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Recurrence of Ovarian Cancer in *BRCA*wt Patients Without Maintenance Therapy: Real-World Evidence

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BACKGROUND

- Development of platinum resistance is a major clinical challenge in the treatment of patients with ovarian cancer (OC)
- In the phase 3 ENGOT-OV16/NOVA trial of the poly(ADP-ribose) polymerase (PARP) inhibitor niraparib, 55% of *BRCA* wild-type (*BRCA*wt) patients receiving placebo developed platinum resistance after their last platinum-based therapy (ie, progressive disease within 6 months of their last chemotherapy [CT] dose)[1]
  - Patients who do not carry a *BRCA* mutation are classified as *BRCA*wt
- Niraparib, a PARP inhibitor approved for the maintenance treatment of adult patients with recurrent OC following platinum-based CT, significantly prolongs progression-free survival (PFS)[2,3]

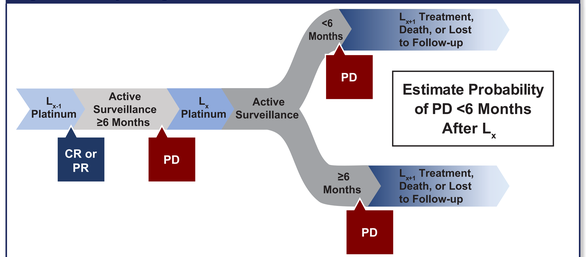
OBJECTIVE

- To assess the risk of platinum eligibility loss for *BRCA*wt patients who did not receive maintenance therapy after platinum-based treatment in a real-world setting

METHODS

- This retrospective study identified patients with OC from January 2011 to October 2018 using data from Flatiron, a longitudinal, demographically and geographically diverse database derived from records of >265 cancer clinics and >2 million US patients with cancer
- *BRCA*wt patients were included who received at least 2 lines of platinum-based CT, had disease progression ≥6 months after their penultimate line of treatment (L_{x-1}), and had received no maintenance therapy (PARP inhibitor, bevacizumab, or CT agents) after their last line of treatment (L_x) (**Figure 1**)
- Time to next treatment (TTNT) was defined as the time from the index date (last date of L_x treatment) to the start date of the next line of treatment (L_{x+1}), death, or the date of the patient's last confirmed activity, whichever occurred first
- Kaplan-Meier methodology was used to estimate the probability of patients initiating the next line of treatment (L_{x+1}) or death, whichever occurred first, within 6 months of their last platinum-based CT
- Median TTNT and its two-sided 95% confidence intervals (CIs) were also provided

Figure 1. Study Design

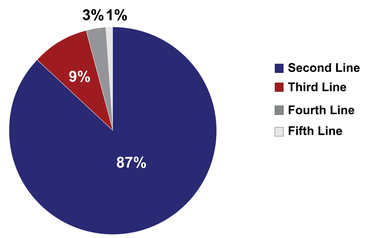


CR=complete response; L_x=last line of chemotherapy; L_{x-1}=penultimate line of chemotherapy; L_{x+1}=next Line of chemotherapy; PD=progressive disease; PR=partial response.

RESULTS

- We identified 5535 patients diagnosed with OC; of these, 147 *BRCA*wt patients met the inclusion/exclusion criteria for this analysis (**Table 1**)
- Eighty-seven percent of *BRCA*wt patients were in the 2nd line, 9% in 3rd line, 3% in 4th line, and 1% in 5th line
- Demographics and baseline characteristics were similar among patients who lost their platinum eligibility and those who maintained their platinum eligibility (**Table 2**)
- An estimated 56% of patients received the next treatment or died within 6 months after their last platinum-based therapy (**Figure 3**)
- The median time to next treatment or death was 5.1 months (95% CI, 3.1–7.2; **Figure 3**)

Figure 2. Distribution of the Last Line of Platinum-Based CT (N=147)



CT=chemotherapy.

Table 1. Study Attrition

Attrition	Patients	%
Ovarian cancer cohort (1/1/2011–10/31/2018)	5535	100%
Patients who received any platinum-based CT	3632	66%
Patients who received at least 2 lines of platinum-based CT	761	14%
Patients whose treatment gap between the prior platinum and current platinum was ≥6 months	463	8%
Patients who had no maintenance after the current platinum-based CT	333	6%
Excluded patients whose follow-up times were missing	292	5%
Patients with *BRCA* wild-type	147	3%

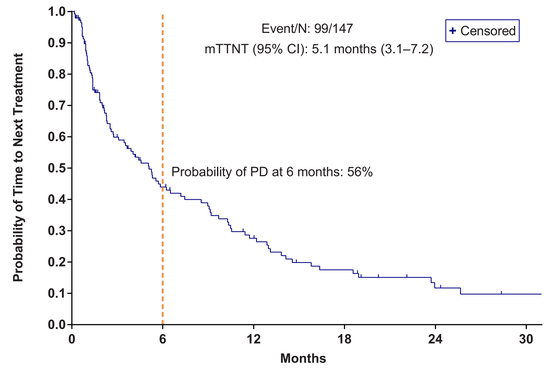
CT=chemotherapy.

Table 2. Patient Demographics and Baseline Characteristics

Characteristic, n (%)	Lost PS[a] (n=68)	Maintained PS[b] (n=31)	Censored[c] (n=48)	*P* Value
Age (years)				0.95
18–65	23 (34%)	9 (29%)	17 (35%)	
65–75	26 (38%)	13 (42%)	20 (42%)	
>75	19 (28%)	9 (29%)	11 (23%)	
Race				0.76
White	53 (78%)	25 (81%)	39 (81%)	
Black	1 (1%)	2 (6%)	2 (4%)	
Asian	1 (1%)	0 (0%)	0 (0%)	
Other race	9 (13%)	2 (6%)	3 (6%)	
Unknown	4 (6%)	2 (6%)	4 (8%)	
Type of therapy				0.99
Adjuvant	42 (62%)	21 (68%)	31 (65%)	
Neoadjuvant	20 (29%)	8 (26%)	14 (29%)	
No surgery	6 (9%)	2 (6%)	3 (6%)	
Stage of OC at initial diagnosis				0.24
I	5 (7%)	1 (3%)	1 (2%)	
II	2 (3%)	3 (10%)	7 (15%)	
III	39 (57%)	15 (48%)	29 (60%)	
IV	15 (22%)	7 (23%)	9 (19%)	
Unknown	7 (10%)	5 (16%)	2 (4%)	
ECOG performance status[d]				0.19
0–1	33 (49%)	16 (52%)	31 (65%)	
2–4	9 (13%)	2 (6%)	1 (2%)	
Missing	26 (38%)	13 (42%)	16 (33%)	
Platelet count,[e] $\times 10^9$/L				0.09
<150	11 (16%)	10 (32%)	15 (31%)	
≥150	36 (53%)	16 (52%)	17 (35%)	
Missing	21 (31%)	5 (16%)	16 (33%)	
Hemoglobin,[e] g/dL				0.62
<10	9 (13%)	5 (16%)	3 (6%)	
≥10	56 (82%)	24 (77%)	42 (88%)	
Missing	3 (4%)	2 (6%)	3 (6%)	
Neutrophil count,[e] $\times 10^9$/L				0.61
<1.5	7 (10%)	1 (3%)	5 (10%)	
≥1.5	26 (38%)	10 (32%)	20 (42%)	
Missing	35 (51%)	20 (65%)	23 (48%)	
Tumor site				
Ovarian	61 (90%)	25 (81%)	42 (88%)	0.46
Fallopian tube	3 (4%)	1 (3%)	4 (8%)	0.63
Primary peritoneal	6 (9%)	7 (23%)	4 (8%)	0.10

[a]Patients who progressed or died within 6 months; [b]Patients who progressed or died after 6 months; [c]Patients who did not progress or die and had a follow-up of <6 months; [d]Defined as the worst value within 6 months before the index date; [e]Defined as the most recent measure before the index date.
ECOG=Eastern Cooperative Oncology Group; OC=ovarian cancer; PS=platinum sensitivity.

Figure 3. Time to Next Treatment in *BRCA*wt Patients



*BRCA*wt=*BRCA* wild-type; CI=confidence interval; mTTNT= median time to next treatment; PD=progressive disease.

CONCLUSIONS

- Our real-world data analysis shows that 56% of *BRCA*wt patients who received platinum-based CT without maintenance therapy had recurrent OC within 6 months of their last platinum-based CT, classifying them as platinum resistant
- The use of maintenance treatment options, such as niraparib, has been shown to significantly prolong PFS after platinum-based CT and may be beneficial in extending the platinum-free interval, enabling patients to remain eligible for further platinum therapy

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ACKNOWLEDGMENTS

Writing and editorial support, funded by TESARO: A GSK Company (Waltham, MA, USA) and coordinated by Heather Ostendorff-Bach, PhD, of TESARO, were provided by Eric Scocchera, PhD, and Frederique H. Evans, MBS, of Ashfield Healthcare Communications (Middletown, CT, USA) and Adrienne M. Schreiber of TESARO.

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Presented at the American Society of Clinical Oncology (ASCO) Annual Congress | May 31–June 4, 2019 | Chicago, IL