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Final overall survival (OS) results from the phase III PAOLA-1/ENGOT-ov25 trial evaluating maintenance olaparib (ola) plus bevacizumab (bev) in patients (pts) with newly diagnosed advanced ovarian cancer (AOC)

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Background

In the PAOLA-1/ENGOT-ov25 (NCT02477644) primary analysis, adding ola to maintenance bev after first-line (1L) platinum-based chemotherapy (PBC) + bev led to a significant progression-free survival (PFS) benefit in AOC (HR 0.59, 95% CI 0.49–0.72; *P*<0.001), particularly in pts with homologous recombination deficiency (HRD+; *BRCA1/2* mutation [BRCAm] and/or genomic instability; Ray-Coquard *et al*NEJM 2019). Here, we report the prespecified final OS analysis.

Methods

Pts with high-grade AOC, in response after PBC + bev, were randomized 2:1 to ola tablets (300 mg bid; up to 24 months [mo]) + bev (15 mg/kg q3w; 15 mo total) or placebo [pbo] + bev. OS (intent-to-treat [ITT] population) was a key secondary endpoint, with analysis planned for 3 years (y) after the primary analysis as part of hierarchical testing.

Results

537 pts were randomized to ola + bev and 269 to pbo + bev (median follow-up 61.7 and 61.9 mo, respectively; OS data maturity: 55.3%). Median OS in the ITT population was 56.5 mo with ola + bev vs 51.6 mo with pbo + bev (HR 0.92, 95% CI 0.76–1.12; *P*=0.4118; OS at 5 y, 47.3 vs 41.5%). In HRD+ pts, OS was prolonged with ola + bev (HR 0.62, 95% CI 0.45–0.85; OS at 5 y, 65.5 vs 48.4%), with benefit in HRD+ pts with or without a tumour BRCAm (tBRCAm; Table). No benefit was seen in HRD- pts (HR 1.19, 95% CI 0.88–1.63). Subsequent PARP inhibitor therapy was received by 105 (19.6%) ola + bev pts vs 123 (45.7%) pbo + bev pts. Myelodysplastic syndrome, acute myeloid leukaemia and aplastic anaemia incidence, and new primary malignancy incidence, was respectively: ola + bev, 9 pts [1.6%] and 22 pts [4.1%]; pbo + bev, 6 pts [2.2%]) and 8 pts [2.9%]).Table: 000LBA29

OS*	No. of events/no. of pts (%)		5 y OS rate, % (95% CI)		HR (95% CI)
	Ola + bev	Pbo + bev	Ola + bev	Pbo + bev	
ITT	288/537 (53.6)	158/269 (58.7)	47.3	41.5	0.92 (0.76–1.12)
HRD+§	93/255 (36.5)	69/132 (52.3)	65.5	48.4	0.62 (0.45–0.85)

OS*	No. of events/no. of pts (%)		5 y OS rate, % (95% CI)		HR (95% CI)
	Ola + bev	Pbo + bev	Ola + bev	Pbo + bev	
tBRCAm§	48/157 (30.6)	37/80 (46.3)	73.2	53.8	0.60 (0.39–0.93)
HRD+ excluding tBRCAm§	44/97 (45.4)	32/55 (58.2)	54.7	44.2	0.71 (0.45–1.13)
HRD-/unknown§	195/282 (69.1)	89/137 (65.0)	30.6	34.9	1.14 (0.89–1.48)
HRD-§	140/192 (72.9)	58/85 (68.2)	25.7	32.3	1.19 (0.88–1.63)

*tBRCAm status by central labs; HRD status by Myriad myChoice HRD Plus §Preplanned exploratory analysis

Conclusions

Despite a high proportion of pts in the control arm receiving a PARP inhibitor post-progression, ola + bev provided a clinically meaningful improvement in OS for 1L HRD+ pts with and without a tBRCAm, confirming ola + bev as standard of care in this setting.

Clinical trial identification

NCT02477644.

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Legal entity responsible for the study

ARCAGY Research.

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Disclosure

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