None - Scientific Plenary

Interim post-progression data and updated survival in patients with newly diagnosed advanced ovarian cancer in ATHENA-MONO

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Objectives:

Rucaparib provided a sustained progression-free survival benefit in patients with newly diagnosed advanced ovarian cancer after first-line treatment. We reported interim secondary and exploratory post-progression endpoints with a 3-year follow-up (data cutoff March 9, 2023).

Methods:

Patients with stage III–IV high-grade ovarian cancer (OC) who had completed cytoreductive surgery (R0 permitted) and 4–8 cycles of first-line platinum-doublet (bevacizumab allowed with chemotherapy) with a response were randomized 4:1 to oral rucaparib 600 mg BID or placebo. The primary endpoint was PFS assessed by the investigator. Overall survival (OS) is a key secondary endpoint, and second progression-free survival (PFS2) is an exploratory endpoint. Time to first subsequent treatment (TFST), PFS2, and OS analyses were updated based on a regulatory agency request.

Results:

A total of 427 patients were randomized to rucaparib and 111 patients to placebo. Updated post-progression outcomes and overall survival are reported in Table 1. In the overall population, rucaparib treatment was associated with a longer TFST (HR: 0.52; 95% CI: 0.40–0.67) and PFS2 (HR: 0.84; 95% CI: 0.63–1.13) than among patients receiving placebo. Among patients with HRD tumors, the TFST (HR: 0.50; 95% CI: 0.33–0.76) was longer among patients receiving rucaparib than patients receiving placebo; the median PFS2 had not been reached in the rucaparib arm compared with 39.9 months in the placebo arm (HR: 0.75; 95% CI: 0.46–1.24). In the overall population, OS was not reached in the rucaparib arm compared to 46.2 months in the placebo arm (HR: 0.83; 95% CI: 0.58–1.17). OS was not reached in either arm (HR: 0.84; 95% CI: 0.44–1.58) for the HRD comparison.

Conclusions:

Interim data on post-progression outcomes continue to support the benefit of rucaparib maintenance treatment in newly diagnosed ovarian cancer patients following response to first-line chemotherapy. Final post-progression endpoints will be analyzed when the protocol-specified number of events is reached.

Table 1 **Interim Post-progression Outcomes in ATHENA-MONO**

	Events/N (%)	Median, mo		HR (95% CI)
		Rucaparib	Placebo	
PFS[a]				
HRD	111/234 (47.4)	28.7	11.3	0.47 (0.31 to 0.72)
ITT	305/538 (56.7)	20.2	9.2	0.52 (0.40 to 0.68)
TFST				
HRD	123/234 (52.6)	32.7	15.1	0.50 (0.33, 0.76)
ITT	326/538 (60.6)	23.3	12.1	0.52 (0.40, 0.67)
PFS2				
HRD	92/234 (38.9)	NR	39.9	0.75 (0.46, 1.24)
ITT	266/538 (48.4)	36.0	26.8	0.84 (0.63, 1.13)
OS				
HRD	58/234 (24.8)	NR	NR	0.84 (0.44, 1.58)
ITT	186/538 (34.6)	NR	46.2	0.83 (0.58, 1.17)

Visit cutoff March 09, 2023, unless otherwise noted.
HRs estimated with a Cox proportional hazards model.
[a]Visit cutoff March 23, 2022 (date of unblinding for primary efficacy analysis).
CI, confidence interval; HR, hazard ratio

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Patient-reported outcome results from phase III MIRASOL trial of mirvetuximab soravtansine versus investigator's choice of chemotherapy in FRα-positive, platinum-resistant ovarian cancer

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Objectives:

Mirvetuximab soravtansine (MIRV), an antibody-drug conjugate targeting folate receptor-alpha (FRα), is the first novel treatment to demonstrate a benefit in overall survival (OS) in platinum-resistant ovarian cancer (PROC) in a phase III trial. MIRASOL is the confirmatory, randomized, global phase III trial of MIRV versus standard of care chemotherapy among patients with PROC, which met its primary and key secondary endpoints with statistically significant results in progression-free survival (PFS; INV), objective response rate (ORR; INV), and OS. Here, we described the primary patient-reported outcomes (PROs) from the European Organization for Research and Treatment of Cancer (EORTC) QLQ-OV28 for patients enrolled in MIRASOL.

Methods:

A total of 453 FRα-positive PROC patients (Roche FOLR1 Assay) with 1-3 prior lines of therapy were randomized 1:1 to MIRV 6 mg/kg, adjusted ideal body weight, day 1 of a 21-day cycle or investigator's choice (IC) of paclitaxel, pegylated liposomal doxorubicin, or topotecan. The primary PRO assessment was defined as the number of patients achieving at least 15-point improvement at week 8/9 in the abdominal/GI symptom scale of EORTC QLQ-OV28. This primary PRO assessment was the last of 3 key secondary endpoints tested in hierarchical order (ORR, OS), both of which were met. As a pre-specified and exploratory analysis, the change from baseline on the OV28 was analyzed with mixed model repeated measures (MMRM). Post-hoc sensitivity and anchor-based meaningful change analyses using the Patient's Global Impression of Severity (PGIS) were completed.

Results:

A total of 21% of MIRV patients and 15.3% of IC Chemotherapy patients met the threshold of a 15-point improvement at week 8/9 (P=0.2611). At all time points, statistically significant differences favoring MIRV over IC on the abdominal/GI symptom scale occurred in mean change from baseline at week 8/9 with a difference of -5.0 (95% CI: -8.3 – -1.6; P= 0.0041) with continuous improvement at week 24 of -6.0 (-10.2 – -1.8; P= 0.0056). Anchor-based analyses demonstrated that an 11-point change in subscale score was clinically meaningful. Sensitivity analysis using the 11-point threshold showed that 29% of MIRV patients and 18% of IC Chemotherapy patients met the improvement threshold at week 8/9 (P=0.0318).