Disease Progression in Patients with Ovarian Cancer Who Received First-Line Maintenance Therapy or Active Surveillance, a US Real-World Analysis

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**Employed by GlaxoSmithKline when the study was conducted.*

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 in women; almost 80% of patients have regional or distant disease at diagnosis[1]
- In patients with advanced epithelial OC, recurrence is common, and the 5-year overall survival rate is approximately 30%[1,2]
- In recent years, the treatment landscape for advanced OC has expanded to include maintenance therapies, which have been shown to extend progression-free survival across multiple patient populations in clinical trials[2,3]
- Risk factors for progression of advanced OC include visible residual disease after surgery, disease stage, therapy modality, and *BRCA* mutation status[1,3,4]
- In the real-world setting, limited evidence exists on the interaction of risk factors for progression and outcomes for patients with advanced OC who are treated with maintenance therapy or active surveillance

Conclusions

- In this real-world analysis of patients with advanced OC treated in clinical practice, over 95% of patients had 1 or more high-risk factors, and 25.8% of patients received first-line (1L) maintenance therapy
- The number of high-risk factors impacted the risk of disease progression, irrespective of the type of therapy the patient received after completion of 1L treatment
- For high-risk patients, median time to next treatment (TTNT) was longer in patients who received 1L maintenance therapy than in patients treated with active surveillance

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Conflicts of Interest

Dr. Chase reports speakers' bureau fees and/or advisory roles from AstraZeneca, Clovis, GlaxoSmithKline, Merck, Roche, and Takeda. **Ms. Perhanidis and Drs. Gupta, Kalilani, and Lechpammer** are employees of GlaxoSmithKline. **Ms. Woodward** is a former employee of GlaxoSmithKline. **Dr. González-Martín** reports consulting or advisory roles from Amgen, AstraZeneca, Clovis Oncology, Genmab, Immunogen, Mersana, MSD, Roche, Sotio, and Takeda; speakers' bureau with AstraZeneca, Clovis, GlaxoSmithKline, MSD, and Roche; institutional research funding from GlaxoSmithKline and Roche; travel support from AstraZeneca, GlaxoSmithKline, and Roche.

Objective

- This retrospective real-world study assessed whether the number of high-risk factors impacted TTNT as a proxy for disease progression in patients with advanced OC treated with maintenance therapy or active surveillance after completing 1L treatment

Methods

- This 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 US nationwide[5,6]; of note, the majority of patients in the database originate from community oncology practices
- This study included patients diagnosed with OC between 1 January 2011 and 28 February 2021. Patients were included if they met the following criteria: ≥18 years old, stage III or IV disease, initiated 1L platinum-based chemotherapy, Eastern Cooperative Oncology Group score of 0 or 1, ≥12 weeks of follow-up time after 1L treatment. Patients were excluded if they had any of the following: incomplete medical history, evidence of surgery but missing either the date of surgery or postoperative residual disease status, or likely misclassification of lines of treatment
- Patients were classified as having moderate- or high-risk disease; high-risk patients were further grouped by number of high-risk factors (Figure 1)
- Patients were followed from end of 1L treatment (index date) until last activity or end of the study period, whichever occurred first. The cloning approach within the target trial emulation framework was used to account for potential selection and immortal time biases.[7] The inverse probability-of-censoring weights were created to control for bias. Patients were classified as having received maintenance therapy if maintenance therapy was started within 120 days of the index date
- Weighted Kaplan-Meier methodology was used to estimate TTNT (time from index date to start of second-line treatment, death, or last activity)

Figure 1. Risk Factor Classification[a]

Moderate risk: have **all** of the following risk factors
- Stage III disease
- NVRD
- PDS
- *BRCA*m

High risk: have **≥1** high-risk factor
- Stage IV disease
- VRD present or no surgery
- IDS or no surgery
- *BRCA*wt, *BRCA*unk, or missing

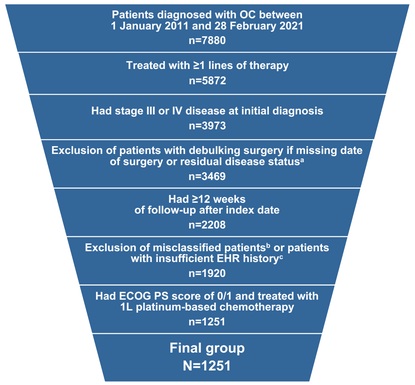
[a]Classification based on known risk factors for progression of advanced OC: disease stage, therapy modality, visible residual disease after surgery, and *BRCA* mutation status.[1,3,4] *BRCA*m, *BRCA* mutated; *BRCA*unk, *BRCA* unknown; *BRCA*wt, *BRCA* wild type; IDS, interval debulking surgery; NVRD, no visible residual disease; OC, ovarian cancer, PDS, primary debulking surgery, VRD, visible residual disease.

Results

- 1251 patients with advanced OC were included in the analysis (Figure 2)
- 25.8% of patients received 1L maintenance therapy, and 74.2% received active surveillance
- In patients who received first-line maintenance therapy, 41.8% received bevacizumab-containing regimens, 38.7% received a poly(ADP-ribose) polymerase (PARP) inhibitor, 6.5% received bevacizumab plus PARP inhibitor combination therapy, and 13.0% of patients received other agents
- At index, median patient age was 65 and 67 years, respectively, in patients who received 1L maintenance therapy and in patients who received active surveillance (Table 1)
- 24.8% of patients who received 1L maintenance therapy had *BRCA*-mutated disease, compared with 14.9% of patients who received active surveillance (Table 1)

Results *(cont'd)*

Figure 2. Study Attrition



[a]Patients with no evidence of debulking surgery were included in the study; [b]Exclusion of patients who were likely misclassified (eg, patients with 1L or 2L PARP inhibitor monotherapy treatment); [c]Exclusion of patients with incomplete EHR history (eg, no visit or noncancelled medication order within 90 days of initial diagnosis or debulking surgery). 1L, first-line; 2L, second-line; ECOG PS, Eastern Cooperative Oncology Group performance status; EHR, electronic health record; OC, ovarian cancer; PARP, poly(ADP-ribose) polymerase.

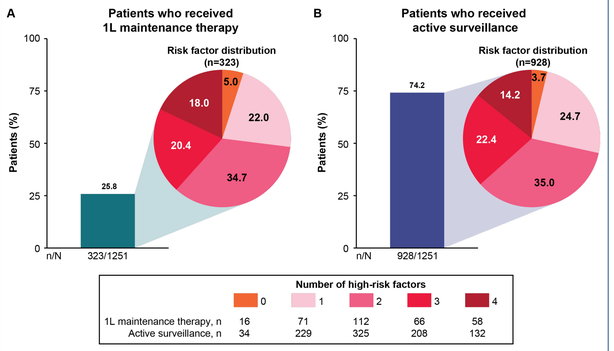
Table 1. Demographic and Clinical Characteristics at Index Date

	1L maintenance (n=323)	Active surveillance (n=928)
Demographic characteristics		
Median age at index (IQR), years	65 (58–72)	67 (58–75)
Practice type, n (%)		
Academic	19 (5.9)	111 (12.0)
Community	304 (94.1)	817 (88.0)
Clinical characteristics		
BRCA mutation status, n (%)[a]		
*BRCA*m	80 (24.8)	138 (14.9)
*BRCA*wt	207 (64.1)	559 (60.2)
*BRCA*unk or missing	36 (11.1)	231 (24.9)
Disease stage at diagnosis, n (%)		
III	198 (61.3)	633 (68.2)
IV	125 (38.7)	295 (31.8)
Therapy type, n (%)		
PDS	144 (44.6)	488 (52.6)
IDS	131 (40.6)	317 (34.2)
No surgery	48 (14.9)	123 (13.3)
Residual disease, n (%)		
NVRD	145 (44.9)	422 (45.5)
VRD or no surgery	178 (55.1)	506 (54.5)

[a]Approximately 3.6% of patients had test results indicating genetic variants of unknown significance or that favoured polymorphism and were grouped as *BRCA*m. 1L, first-line; *BRCA*m, *BRCA* mutated; *BRCA*unk, *BRCA* unknown; *BRCA*wt, *BRCA* wild type; IDS, interval debulking surgery; IQR, interquartile range; NVRD, no visible residual disease; PDS, primary debulking surgery; VRD, visible residual disease.

- In patients who received 1L maintenance therapy, 5.0% of patients were moderate risk (0 high-risk factors), and 95.0% of patients were high risk (≥1 high-risk factors; Figure 3A)
- In patients who received active surveillance, 3.7% of patients were moderate risk (0 high-risk factors), and 96.3% of patients were high risk (≥1 high-risk factors; Figure 3B)

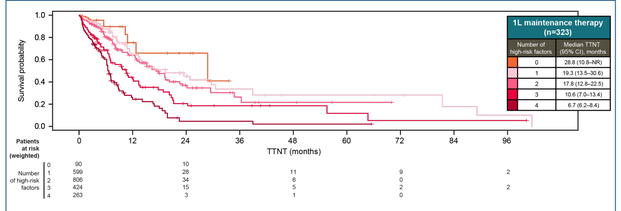
Figure 3. Risk Factor Distribution by 1L Maintenance Therapy Status



1L, first-line.

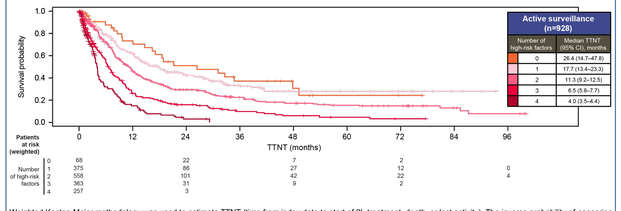
- In patients who were high risk (≥1 high-risk factor), median TTNT was longer in patients who received 1L maintenance therapy than in patients who received active surveillance
  - TTNT for 1L maintenance therapy: 13.3 months (95% CI, 11.1–16.3 months)
  - TTNT for active surveillance: 9.0 months (95% CI, 8.0–9.9 months)
- Median TTNT decreased as the number of high-risk factors increased in patients who received 1L maintenance therapy (Figure 4) and active surveillance (Figure 5)

Figure 4. TTNT by Number of High-Risk Factors in Patients Who Received 1L Maintenance Therapy



Weighted Kaplan-Meier methodology was used to estimate TTNT (time from index date to start of 2L treatment, death, or last activity). The inverse probability-of-censoring weights were created to control for bias. 1L, first-line; 2L, second-line; CI, confidence interval; NR, not reached; TTNT, time to next treatment.

Figure 5. TTNT by Number of High-Risk Factors in Patients Who Received Active Surveillance



Weighted Kaplan-Meier methodology was used to estimate TTNT (time from index date to start of 2L treatment, death, or last activity). The inverse probability-of-censoring weights were created to control for bias. 1L, first-line; 2L, second-line; CI, confidence interval; TTNT, time to next treatment.