%	–	–	Well-tolerated, no unexpected AEs; dose-limiting f and myelosuppression
	5513	Oral adavosertib (225 mg) BID over 2.5 days weekly, weeks 1–3 + IV carboplatin (AUC5) day 1, q3 weeks[d]	Highly selective WEE1 inhibitor; cytotoxic agent	Recurrent, platinum-resistant OC (n = 94 total among four arms, n = 12 in this treatment group[d])	ORR 8 (67%) DCR 12 (100%) Median PFS 10.1 months	–	–	≥G3 ANC 9 (75%), PLTS 9 (75%), An 6 (50%)[d]
	5519	IV pembrolizumab (200 mg) day 1 + carboplatin (AUC2) days 8, 15 of 21-day cycle	Anti-PD-1 antibody; cytotoxic agent	Platinum-resistant, advanced OC/FTC/PPC with progression after systemic therapy, ECOG PS 0–1 (n = 27)	Median PFS 4.6 months PFS at 6 months 40.4% PR 3 (13%) SD 15 (65.2%) PD 5 (21.7%)	–	–	Lymphopenia (18%), An (9%); majority AEs Gr1–2 (93%), Gr4 lymphopenia (7%) and An (7%)
	5520	IV mirvetuximab soravtansine (6 mg/kg)[f] + IV bevacizumab (15 mg/kg)[f] day 1, 21-day cycle	Antibody-drug conjugate comprising a FRα-binding antibody, cleavable linker, and potent tubulin-targeting agent (maytansinoid DM4); anti-VEGF antibody	FRα-positive, platinum-resistant OC with recurrence within 6 months of last platinum therapy (n = 66)	Median PFS 7.1 months Median DOR 8.6 months ORR 27 (41%) The above values were 9.9 months, 12 months, and 56%, respectively among bevacizumab-naïve (n = 16) with 1–2 prior therapies and medium/high FRα levels Among platinum-sensitive (n = 11), platinum-resistant (n = 10), and exploratory cohorts (n = 13):	–	–	Primarily ≤Gr2 d (58%), n (50%), blurred vision (48%); serious AEs were GI-related with small intestinal obstruction in 6%
	5521	Oral olaparib (150 mg) BID + oral cediranib (20 mg) daily	PARP inhibitor; VEGFR tyrosine kinase inhibitor	High-grade serous OC, PARP inhibitor failure (n = 34)	- PFS at 16 weeks was 54.5%, 50%, and 36%, respectively - OS at 1 year was 81.8%, 64.8%, and 39.1%, respectively - gBRCAm in 9 (81.8%), 8 (80%), and 7 (53.8%), respectively - PR in 18%, 20%, and 0%, respectively SD in 18	–	–	An, HTN, d, f; <10% were Gr3 AEs
	5542	IV ofranergene obadenovec (1×10^{13} viral particles) q8 weeks + IV paclitaxel (80 mg/m^2), weekly	Immunotherapy with anti-angiogenic and vascular disrupting effects; cytotoxic agent	Recurrent, platinum-resistant OC (n = 21)	CA-125 GCIG RR 58% Median OS 16.4 months	–	–	Generally well tolerated, mild flu-like symptoms
	5567	Everolimus[h] + letrozole[h]	mTOR kinase inhibitor; aromatase inhibitor	ER+ OC (n = 10), endometrial (n = 7), or PPC (n = 2) with PD following primary and salvage ct (n = 19)	CR 0 (0%) PR 1 (5%) SD 6 (32%) Median time to progression 5 months	–	–	Most common AEs were hyperglycemia, rash, stomatitis, f, An with 7 dose-reductions and 2 discontinuations due to pneumonitis
	5576	SC DPX-Survivac[h] + intermittent, low-dose oral cyclophosphamide[h] BID with or without oral epacadostat[h]	Immunologic Survivin T-cell activator; cytotoxic agent; indoleamine 2,3-dioxygenase 1 inhibitor	Advanced, recurrent OC with metastatic disease (n = 12)	Infiltration of tumors with survivin-specific T cells correlated with the observed tumor regression Among baseline tumor <5 cm (n = 15): - CBR 100% - PR 4 (27%) with "prolonged" PFS	–	–	–
Randomized phase II	5505	Oral niraparib (300 mg) daily vs. oral niraparib (300 mg) daily + IV bevacizumab (15 mg/kg) q3 weeks; randomized 1:1	PARP inhibitor; anti-VEGF antibody	High-grade serous or endometrioid, platinum-sensitive, recurrent OC (n = 97)	Median PFS 5.5 vs 11.9 months HRs in sub-group analyses: - HRD + tumors (n = 54) - HRD- tumors (n = 43)	0.35 0.36 0.47 0.53 0.33	<0.001	Only difference in Gr3–4 AEs were rate of HTN (0 vs. 26.5%) and ANC (2.1 vs. 12.2%)

(continued on next page)

Table 1 (*continued*)

Type	Abs no.	Agents/dose	Mechanism	Type of patients	Results	HR	*P*-value	Major toxicities
					- gBRCAm (n = 34) - Non-gBRCAm (n = 63) - CFI 6–12 months (n = 38) - CFI ≥12 months (n = 59)	0.29 0.42		
	5507	Oral olaparib (300 mg) BID vs. physician's choice[a]; randomized 2:1	PARP inhibitor; various[a]	Platinum-resistant OC (n = 100)	Median PFS 2.9 vs. 3.4 months Median DOR 5.4 vs. 4.5 months ORR 12 (18%) vs. 2 (6%) DCR 24 (35.8%) vs. 14 (42%) Among olaparib monotherapy (n = 67): gBRCAm (n = 13)	–	–	≥Gr3 AEs in 60% vs. 52%
					- ORR 5 (38%) - DCR 8 (62%) - gBRCAwt (n = 54) - ORR 7 (13%) - DCR 16 (30%)			
	5508	P/C[b] day 1 q3 weeks vs. carboplatin monotherapy[b] vs. weekly carboplatin + paclitaxel[b]; randomized 1:1:1	Cytotoxic agents	Age ≥ 70 years; Geriatric Vulnerability Score ≥ 3; first-line FIGO stage III/IV EOC (n = 120)	Prematurely closed study due to significantly worse survival in ArmB Median PFS 12.5 vs. 4.8 vs. 8.3 months Median OS NR vs. 7.4 vs. 17.3 months Protocol feasibility 65 vs. 47 vs. 60% PD 3 (7.5%) vs. 12 (30%) vs. 1 (2%)	–	<0.001 0.001 0.15 0.004	Treatment discontinued due to toxicity in 20 vs 15 vs 22.5% ($p = 0.771$)
	5511	IV avelumab (10 mg/kg) q2 weeks + oral entinostat (5 mg) weekly vs. IV avelumab (10 mg/kg) q2 weeks + placebo; randomized 2:1	Human anti-PD-L1 monoclonal antibody; Class I selective HDAC inhibitor	EOC which progressed or recurred after 3–6 lines of 1st-line platinum therapy (n = 126)	Median PFS 1.64 vs. 1.51 months ORR 6 vs. 5% OS NE vs. 11.3 months Duration of therapy 4 vs. 5 months	0.90	0.31 NS NS	Gr3–4 AEs 41 vs 10%; any grade 93 vs. 78%; discontinuation due to AEs 21 vs 17.5%; Among non-placebo: f (46%), n (31%), d (26%), An (26%), chills (20%); Gr3–4 f (9%), ANC (8%)
	5512	P/C[c] before/after interval debulking surgery, 6 total cycles + oral nintedanib (200 mg) vs. placebo, days 2–21 q3 weeks cycles 1, 2, 5, 6, ≤2 year maintenance; randomized 2:1	Cytotoxic agents; VEGFR, FGFR, and PDGFR inhibitor	FIGO stage IIIC/IV, ct-naïve EOC unresectable after laparoscopic evaluation (n = 188)	Median PFS 14.4 vs. 16.8 months Median OS 37.7 vs. 44.1 Debulking surgery in 58.1 vs. 76.6% ORR to pre-surgery debulking therapy 35.1 vs. 55.9% Similar among all debulking subjects: - Complete cytoreduction rate 76% - Peri-/post-op complications 11.2%	1.50 1.54	0.02 0.053	Gr3–4 AEs 92 vs. 71%; early treatment discontinuation in 14.5 vs. 6.2%
	5514	Dose-dense early post-op intraperitoneal cisplatin (50 mg/m^2) + IV etoposide (100 mg/m^2) followed by IV P/C[e] q3 weeks, 6 cycles vs. IV P/C[e] alone; randomized 1:1	Cytotoxic agents; topoisomerase II inhibitor	FIGO stage IIIC/IV OC and optimal debulking with residual disease ≤1 cm (n = 215)	OS 67.5 vs. 46.3 months Median PFS 21.7 vs. 16.8 months TFST 25.1 vs. 18.0 months TSST 42.2 vs. 29.3 months Median follow-up (f/u) of 61.9 months - Alive at f/u 52 (49%) vs. 41 (38%) PFS/OS benefit among gBRCAwt ($n = 68$; $n = 23$ for gBRCAm)	0.70 0.64 0.62 0.66 0.46	0.047 0.003 0.002 0.019	Gr3–4 ANC (53.8 vs. 35.2%), An (23.6 vs. 5.6%), GI events (10.4 vs. 1.9%)
	5518	IV gemcitabine (1000 mg/m^2) days 1, 8, 15 of 28-day cycle + oral adavosertib (175 mg) daily, days 1, 2, 8, 9, 15, 16 vs. IV gemcitabine + placebo; randomized 2:1	Cytotoxic; highly selective WEE1 inhibitor	Recurrent, platinum-resistant/refractory high-grade serous OC (n = 99)	Median PFS 3.0 vs. 4.6 months Median OS 7.2 vs. 11.5 months PR 13 (21%) vs. 1 (3%)	0.56 0.56	0.015 0.022 0.02	≥Gr3 An (31 vs. 18%), PLTS (31 vs. 6%), ANC (62 vs 30%)
	5537	Oral ralimetinib (200 mg) BID days 1–10 of 21-day cycle + IV gemcitabine/carboplatin[g] vs. placebo + IV gemcitabine/carboplatin, 6 cycles; followed by oral ralimetinib (300 mg) BID days 1–14, q28 days; randomized 1:1	Selective small-molecule inhibitor of p38α/β MAPKs; cytotoxic agents	Recurrent, platinum-sensitive EOC/FTC/PPC after first-line treatment (n = 110)	Median PFS 10.3 vs. 7.9 months Median OS 29.2 vs. 25.1 months ORR 46.6 vs. 46.2% Normalized CA-125 at end of cycle 6 in 32.4 vs. 25.0%	0.773 0.827	0.246 0.469 0.967	≥1 Gr3–4 AEs in 95.5% vs. 92.3%; ANC (60.6 vs. 76.9%), PLTS (43.9 vs. 38.5%), decreased WBCs, (30.3 vs. 26.9%), An (22.7 vs. 25.0%), increased ALT (19.7 vs. 3.8%)

finding was due to successful salvage therapy following recurrence. For cases with preoperative tumor size ≤2 cm, there were 5/121 (4.1%) recurrences in open and 25/415 (6%) recurrences in MIS group (p = 0.34). However, the authors note than in 25% of cases, when surgeons estimated a tumor was <2 cm, the final pathology showed that the tumor was actually larger than 2 cm. Dr. Uppal ended his presentation with the observation that the total number of radical hysterectomies of any type are decreasing in the United States (US), and therefore the question of MIS versus open radical hysterectomy may not be "a fight worth fighting." During the MIS debate in the Education Session called "Gynecologic Cancers: Is it Time to Put Away the Knife?", Dr. Ramirez effectively countered most of the criticisms against the LACC trial. Dr. Boggess, an expert robotic surgeon, made the point that the lay press had over-interpreted the results of the LACC trial, specifically with respect to robotic surgery, and had effectively ended robotic surgery for early stage cervical cancer in the US prior to sufficient vetting of the data.

2.2. Chemotherapy followed by surgery in stage Ib2-IIb cervical cancer: is there a role?

Dr. Kenter presented the results of EORTC 55994, a large phase 3 study (620 patients) of neoadjuvant chemotherapy (NACT) followed by surgery compared with chemoradiation (chemoRT) for stage Ib2-IIB cervical cancer (**5503**). There was no OS difference between the two arms; however, progression free survival (PFS) was statistically superior in the chemoRT arm (57% NACT plus surgery versus 66% chemoRT, p = 0.021). There was a trend toward better survival results for NACT plus surgery for patients with stage 1b2 disease.

3. Ovarian cancer

3.1. Parp inhibitors and ovarian cancer: better option than chemotherapy?

The last few years have brought many new, noncytotoxic chemotherapy options to patients with advanced and recurrent ovarian cancer. In particular, the role of PARPi's as single agents, in combination with chemotherapy and/or other targeted agents, and as maintenance therapy has continued to evolve. At ASCO 2019 studies focused on PARPi as a non-cytotoxic chemotherapy option in patients with recurrent disease.

The results of GOG 9923, one of the largest phase I studies ever to be completed (424 patients), were discussed in the Poster Discussion Session (**5523**). In this study, the PARPi veliparib was dose-escalated along standard of care chemotherapy paclitaxel and carboplatin given with bevacizumab. Chemotherapy was given every 3 weeks, weekly, or intraperitoneal (using the regimen defined by the GOG phase I study 9921) and veliparib was given continuously or intermittently. GOG 9923 defined the dose and regimen to be used in the subsequent randomized phase 3 study GOG 3005, which has since completed accrual (results pending).

Two studies considered PARPi single agent therapy in place of chemotherapy in the recurrent setting. The CLIO trial evaluated olaparib single-agent therapy versus standard of care (SOC) chemotherapy in platinum sensitive (PSOC) and platinum-resistant ovarian cancer (PROC); the results for PROC were reported (**5507**). Eligible patients with measurable disease and ≥1 prior line of chemotherapy were randomized 2:1 to olaparib monotherapy (300 mg tablets, BID) or physician's choice chemotherapy. Cross-over was allowed, and the primary endpoint was overall disease response. 100 patients were randomized. Overall response rate (ORR) was 18% in the olaparib arm versus 6% in the chemotherapy arm (p = ns). ORR was higher for olaparib in the BRCA mutated patients (36%) compared to the BRCA wildtype (13%). The ORR for olaparib was 23% in patients with ≥4 prior lines of treatment. There was no difference between olaparib and chemotherapy for PFS or clinical benefit rate. Notably, there were 6 patients in the olaparib arm who experienced clinical benefit for longer than 1 year; only 1 of these 6 had a germline BRCA mutation (gBRCAm). The CLIO study demonstrated a response rate in heavily pretreated patients with PROC without a gBRCAm.

Dr. Penson and his colleagues reported the results of SOLO3, a randomized phase 2 trial of olaparib versus non-platinum chemotherapy in gBRCAm patients with PSOC (**5506**). As in the CLIO study, patients were randomized 2:1 to olaparib tablets 300 mg BID or non-platinum chemotherapy treatment of physician's choice. 266 patients were randomized and 223 were eligible for the ORR endpoint. ORR was 72% for olaparib versus 51% for chemotherapy (OR 2.53, 95% CI 1.40–4.58; p = 0.002). HR for PFS by blinded independent central review was 0.62 (95% CI 0.43–0.91; p = 0.013; median 13.4 vs 9.2 months [olaparib vs chemotherapy]) and by investigator assessment was 0.49 (95% CI 0.35–0.70; p < 0.001; median 13.2 vs 8.5 months, respectively). During the plenary session, the study design was criticized for not allowing platinum as the comparator arm.

Finally, NSGO-AVANOVA2/ENGOT-OV24 was a randomized phase 2 study of niraparib and bevacizumab versus niraparib alone as treatment of recurrent PSOC (**5505**). Women with measurable/evaluable, high-grade serous or endometrioid recurrent PSOC were randomized 1:1 to niraparib 300 mg QD or the combination of niraparib 300 mg QD and bevacizumab 15 mg/kg IV every 3 weeks until disease progression. The primary endpoint was PFS. Stratification was according to homologous recombination-deficiency (HRD) status (MyChoice HRD) and chemotherapy-free-interval (CFI) (6–12 months (mo) vs. >12 mo). First-line maintenance bevacizumab was permitted. Compared to niraparib alone, the chemotherapy-free regimen of niraparib and

Notes to Table 1

KEY: AEs = adverse events; An = anemia; ANC = absolute neutrophil count/neutropenia; CBR = clinical benefit rate; CFI = chemotherapy-free interval; CR = complete response; ct = chemotherapy/chemotherapeutic; d = diarrhea; DCR = disease control rate; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; EOC = epithelial ovarian carcinoma; ER+ = estrogen receptor positive; f = fatigue; FIGO = International Federation of Gynecology and Obstetrics; FRα = folate receptor alpha; FTC = fallopian tube carcinoma; (g) BRCA(m/wt) = (germline) BRCA (mutation/wild-type); GCIG = Gynecological Cancer Intergroup; HRD = homologous recombination deficiency; HTN = hypertension; n = nausea; NR (or NE) = not reached/reported/evaluable; NS = not significant; OC = ovarian cancer; ORR = overall response rate; OS = overall survival; PD = progressive disease/disease progression; PFS = progression-free survival; PLTS = platelets/thrombocytopenia; PPC = primary peritoneal carcinoma; PR = partial response; PS = performance status; qd/bid = once/twice per day; q*n* days = every *n* days; q*n* weeks = every *n* weeks; RR = response rate; SC = subcutaneous; SD = stable disease; TFST = time to first subsequent therapy (or death); TSST = time to second subsequent therapy (or death).

[a] Physician's choice/standard of care chemotherapy = IV pegylated liposomal doxorubicin (40 mg/m^2) q4 weeks; IV topotecan (1.25 mg/m^2) days 1–5 q3 weeks; IV paclitaxel (80 mg/m^2) days 1, 8,15 q3 weeks; IV gemcitabine (1000 mg/m^2) day 1, 8, 15 q4 weeks.

[b] P/C = IV paclitaxel (175 mg/m^2) + carboplatin (AUC5–6) day 1 q3 weeks; carboplatin monotherapy = IV carboplatin (AUC5–6) day 1, q3 weeks; weekly carboplatin + paclitaxel = IV carboplatin (AUC2) + IV paclitaxel (60 mg/m^2) days 1, 8, 15 q4 weeks.

[c] P/C = IV carboplatin (AUC 5 mg/mL/min) + IV paclitaxel (175 mg/m^2), 3–4 cycles before interval debulking surgery followed by 2 to 3 more cycles for total of 6 cycles.

[d] Four-arm study of oral adavosertib (either 175 or 225 mg) + various chemotherapies (carboplatin, gemcitabine, weekly paclitaxel, or pegylated liposomal doxorubicin) in 3- or 4-week cycles. Given adavosertib (225 mg) BID over 2.5 days weekly, weeks 1–3 + IV carboplatin (AUC5) day 1, q3 weeks showed greatest benefit, this data alone was chosen to be included in the table due to space restrictions.

[e] P/C = paclitaxel (175 mg/m^2) + carboplatin (AUC5) or docetaxel (60–75 mg/m^2) + carboplatin (AUC5).

[f] Using adjusted ideal body weight.

[g] IV gemcitabine (1000 mg/m^2) days 3, 10 + carboplatin (AUC4) day 3, 6 cycles.

[h] Dose not specified.

Table 2
Phase II trials of novel agents and treatment strategies in endometrial, uterine, and cervical carcinomas.

Type	Abs no.	Agents/dose	Mechanism	Type of patients	Results	HR	*P*-value	Major toxicities
Phase II single agent	5501	IV durvalumab (1500 mg), q4 weeks	Anti-PD-L1 antibody	Advanced EC (n = 71)	Deficient MMR (n = 35) vs. proficient MMR status (n = 36): - CR 4 (11%) vs. 0 (0%) - PR 10 (29%) vs. 1 (3%) - SD 7 (20%) vs. 6 (17%) - 16-week DCR 60% vs. 19% - - Objective tumor response 14 (40%) vs. 1 (3%) Deficient MMR and/or mutation in exonuclease POLE domain (n = 15) vs. normal MMR (n = 16):	–	–	14 (20%) immune-related AEs: 6 (8%) hyperthyroidism, 6 (8%) hypothyroidism, 1 (1%) pneumonitis, 1 (1%) hepatitis
	5502	IV avelumab (10 mg/kg), q2 weeks	Anti-PD-L1 antibody	EC (n = 33)	- ORR 26.7% vs. 6.25% - 6-month PFS 6 (40%) vs. 1 (6.25%) 6-month PFS in pts with ≥3 lines of prior therapy with PD-L1 negative tumors by IHC 5/6 (83%)	– 0.011		AEs in 22 (71%); G3 AEs in 6 (19%)
Phase II combination	5510	Oral ribociclib (400 mg) daily + oral letrozole (2.5 mg) daily	Cyclin kinase inhibitor; aromatase inhibitor	ER+ OC or EC with measurable disease and not previously treated with ribociclib or aromatase inhibitor (n = 40)	ER+ OC (n = 20) vs. EC (n = 20): 12-week PFS 10 (50%) vs. 11 (55%)	–	–	Leukopenia (18%), lymphopenia (18%), ANC (13%), f (13%)
	5532	Radiotherapy (50.4 Gy/28 F on pelvic field ± extended-field radiation + additional 30–36 Gy) + IV cisplatin (40 mg/m^2) weekly + IV nimotuzumab (200 mg) weekly	Radiation therapy; cytotoxic agent; humanized monoclonal anti-EGFR antibody	Locally advanced, FIGO Stage IB2-IVA cervical SCC (n = 31)	CR 30 (96.8%) 1-year DFS 27 (87.1%) 1-year local PFS 28 (90.3%) 1-year OS 31 (100%) 3-year DFS (74.8%) 3-year local PFS (90.3%) 3-year OS (86.7%)	–	–	No life-threatening AEs; Gr3 bone-marrow toxicity 51.6%, Gr3 GI reactions 9.7%; late AEs in 22.6% (vaginal-rectal fistula, intestinal obstruction, vaginal stenosis, hematuria, rectal hemorrhage)
	5584	IV paclitaxel (80 mg/m^2) days 1, 8, 15 + IV carboplatin (AUC5) day 1, q3 weeks	Cytotoxic agents	Histologically-confirmed uterine corpus FIGO stage III with residual tumors, FIGO stage IV, recurrence after first-line radical treatment or second-line ct or radiotherapy, age 20–75 years (n = 45)	ORR 33 (73.3%) CR 13 (28.9%) PR 20 (44.4%)	–	–	AEs not reported
	11,051	Oral temozoromide (80 mg) daily + IV bevacizumab (2 mg/kg) days 1, 8, 15, q4 weeks with oral cabozantinib (140 mg/kg) weekly added in 14 of 29 patients	Cytotoxic; anti-VEGF antibody; multi-kinase inhibitor of MET, AXL, RET, and VEGFR2	Heavily pretreated uterine sarcomas (n = 29, 23 patients evaluable)	Median PFS 6.5 months RR 8 (35%) CR 5 (22%), PR 3 (13%) SD 6 (26%) DCR 70% (in cabozantinib group, DCR improved from 64% to 75%) Immunotherapy increased:	–	–	AEs mostly mild and manageable; 2 died from perforation
	e17005	Standard ct + radiotherapy with dendritic cell vaccination[a] vs. standard ct + radiation therapy[a] alone	Immunotherapy; cytotoxic agents; radiation therapy	T2b-4a/N0-1/M0-1 CC (n = 17) vs. locally advanced CC (n = 19)	- CD3+/CD8+ cells from 19.0 ± 2.0 to 28.8 ± 1.5% - NK cells from 12.0 ± 2.0 to 21.2 ± 1.9% - Tm 51.7 ± 6.3 to 69.7 ± 4.3% - While in remission, CD8+ Tm rose from 28.5 ± 2.1 to 40.4 ± 5.3%	–	<0.05 for all	No serious AEs
Randomized phase II	5503	Neoadjuvant cisplatin therapy (minimum dose of 225 mg/m^2, cumulative) followed by surgery vs. radiation (45–50 Gy + boost) + IV cisplatin (40 mg/m^2), weekly;	Cytotoxic agent; surgery; radiation therapy	FIGO stage Ib2-IIB CC (n = 620)	Neoadjuvant ct + surgery (n = 311) vs. ct + radiation (309): - 5-year OS 72% vs. 76% 191 deaths (31%)	0.87	0.332	Short-term severe ≥G3 AEs more frequent in surgery arm (35% vs 21%, $p < 0.001$)

randomized 1:1						
	IV durvalumab (1500 mg) q4 weeks vs. IV durvalumab (1500 mg) + IV tremelimumab (75 mg) q4 weeks, 4 cycles, followed by IV durvalumab (1500 mg) q4 weeks; randomized 1:1	Anti-PD-L1 antibody; anti-CTLA4 antibody	Persistent or recurrent EC or endometrial carcinosarcoma (n = 54)	Among single vs. combination treatment groups (n = 27 each): - Median PFS 7.6 vs. 8.1 weeks - 24-week PFS 13.3% vs. 18.5% - Median DOR 16 vs. 8 weeks - ORR 14.8% vs. 11.1% - CR 1 (4%) vs. 2 (7%) - PR 3 (11%) vs. 1 (4%)	– –	Gr3 AEs in 2 (7%) vs. 9 (32%), Gr4 in 1 (4%) vs. 3 (11%); 2 patients excluded due to early death; f (23%), d (20%), nausea (14%), v (13%), pruritis (11%)
	5582					

KEY: AEs = adverse events; ANC = absolute neutrophil count/neutropenia; CC = cervical cancer; CR = complete response; ct = chemotherapy/chemotherapeutic; d = diarrhea; DCR = disease control rate; DFS = disease-free survival; ER+ = estrogen-receptor positive; MMR = DNA mismatch repair; DOR = duration of response; EC = endometrial cancer; f = fatigue; FIGO = International Federation of Gynecology and Obstetrics; OC = ovarian cancer; ORR = overall response rate; OS = overall survival; PFS = progression-free survival; PR = partial response; *qn* days = every *n* days; *qn* weeks = every *n* weeks; SCC = squamous cell carcinoma; SD = stable disease; v = vomiting.

[a] Standard chemotherapy, radiation, and vaccine doses were not reported.

bevacizumab significantly improved PFS in women with PSROC, regardless of HRD status and duration of CFI (median PFS 11.9 vs. 5.5 mo; hazard ratio (HR) adjusted for stratification factors 0.35; 95% confidence interval (CI),[0.21 to 0.57]; $p < 0.001$).

Taken together, these studies suggest that PARPi may be substituted for chemotherapy in patients with recurrent ovarian cancer, regardless of platinum sensitivity or gBRCAm status, without increased toxicity.

Multiple other PARPi studies were presented in the poster session. We continue to learn from the extensive SOLO1 data as investigators perform subset analyses of the data to ask specific questions. Examples: the adverse events seen with olaparib in SOLO1 were detailed in abstract **5539**; the treatment effect of olaparib in Chinese women in SOLO1 was discussed in abstract **5554**; olaparib efficacy was evaluated by timing of surgery, presence of residual tumor following surgery, and response status after completion of chemotherapy in SOLO1 in abstract **5541**; and PFS by mutation (BRCA1 versus BRCA2) was analyzed in abstract **5551**.

The issue of PARPi treatment after PARPi failure remains unresolved. Dr. Lherueux and colleagues theorized that PARPi resistance could be overcome by adding an anti-angiogenic. They reported the results of the phase 2 study of cediranib and olaparib after PARPi failure in high grade serous ovarian cancer (**5521**). Treatment with the combination was feasible and efficacious in all three cohorts studied: PSOC after PARPi, PROC after PARPi, and an exploratory cohort of patients re-challenged with chemotherapy after PARPi progression. Matched pre- and post-PARPi progression biopsies were obtained and analyzed; it is notable that archived tumor tissue and baseline study biopsies post PARPi often did not match with respect to relevant biomarkers.

3.2. Wee-1 inhibitor adavosertib with chemotherapy in ovarian cancer

Two clinical trials utilizing the wee-1 inhibitor adavosertib in combination with chemotherapy were discussed. Dr. Moore presented the results of an open label 4 arm phase 2 study of adavosertib with chemotherapy in patients with PROC (**5513**). Patients received adavosertib in combination with carboplatin, gemcitabine, weekly paclitaxel, or pegylated doxorubicin. Patients in the carboplatin arm showed the greatest benefit, with ORR of 67% and median PFS 10.1 months. Dr. Lleureux and colleagues presented a randomized phase 2 study of adavosertib plus gemcitabine versus gemcitabine alone in the same patient population, demonstrating an improved response rate, PFS and OS with manageable toxicity (**5518**). Given these results, this wee-1 inhibitor in combination with chemotherapy deserves future study and we will likely see more exciting results in the future, including predictive biomarker results.

4. New options in endometrial cancer: a focus on targeted therapy, obesity, and rare tumors

As noted above, Dr. Powell's presentation of GOG 261 study was much anticipated and validates the change in standard of care that many practitioners have already made in the treatment of endometrial and ovarian carcinosarcomas. Two studies of immunotherapy (avelumab (**5502**) and durvalumab (**5501**)) were also presented in the oral plenary session. Both demonstrated the futility of a PDL1 inhibitor in microsatellite stable (MSS) disease, as well as durable responses in those patients with MSI disease.

Other studies in endometrial (and ovarian) cancer suggest biomarkers for future studies. Using samples from GOG 210, Dr. Huang and colleagues found that circulating insulin and estradiol, and tissue phosphorylated (activated) IGR1R/IR were independently associated with recurrence, suggesting their clinical utility as prognostic biomarkers (**5509**). Dr. Colon-Otero and colleagues presented results of a phase 2 clinical trial of the combination of ribociclib and letrozole in patients with relapsed ER positive OC or EC (**5510**). The combination was

associated with a promising 50% and 55% PFS12 in patients with ER positive relapsed OC or EC respectively.

5. Other notable abstracts

There were several other notable abstracts deserving of mention; we will discuss 4 of them briefly here. First, Dr. Falandry and colleagues presented EWOC-1, a randomized trial in elderly women with ovarian cancer (**5508**). The validated Geriatric Vulnerability Score (GVS) was used to identify eligible patients age ≥70 with newly diagnosed ovarian cancer, who were then randomized to receive carboplatin and paclitaxel every 3 weeks (standard arm), weekly carboplatin and paclitaxel, or carboplatin alone as adjuvant therapy. The study was stopped early by the data safety monitoring board due to significantly worse survival in the single agent carboplatin arm, thus establishing Q3 week carboplatin and paclitaxel as the standard of care even in this most vulnerable group of patients.

Abstract **11051**, presented in the sarcoma track, was a prospective phase 2 study of temozoromide and bevacizumab with or without cabozatinib in patients with heavily pretreated uterine sarcomas. 23 of 29 patients were evaluable. There were 5 (22%) CRs, 3 (13%) PRs and 6 (26%) stable disease for a disease control rate of 70%. Based on these remarkable results, this combination is worthy of further study.

Dr. Jazaeri and colleagues presented study C-145-04, an ongoing open-label multicenter phase 2 clinical trial evaluating the safety and efficacy of LN-145 TIL therapy in patients with advanced cervical cancer (**2538**). At the time of reporting, 27 patients had been treated, with an ORR of 44% (1 CR, 9 PR, 2 uPR). DCR was 89% at 3.5 month median study follow-up with 11/12 patients maintaining response. The results of this study led to breakthrough FDA approval.

Finally, abstract **LBA10502** highlighted sexual harassment in the workplace determined by a survey of Society of Gynecologic Oncology physician members. Over 70% of female and 50% of male responders reported they had experienced sexual harassment in training or practice, yet only 15% of these were reported. Despite data presented by the study authors supporting a significant gender pay gap in Gyn-Onc (>$100 K), 91% of male responders did not feel there was a gender pay gap.

6. Conclusion

This year's ASCO meeting continued the theme of defining the role of PARPi in ovarian cancer. There were also promising early studies of new targeted therapies and combinations for ovarian cancer, immunotherapy in endometrial cancer, and a new standard of care for gynecologic carcinosarcoma, among others. As we continue to develop promising new targeted therapies and define the role of treatment, including surgery, for gynecologic cancer, we also embrace the theme of the meeting, as we care for and learn from every patient.