Risk Factors for Progression or Death in Ovarian Cancer Patients Who Completed First-Line Platinum Treatment

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BACKGROUND

- Although most patients with ovarian cancer (OC) respond to frontline treatment, approximately 70% will experience recurrence within 3 years[1]
- The American Joint Committee on Cancer recognizes several prognostic factors in patients with OC: International Federation of Gynecology and Obstetrics (FIGO) staging, histology, and grade of OC[2]
  - Residual disease after cytoreductive surgery is the most important prognostic factor in patients with advanced disease.[2] Residual tumor size, number of residual sites, and residual disease locations are also recognized as prognostic factors[2]
- This study used a large real-world dataset to identify prognostic factors associated with the risk of progression or death in patients with OC following response to frontline treatment

OBJECTIVE

- To assess the effect of potential prognostic risk factors on outcomes (time to next treatment [TTNT] and overall survival [OS]) among OC patients who completed first-line platinum-based chemotherapy (CT)

METHODS

- This retrospective study identified patients diagnosed with OC from January 2011 to October 2018 using the Flatiron Health database, a longitudinal, demographically and geographically diverse database derived from electronic health records of >265 cancer clinics and >2 million US patients with cancer

Underlying Cohort

- Patients with FIGO stage III/IV OC who completed first line platinum-based CT for 5–10 cycles after primary debulking surgery, 2–10 cycles after interval debulking surgery, or 3–10 cycles without surgery were included. Patients who received any poly(ADP-ribose) polymerase inhibitor as first-line treatment or any maintenance therapy after first-line treatment were excluded. Only patients who started second-line treatment ≥2 months after first-line treatment were selected

Outcomes

- TTNT was defined as the time from the index date (last date of first-line platinum-based CT) to the start date of the second-line treatment, death, or the date of the patient's last confirmed activity (last structured visit, laboratory test, medication administration, or abstracted end date for an oral span), whichever occurred first
- OS was defined as the time from the index date (last date of first-line platinum-based CT) to death or the date of the patient's last confirmed activity (last structured visit, laboratory test, medication administration, or abstracted end date for an oral span), whichever occurred first

Statistical Methods

- Cox proportional hazards model was used to assess the association between baseline factors (neoadjuvant CT, disease stage, residual disease, *BRCA* mutation status, Eastern Cooperative Oncology Group [ECOG] performance status, age, platelet count, hemoglobin count, and neutrophil count) and the TTNT or OS in patients with OC who completed first-line platinum-based CT. Significant risk factors were reported where the 90% confidence interval excluded 1
- Kaplan-Meier analysis was performed to compare the patient prognosis of some key risk factors (*BRCA* mutation status, neoadjuvant CT, and disease stage)
- A sensitivity analysis was conducted that included patients who started second-line treatment ≥3 months after first-line treatment

RESULTS

- Patient attrition is shown in **Table 1**

Table 1. Study Attrition

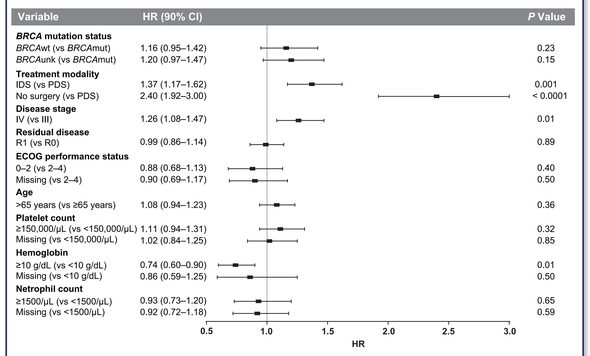
Attrition	Patients, n (%)
Ovarian cancer cohort (1/1/2011–10/31/2018)	5535 (100)
Patients received 1L treatment	4081 (74)
Patients received 1L platinum-based CT	3499 (63)
Patients had stage III/IV disease	2314 (42)
Excluded patients whose surgery date was unknown	2312 (42)
Platinum-based CT criteria: a. Patients without surgery in the 1L must have had ≥3 and ≤10 cycles of platinum-based CT; b. Patients treated with primary debulking surgery must have had ≥5 and ≤10 cycles of platinum-based CT; c. Patients must have had ≥2 and ≤10 postoperative cycles of platinum-based CT following interval debulking surgery	1346 (24)
Excluded patients who received 1L PARP inhibitor treatment	1345 (24)
Patients who had active surveillance after 1L treatment	1217 (22)
Excluded patients who started 2L treatment within 2 months	1064 (19)
Sensitivity analysis Excluded patients who started 2L treatment within 3 months	1018 (18)

1L=first-line; 2L=second-line; CT=chemotherapy; PARP=poly(ADP-ribose) polymerase.

Time to Next Treatment

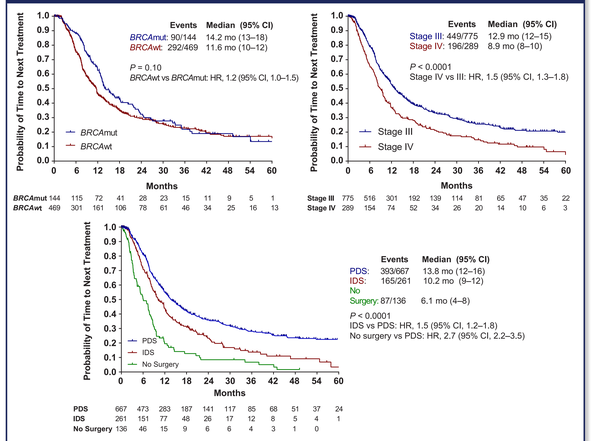
- Patients who received neoadjuvant CT had a shorter TTNT than those who did not, after adjusting for other covariates (**Figure 1**; **Figure 2**)
- Patients with stage IV OC had a shorter TTNT than patients with stage III OC, after adjusting for other covariates

Figure 1. Cox Proportional Hazards Model Analysis (TTNT)



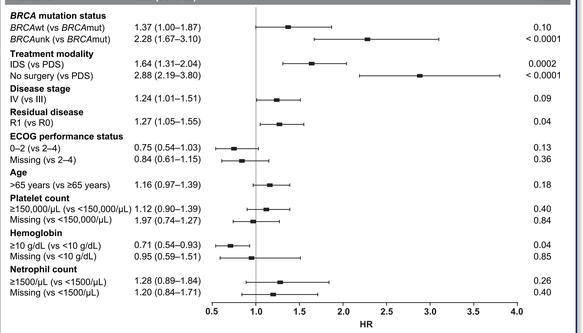
The multivariable model adjusted for all variables shown in the forest plot. A hazard ratio greater than 1.0 indicates an increased TTNT.
*BRCA*mut=*BRCA* mutated; *BRCA*wt=*BRCA* wild-type; *BRCA*unk=*BRCA* unknown; CI=confidence interval; ECOG=Eastern Cooperative Oncology Group; HR=hazard ratio; IDS=interval debulking surgery; PDS=primary debulking surgery; R0=no residual disease after surgery; R1=presence of residual disease after surgery; TTNT=time to next treatment.

Figure 2. Kaplan-Meier Analysis (TTNT)



*BRCA*mut=*BRCA* mutated; *BRCA*wt=*BRCA* wild-type; CI=confidence interval; HR=hazard ratio; IDS=interval debulking surgery; mo=months; PDS=primary debulking surgery; TTNT=time to next treatment.

Figure 3. Cox Proportional Hazards Model Analysis (OS)

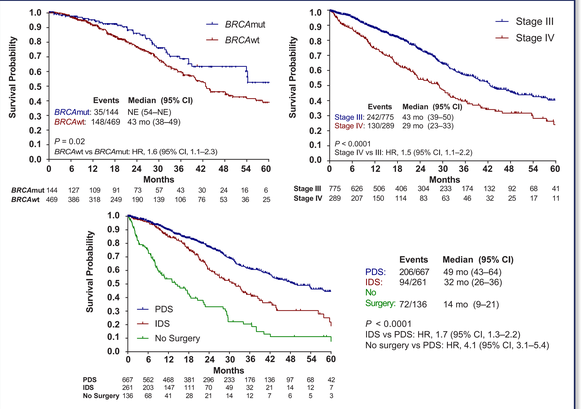


The multivariable model adjusted for all variables shown in the forest plot. A hazard ratio greater than 1.0 indicates an increased risk of shorter OS.
*BRCA*mut=*BRCA* mutated; *BRCA*wt=*BRCA* wild-type; *BRCA*unk=*BRCA* unknown; CI=confidence interval; ECOG=Eastern Cooperative Oncology Group; HR=hazard ratio; IDS=interval debulking surgery; OS=overall survival; PDS=primary debulking surgery; R0=no residual disease after surgery; R1=presence of residual disease after surgery.

Overall Survival

- Patients receiving neoadjuvant CT had a shorter OS than those who did not, after adjusting for other covariates (**Figure 3**; **Figure 4**)
- Patients with stage IV OC had a shorter OS than patients with stage III OC, after adjusting for other covariates
- Patients with any residual disease had a worse OS than those without residual disease
- Patients with *BRCA* wild-type (*BRCA*wt) tumors had a worse OS than patients with *BRCA*-mutated (*BRCA*mut) tumors

Figure 4. Kaplan-Meier Analysis (OS)



*BRCA*mut=*BRCA* mutated; *BRCA*wt=*BRCA* wild-type; CI=confidence interval; HR=hazard ratio; IDS=interval debulking surgery; mo=months; NE=not evaluable; OS=overall survival; PDS=primary debulking surgery.

- The sensitivity analysis yielded similar results

CONCLUSIONS

- In this retrospective analysis of a real-world data set, *BRCA*wt mutation status was associated with a higher risk of death
- Receipt of neoadjuvant CT, higher stage of disease at diagnosis, and presence of residual disease after surgery were also associated with shorter TTNT or a higher risk of death
- These real-world data confirm previously identified prognostic factors

REFERENCES

1. Ledermann JA, et al. *Ann Oncol*. 2013;24(Suppl 6):vi24–vi32.
2. Prat J, et al. Ovary, fallopian tube, and primary peritoneal carcinoma. In: *AJCC Cancer Staging Manual*. 8th ed. Chicago, IL: Springer; 2017:681–690.

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