Reasons for First-Line Maintenance Therapy Discontinuation Among Patients with Newly Diagnosed Advanced Ovarian Cancer Treated in Real-World Settings

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Background

- In the United States, ovarian, fallopian tube, and primary peritoneal cancer, collectively referred to as ovarian cancer (OC), is the fifth leading cause of cancer-related death among women[1]
- At diagnosis, approximately 20% and 60% of patients present with regional or distant disease, respectively; 5-year survival rates in these groups are approximately 75% and 30%, respectively[1]
- Although a combination of surgery and chemotherapy remains a mainstay of treatment for patients with newly diagnosed advanced OC, poly(ADP-ribose) polymerase (PARP) inhibitors and bevacizumab have been integrated as first-line (1L) maintenance therapy options following demonstrations of their efficacy in clinical trials[2-4]
- However, because of adverse events, the rate of PARP inhibitor 1L maintenance treatment discontinuation was more than 10%, compared with ≈2% among placebo-treated patients in the SOLO-1 clinical trial[5]
- To date, few real-world studies have assessed 1L maintenance treatment use and reasons for treatment discontinuation in clinical practice

Conclusions

- In this real-world analysis of patients with advanced OC who received 1L maintenance therapy in clinical practice, bevacizumab and PARP inhibitors were the most common treatments
- Disease progression followed by treatment-related toxicity were the most common reasons for 1L maintenance therapy discontinuation
- Overall, the rates of toxicity-related treatment discontinuations for PARP inhibitors were comparable with those reported in the SOLO-1 clinical trial[5]
- Potential limitations of the analysis include the retrospective observational design; the small sample size, which limited the ability to separate monotherapy and combination therapy; and the limitations of electronic health record data, which are subject to incomplete data entry and coding errors. In addition, the rapidly changing 1L maintenance treatment landscape resulted in different follow-up times and tracking for available 1L maintenance treatment options

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Conflicts of Interest

Drs. Liu, Kalilani, 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 STATinMED, a consulting company that has provided paid consulting services to GlaxoSmithKline, which funded the development and conduct of this study and poster. **Mr. Mallampati** was an employee of STATinMED when the analysis was conducted. **Dr. Maiese** was an employee of GlaxoSmithKline when the analysis was conducted. **Dr. Chan** reports research, consulting, and speakers' bureau fees from Abbvie, Acerta, Aravive, AstraZeneca, Clovis, Eisai, GlaxoSmithKline, Merck, and Roche.

Objective

- This real-world analysis of patients with advanced OC treated in clinical practice evaluated patterns of 1L maintenance treatment use and reasons for treatment discontinuation, with a focus on PARP inhibitors

Methods

- This real-world retrospective cohort study used the Flatiron Health database, a longitudinal electronic health record–derived database consisting of deidentified patient-level structured and unstructured data that are curated via technology-enabled abstraction from approximately 280 cancer clinics (≈800 sites of care) representing patients with cancer in the United States nationwide[6,7]; of note, the majority of patients in the database originate from community oncology practices
- Patients were included if they had OC initially diagnosed between January 1, 2016, and February 29, 2020, and met the following criteria: ≥18 years old, stage III or IV disease at initial diagnosis, and received primary systemic treatment for OC. Patients were excluded if they had incomplete data in the Flatiron Health database, were pregnant, received 1L maintenance treatment with niraparib, or had borderline tumor histology
- Upon selection, patients were classified into cohorts based on whether they had received maintenance treatment or active surveillance after 1L systemic treatment; patients were excluded from analysis if they did not have at least 90 days of follow-up to define maintenance therapy use. 1L maintenance therapy determinations were made according to Flatiron Health database rules and did not distinguish between investigational, off-label, or approved use

Therapies eligible for classification as maintenance treatment per Flatiron Health database definitions[a]

Antiangiogenic	Chemotherapy	PARPi[a]	Combination
Bevacizumab	Gemcitabine	Olaparib	Bevacizumab + olaparib
	Paclitaxel	Rucaparib	Bevacizumab + paclitaxel
			Bevacizumab + gemcitabine

[a]Maintenance therapy classification depends on treatment sequence, treatment timing, and discontinuation of other drugs in combination therapy regimens; [b]Niraparib was eligible to be considered a maintenance treatment per Flatiron Health database definitions; however, per study protocol, patients who received niraparib 1L maintenance treatment were excluded from the analysis.
1L, first-line; PARPi, poly(ADP-ribose) polymerase inhibitor.

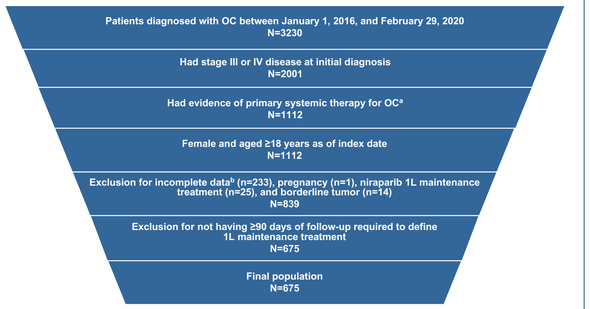
- The end of 1L systemic therapy was defined as the index date, and patients were followed from the index date until patient death, the end of the study period, or the date of the last recorded visit, whichever occurred first

Results

- In total, 839 patients met all eligibility criteria; within this population, 675 patients had sufficient follow-up data to determine 1L maintenance therapy status and were included in the analysis (Figure 1)
- 144 (21.3%) patients received any 1L maintenance treatment, and 531 (78.7%) received active surveillance
- Demographic and clinical characteristics are shown in Table 1
- The median times from initial diagnosis to initiation of index treatment were 197 and 188 days in patients who received 1L maintenance treatment and active surveillance, respectively

Results *(cont'd)*

Figure 1. Study Attrition



[a]Primary systemic therapy for OC (paclitaxel, doxorubicin, docetaxel, bevacizumab, cisplatin, carboplatin, oxaliplatin) as 1L treatment on or after the index date during the identification period (January 1, 2017, to August 31, 2019); [b]Incomplete data was defined as a gap of >90 days between initial OC diagnosis date and any structured activity such as record of any procedures, medication use, or hospitalization.
1L, first-line; OC, ovarian cancer.

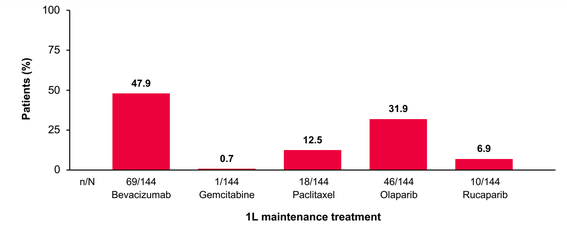
Table 1. Demographic and Clinical Characteristics at Index Date

	1L maintenance treatment (n=144)	Active surveillance (n=531)
Age		
Mean age (StDev), years	65.0 (10.9)	67.9 (11.3)
Race, n (%)		
White	102 (70.8)	379 (71.4)
African American	5 (3.5)	37 (7.0)
Asian	2 (1.4)	10 (1.9)
Other race[a]/missing	35 (24.3)	105 (19.8)
Ethnicity, n (%)		
Non-Hispanic/Non-Latino	125 (86.8)	499 (94.0)
Hispanic/Latino	19 (13.2)	32 (6.0)
Practice type, n (%)		
Community	134 (93.1)	465 (87.6)
Academic institution	10 (6.9)	66 (12.4)
***BRCA* mutation status, n (%)**		
*BRCA*m	30 (20.8)	60 (11.3)
*BRCA*wt	96 (66.7)	351 (66.1)
Other/missing[b]	18 (12.5)	120 (22.6)
ECOG PS, n (%)		
0–1	117 (81.3)	391 (73.6)
2–4	13 (9.0)	56 (10.5)
Missing	14 (9.7)	84 (15.8)
History of debulking surgery, n (%)		
Yes	126 (87.5)	481 (90.6)
No	18 (12.5)	50 (9.4)
Residual disease status, n (%)		
Residual disease	46 (31.9)	227 (42.7)
No residual disease	43 (29.9)	156 (29.4)
Missing	55 (38.2)	148 (27.9)
Year of 1L treatment, n (%)		
2017	15 (10.4)	212 (39.9)
2018	39 (27.1)	178 (33.5)
2019	90 (62.5)	141 (26.6)

[a]Includes Hispanic/Latino; [b]Includes genetic variant of unknown significance, *BRCA* 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; StDev, standard deviation.

- In patients who received 1L maintenance treatment, bevacizumab and olaparib were the most common treatments (Figure 2)

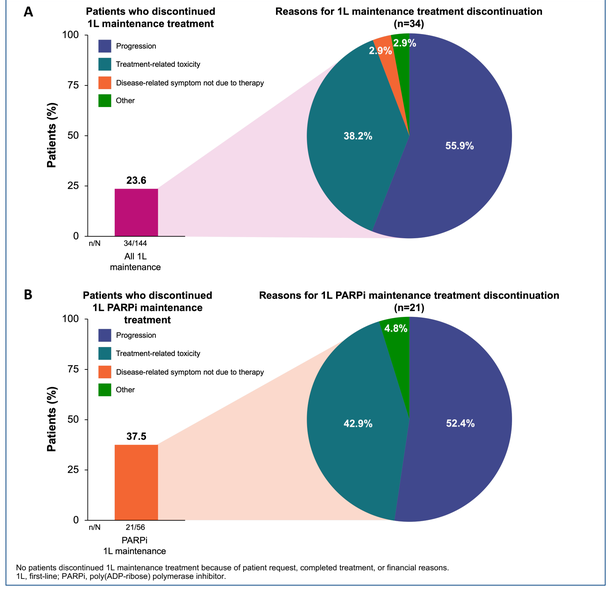
Figure 2. 1L Maintenance Treatment Use



1L, first-line.

- In the overall 1L maintenance treatment population, 34 of 144 (23.6%) patients discontinued 1L maintenance treatment (Figure 3A)
- In the PARP inhibitor (olaparib, rucaparib) 1L maintenance population, 21 of 56 (37.5%) patients discontinued 1L maintenance treatment (Figure 3B)
- In patients who discontinued 1L maintenance treatment, the most common reason for discontinuation was disease progression, followed by treatment-related toxicity (Figure 3)

Figure 3. Treatment Discontinuation Rates and Reasons



No patients discontinued 1L maintenance treatment because of patient request, completed treatment, or financial reasons.
1L, first-line; PARPi, poly(ADP-ribose) polymerase inhibitor.