PARPi-resistant ovarian cancer (OC), demonstrated efficacy and moderate toxicity. We report updated progression-free survival (PFS) and clinical/molecular features associated with clinical benefit from adavosertib (A) +/- olaparib (O).

Methods Eligible patients had recurrent OC after progression on PARPi, measurable disease, and adequate end-organ function. Primary endpoint was objective response rate (ORR) per RECIST v1.1. Secondary endpoints included PFS and clinical benefit (ORR/stable disease > 4 months) based on BRCA status, homologous recombination deficiency (HRD), platinum sensitivity, and intervening alternate therapy after prior PARPi before trial enrollment. Replication stress and HRD are being assessed using novel pRPA32 and Rad51 foci.

Results There were 35 evaluable patients on each arm. Patients received a median of 4 prior therapies (range 1–11), including olaparib (41%). Median PFS was 5.5 months (95% CI, 3.9–6.9) from A and 6.8 months (95% CI, 4.3–8.3) from A/O. Table 1 demonstrates clinical benefit based on clinical/molecular features. Clinical benefit was observed on both arms regardless of BRCA status, platinum sensitivity, or use of intervening therapy after PARPi. Figure 1 demonstrates clinical benefit based on platinum sensitivity, with intriguing activity in platinum-resistant disease.

Conclusion/Implications Efficacy of adavosertib +/- olaparib was retained across multiple clinical cohorts of PARPi-resistant OC, including BRCAwt and platinum-resistant disease. Ongoing analysis using a novel functional HRD assay consisting of concordant measurement of Rad51, gH2AX and geminin foci will elucidate the role of HRD in clinical benefit.

Abstract PR073/#425 Table 1

<table>
<thead>
<tr>
<th></th>
<th>Fully platinum sensitive (n=38)</th>
<th>Partially platinum sensitive (n=53)</th>
<th>2L prior CT (n=64)</th>
<th>≥ 3L prior CT (n=27)</th>
<th>Overall (n=91)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR, %</td>
<td>65.8% (48.6–79.9)</td>
<td>54.7% (40.6–68.2)</td>
<td>64.1% (51.0–75.4)</td>
<td>48.1% (29.2–67.7)</td>
<td>59.3% (48.4–69.2)</td>
</tr>
<tr>
<td>DCR, %</td>
<td>97.4% (84.6–99.9)</td>
<td>90.6% (78.6–96.5)</td>
<td>93.8% (84.0–98.0)</td>
<td>92.6% (74.2–98.7)</td>
<td>93.4% (86.2–97.5)</td>
</tr>
<tr>
<td>DOR, mo</td>
<td>12.0 (10.2–NR)</td>
<td>8.2 (6.8–9.6)</td>
<td>11.1 (9.1–13.0)</td>
<td>9.1 (6.8–11.5)</td>
<td>10.3 (8.2–12.0)</td>
</tr>
<tr>
<td>PFS, mo</td>
<td>13.9 (10.6–17.1)</td>
<td>8.3 (7.1–9.5)</td>
<td>12.3 (9.2–15.3)</td>
<td>9.1 (7.8–10.4)</td>
<td>11.1 (8.3–13.8)</td>
</tr>
</tbody>
</table>

Introduction Senaparib (IMP4297) showed promising antitumor activity for advanced ovarian cancer (OC). This study aimed to evaluate the efficacy and safety of senaparib in patients(pts) with BRCA1/2 mutated platinum sensitive recurrent OC. Here we assessed the efficacy by prior therapies and platinum sensitive.

Abstracts

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PR073/#425 SENAPARIB, A PARP INHIBITOR, IN PATIENTS WITH BRCA1/2 MUTATED PLATINUM SENSITIVE RECURRENT OVARIAN CANCER: SUBGROUP ANALYSIS FROM SABRINA STUDY

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Abstract PR073/#425 Table 1
Methods This open label, multicenter, single arm, phase II study (NCT04089189) enrolled recurrent OC pts with germ-line and/or somatic BRCA mutation who had previously received ≥ 2 lines of platinum-based chemotherapy (CT). Senaparib (100 mg oral QD) was administered until disease progression or unacceptable toxicity. The primary endpoint was independent review committee (IRC)-assessed objective response rate (ORR) per RECIST v1.1.

Results As of 30 Jan 2023, 93 pts were enrolled. 59%/41% pts were partially/fully platinum sensitive. Median lines of prior systemic chemotherapy (CT) was 2 (range 2–7), and 71%/29% received 2/3 lines of CT. After a median follow up of 15.7 months, efficacy was assessed in 91 pts who received treatment of senaparib and ≥ 1 tumor evaluated and met the criteria for the response evaluable set. IRC had not finished the assessment and the efficacy assessed by investigators was showed in table 1.

Conclusion/Implications Senaparib demonstrated clinically meaningful antitumor activity in OC pts of fully or partially platinum sensitive who had previously received ≥ 2 lines of CT.