Survival in Patients with Advanced Ovarian Cancer Changes with Cumulative Number of Risk Factors, 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 and will result in an estimated 13,770 deaths in 2021[1]
- Although most patients with advanced epithelial OC respond to first-line (1L) treatment, the rate of recurrence is high (≈70%), and the 5-year overall survival (OS) rate is approximately 30%[1,2]
- Disease stage, therapy modality, visible residual disease after surgery, and *BRCA* mutation status are known risk factors for progression of advanced OC[1,3,4]
- However, the cumulative impact of these risk factors on disease progression and OS are unknown, particularly in the real-world setting

Conclusions

- These real-world analyses demonstrate a decrease in time to next treatment (TTNT) and OS by the cumulative number of high-risk factors
- Confirmatory studies are needed to validate the clinical utility of cumulative risk factors assessment as a stratification factor for 1L OC trials

Poster #742P

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Presented at the European Society for Medical Oncology (ESMO) 2021 Congress, 16–21 September 2021.

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Acknowledgments

This study (OneCDP 213807) was funded by GlaxoSmithKline. Writing and editorial support, funded by GlaxoSmithKline (Waltham, MA, USA) and coordinated by Johanna C. Bruneau, PhD, of GlaxoSmithKline, were provided by Betsy C. Taylor, PhD, CMPP, and Jennifer Robertson, PhD, of Ashfield MedComms, an Ashfield Health company (Middletown, CT, USA).

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.

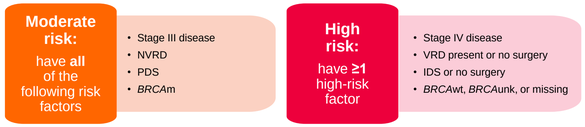
Objective

- This retrospective real-world study was conducted to assess whether the number of high-risk factors impacted TTNT, a proxy for disease progression, and OS among patients with advanced OC treated in clinical practice

Methods

- This study used the Flatiron Health database, a longitudinal electronic health record–derived database consisting of de-identified 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 January 1, 2011, and February 28, 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, and patients with high-risk disease were further grouped by the number of high-risk factors (Figure 1). Patients were followed from the end of 1L treatment (index date) until last activity or end of study period, whichever occurred first
- Kaplan-Meier methodology was used to estimate TTNT (time from index date to start of 2L treatment, death, or last activity) and OS (time from index date to death or last activity)

Figure 1. Risk Factor Classification[a]



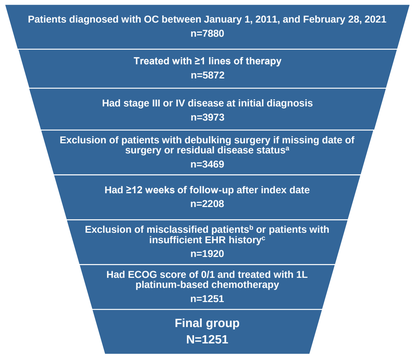
[a]Classification based on known risk factors for progression of advanced OC: disease stage, therapy modality, visible residual disease after surgery, and *BRCA* mutation status.[1,3,4]
BRCAm, *BRCA* mutated; *BRCAunk*, *BRCA* unknown; *BRCAwt*, *BRCA* wild type; IDS, interval debulking surgery; NVRD,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

Results

- In total, 1251 patients with advanced OC were included in the analysis (Figure 2)
- At index, median patient age was 67 years, and 89.6% of patients were treated in the community setting (Table 1)
- 66.4% of patients had stage III disease at diagnosis, and 54.7% of patients had visible residual disease following debulking surgery (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, Eastern Cooperative Oncology Group; EHR, electronic health record; OC, ovarian cancer; PARP, poly(ADP-ribose) polymerase.

Table 1. Demographic and Clinical Characteristics at Index Date

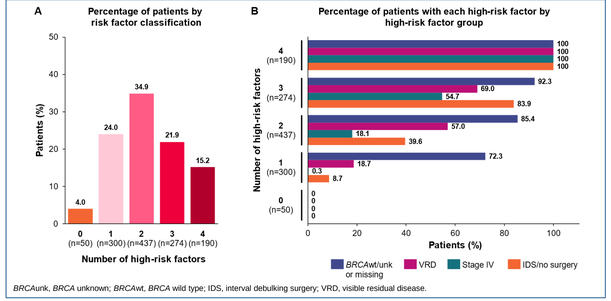
	Overall population (N=1251)
Demographic characteristics	
Median age at index (IQR), years	67 (58–74)
Race, n (%)[a]	
White	906 (72.4)
Black	75 (6.0)
Asian	27 (2.2)
Other	163 (13.0)
Missing	80 (6.4)
Ethnicity, n (%)[b]	
Hispanic or Latino	84 (6.7)
Practice type, n (%)	
Academic	130 (10.4)
Community	1121 (89.6)

	Overall population (N=1251)
Clinical characteristics	
BRCA mutation status, n (%)[c]	
*BRCA*m	218 (17.4)
*BRCA*wt	766 (61.2)
*BRCA*unk or missing	267 (21.3)
Disease stage at diagnosis, n (%)	
III	831 (66.4)
IV	420 (33.6)
Therapy type, n (%)	
PDS	632 (50.5)
IDS	448 (35.8)
No surgery	171 (13.7)
Residual disease, n (%)	
NVRD	567 (45.3)
VRD or no surgery	684 (54.7)

[a]Hispanic/Latino is grouped with other category because of the small number of patients; [b]Ethnicity data were collected separately from race in the database; [c]Approximately 3.6% of patients had test results of genetic variants of unknown significance or favored polymorphism were grouped as *BRCA*m. *BRCA*m, *BRCA* mutated; *BRCA*unk, *BRCA* unknown; *BRCA*wt, *BRCA* wild type; IDS, interval debulking surgery; IQR, interquartile range; NVRD, nonvisible residual disease; PDS, primary debulking surgery; VRD, visible residual disease.

- 4.0% of patients were moderate risk (0 high-risk factors), and 96.0% of patients were high risk (≥1 high-risk factors) (Figure 3A)
- The percentages of patients with 1, 2, 3, or all 4 high-risk factors were 24.0%, 34.9%, 21.9%, and 15.2%, respectively (Figure 3A)
- Within high-risk factor groups 1, 2, and 3, the most common high-risk factor was *BRCA* wild type, *BRCA* unknown, or missing (72.3%–92.3%), and the least common high-risk factor was stage IV disease at diagnosis (0.3%–54.7%; Figure 3B)

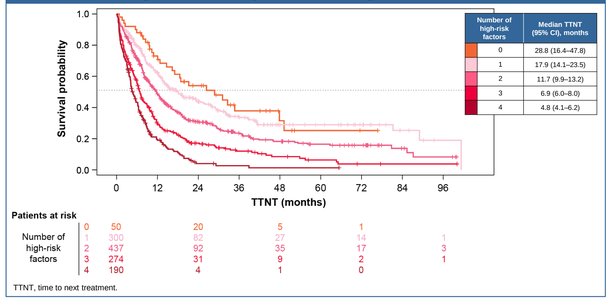
Figure 3. Risk Factor Classification and Distribution



*BRCA*unk, *BRCA* unknown; *BRCA*wt, *BRCA* wild type; IDS, interval debulking surgery; VRD, visible residual disease.

- Median TTNT was 10.1 months (95% CI, 9.0–11.0 months) in the overall population (N=1251) (Figure 4)
- Median TTNT decreased as the number of high-risk factors increased

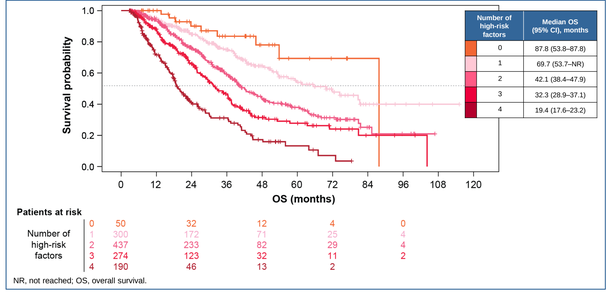
Figure 4. TTNT by Number of High-Risk Factors



TTNT, time to next treatment.

- Median OS was 40.9 months (95% CI, 38.4–44.2 months) in the overall population (N=1251) (Figure 5)
- Median OS decreased as the number of high-risk factors increased

Figure 5. OS by Number of High-Risk Factors



NR, not reached; OS, overall survival.