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Fuzuloparib (FZPL) monotherapy or in combination with apatinib (APA) as first-line (1L) maintenance therapy in advanced ovarian cancer (OC): Final analysis of the FZOCUS-1 trial

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Background

PARP inhibitor (PARPi) +/- antiangiogenic was approved as 1L maintenance therapy for advanced OC. However, the efficacy of PARPi + antiangiogenic compared to PARPi alone lacks evidence, especially in *BRCA*m/homologous recombination deficiency (HRD) pts. We conducted FZOCUS-1, a randomized, double-blind, placebo-controlled phase 3 trial, to assess the efficacy and safety of FZPL, a novel PARPi, with/without APA, a VEGFR-2 inhibitor, as 1L maintenance in OC. Here, we report the final analysis results, after ⊠40 mo of follow-up.

Methods

Patients (pts) with newly diagnosed OC after a response to 1L platinum-based chemotherapy were randomized 2:2:1 to receive FZPL (150 mg BID), FZPL (100 mg BID) + APA (375 mg QD), or matching placebo as maintenance therapy. The primary endpoint was PFS by BIRC per RECIST v1.1, with the primary objectives of testing FZPL and FZPL+APA vs placebo in the overall population and g*BRCA1/2*m subpopulation. As of Nov 1, 2024, 385 PFS events occurred and a final analysis was performed.

Results

674 pts were randomized to FZPL (n = 269), FZPL+APA (n = 269), and placebo (n = 136). FZPL and FZPL+APA significantly prolonged PFS by BIRC vs placebo, regardless of g*BRCA1/2* mutation status. Median PFS in g*BRCA1/2*m subgroup was 45.1 mo (HR 0.50, 95% CI 0.30-0.84) in FZPL+APA and 47.8 mo (HR 0.51, 95% CI 0.30-0.86) in FZPL, vs 16.6 mo in placebo. Notably, in HRD (including *BRCA*m) pts, FZPL+APA resulted in similar PFS as FZPL monotherapy, while in homologous recombination proficient (HRP) pts, FZPL+APA showed PFS benefit trend over FZPL (Table). OS data were not mature. Grade >=3 TRAEs (mostly hematologic) were reported by 48.7%, 45.7%, and 7.4% of pts in the FZPL+APA, FZPL, and placebo group.Table: 1063O

Efficacy summary

	FZPL+APA (N = 269)	FZPL (N = 269)	Placebo (N = 136)
Overall population			
mPFS, mo (95% CI)	26.9 (20.3, 36.6)	29.9 (22.1, 36.1)	11.1 (8.3, 16.6)
HR, vs placebo (95% CI)	0.57 (0.44, 0.75)	0.58 (0.44, 0.75)	

	FZPL+APA (N = 269)	FZPL (N = 269)	Placebo (N = 136)
HR, vs FZPL (95% CI)	1.04 (0.83, 1.32)		
HRD, including BRCAm (n=486)			
mPFS, mo (95% CI)	34.1 (22.4, 41.2)	35.8 (27.3, NR)	16.6 (8.3, 31.1)
HR, vs placebo (95% CI)	0.67 (0.48, 0.93)	0.62 (0.45, 0.87)	
HR, vs FZPL (95% CI)	1.09 (0.83, 1.44)		
HRP (n=118)			
mPFS, mo (95% CI)	16.6 (10.2, 22.1)	11.0 (6.5, 16.6)	5.5 (3.3, 13.8)
HR, vs placebo (95% CI)	0.51 (0.30, 0.86)	0.68 (0.40, 1.15)	
HR, vs FZPL (95% CI)	0.73 (0.45, 1.19)		

Conclusions

Adding antiangiogenic APA to FZPL did not enhance PFS among HRD pts in the 1L maintenance setting, while HRP pts showed PFS benefit trend with FZPL+APA compared to FZPL alone.

Clinical trial identification

NCT04229615.

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Disclosure

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