

LBA33

Maintenance olaparib rechallenge in patients (pts) with ovarian carcinoma (OC) previously treated with a PARP inhibitor (PARPi): Phase IIIb OReO/ENGOT Ov-38 trial

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Background

OReO/ENGOT Ov-38 (NCT03106987), a randomized, double-blind trial, is the first Phase III study to evaluate PARPi maintenance rechallenge.

Methods

Pts had non-mucinous platinum-sensitive relapsed (PSR) OC, one prior line of PARPi maintenance and were in response to their most recent platinum-based chemotherapy (PBC). Pts enrolled in BRCA1/2 mutated (BRCAm) (≥ 18 months [m] first-line [1L] or ≥ 12 m 2L+ prior PARPi exposure [PPE]) and non-BRCAm (≥ 12 m 1L or 6 m 2L+ PPE) cohorts were randomized (2:1; stratified by prior bevacizumab [yes vs no] and prior lines of PBC [≤ 3 vs ≥ 4]) to olaparib (O) tablets (300 mg bid [or 250 if 300 not previously tolerated]) or placebo (P) until progression. Primary endpoint was investigator-assessed progression-free survival (PFS; RECIST v1.1).

Results

112 pts were randomized in the BRCAm cohort (O: n=74; P: n=38); 108 in the non-BRCAm cohort (O: n=72; P: n=36). Pts were heavily pre-treated with 93% (BRCAm) and 86% (non-BRCAm) receiving ≥ 3 prior lines of any chemotherapy (see the table for other baseline characteristics). In the BRCAm cohort median PFS was 4.3 (O) vs 2.8 (P) m (hazard ratio [HR] 0.57; 95% CI 0.37–0.87; $P=0.022$); PFS rates (Kaplan–Meier method) were 35% vs 13% at 6 m and 19% vs 0% at 12 m. In the non-BRCAm cohort median PFS was 5.3 (O) vs 2.8 (P) m (HR 0.43; 95% CI 0.26–0.71; $P=0.002$); PFS rates were 30% vs 7% at 6 m and 14% vs 0% at 12 m. Subgroup analyses by HRD status in non-BRCAm pts will be presented. Grade ≥ 3 adverse events (AEs) occurred in 15% of O vs 5% of P BRCAm pts and 21% vs 8% of non-BRCAm pts. 3% BRCAm pts and 1% non-BRCAm pts discontinued O because of an AE vs no P pts. Table: LBA33

	BRCAm*		Non-BRCAm†	
	O	N=74	P	N=38
Median age, y	58.5	61.5	66.5	62.5
No. of prior lines of PBC, %				
≤ 3	64	61	65	67

	BRCaM*		Non-BRCaM†	
	O N=74	P N=38	O N=72	P N=36
≥4	36	39	35	33
Response to prior PBC, %				
Complete	20	34	26	31
Partial	78	66	74	69
Missing	1	0	0	0
Median duration of prior PARPi, m	21.2	18.3	12.6	12.4
HRD status, %				
HRD+‡	–	–	40	44
HRD–§	–	–	42	31

*Previously documented gBRCaM or sBRCaM by local testing. †gBRCaM negative by local testing; may include pts with undetected sBRCaM. ‡GIS ≥42 and/or a qualifying tBRCaM based on retrospective tumour testing (Myriad myChoice CDx); §GIS <42 and no qualifying tBRCaM. BRCaM, *BRCA1* and/or *BRCA2* mutation; g, germline; GIS, genomic instability score; HRD, homologous recombination deficiency; s, somatic; t, tumour

Conclusions

The OReO/ENGOT Ov-38 trial is the first to provide data on PARPi rechallenge in PSR OC pts. The trial met its primary PFS endpoint. Maintenance O provided a significant improvement in PFS vs P, irrespective of BRCaM status. A proportion of pts derived clinically relevant long-term benefit. Safety was consistent with the known profile of O.

Clinical trial identification

NCT03106987.

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Legal entity responsible for the study

AstraZeneca.

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Disclosure

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