SGO 2021 VIRTUAL ANNUAL MEETING ON WOMEN'S CANCER®

# An Open-Label Phase 2 Study of Dostarlimab, Bevacizumab, and Niraparib Combination in Patients with Platinum-Resistant Ovarian Cancer: Cohort A of the OPAL Trial

Society of Gynecologic Oncology


*Joyce F. Liu,[1] Stéphanie Gaillard,[2] Andrea E. Wahner Hendrickson,[3] John W. Moroney,[4] Oladapo Yeku,[5] Elisabeth Diver,[6] Camille Gunderson-Jackson,[7] Rebecca Arend,[8] Elena Ratner,[9] Vivek Samnotra,[10] Divya Gupta,[10] Lena Evilevitch,[10] Zebin Wang,[10] Ping Wang,[10] Joseph Tang,[10] Emeline Bacqué,[10] Xiaohong Liu,[10] Gottfried E. Konecny[11]*

*[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA; [3]Mayo Clinic Rochester, Rochester, NY, USA; [4]University of Chicago Medicine Comprehensive Cancer Center, Chicago, IL, USA; [5]Massachusetts General Cancer Center, Boston, MA, USA; [6]Stanford Women's Cancer Center, Palo Alto, CA, USA; [7]University of Oklahoma Stephenson Cancer Center, Oklahoma City, OK, USA; [8]The University of Alabama at Birmingham, UAB Comprehensive Cancer Center, Birmingham, AL, USA; [9]Yale University, New Haven, CT, USA; [10]GlaxoSmithKline, Waltham, MA, USA; [11]Ronald Reagan UCLA Medical Center, Los Angeles, CA, USA.*


## Background

- Preclinical evidence suggests that poly(ADP-ribose) polymerase inhibition (PARPi), anti–programmed cell death 1 (anti–PD-1) therapy, and antiangiogenic therapies have interactions that may support synergistic antitumor activity in patients with platinum-resistant ovarian cancer (PROC)
  - A phase 1/2 trial of niraparib + pembrolizumab demonstrated an objective response rate (ORR) of 18% in patients with PROC or who were otherwise ineligible for further platinum-based therapies[1]
- This phase 2 study evaluated the antitumor activity of adding an anti-VEGF monoclonal antibody to niraparib + anti–PD-1
  - The OPAL study tested combination therapy with niraparib, dostarlimab, and bevacizumab in patients with PROC

## Conclusions

- Triplet therapy with niraparib, dostarlimab, and bevacizumab is tolerable and demonstrated clinical activity in patients with PROC
  - The majority of patients enrolled had *BRCA*wt or HRRwt tumors, which are predictive factors associated with lower responses to therapy
  - Several patients were primary platinum resistant (43.9%), which is also associated with worse outcomes
  - There were no clear response trends based on biomarkers
- TRAEs were consistent with the prior experience for each drug

Poster #23

Scan to download a copy of this poster


joyce_liu@dfci.harvard.edu





*Presented at the Society of Gynecologic Oncology (SGO) 2021 Annual Meeting on Women's Cancer, Virtual Meeting, March 19–25, 2021.*

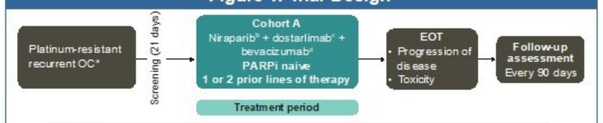

## Objectives

- Here we report on the safety and antitumor activity in the OPAL trial (NCT03574779)

## Methods

- Eligible patients had high-grade, platinum-resistant (progressed ≤6 months after completion of ≥4 cycles of platinum-based chemotherapy), recurrent epithelial ovarian, fallopian tube, primary peritoneal cancer, or recurrent carcinosarcoma of the ovary (high-grade mixed histology permitted)
- Patients had 1–2 prior lines of anticancer therapy for ovarian cancer and no prior therapy with an anti–PD-1/PD-L1 or PARPi
- Patients received a regimen of 500 mg dostarlimab IV every 3 weeks (Q3W) for the first 4 doses, then 1000 mg every 6 weeks (Q6W) thereafter, with 15 mg/kg bevacizumab IV Q3W up to 15 months + niraparib 300 mg or 200 mg QD (for weight <77 kg or platelet count <150,000/μL at screening) orally once daily until discontinuation (Figure 1)

**Figure 1. Trial Design**




[a]Niraparib
Starting dose is as follows:
- 300 mg in patients with baseline body weight ≥77 kg *and* platelets ≥150,000/μL
- 200 mg in patients with baseline weight <77 kg *or* baseline platelet count <150,000/μL
- Administered QD until disease progression

[b]Dostarlimab
500 mg on day 1 Q3W for 4 cycles, followed by 1000 mg every other cycle (Q6W) beginning on day 1/cycle 5.

[c]Bevacizumab
15 mg/kg on day 1 of every 21-day cycle Q3W; only up to 15 months.

[a]Patients with platinum-refractory OC were not eligible for enrollment.
EOT, end of treatment.

- The primary endpoint was investigator-assessed ORR per RECIST v1.1
- Secondary objectives were progression-free survival (PFS), safety, and disease control rate (DCR)
- A post hoc analysis by biomarker (*BRCA* mutation [*BRCA*m] status, homologous recombination repair mutation [HRRm; determined by mutation status of 15 HRR genes (including *BRCA1* and *BRCA2*) in the Myriad myChoice Plus IDE validated panel], and PD-L1 status using combined positive score [CPS ≥1%; a measure of tumor and immune infiltrate PD-L1 expression][2]) prior lines of therapy, and prior bevacizumab use was performed
- Data presented are from a data cutoff date of July 24, 2020

## Results

- In total, 41 patients were enrolled and dosed (safety population)
- Patient demographics and baseline characteristics are shown in Table 1

**Table 1. Patient Demographics and Baseline Characteristics**

| Characteristic | Cohort A (N=41) |
|---|---|
| Age, median (range), y | 66 (37–83) |
| Bodyweight, mean (StDev), kg | 72 (15.5) |
| ECOG performance status, n (%) | |
| 0 | 19 (46.3) |
| 1 | 22 (53.7) |
| Prior lines of therapy, n (%) | |
| 1 | 18 (43.9) |
| 2 | 23 (56.1) |
| Prior bevacizumab, n (%) | |
| Yes | 18 (43.9) |
| No | 23 (56.1) |
| t*BRCA* status, n (%) | |
| *BRCA*m | 4 (9.8) |
| *BRCA*wt | 34 (82.9) |
| Unknown | 3 (7.3) |
| HRRm status, n (%) | |
| HRRm | 7 (17.1) |
| HRRwt | 31 (75.6) |
| Unknown | 3 (7.3) |
| PD-L1 status | |
| Positive | 28 (68.3) |
| Negative | 9 (22.0) |
| Unknown | 4 (9.8) |

t, tumor; StDev, standard deviation.

## Results *(cont'd)*

### Antitumor activity

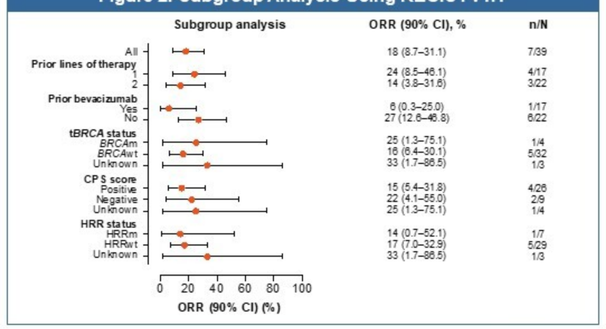
- Antitumor activity was assessed in the response-evaluable population (n=39)
  - 2 patients in the safety population did not have a postbaseline scan and were excluded from the response-evaluable population
- Response data required that patients with a best response of CR or PR had a confirmation scan ≥4 weeks after the first scan in which a response was observed

**Table 2. Antitumor Activity per RECIST v1.1**

| Variable, n (%) | Response-evaluable population (n=39) |
|---|---|
| Complete response | 0 |
| Partial response | 7 (17.9) |
| Stable disease | 23 (59.0) |
| Progressive disease | 8 (20.5) |
| Inconclusive | 1 (2.6) |
| **ORR (90% CI), %** | 17.9 (8.7–31.1) |
| **DCR (90% CI), %** | 76.9 (63.2–87.4) |

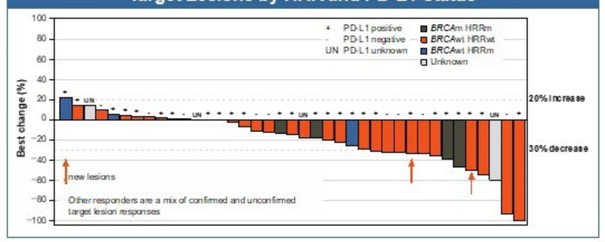
- A subgroup analysis showed that ORR was consistent across most subgroups, but that patients who received prior bevacizumab showed a lower response rate (nonsignificant; Figure 2)

**Figure 2. Subgroup Analysis Using RECIST v1.1**



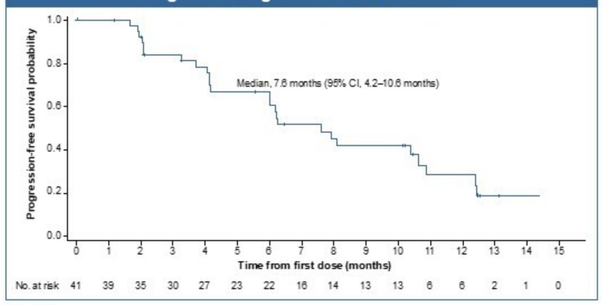

- Best percent change in baseline lesion size by HRR status is shown in Figure 3

**Figure 3. Best Percent Change from Baseline Sum of Target Lesions by HRR and PD-L1 Status**




- Median PFS in the safety population (n=41) was 7.6 months (95% CI, 4.2–10.6 months; Figure 4)

**Figure 4. Progression-Free Survival**




### Safety

- Overall, 97.6% of patients reported at least 1, any-grade treatment-related adverse event (TRAE; Table 3)
  - TRAEs are shown by the drug they were assessed as related to by investigators

**Table 3. Any-Grade TRAEs That Occurred with an Overall Incidence of ≥10%**

| | Cohort A (N=41) | | | |
|---|---|---|---|---|
| Preferred term, n (%) | Niraparib | Dostarlimab | Bevacizumab | Total[a] |
| Any TRAE | 39 (95.1) | 34 (82.9) | 33 (80.5) | 40 (97.6) |
| Fatigue | 24 (58.5) | 15 (36.6) | 9 (22.0) | 25 (61.0) |
| Thrombocytopenia event[b] | 20 (48.8) | 1 (2.4) | 2 (4.9) | 20 (48.8) |
| Hypertension | 13 (31.7) | 1 (2.4) | 17 (41.5) | 18 (43.9) |
| Nausea | 17 (41.5) | 2 (4.9) | 2 (4.9) | 17 (41.5) |
| Anemia event[c] | 14 (34.1) | 0 | 0 | 14 (34.1) |
| Vomiting | 13 (31.7) | 2 (4.9) | 2 (4.9) | 13 (31.7) |
| Neutropenia event[d] | 12 (29.3) | 2 (4.9) | 3 (7.3) | 12 (29.3) |
| Decreased appetite | 8 (19.5) | 2 (4.9) | 2 (4.9) | 9 (22.0) |
| Aspartate aminotransferase increased | 5 (12.2) | 7 (17.1) | 0 | 8 (19.5) |
| Constipation | 8 (19.5) | 4 (9.8) | 2 (4.9) | 8 (19.5) |
| Diarrhea | 6 (14.6) | 4 (9.8) | 1 (2.4) | 7 (17.1) |
| Insomnia | 7 (17.1) | 1 (2.4) | 1 (2.4) | 7 (17.1) |
| Rash | 3 (7.3) | 7 (17.1) | 1 (2.4) | 7 (17.1) |
| Alanine aminotransferase increased | 4 (9.8) | 5 (12.2) | 0 | 6 (14.6) |
| Hypothyroidism | 0 | 6 (14.6) | 1 (2.4) | 6 (14.6) |
| Proteinuria | 0 | 0 | 6 (14.6) | 6 (14.6) |
| Pruritus | 2 (4.9) | 6 (14.6) | 1 (2.4) | 6 (14.6) |
| Epistaxis | 0 | 0 | 5 (12.2) | 5 (12.2) |

[a]TRAEs could be assigned as related to more than one drug; the total represents the number of individual patients with that TRAE; [b]Includes thrombocytopenia and platelet count decreased; [c]Includes anemia and red blood cell count decreased; [d]Includes neutropenia and neutrophil count decreased.

- Overall, 78.0% of patients reported at least 1 grade ≥3 TRAE (Table 4)

**Table 4. Grade ≥3 TRAEs with an Overall Incidence of ≥5%**

| | Cohort A (N=41) | | | |
|---|---|---|---|---|
| Preferred term, n (%) | Niraparib | Dostarlimab | Bevacizumab | Total[a] |
| Hypertension | 6 (14.6) | 0 | 9 (22.0) | 9 (22.0) |
| Thrombocytopenia event[b] | 9 (22.0) | 1 (2.4) | 0 | 9 (22.0) |
| Anemia event[c] | 7 (17.1) | 0 | 0 | 7 (17.1) |
| Fatigue | 7 (17.1) | 2 (4.9) | 2 (4.9) | 7 (17.1) |
| Neutropenia event[d] | 4 (9.8) | 0 | 0 | 4 (9.8) |

[a]TRAEs could be assigned as related to more than one drug; the total represents the number of individual patients with that TRAE; [b]Includes thrombocytopenia and platelet count decreased; [c]Includes anemia and red blood cell count decreased; [d]Includes neutropenia and neutrophil count decreased.

- 34.1% of patients discontinued at least 1 of the 3 study drugs because of a TRAE
- No treatment-emergent adverse event resulted in death
- 6 patients (14.6%) developed grade ≥3 small-intestinal obstructions, all assessed as not related to the study drug
- 1 patient developed a grade 4 small-intestinal perforation that was assessed as related to bevacizumab

### References


1. Konstantinopoulos PA, et al. *JAMA Oncol* 2019;5(8):1141–1149.
2. Shitara K, et al. *Lancet* 2018;392:123.


### Acknowledgments


- Writing and editorial support, funded by GlaxoSmithKline (Waltham, MA, USA) and coordinated by Johanna C. Bruneau, PhD, of GlaxoSmithKline, was provided by Nicole Renner, PhD, and Jennifer Robertson, PhD, of Ashfield MedComms, an Ashfield Health Company (Middletown, CT, USA)
- This study (NCT02715284) was funded by GlaxoSmithKline


### Conflicts of Interest

**Dr. J Liu** reports personal fees from AstraZeneca, Clovis, Genentech, Merck, Regeneron, and GlaxoSmithKline. **Dr. Gaillard** reports personal fees from Immunogen, AstraZeneca, and Sermonix Pharmaceuticals; institutional fees from Rigel; institutional grants from PharmaMar, Genentech/Roche, Iovance Biotherapeutics, Abbvie, AstraZeneca, Pfizer, and GlaxoSmithKline; and patents, royalties, or other intellectual property at Sermonix Pharmaceuticals. **Dr. Diver** reports personal fees from Clovis Oncology and GlaxoSmithKline. **Dr. Gunderson** reports personal fees from Agenus. **Dr. Ratner** reports personal fees from GlaxoSmithKline. **Dr. Konecny** reports personal fees from AstraZeneca, Clovis, and GlaxoSmithKline; and institutional grants from Pfizer, Merck, and Lilly. **Drs. Wahner Hendrickson, Moroney, Yeku,** and **Arend** have nothing to disclose. **Drs. Samnotra, Gupta, Evilevitch, Z Wang, P Wang, Tang, Bacqué,** and **X Liu** are employees of GlaxoSmithKline.