Final overall survival (OS) results from the phase III PAOLA-1/ENGOT-ov25 trial evaluating maintenance olaparib (ola) plus bevacizumab (bev) in patients (pts) with newly diagnosed advanced ovarian cancer (AOC)


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Background

In the PAOLA-1/ENGOT-ov25 (NCT02477644) primary analysis, adding ola to maintenance bev after first-line (1L) platinum-based chemotherapy (PBC) + bev led to a significant progression-free survival (PFS) benefit in AOC (HR 0.59, 95% CI 0.49–0.72; P < 0.001), particularly in pts with homologous recombination deficiency (HRD+; BRCA1/2 mutation [BRCAm] and/or genomic instability; Ray-Coquard et al. NEJM 2019). Here, we report the prespecified final OS analysis.

Methods

Pts with high-grade AOC, in response after PBC + bev, were randomized 2:1 to ola tablets (300 mg bid; up to 24 months [mo]) + bev (15 mg/kg q3w; 15 mo total) or placebo [pbo] + bev. OS (intent-to-treat [ITT] population) was a key secondary endpoint, with analysis planned for 3 years (y) after the primary analysis as part of hierarchical testing.

Results

537 pts were randomized to ola + bev and 269 to pbo + bev (median follow-up 61.7 and 61.9 mo, respectively; OS data maturity: 55.3%). Median OS in the ITT population was 56.5 mo with ola + bev vs 51.6 mo with pbo + bev (HR 0.92, 95% CI 0.76–1.12; P=0.4118; OS at 5 y, 47.3 vs 41.5%). In HRD+ pts, OS was prolonged with ola + bev (HR 0.62, 95% CI 0.45–0.85; OS at 5 y, 65.5 vs 48.4%), with benefit in HRD+ pts with or without a tumour BRCAm (tBRCAm; Table). No benefit was seen in HRD- pts (HR 1.19, 95% CI 0.88–1.63). Subsequent PARP inhibitor therapy was received by 105 (19.6%) ola + bev pts vs 123 (45.7%) pbo + bev pts. Myelodysplastic syndrome, acute myeloid leukaemia and aplastic anaemia incidence, and new primary malignancy incidence, was respectively: ola + bev, 9 pts [1.6%] and 22 pts [4.1%]; pbo + bev, 6 pts [2.2%]) and 8 pts [2.9%]).

<table>
<thead>
<tr>
<th>OS*</th>
<th>No. of events/no. of pts (%)</th>
<th>5 y OS rate, % (95% CI)</th>
<th>HR (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Ola + bev</td>
<td>288/537 (53.6)</td>
<td>158/269 (58.7)</td>
<td>47.3</td>
</tr>
<tr>
<td>Pbo + bev</td>
<td>93/255 (36.5)</td>
<td>69/132 (52.3)</td>
<td>65.5</td>
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Table: 000LBA29

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*OS: overall survival; HR: hazard ratio; PBC: platinum-based chemotherapy; bev: bevacizumab; ITT: intent-to-treat; HRD: homologous recombination deficiency; BRCAm: BRCA1/2 mutation; tBRCAm: tumour BRCAm
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<td>Ola + bev</td>
<td>Pbo + bev</td>
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<tr>
<td>tBRCAm§</td>
<td>48/157   (30.6)</td>
<td>37/80   (46.3)</td>
</tr>
<tr>
<td>HRD+ excluding tBRCAm§</td>
<td>44/97   (45.4)</td>
<td>32/55   (58.2)</td>
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<tr>
<td>HRD-/unknown§</td>
<td>195/282  (69.1)</td>
<td>89/137  (65.0)</td>
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<tr>
<td>HRD.+</td>
<td>140/192  (72.9)</td>
<td>58/85   (68.2)</td>
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*tBRCAm status by central labs; HRD status by Myriad myChoice HRD Plus §Preplanned exploratory analysis

Conclusions

Despite a high proportion of pts in the control arm receiving a PARP inhibitor post-progression, ola + bev provided a clinically meaningful improvement in OS for 1L HRD+ pts with and without a tBRCAm, confirming ola + bev as standard of care in this setting.

Clinical trial identification

NCT02477644.

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ARCAGY Research.

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Disclosure


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