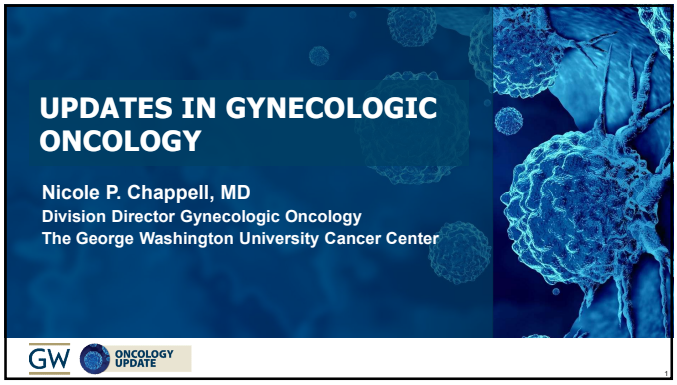


Brief Highlights of ASCO and SGO 2021

- Use of Biomarkers to improve outcomes in Ovarian Cancer
- Updates on PARP-inhibitor landscape in Ovarian Cancer
  - Large Trial Subgroup Analysis (SOLO1 and ARIEL4)
  - PARP-inhibitors and Combination Therapy
  - Evaluation of Platinum therapy after recurrence on PARP-inhibitors
- Cervical Cancer
  - Late Breaking Abstract at ASCO 2021: OUTBACK
  - State of HPV-associated cancers in the United States
- Endometrial Cancer
  - Multigene panel testing pilot study
  - Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) study

Moore, et al. *Lancet Oncol.* 2021;22(5):632-642.

GW ONCOLOGY UPDATE 2

Use of Biomarkers to Improve Outcomes in Ovarian Cancer

- An Umbrella study of biomarker-driven targeted therapy in patients with platinum-resistant recurrent ovarian cancer (PRROC) (KGOG 3045, AMBITION)
  - Background: Prognosis remains poor in this patient population, anticancer therapies based on molecular biomarkers were looked at with Olaparib, O; cediranib, C; durvalumab,D; tremelimumab, T), in arms 3, 4 and 5 (partial or complete biomarker negative subgroups, standard chemotherapy combined with targeted therapy).
  - 70 patients with PRROC with 2 or more prior lines of chemotherapy
    - In screening phase tumor samples were tested for HRD and PD-L1 status→ treatment arms were allocated according to the test results
  - First biomarker-driven umbrella study conducted in patients with platinum-resistant recurrent ovarian cancer

Lee, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 5520)

GW ONCOLOGY UPDATE 3

Use of Biomarkers to Improve Outcomes in Ovarian Cancer

Among all patients, the ORR was 35.7% (25/70, 95% CI: 24.6%-48.0%); complete response was observed in two patients.

- preliminary evidence on the clinical benefit of biomarker-driven targeted therapy.

	Drug	Biomarker	ORR, % (95% CI)	Tx Related Gr 3 /4 AEs
Arm 1 (N = 16)	O+C	HRD+	50 (24.7-75.4)	37.5%
Arm 2 (N = 14)	O+D	HRD+	35.7 (12.8-64.9)	35.7%
Arm 3 (N = 5)	D+CT	HRD- & PD-L1+	20 (0.5-71.6)	20%
Arm 4 (N = 18)	D+T75+CT	HRD- & PD-L1-	33.3 (13.3-59.0)	66.7%
Arm 5 (N = 17)	D+T300+CT	HRD- & PD-L1-	29.4 (10.3-56.0)	35.3%

Lee, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 5520)

GW ONCOLOGY UPDATE 4

Use of Biomarkers to Improve Outcomes in Ovarian Cancer

- Evaluation of a RAD51 functional assay in advanced ovarian cancer, a GINECO/GINEGEPS study.
  - Objective: Describe Homologous recombination deficiency (HRD) using this RAD51 functional assay in EOC and correlate RAD51 status to platinum response and *BRCA*mut.
  - **patients with RAD51-deficient tumors had significantly higher overall response rates to neoadjuvant platinum (68% vs 37%, p = 0.04)** longer median PFS (HR 0.50, IC95% 0.25-0.98, p = 0.02).
  - RAD51-deficient EOC have improved outcome after neoadjuvant platinum. Conversely, the RAD51 assay also identified a small subset of RAD51-high *BRCA*mut tumors with poor platinum response. **Whether this RAD51 functional assay may also predict PARP inhibitor benefit is currently being investigated.**

Blanc-Durand, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 5513).

GW ONCOLOGY UPDATE 5

Outcomes of ovarian cancer patients treated with platinum or non-platinum based chemotherapy after PARP inhibitor maintenance.

- Assessed patients for treatment time on PARP inhibitors (PFS), type of chemotherapy regimen following PARP inhibitor maintenance, and time to progression on subsequent therapy following PARP inhibitors.
- 83 ovarian cancer patients treated with PARPi identified for study, 29 documented progression:
  - 21/29 (72.4%) received subsequent Platinum based chemotherapy (PC)
    - 14/21 (66.7%) had a PFS2 of over six months
    - 5/21 (23.8%) had a PFS2 of over 12 months
  - 8/29 (27.6%) received non-platinum based chemotherapy (NPC).
    - 7/8 (87.5%) had a PFS2 of over six months
    - 2/8 (25.0%) had a PFS2 of over 12 months.

Brann, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 5563)

GW ONCOLOGY UPDATE 6

Outcomes of ovarian cancer patients treated with platinum or non-platinum based chemotherapy after PARP inhibitor maintenance.

- Women who had progression while on PARP inhibitors responded to both platinum-based chemotherapy and non-platinum-based chemotherapy
- Conclusion: **Retreatment** with **platinum-based chemotherapy** prior to switching to other types of chemotherapy following progression on PARPi maintenance should still be considered

Brann, et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5563)

GW ONCOLOGY UPDATE 7

PARP inhibitor large trial subgroup analysis

- Subgroup analysis of **rucaparib** versus chemotherapy (CT) as treatment for BRCA-mutated, advanced, relapsed ovarian carcinoma: Effect of platinum sensitivity in the randomized, phase 3 study **ARIEL4**
  - prespecified exploratory analysis to investigate effect of platinum sensitivity on the efficacy of rucaparib vs CT in **ARIEL4**
  - Pts randomized 2:1 to oral rucaparib 600 mg twice daily or CT and stratified based on progression-free interval
  - ≥1 to <6 months = platinum resistant;
  - ≥6 to <12 months = partially platinum sensitive;
  - ≥12 months = fully platinum sensitive).
  - In the CT group, patients with platinum-resistant or partially platinum-sensitive disease received weekly paclitaxel 60–80 mg/m^2; patients with fully platinum-sensitive disease received investigator's choice of platinum-based CT (single-agent carboplatin or cisplatin, or platinum doublet).

Oza, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 5517)

GW ONCOLOGY UPDATE 8

PARP inhibitor large trial subgroup analysis

- Subgroup analysis of rucaparib versus chemotherapy (CT) as treatment for BRCA-mutated, advanced, relapsed ovarian carcinoma: Effect of platinum sensitivity in the randomized, phase 3 study ARIEL4
- Conclusion: Rucaparib is a reasonable treatment option for heavily pretreated patients across all platinum sensitivity subgroups

	Platinum resistant		Partially platinum sensitive		Fully platinum sensitive	
	Rucaparib (n=110)	CT (n=51)	Rucaparib (n=62)	CT (n=28)	Rucaparib (n=48)	CT (n=26)
Median PFS, months (95% CI)	6.4 (5.5–7.4)	5.7 (3.7–7.3)	8.0 (7.0–11.0)	5.5 (2.0–5.6)	12.9 (9.2–14.8)	9.6 (7.5–15.4)
	HR 0.782 (95% CI 0.542–1.127)		HR 0.397 (95% CI 0.242–0.650)		HR 0.689 (95% CI 0.368–1.292)	
ORR, n/N (% [95% CI])	25/107 (23 [16–33])	13/48 (27 [15–42])	32/60 (53 [40–66])	5/25 (20 [7–41])	28/44 (64 [48–78])	13/23 (57 [34–77])

Oza, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 5517)

GW ONCOLOGY UPDATE 9

Ovarian Cancer PARP inhibitor 5-year follow up of SOLO-1

- Maintenance olaparib for patients with newly diagnosed, advanced ovarian cancer and a BRCA mutation: 5-year follow-up from SOLO1
  - Patients with High grade serous ovarian cancer or endometrioid ovarian cancer were randomized 2:1 to olaparib maintenance vs. placebo for two years
  - Median PFS was 56 months in the Olaparib arm, vs. 12 months in the placebo
  - Almost half of the patients treated with olaparib in the study were disease-free at 5 years, vs 20% of those treated with placebo

SGO Virtual Meeting https://ascopost.com/videos/sgo-2021-virtual-annual-meeting-on-womens-cancer/william-bradley-on-ovarian-cancer-5-year-follow-up-on-maintenance-olaparib/

Moore, et al. *Lancet Oncol.* 2021;22(5):632-642.

GW ONCOLOGY UPDATE 10

Ovarian Cancer PARP inhibitors and combination therapy

- An Open-Label Phase 2 Study of Dostarlimab (TSR-042), Bevacizumab (bev), and Niraparib Combination in Patients (pts) with Platinum-Resistant Ovarian Cancer (PROC): Cohort A of the OPAL Trial.
  - **Dostarlimab (a PD-1 inhibitor) plus niraparib (Zejula) and bevacizumab (Avastin) showcased favorable antitumor activity and tolerability in patients with platinum-resistant recurrent ovarian cancer**
  - Median patient age of 66 years (range, 37-83) with ECOG performance score was 0 (46.3%) or 1 (53.7%).
  - Eighteen (43.9%) patients had received prior bevacizumab.
  - Biomarker analysis at baseline:
    - 9.8% of patients had *BRCA*m
    - 82.9% of patients had *BRCA* wild-type disease (*BRCA*wt)
    - 7.3% had unknown *BRCA* status.
    - 68.3%) had positive PD-L1 status.
  - Objective response rate was 17.9% [90% CI, 8.7%-31.1%] with 7 partial responses and zero complete responses. **No clear response trends based on biomarkers**

Liu, et al. Society of Gynecologic Oncology 2021 Virtual Annual Meeting on Women's Cancer; March 19-25, 2021; Virtual Abstract 23

GW ONCOLOGY UPDATE 11

Ovarian Cancer PARP inhibitors and combination therapy

- Progression-free survival (PFS) and second PFS (PFS2) by disease stage in patients (pts) with homologous recombination deficiency (HRD)-positive newly diagnosed advanced ovarian cancer receiving **bevacizumab (bev) with olaparib**/placebo maintenance in the **phase III PAOLA-1/ENGOT-ov25 trial.**
- Conclusion: In the PAOLA-1 study, maintenance olaparib + bev provided a PFS and PFS2 benefit over pbo + bev in HRD+ pts, irrespective of FIGO stage and residual disease after upfront surgery

PFS and PFS2 by FIGO stage in HRD+ pts in PAOLA-1.

	Olaparib + bev	Pbo + bev	HR (95% CI)
Median PFS, mo (95% CI)			
Stage III	39.3 (36.0–NE) (n=182)	19.9 (17.7–23.4) (n=90)	0.32 (0.22–0.47)
Stage IV	25.1 (22.0–37.2) (n=73)	12.8 (10.4–15.8) (n=42)	0.32 (0.20–0.52)
Median PFS2, mo (95% CI)			**HR (95% CI)**
Stage III	NE (50.3–NE) (n=182)	43.0 (35.3–NE) (n=90)	0.57 (0.38–0.87)
Stage IV	37.8 (29.7–NE) (n=73)	25.6 (22.6–35.2) (n=42)	0.56 (0.35–0.91)

Pautier, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 5514)

GW ONCOLOGY UPDATE 12

CERVICAL CANCER: Late Breaking at ASCO 2021

- Adjuvant chemotherapy following chemoradiation as primary treatment for locally advanced cervical cancer compared to chemoradiation alone: The randomized phase III OUTBACK Trial (ANZGOG 0902, RTOG 1174, NRG 0274)
  - Standard treatment for locally advanced disease is chemoradiation. However, a significant percentage of women still relapse and die from the development of distant metastatic disease. OUTBACK was designed to determine the effects of giving adjuvant chemotherapy after chemoradiation on survival.

Mileshkin, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr LBA3).

GW ONCOLOGY UPDATE 13

OUTBACK Trial Summary

- 463 assigned Adj CT vs. 456 control
  - ACT was started in 361 (78%) women assigned to receive it
  - Median follow-up 60 months
  - OS at 5 years was similar in those assigned ACT versus control (72% vs 71%, difference <1%, P = 0.91).
- Additional Chemotherapy does not offer Survival benefit for patients with locally advanced cervical cancer
  - Serious adverse events (grade 3-5) were experienced by more patients up to 1 year after randomisation
    - 81% of patients in the adjuvant chemotherapy group versus 62% in the standard treatment
- The study confirms that chemoradiotherapy alone is currently our best possible treatment for women with locally advanced cervical cancer

Mileshkin, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr LBA3).

GW ONCOLOGY UPDATE 14

Cervical Cancer/HPV Update

- HPV-associated cancers in the United States over the last 15 years: Has screening or vaccination made any difference?
  - **Cervical cancer rates drop; other HPV-related cancers are on the rise**
    - In the population-based study, the researchers found that cervical cancer accounted for 52% of all HPV-related cancers in the United States (U.S.) from 2001 to 2017, and that the incidence of the disease has decreased annually by 1%
    - OF NOTE in 2006, the HPV vaccine was first approved for girls and young women aged 9-26 years to prevent HPV infection and the development of cervical cancer lesions.
      - 2011, recommendations for HPV vaccination were extended to boys
      - Currently it is approved for everyone from age 9-45

Liao, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 107).

GW ONCOLOGY UPDATE 15

Cervical Cancer /HPV Updates

- Overall, there was a decrease in cervical cancer incidence likely due to screening or vaccination
- **HPV-related Cancer prevalence, especially in rates of anal and rectal cancers, is expected to continue to grow and to surpass that of cervical cancer in every age group over 50 by 2025**.
- Overall **annual increase in incidence of oropharyngeal, anal, rectal, and vulvar cancers among women was 1.3% per year.**
- Over 80% of Men with HPV-related cancer had oropharyngeal cancers from 2001 to 2017 – a nearly fivefold higher incidence compared to women.
- Over the last 16 years there was an overall annual increase in HPV-related cancers in men of 2.36% per year, with the highest increase in oropharyngeal cancer.

Liao, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 107).

GW ONCOLOGY UPDATE 16

Endometrial Cancer Updates

- High prevalence of actionable germline variants in unselected endometrial cancer (EC) patients
- Upfront multi-gene panel testing (MGPT) for EC has been evaluated as an alternative approach to identifying Lynch Syndrome with the potential to simultaneously find actionable germline variants in other cancer susceptibility genes (CSGs). Objective: to determine the frequency and types of actionable germline variants in a large, unselected group of women with EC.
- This study shows that upfront germline testing may help identify patients with Lynch Syndrome or *BRCA* mutations that would not have been identified with tumor testing alone

Levine, *J Clin Oncol* 39, 2021 (suppl 15; abstr 5577).

GW ONCOLOGY UPDATE 17

Endometrial Cancer Updates

- High prevalence of actionable germline variants in unselected endometrial cancer (EC) patients
  - 961 unselected EC cases
    - 101 likely pathogenic (LP) or pathogenic variants (PV) identified in 98 women (10.2%)
    - LP/PVs in LS genes were most common: 29 LS cases were identified (3.02%, 95% CI 2.1 - 4.3%).
    - MGPT found 9 cases (one-third of LS cases) that were not identified by tumor screening
- **Over half of the women carrying germline *BRCA1/2* pathogenic variants had type-II endometrial cancers**, which tend to be aggressive and more difficult to treat.
- The high yield of potentially actionable germline variants seen in this study provides evidence to support the routine clinical implementation of upfront multigene panel testing for all patients with endometrial cancer,
- Conclusion: Upfront MGPT in EC provides clinically impactful information and should be adopted into routine clinical care

Levine, *J Clin Oncol* 39, 2021 (suppl 15; abstr 5577).

GW ONCOLOGY UPDATE 18

Endometrial Cancer Updates

- Pertuzumab plus trastuzumab (P+T) in patients (Pts) with uterine cancer (UC) with *ERBB2 or ERBB3* amplification, overexpression or mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) study.
- TAPUR is a phase II basket study evaluating anti-tumor activity of commercially available targeted agents in pts with advanced cancers with genomic alterations. Results in a cohort of UC pts with *ERBB2 or ERBB3* amplification, overexpression or mutation treated with P+T are reported.
- P+T demonstrated evidence of anti-tumor activity in heavily pre-treated UC pts with *ERBB2* amplification or certain mutations. Additional study is warranted to confirm the efficacy of P+T in this pt population

Ali Ahmad, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 5508).

GW ONCOLOGY UPDATE 19

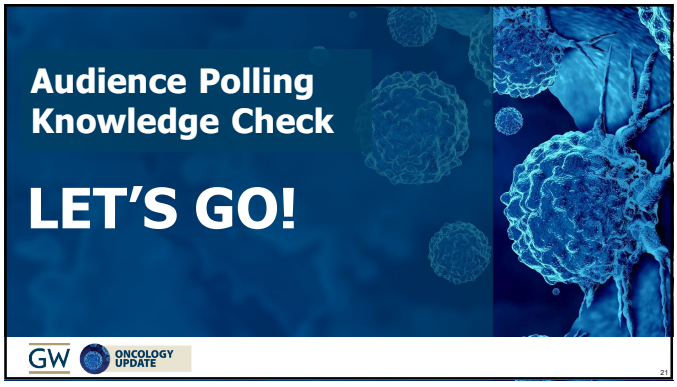
Endometrial Cancer Updates

- Pertuzumab plus trastuzumab (P+T) in patients (Pts) with uterine cancer (UC) with *ERBB2 or ERBB3* amplification, overexpression or mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) study.
- P+T demonstrated evidence of anti-tumor activity in heavily pre-treated UC pts with *ERBB2* amplification or certain mutations. Additional study is warranted to confirm the efficacy of P+T in this pt population

Demographics and efficacy outcomes (N=28)	
Median age, yrs (range)	**69 (44, 90+)**
Prior systemic regimens, %	
1-2	43%
3 or >	57%
DC rate, % (OR or SD16+) (95% CI)	37 (95% CI 21-50%)
OR rate, % (95% CI)	7.1 (0.8, 24)
1 year OS, % (95% CI)	53.4 (36.7, 77.8)

Ali Ahmad, et al. *J Clin Oncol* 39, 2021 (suppl 15; abstr 5508).

GW ONCOLOGY UPDATE 20



GW ONCOLOGY UPDATE 21

Question 1- Based on SOLO-1 data, women with ovarian cancer and a BRCA mutation should receive _____ as maintenance following adjuvant chemotherapy

1. Niraparib (Zejula)
2. Rucaparib (Rubraca)
3. Olaparib (Lynparza)
4. Pemprolizumab (Keytruda)
5. Bevacizumab (Avastin)

GW ONCOLOGY UPDATE 22

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3. Olaparib (Lynparza)
4. Pemprolizumab (Keytruda)
5. Bevacizumab (Avastin)

GW ONCOLOGY UPDATE 23

Question 2- What is the standard primary treatment for locally advanced cervical cancer?

1. High dose cervical Brachytherapy
2. Systemic chemotherapy with carboplatin and paclitaxel
3. External Beam radiation
4. Chemoradiation (weekly cisplatin concurrent with radiation)
5. Chemoradiation followed by systemic chemotherapy with carboplatin and paclitaxel

GW ONCOLOGY UPDATE 24

Question 2- What is the standard primary treatment for locally advanced cervical cancer?

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2. Systemic chemotherapy with carboplatin and paclitaxel
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4. Chemoradiation (weekly cisplatin concurrent with radiation)
5. Chemoradiation followed by systemic chemotherapy with carboplatin and paclitaxel

GW ONCOLOGY UPDATE 25

Question 3- The Human Papillomavirus 9-valent Vaccine is FDA approved for which age group?

1. Females age 9-26
2. Males and Females age 9-26
3. Males and Females age 27-45
4. Males and Females age 9-45
5. All of the above

GW ONCOLOGY UPDATE 26

Question 3- The Human Papillomavirus 9-valent Vaccine is FDA approved for which age group?

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2. Males and Females age 9-26
3. Males and Females age 27-45
4. Males and Females age 9-45
5. All of the above

GW ONCOLOGY UPDATE 27

Question 4- True Or False: Over the last 17 years there has been an overall annual decrease in HPV-related cancers in men of over 2%

1. False
2. True

GW ONCOLOGY UPDATE 28

Question 4- True Or False: Over the last 17 years there has been an overall annual decrease in HPV-related cancers in men of over 2%

1. False
2. True

GW ONCOLOGY UPDATE 29

Question 5- What type of uterine cancers do women carrying germline BRCA pathogenic variants appear to be more prone to have?

1. Type I (low grade endometrioid)
2. Type II (high grade serous)
3. Leiomyosarcoma
4. Gestational Trophoblastic Neoplasia

GW ONCOLOGY UPDATE 30

Question 5- What type of uterine cancers do women carrying germline BRCA pathogenic variants appear to be more prone to have?

1. Type I (low grade endometrioid)
2. Type II (high grade serous)
3. Leiomyosarcoma
4. Gestational Trophoblastic Neoplasia

GW ONCOLOGY UPDATE 31

THANK YOU

GW ONCOLOGY UPDATE 32