Maintenance olaparib for BRCA-mutated ovarian cancer (OC) patients in first-line and platinum-sensitive relapsed (PSR) settings: maximizing treatment opportunities

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Introduction

- Olaparib (Lynparza®) is approved for maintenance treatment in women with advanced BRCA-mutated (BRCAm) OC who have achieved a complete or partial response (CR/PR) following completion of first-line platinum-based chemotherapy (PBC). It is also approved for maintenance treatment in PSR OC, irrespective of BRCA mutation status.
- In Phase III randomized trials, maintenance therapy with olaparib demonstrated an efficacy benefit versus placebo in patients with BRCAm advanced OC who had a CR/PR to PBC in the newly diagnosed (SOLO-1; NCT01844986)¹ and PSR OC (SOLO-2 /ENGOT-Ov21; NCT01874353)² settings.
- Based on the SOLO-1 study results, olaparib maintenance therapy for women with newly diagnosed BRCAm advanced OC also provides an apparent enduring treatment benefit, which is important in preventing or delaying platinum resistance and in reducing or delaying the burden of disease and adverse events associated with multiple lines of PBC in relapsed settings.
- The direct cost burden of OC after first-line therapy has been reported to escalate for women with PSR OC as a result of second-line treatment costs, hospitalizations and the management of treatment-related adverse events.³
- Cost analysis of maintenance therapy with olaparib in women with newly diagnosed BRCAm advanced OC has found that the cost of maintenance therapy stabilizes after 2 years and reduces to a low level over the remainder of the patient's lifetime.⁴
- Moreover, the costs for women with newly diagnosed BRCAm advanced OC who do not receive olaparib maintenance following first-line PBC, regardless of disease progression status, increase after 2 years because of second or later-line treatment.⁴
- Here, we investigate missed opportunities for olaparib maintenance therapy in the setting of newly diagnosed OC.

Methods

Data identification

- A targeted literature review was conducted to obtain response rates to PBC in newly diagnosed patients with advanced BRCAm OC and those with BRCAm PSR OC.
- The search yielded few results in either cohort. The use of an adjustment factor was considered.

Newly diagnosed BRCAm OC

- Searching relevant manuscripts did not reveal PBC response rates applicable in the newly diagnosed setting.
- GOG 218 study authors previously predicted response rates to PBC to be 75%⁵ in a newly diagnosed non-biomarker-specific population. As this response rate was obtained from a non-biomarker-specific population, a BRCA response rate adjustment factor was applied.

BRCAm PSR OC

- Searching relevant manuscripts identified a 64.6% response rate to PBC in BRCAm patients in the second-line setting published by Alsop *et al.*⁶
- Platinum sensitivity data for second-line PBC was determined from the proportion of patients in the placebo arm of the SOLO-1 trial who were progression free after 6 months (80.6%).⁷

BRCA response rate factor

- To determine the BRCAm population response rates to PBC, a BRCA mutation response rate factor was derived from two studies that assessed PSR OC patient populations:
  - Aghajanian *et al.*⁸ reported response rates in non-biomarker patients as 57.4%
  - Alsop *et al.*⁶ determined response rates in BRCAm patients as 64.6%
  - The BRCA mutation response rate factor was calculated as (BRCA mutation response rate [Alsop 64.6%])/(non-biomarker response rate [Aghajanian 57.4%]) = 1.125
  - It was assumed that the numerical relationship between the BRCA mutation and non-biomarker response rates in the PSR OC population would apply to the newly diagnosed population.

Missed opportunity for olaparib treatment calculation

- The proportion of newly diagnosed BRCAm patients who are eligible for olaparib and who would experience possible resistance to, and potential failure of, second-line PBC was calculated by ([proportion of newly diagnosed BRCAm patients eligible for olaparib – proportion of BRCAm PSR OC patients eligible for olaparib]/[proportion of newly diagnosed BRCAm patients eligible for olaparib]) x 100%.

Results

- In a hypothetical cohort of 1000 BRCAm patients, 844 (84%; Figure 1) will be eligible for maintenance olaparib following first-line PBC, and 439 (44%; Figure 2) will be eligible for olaparib in the PSR OC setting (Table 1).
- Based on this, 48% ([844-439]/844) of patients who were eligible for olaparib in the newly diagnosed setting may not receive olaparib maintenance therapy in the second-line setting.

Table 1. Estimation of proportion of patients with BRCAm OC who have achieved a complete or partial response to PBC and are eligible for olaparib maintenance therapy in both the newly diagnosed OC and PSR OC settings

Patient setting	Cohort, n	Calculation	BRCAm population eligible for olaparib, n (%)
Newly diagnosed BRCAm OC	1000	1000 x 0.75 (first-line response rate) x 1.125 (BRCA response rate factor)	844 (84)
BRCAm PSR OC	1000	1000 x 0.75 (first-line response rate) x 1.125 (BRCA response rate factor) x 0.806 (platinum sensitivity) x 0.646 (second-line response rate)	439 (44)

Figure 1. Proportion of BRCAm patients eligible for olaparib following first-line PBC

Figure 2. Proportion of BRCAm PSR OC patients eligible for olaparib

Conclusions

- These analyses demonstrate that an additional 48% of BRCAm OC patients may obtain the treatment benefit from olaparib demonstrated in the SOLO-1 study if treated following first-line PBC rather than in a PSR setting.
- Potential advantages of olaparib maintenance therapy following first-line PBC may include:
  - Prevention or delay of relapse or resistance and extension of the time until subsequent treatment is required
  - Reduction in the adverse events, poor quality of life, disease burden and direct costs associated with progressive disease.
- A limitation of this analysis was not identifying published response rates for newly diagnosed BRCAm patients; a derived BRCA response rate factor was used to determine those response rates.

References

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