INTRODUCTION

ARIEL3 (NCT01968313) was a phase 3 study of rucaparib (800 mg twice daily) vs placebo as maintenance therapy to platinum-based chemotherapy for recurrent ovarian cancer (Figure 1).

Rucaparib significantly improved progression-free survival (PFS) in all patients with platinum-sensitive recurrent ovarian cancer, including patients with BRCA mutations.

Validation of a genomic LOH cutoff in ARIEL3 was the first trial to prospectively test the genomic LOH cutoff discriminator and tumor molecular testing is not required for use, based on the prespecification studies.

METHODS

Patient Eligibility

Signatures

Response to recent chemotherapy

Platinum sensitivity

FIGURE 1. Study Design

RESULTS

Patient Demographics

Table 1. Baseline Demographics (All Randomized Patients)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Rucaparib (n=375)</th>
<th>Placebo (n=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), years</td>
<td>61 (39-84)</td>
<td>62 (50-82)</td>
</tr>
<tr>
<td>HPV status</td>
<td>Non-BRCA wild-type (HRD)</td>
<td>Non-BRCA wild-type (HRD)</td>
</tr>
<tr>
<td>Response to recent platinum chemotherapy</td>
<td>86% (25/30)</td>
<td>86% (21/24)</td>
</tr>
<tr>
<td>Ectopic ovarian cancer</td>
<td>32 (8.8)</td>
<td>10 (9.3)</td>
</tr>
<tr>
<td>Fallopian tube cancer</td>
<td>32 (8.8)</td>
<td>10 (9.3)</td>
</tr>
<tr>
<td>Primary peritoneal cancer</td>
<td>31 (8.3)</td>
<td>19 (18.0)</td>
</tr>
<tr>
<td>BRCA-wild-type ovarian cancer</td>
<td>130 (34.7)</td>
<td>66 (62.2)</td>
</tr>
<tr>
<td>BRCA1</td>
<td>80 (21.3)</td>
<td>37 (34.5)</td>
</tr>
<tr>
<td>BRCA2</td>
<td>50 (13.5)</td>
<td>29 (27.0)</td>
</tr>
<tr>
<td>Germline</td>
<td>82 (21.6)</td>
<td>46 (43.0)</td>
</tr>
<tr>
<td>RP58</td>
<td>42 (11.2)</td>
<td>15 (14.0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (2.1)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>BRCA wild-type</td>
<td>245 (65.4)</td>
<td>123 (115.0)</td>
</tr>
<tr>
<td>Germline LOH &gt;16%</td>
<td>108 (28.3)</td>
<td>52 (48.6)</td>
</tr>
<tr>
<td>Germline LOH &lt;16%</td>
<td>127 (33.8)</td>
<td>54 (50.0)</td>
</tr>
<tr>
<td>Germline LOH uninterpretable</td>
<td>32 (8.5)</td>
<td>17 (15.8)</td>
</tr>
</tbody>
</table>

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥6% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥16% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥16% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥16% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥16% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥16% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥16% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥16% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥16% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥16% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥16% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%

- Of the 368 patients with BRCA4 wild-type recurrent ovarian cancer, LOH was ≥16% for 518 (81%) patients, <16% for 107 (28.5%) patients,

- The interaction between treatment with rucaparib and LOH was evaluated using the rank sum test.

- The treatment-by-LOH subgroup interaction was non-significant (P=0.4016) using the prespecified cutoff of 16%