Clinical and molecular characteristics of patients with short- and long-term progression-free survival in the Phase IIb OPINION study of maintenance olaparib for patients with non-germline BRCAl/BRCAl2-mutated platinum-sensitive relapsed ovarian cancer

Introduction

• The Phase IIb OPINION study was the first to prospectively evaluate maintenance therapy with the PARP inhibitor olaparib in patients with PSR OC and without a gBRCAm.

• Median PFS in OPINION was 0.2 months (95% confidence interval [CI] 1.7–10.6) overall, demonstrating clinical benefit relative to historical controls.

• We sought to characterize clinical and molecular characteristics in the OPINION study in patients with long- and short-term PFS.

Objective

• To explore the clinical and molecular characteristics of patients with long- and short-term progression-free survival (PFS) in the OPINION study.

• The Phase IIIb OPINION study was the first to prospectively study the maintenance of olaparib in patients with platinum-sensitive relapsed ovarian cancer (PSR OC) without a germline or somatic BRCA mutation (non-gBRCA).

Conclusions

• Patients with long-term PFS (>18 months) in OPINION more commonly had homologous recombination deficiency (HRD), along with genetic mutations that may be associated with ovarian cancer.

• Overlap between tBRCAm, HRD, non-BRCA HRRm, and non-HRR gene mutations identified in patients with long-term PFS (Figure 2).

• Patients with long-term PFS (>18 months) and non-BRCA HRRm had HRD-positive tumors, a tBRCAm, and a non-BRCA HRRm (Table 2).

• Among patients with long-term PFS, the most common non-BRCA HRR genes were with a deleterious or suspected deleterious mutation were RAD51C (seven patients; 10%) and NAP10 (five patients; 7%).

• The most commonly mutated non-BRCA and non-HRR gene was ATM (13 patients; 22%).

Results and interpretation

Table 1. Baseline demographics and clinical characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Long-term PFS (n=67)</th>
<th>Short-term PFS (n=65)</th>
<th>Total enrolled [n=272]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (range) age, years</td>
<td>64 (44–82)</td>
<td>61 (27–84)</td>
<td>65 (27–84)</td>
</tr>
<tr>
<td>Median (range) no. prior lines of PBC</td>
<td>2 (0–10)</td>
<td>2 (0–10)</td>
<td>2 (0–10)</td>
</tr>
<tr>
<td>Median (range) time from diagnosis, years</td>
<td>1 (1.3–14)</td>
<td>2 (0–22.5)</td>
<td>2 (0–22.5)</td>
</tr>
</tbody>
</table>

Table 2. Median (range) time (months) to PFS event by study subgroup

<table>
<thead>
<tr>
<th>Study subgroup</th>
<th>Median (range) time to PFS event</th>
<th>[n=272]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term PFS</td>
<td>9.2 (40–85)</td>
<td>2 (9.2)</td>
</tr>
<tr>
<td>Short-term PFS</td>
<td>2.5 (42–84)</td>
<td>1 (2.5)</td>
</tr>
</tbody>
</table>

Table 2. HRR, BRCAm, and non-BRCA HRRm status

Characteristic, %  

<table>
<thead>
<tr>
<th>Long-term PFS</th>
<th>Short-term PFS</th>
<th>Total enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRR-positive tumors</td>
<td>12% (40/347)</td>
<td>32% (112/351)</td>
</tr>
<tr>
<td>BRCAm</td>
<td>15% (57/390)</td>
<td>15% (56/390)</td>
</tr>
<tr>
<td>Non-BRCA HRRm</td>
<td>15% (56/373)</td>
<td>15% (55/373)</td>
</tr>
</tbody>
</table>

Methods

• Inclusion criteria

• Patients with non-germline BRCAl/BRCAl2 mutations or with a suspected deleterious, deleterious, or likely deleterious mutation in HRD driving genes identified in the PSR OC setting.

• Maintenance therapy

• Olaparib tablets twice every day until their cancer progressed or unacceptable side effects occurred.

• All patients began taking olaparib following failure of three prior chemotherapy regimens:

• Tumor samples were analyzed using the Myriad myChoice HRD plus assay on archival tissue or EDT blood. No archival tissue was available; gBRCA was deleted using the BRACalc analysis CDx assay.

• Additional information on the study design, molecular analysis, and cut-off timings is available in the Supplement, which is accessible via QR code.

Acknowledgments

This study was funded by AstraZeneca and is part of an alliance between Antoni de Capitán and Merck Sharpe & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. Medical writing assistance was provided by Adam Gill, PhD, at Censis, funded by AstraZeneca and Merck Sharpe & Dohme Corp, a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

References