OLAPARIB TREATMENT IN PATIENTS WITH PLATINUM-SENSITIVE RELAPSED OVARIAN CANCER BY BRCA MUTATION AND HOMOLOGOUS RECOMBINATION DEFICIENCY STATUS: PHASE II LIGHT STUDY
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Introduction
- In BRCArec (NCT02320223), patients with germline BRCA-mutated (gBRCAm) platinum-sensitive relapsed (PSR) ovarian cancer (OC) who had received at least two prior lines of platinum-based chemotherapy and were then treated with olaparib tablets (300 mg b.i.d) in patients with PSR OC for differences in gBRCAm, somatic BRCAm (sBRCAm) and HRD status determined by Myriad therAniC test score ≥42.
- Therefore, the goal of this study was to investigate olaparib treatment in patients with PSR OC by BRCAm and HRD status.
- As previously observed in the maintenance setting, all TEAEs were significantly reduced in the HRD-positive cohort compared with the HRD-negative cohort (4).

Methods
- Patients were assigned to one of four cohorts according to BRCAm and HRD status determined by Myriad therAniC test score ≥42.
- Patients categorized as having an HRD-positive tumor (Cohort 3) had a Myriad myChoice test score ≥42.

Results
- Of the 272 patients enrolled, 271 were treated with at least one dose of olaparib and 270 had measurable disease at baseline.
- The ORR for each cohort is shown in Figure 1.
- Patient characteristics in each cohort are described in Table 1.
- In the maintenance setting for PSR OC, both patients with a BRCAm and patients without a BRCAm had a PFS benefit when treated with olaparib vs placebo.
- Therefore, the goal of this study was to investigate olaparib treatment in patients with PSR OC by BRCAm and HRD status.

Conclusions
- LIGHT is the first study to report the activity of olaparib tablet monotherapy in PSR OC patients who had received at least one prior line of platinum-based chemotherapy (2L+ or who were prospectively assigned to separate cohorts according to BRCAm and HRD status.
- As expected with a PARP inhibitor, and consistent with previously reported, we saw a greater magnitude of benefit in the BRCAm and HRD-positive cohorts than in the HRD-negative cohort.

Implications
- There were two cases of pneumonitis (Grade 2 and 3), one case of pulmonary fibrosis (Grade 2), and no cases of acute myeloid leukemia or myelodysplastic syndromes.

Table 1. Patient characteristics (full analysis set)

<table>
<thead>
<tr>
<th>Cohort</th>
<th>BRCAm</th>
<th>sBRCAm</th>
<th>HRD+ve (n=68)</th>
<th>HRD-ve (n=68)</th>
<th>Overall (n=272)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort 1</td>
<td>61 (69)</td>
<td>36 (53)</td>
<td>36 (49)</td>
<td>25 (34)</td>
<td>66 (25)</td>
</tr>
<tr>
<td>Cohort 2</td>
<td>71 (78)</td>
<td>54 (61)</td>
<td>54 (61)</td>
<td>27 (34)</td>
<td>71 (28)</td>
</tr>
<tr>
<td>Cohort 3</td>
<td>64 (86)</td>
<td>56 (78)</td>
<td>56 (78)</td>
<td>28 (37)</td>
<td>64 (24)</td>
</tr>
<tr>
<td>Cohort 4</td>
<td>64 (60)</td>
<td>48 (60)</td>
<td>33 (47)</td>
<td>31 (43)</td>
<td>64 (24)</td>
</tr>
</tbody>
</table>

Grade ≥3 TEAE, n (%)
- Anaemia 18 (67), neutropenia 16 (59)
- Other 33 (12), fatigue 25 (9)

TEAE leading to discontinuation, n (%)
- Anaemia 18 (67), neutropenia 16 (59)
- Other 33 (12), fatigue 25 (9)

TEAE leading to dose interruption, n (%)
- Anaemia 18 (67), neutropenia 16 (59)
- Other 33 (12), fatigue 25 (9)

TEAE leading to dose reduction, n (%)
- Anaemia 18 (67), neutropenia 16 (59)
- Other 33 (12), fatigue 25 (9)

TEAE leading to dose interruption, n (%)
- Anaemia 18 (67), neutropenia 16 (59)
- Other 33 (12), fatigue 25 (9)

TEAE leading to dose reduction, n (%)
- Anaemia 18 (67), neutropenia 16 (59)
- Other 33 (12), fatigue 25 (9)

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References

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