Real-World Patterns and Predictors of First-Line Maintenance Use Among Patients with Newly Diagnosed Advanced Ovarian Cancer: Is There an Opportunity for Change?

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Background

- In the United States, ovarian cancer (OC) is the fifth leading cause of cancer-related death among women[1]
- Advanced disease at diagnosis is common, and OC recurs within 5 years in approximately 70% of patients following initial treatment[1–3]
- In clinical trials, maintenance treatment with poly(ADP-ribose) polymerase (PARP) inhibitors following a complete or partial response to first-line (1L) platinum-based chemotherapy resulted in a significant progression-free survival benefit in patients with newly diagnosed advanced OC[3,4]
- To date, few real-world studies have assessed 1L maintenance treatment use and treatment outcomes among patients with OC treated in clinical practice

Conclusions

- In this real-world analysis, most patients with advanced stage OC treated in clinical practice did not receive 1L maintenance treatment; however, maintenance treatment use did increase over time
- Year of 1L treatment and *BRCA*-mutation status were significant predictors of 1L maintenance treatment; other factors such as age, OC stage at diagnosis, and postoperative residual disease status were not predictive of 1L maintenance treatment
- Potential limitations of the analysis include the retrospective observational design, the limitations of the database (eg, potentially missing data due to documentation patterns or treatment outside of the network), and the rapidly changing treatment landscape, which resulted in different follow-up times and tracking for 1L maintenance treatments
- Additional research is warranted to address barriers to the appropriate use of maintenance treatments, including PARP inhibitors, in real-world clinical practice

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Objective

- This real-world analysis of patients with advanced OC treated in clinical practice described the overall use of 1L maintenance treatment and sought to identify factors predictive of 1L maintenance treatment use in patients who were responsive to 1L platinum-based chemotherapy and would have been considered eligible for PARP inhibitor maintenance treatment

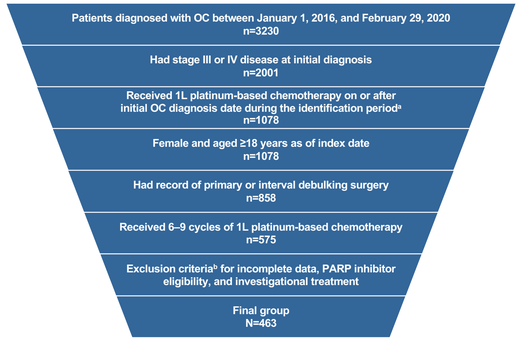
Methods

- This real-world study used the Flatiron Health database, a longitudinal electronic health record–derived database consisting of de-identified patient-level structured and unstructured data that is curated via technology-enabled abstraction from approximately 280 cancer clinics (≈800 sites of care) representing patients with cancer in the United States nationwide[5,6]; of note, the majority of patients in the database originate from community oncology practices
- This retrospective cohort study included patients in the database diagnosed with OC between January 1, 2016, and February 29, 2020. Patients were included if they met the following criteria: ≥18 years old, stage III or IV disease, and received 6–9 cycles of 1L platinum-based chemotherapy and primary debulking surgery or interval debulking surgery following neoadjuvant chemotherapy. Patients were excluded if they started second-line chemotherapy within 2 months of completing 1L treatment or received niraparib for 1L maintenance treatment
- Upon selection, patients were classified into 2 cohorts based on whether or not they had received 1L maintenance treatment with bevacizumab, a PARP inhibitor (olaparib, rucaparib), paclitaxel, or gemcitabine
- The end of the last cycle of 1L platinum-based chemotherapy was defined as the index date. Logistic regression was used to analyze variables predictive of 1L maintenance use

Results

- In total, 463 patients with advanced OC who received 1L platinum-based chemotherapy and were considered to be PARP-inhibitor eligible were included (Figure 1)

Figure 1. Study Attrition



[a]Identification period: January 1, 2017, to August 31, 2019; [b]Incomplete data defined as patients who had initial OC diagnosis date but no records for any procedures, medication use, or hospitalization for >90 days before and after the index date. Patients who died within 30 days of the index date were excluded from the definition of incomplete data. Patients who started 2L treatment within 2 months of the index date were excluded. Patients who were pregnant or used niraparib, which was investigational at the time of the study, were also excluded from the analysis. 1L, first-line; OC, ovarian cancer; PARPi, poly(ADP-ribose) polymerase inhibitor.

- Overall, 21.0% of patients received 1L maintenance treatment, and 79.0% received active surveillance
- Demographic and clinical characteristics are shown in Table 1; overall, most patients had stage III disease at diagnosis (≈71%) and were assessed for *BRCA* mutation status (≈84%)

Results *(cont'd)*

- The mean time to 1L treatment start day was 45.3 and 42.0 days in the patients who did and did not receive 1L maintenance therapy, respectively
- In patients who received 1L maintenance treatment, the mean time from index date to initiation of maintenance treatment was 41.1 days

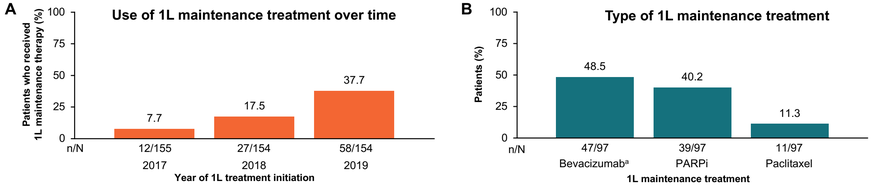
Table 1. Demographic and Clinical Characteristics at Index Date

	1L maintenance therapy (n=97)	Active surveillance (n=366)	Standardized difference
Mean age (StDev), years	63.8 (10.7)	66.3 (11.1)	
Race, n (%)			7.7
Asian	1 (1.0)	4 (1.1)	
African American	4 (4.1)	25 (6.8)	
White	68 (70.1)	271 (74.0)	
Other race/missing	24 (24.7)	66 (18.0)	
Practice type, n (%)			21.1
Community	90 (92.8)	316 (86.3)	
Academic institution	7 (7.2)	50 (13.7)	
Year of 1L treatment initiation, n (%)			6.0
2017	12 (12.4)	143 (39.1)	
2018	27 (27.8)	127 (34.7)	
2019	58 (59.8)	96 (26.2)	
ECOG PS, n (%)			10.9
0–1	82 (84.5)	277 (75.7)	
2–4	7 (7.2)	23 (6.3)	
Missing	8 (8.2)	66 (18.0)	
Ovarian cancer stage,[a] n (%)			20.1
Stage III	62 (63.9)	268 (73.2)	
Stage IV	35 (36.1)	98 (26.8)	
BRCA mutation, n (%)			18.6
*BRCA*m	28 (28.9)	46 (12.6)	
*BRCA*wt	64 (66.0)	249 (68.0)	
Other/missing[b]	5 (5.2)	71 (19.4)	
Residual disease status, n (%)			7.1
Residual disease	37 (38.1)	171 (46.7)	
No residual disease	35 (36.1)	117 (32.0)	
Missing	25 (25.8)	78 (21.3)	

[a]In cases where both International Federation of Gynecology and Obstetrics (FIGO) stage and American Joint Committee on Cancer (AJCC) stage were reported in the patient record, FIGO stage was used for the group stage variable; if the group stage was not explicitly documented but there was clear evidence of distant metastases at the time of diagnosis, stage IV was selected; [b]Includes genetic variant of unknown significance, *BRCA* mutation not otherwise specified, other, and missing.
1L, first-line; *BRCA*m, *BRCA* mutated; *BRCA*wt, *BRCA* wild type; ECOG PS, Eastern Cooperative Oncology Group performance status; NA, not applicable; StDev, standard deviation.

- Overall maintenance treatment use increased during the study period, from 7.7% of patients who started 1L treatment in 2017 to 37.7% of patients who started 1L treatment in 2019 (Figure 2A)
- Bevacizumab and PARP inhibitors were the most used 1L maintenance treatments (Figure 2B)

Figure 2. 1L Maintenance Treatment Use

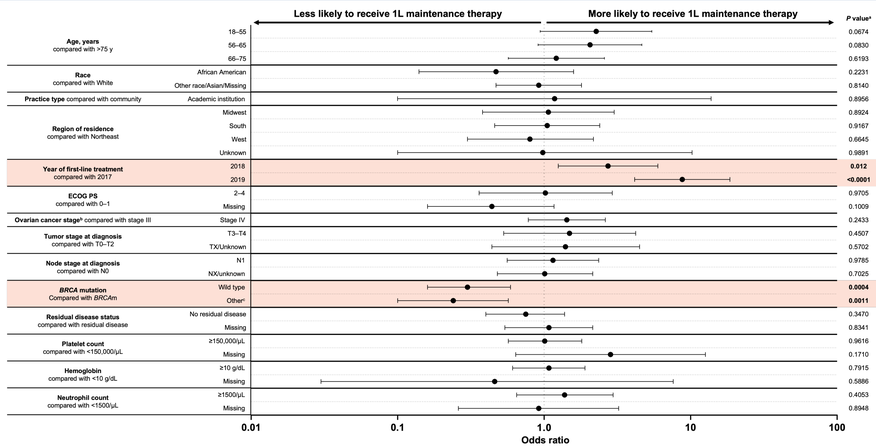


[a]Includes patients who received maintenance treatment with bevacizumab alone or in combination with other agents, including PARP inhibitors.
1L, first-line; PARPi, poly(ADP-ribose) polymerase inhibitor.

Multivariate logistic regression analyses

- Year of 1L treatment initiation and *BRCA*-mutation status were statistically significant predictors of 1L maintenance treatment use (Figure 3)
  - Patients treated in 2019 (odds ratio, 8.78; 95% CI, 4.15–18.55) and 2018 (odds ratio, 2.73; 95% CI, 1.25–5.98) were significantly more likely to receive 1L maintenance treatment than patients treated in 2017
  - Patients with *BRCA*–wild-type OC were significantly less likely to receive maintenance treatment (odds ratio, 0.30; 95% CI, 0.16–0.59) than patients with *BRCA*-mutated OC
- Other demographic or clinical characteristics were not predictive of receiving 1L maintenance treatment

Figure 3. Characteristics Predictive of 1L Maintenance Treatment Use



[a]Reported *P* values tested whether the null hypothesis for each coefficient was equal to zero. *P* values <0.05 indicated that the null hypothesis could be rejected and that the coefficient was a significant predictor of 1L maintenance use; [b]In cases where both International Federation of Gynecology and Obstetrics (FIGO) stage and American Joint Committee on Cancer (AJCC) stage were reported in the patient record, FIGO stage was used for the group stage variable; if the group stage was not explicitly documented but there was clear evidence of distant metastases at the time of diagnosis, stage IV was selected; [c]Genetic variant of unknown significance/*BRCA* mutation not otherwise specified/other/missing.
1L, first-line; ECOG PS, Eastern Cooperative Oncology Group performance status; m, mutated; N, node; T, tumor; y, year.

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Conflicts of Interest

Drs. Liu and Hurteau are current employees of GlaxoSmithKline. **Dr. Thaker** reports institutional grants from GlaxoSmithKline and Merck; and personal fees from AstraZeneca, Celsion, GlaxoSmithKline, Iovance, Novocure, and Seagen. **Ms. Sah** is an employee of STATinMED, a consulting company that has provided paid consulting services to GlaxoSmithKline, which funded the development and conduct of this study and poster. **Dr. Maiese** was an employee of GlaxoSmithKline at the time the analysis was conducted. **Mr. Bee** was an employee of STATinMED at the time the analysis was conducted. **Dr. Chan** reports research, consulting, and speakers' bureau fees from Abbvie, Acerta, Aravive, AstraZeneca, Clovis, Eisai, GlaxoSmithKline, Merck, and Roche.