or *PALB2* and were deemed eligible for NACT by laparoscopic scoring or imaging. After 2 cycles (56 days) of olaparib at 300 mg PO BID daily, patients were assessed with imaging. Patients without the progressive disease (PD) were considered for TRS. Those deemed not amenable to surgery or with PD received CT. Patients who underwent immediate TRS received postoperative adjuvant therapy at provider/patient discretion. Feasibility was defined as the ability to receive 2 cycles of olaparib without unacceptable toxicity or PD. Toxicity was assessed by CTCAE v5.0, and the response was assessed by RECIST v1.1 in patients with measurable disease. Pre- and post-treatment tissue and blood were obtained for translational studies.

Results

Overall, 15 patients were treated; all were evaluable for toxicity, and 13 were evaluable for response. The median age was 56 years, and 40% had stage IV disease. Mutations included *BRCA1* ($n = 11$), *BRCA2* ($n = 2$), *PALB2* ($n = 1$), and *RAD51C* ($n = 1$). All patients were able to complete 2 cycles of NA olaparib. Thirteen (87%) underwent TRS immediately after olaparib, and 2 (13%) received CT prior to TRS; however, one of the two did not undergo TRS due to performance status. Of 14 patients who had undergone surgery, 100% had optimal TRS, 12 (86%) had a complete gross resection, and 1 patient (8%) had a pathologic complete response. Of 13 evaluable patients with measurable disease, 54% had a partial response (PR), and 46% had stable disease. No patients had PD on olaparib; 13 patients have completed all NA and adjuvant CT. Eleven (85%) have no evidence of disease (NED), 1 (8%) PR, and 1 (8%) PD. To date, only 2 patients have had progression after adjuvant therapy (one immediately at completion of adjuvant therapy and one at 3 months after therapy). Adverse events (AEs) during olaparib were as expected, with abdominal pain (47%), constipation (27%), anemia (20%), nausea (13%), and pain (13%) observed most commonly. The only grade 3/4 AEs reported were 3 patients (20%) with G3 anemia.

Conclusions

Neoadjuvant olaparib is feasible and has a good safety profile in patients with advanced-stage ovarian cancer with mutations in *BRCA1* or *2, PALB2,* or *RAD51C*. Even in those with stage IV disease, surgical outcomes are excellent after only two cycles of olaparib. These results justify further study to determine if PARPi can be given in lieu of chemotherapy in the NA setting.

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Mirvetuximab soravtansine (MIRV) in patients with platinum-resistant ovarian cancer with high folate receptor alpha (FRα) expression: Evaluation of sequence of therapy on anti-tumor activity in the SORAYA study (002)

Robert Coleman[a], Ana Oaknin[b], Sandro Pignata[c], Hannelore Denys[d], Nicoletta Colombo[e], Toon Van Gorp[f], Jason Konner[g], Margarita Romeo Marin[h], Philipp Harter[i], Conleth Murphy[j], Brooke Esteves[k], Michael Method[k], Domenica Lorusso[l], Ursula Matulonis[m]

[a]*US Oncology Research, The Woodlands, TX, United States;* [b]*Vall d'Hebron Institute of Oncology, Barcelona, Spain;* [c]*Istituto Nazionale Tumori di Napoli Fondazione G Pascale IRCCS, Napoli, Italy;* [d]*Ghent University Hospital, Gent, Belgium;* [e]*European Institute of Oncology IRCCS, Milan, Italy;* [f]*University Hospital Leuven, Leuven, Belgium;* [g]*Memorial Sloan Kettering Cancer Center, New York, NY, United States;* [h]*Institut Català d'Oncologia/Hospital Universitari Germans Trias i Pujol, Badalona, Spain;* [i]*Kliniken Essen-Mitte, Essen, Germany;* [j]*Bon Secours Hospital Cork and Cancer Trials, Cork, Ireland;* [k]*ImmunoGen Inc, Waltham, MA, United States;* [l]*Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome, Italy;* [m]*Dana-Farber Cancer Institute, Boston, MA, United States*

Objectives

SORAYA is a global single-arm phase III study evaluating Mirvetuximab soravtansine (MIRV) in patients (pts) with folate receptor alpha (FRα) high platinum-resistant ovarian cancer (PROC). MIRV is an antibody-drug conjugate comprising an FRα-binding antibody, cleavable linker, and maytansinoid DM4, a potent tubulin-targeting agent. In this study, MIRV demonstrated activity in a broad population of PROC, regardless of the number of prior lines of therapy or prior PARPi (Matulonis, SGO 2022). Here we described details of the clinical response to MIRV throughout the treatment journey, which are important for clinical decision making.

Methods

SORAYA enrolled PROC pts. with high FRα expression by immunohistochemistry (Roche FOLR1 Assay ≥75% of cells with PS2 + staining intensity) who had received 1–3 prior therapies, including required prior bevacizumab. Pts received intravenous MIRV at 6 mg/kg, adjusted ideal body weight, on day 1 of a 21-day cycle until disease progression or unacceptable toxicity. The primary endpoint was the confirmed objective response rate (ORR) per RECIST v1.1 by the investigator (INV), and the key secondary endpoint was the duration of response (DOR) safety and tolerability.

Results

A total of 106 pts. were enrolled; 51% had 3 prior lines, 48% had 1–2 prior lines of therapy, 37% of pts. had prior treatment in the PROC setting, and 100% of pts. received prior BEV, with 16% in the PROC setting. ORR by INV was 32.4% (95% CI: 23.6%–42.2%), including five complete responses, and DOR was 6.9 mos (95% CI: 5.6–9.7). The ORR in pts. who received prior treatment in the PROC setting was 28% (95% CI: 15.0%–44.9%) versus 35% (95% CI: 23.5%–47.6%) for pts. who received MIRV as the first treatment in the PROC setting. Pts who received BEV in the platinum-sensitive setting as maintenance or combination had an ORR of 34% (95% CI: 24.6%–44.5%) versus 18% (95% CI: 3.8%–43.4%) in pts. who received BEV in the PROC setting. The most common treatment-related adverse events (TRAE; all grade, grade 3–4) included blurred vision (41%, 6%), keratopathy (29%, 9%), and nausea (29%, 0%). TRAEs led to dose delays in 33%, dose reductions in 20%, and discontinuations in 9% of pts.; one patient discontinued treatment due to an ocular event. The tolerability profile of MIRV consists of low-grade, reversible ocular and GI events, managed with dose modifications and supportive care.

Conclusions

Treatment options for pts. with PROC are limited. MIRV is the first biomarker-directed therapy demonstrating antitumor activity in pts. with FRα high PROC. These results support the clinically meaningful impact MIRV has for pts. with FRα high PROC, irrespective of the sequence of prior therapies. Trial Information: NCT04209855.

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