INTRODUCTION

In the randomised, placebo-controlled, double-blind, phase 3 ARIEL3 (NCT01482121), the poly(ADP-ribose) polymerase inhibitor rucaparib significantly improved progression-free survival in patients with platinum-sensitive, recurrent ovarian cancer who were in complete or partial response to frontline platinum-based chemotherapy. Here we present an analysis of treatment-emergent adverse events (TEAEs) with 2 years of additional follow-up for patients continuing treatment in ARIEL3 compared with the previous safety report, as well as an analysis of the median time to and median duration of first occurrence of TEAEs.

METHODS

Safety data were summarised for all patients who were randomised into ARIEL3 and who received at least one dose of study treatment. TEAEs were classified per MedDRA version 10.1 and graded per the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.03).

Additional safety analyses included:

- Prevalence of nausea and anemia/decreased haemoglobin over time.
- Median duration of first TEAE, defined as the duration of first TEAE regardless of grade. TEAEs overlapping by 10 days were considered as the same consecutive event. TEAEs occurring after the first event were not included in the duration calculation.
- AE duration was calculated using Kaplan-Meier methodology, in which ongoing events without a known date were censored at the date of the last dose plus 28 days.

RESULTS

Safety Overview

The current analysis of TEAEs in ARIEL3 remains consistent with previous reports, with no new safety signals.

- As of the previous safety data cutoff (31 Dec 2017), 363/372 patients in the safety population were still receiving rucaparib and 189/372 patients were on placebo.
- Median treatment duration was 6.3 months in the rucaparib arm and 5.5 months in the placebo arm.
- Among the previous and current safety data cutoff.

- All patients in the rucaparib arm and 182/189 (97%) patients in the placebo arm experienced ≥1 TEAEs.
- Grade ≥3 TEAEs were reported by 176/363 (49%) patients in the rucaparib arm and 72/189 (38%) patients in the placebo arm (Table 1).

The most frequent TEAEs in the rucaparib arm were neutropenia/thrombocytopenia and decreased neutrophils (71/363 patients [19.6%]).

Table 1: Summary of TEAEs

<table>
<thead>
<tr>
<th>TEAE</th>
<th>Rucaparib (n=372)</th>
<th>Placebo (n=189)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment duration, median (range), mo</td>
<td>6.3 (0-27)</td>
<td>5.5 (0-27)</td>
</tr>
<tr>
<td>Patients with at least 1 grade 3 TEAEs</td>
<td>363/372 (98%)</td>
<td>189/189 (100%)</td>
</tr>
<tr>
<td>Treatment interruption and dose reduction due to TEAEs</td>
<td>271 (72.9)</td>
<td>37 (19.5)</td>
</tr>
<tr>
<td>Discontinued due to TEAE</td>
<td>44 (12%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Deaths due to TEAE</td>
<td>6 (1.6%)</td>
<td>0.5%</td>
</tr>
<tr>
<td>Deaths due to disease progression</td>
<td>2 (0.5%)</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

In the rucaparib arm, the most frequently reported TEAEs of any grade were nausea (284/372 [76.1%] and anemia/hypochromia (290/372 [78.1%]), the most frequently reported grade ≥3 TEAEs were neutropenia/thrombocytopenia (271/372 [72.9%]), and proteinuria (92/372 [24.8%]).

- Of the patients who experienced MD or AML, 3 had a germline BRCA-mutant carcinoma, 1 had a BRCA wild-type/low loss of heterozygosity carcinoma.
- No patients in the placebo arm reported treatment-emergent MDS or AML.

HIGHLIGHTS

- The overall safety profile of rucaparib maintenance treatment in patients with recurrent ovarian cancer from ARIEL3 remains consistent with previous reports, with no new safety signals identified.
- Prevalence of any-grade nausea declined progressively over the 24-month evaluation period.
- Prevalence of any-grade anaemia/decreased haemoglobin peaked at month 4, decreasing to a plateau at month 8.3.
- The first onset of frequently reported TEAEs generally occurred early in treatment (≤45 days). The median duration of the first event of frequently reported TEAEs was generally <60 days (Figure 3).

REFERENCES

1. St John of God Subiaco Hospital, Australia; Vithas Marbella Cancer Center, University Health Network, Toronto, Canada; Torrance Cancer Institute, University of Alberta; Memorial Sloan Kettering Cancer Center, New York, USA; Vizient University Hospital, Vizient Other Institute of Oncology (VIO), Barquisimeto, Spain; European Institute of Oncology (IEO) and University of Milan-Bicocca, Italy.
2. ESMO Congress. In: St John of God Subiaco Hospital, Australia; Vithas Marbella Cancer Center, University Health Network, Toronto, Canada; Torrance Cancer Institute, University of Alberta; Memorial Sloan Kettering Cancer Center, New York, USA; Vizient University Hospital, Vizient Other Institute of Oncology (VIO), Barquisimeto, Spain; European Institute of Oncology (IEO) and University of Milan-Bicocca, Italy.
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PRESENTING AUTHOR DISCLOSURE

The Corresponding Author has read and approved the final manuscript. The Corresponding Author is theFileVersion4.03.0001

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