IGCS meeting abstracts

Plenary Sessions

Plenary 1

IGCS19-0523

1 MILO/ENGOT-OV11: PHASE-3 STUDY OF BINIMETINIB VERSUS PHYSICIAN'S CHOICE CHEMOTHERAPY (PCC) IN RECURRENT OR PERSISTENT LOW-GRADE SEROUS CARCINOMAS OF THE OVARY, FALLOPIAN TUBE, OR PRIMARY PERITONEUM

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Objectives Low-grade serous ovarian carcinomas (LGSOC) have historically low chemotherapy responses. Alterations affecting the MAPK pathway, most commonly KRAS/BRAF, are present in 30–60% of LGSOC. A phase II study of the MEK inhibitor selumetinib showed promising response rate of 15% in LGSOC and binimetinib, a potent MEK1/2 inhibitor, has demonstrated activity across multiple cancers.

Methods MILO (MEK-Inhibitor in Low-grade Serous Ovarian Cancer)/ENGOT-ov11 was an open-label, 2:1-randomized study of binimetinib (45-mg BID) vs PCC in LGSOC. Eligible patients had recurrent or persistent measurable LGSOC following ≥ 1 prior platinum-based chemotherapy, ≤ 3 prior chemotherapy lines, and no prior MEK-or BRAF-inhibitor. The primary endpoint was progression-free survival (PFS) by blinded central review; additional assessments: overall survival (OS), overall response rate (ORR), duration of response (DOR), clinical-benefit rate, biomarkers, and safety. (NCT01849874).

Results 303 patients were randomized (201 binimetinib, 102 PCC). Median PFS was 9.1 months (95% CI: 7.3, 11.3) for binimetinib and 10.6 months (95% CI: 9.2, 14.5) for PCC (HR: 1.21 (0.79, 1.86); closed early for futility). Secondary efficacy endpoints were similar in the two groups: ORR 16%

(complete/partial responses [CR/PRs] = 32) vs 13% (CR/PRs = 13); median DOR 8.1 (range: 0.3–12.0+ months) vs 6.7 (0.3–9.7+ months); and median OS 25.3 vs 20.8 months, for binimetinib and PCC, respectively. Safety results were consistent with known safety profile of binimetinib; most common $\geq$ grade 3 events were blood CK increased (20%) and hypertension (20%). Post-hoc analysis suggests a possible association between KRAS mutation and response to binimetinib.

Conclusions Although MILO did not meet its primary endpoint, binimetinib showed activity in LGSOC across the efficacy endpoints evaluated. Chemotherapy responses were higher than predicted. Further evaluation is warranted.

IGCS19-0455

2 EXPLORATORY ANALYSIS OF POSTPROGRESSION AND PATIENT-CENTERED OUTCOMES IN ARIEL3: A PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED STUDY OF RUCAPARIB MAINTENANCE TREATMENT IN PATIENTS WITH RECURRENT OVARIAN CARCINOMA

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Objectives In ARIEL3, rucaparib maintenance treatment significantly improved progression-free survival (PFS) vs placebo. A prespecified exploratory analysis investigated postprogression outcomes. Additionally, a post hoc exploratory analysis investigated patient-centered outcomes during rucaparib maintenance treatment.

Methods Patients were randomized 2:1 to receive oral rucaparib (600 mg BID) or placebo. Postprogression endpoints included time to start of first subsequent therapy (TFST), time to second investigator-assessed PFS or death (PFS2), and time to start of second subsequent therapy (TSST); overall survival data are not yet mature. Patient-centered outcomes included quality-adjusted

Abstract 2 Table 1

	BRCA mutant		ITT	
	Rucaparib (n=130)	Placebo (n=66)	Rucaparib (n=375)	Placebo (n=189)
Prespecified exploratory analyses				
Investigator-assessed TFST				
Median, mo	19.0	7.2	12.5	7.4
HR (95% CI); P value	0.29 (0.20–0.42); P<0.0001		0.43 (0.35–0.53); P<0.0001	
Investigator-assessed PFS2				
Median, mo	26.1	17.9	21.1	16.5
HR (95% CI); P value	0.44 (0.29–0.69); P=0.0003		0.62 (0.48–0.79); P=0.0001	
Investigator-assessed TSST				
Median, mo	NR	19.4	22.2	18.6
HR (95% CI); P value	0.49 (0.31–0.78); P=0.0024		0.70 (0.54–0.91); P=0.0064	
Post hoc exploratory analyses				
QA-PFS ^a				
Mean, mo	15.28	5.92	12.02	5.74
Mean difference (95% CI)	9.37 (6.65–11.85)		6.28 (4.85–7.47)	
Q-TWiST ^b				
Mean, mo	16.42	6.70	13.32	6.44
Expected mean difference (95% CI)	9.73 (7.10–11.94)		6.88 (5.71–8.23)	

Visit cutoff April 15, 2017 (date of unblinding for primary efficacy analyses).

^aQA-PFS was calculated as PFS function × EQ-5D index score function.

^bQ-TWiST was calculated as (μTOX × TOX) + TWiST; TOX represents duration with grade ≥3 adverse events (AEs); TWiST represents progression-free duration without AEs or symptoms of progression (ie, PFS minus time with toxicities); μTOX represents the utility weight for the TOX state; observed utility data from EQ-5D was incorporated as a per-person utility weight (0.90 for the BRCA-mutant cohort and 0.89 for the ITT population).

HRs estimated with a Cox proportional hazards model.

CI, confidence interval; HR, hazard ratio; NR, not reached.

investigator-assessed PFS (QA-PFS) and quality-adjusted progression-free time without symptoms or toxicity (Q-TWiST). Analyses are presented for the predefined BRCA-mutant cohort and the intent-to-treat (ITT) population.

Results The visit cutoff dates for efficacy and safety were April 15, 2017, and December 31, 2017, respectively. Post-progression and patient-centered outcome data are given in the table 1. The most common treatment-emergent adverse events (TEAEs) of any grade (rucaparib vs placebo) were nausea (75.8% vs 36.5%), asthenia/fatigue (70.7% vs 44.4%), dysgeusia (39.8% vs 6.9%), and anemia/decreased hemoglobin (39.0% vs 5.3%). Any grade TEAEs of nausea, asthenia/fatigue, and anemia/decreased hemoglobin led to discontinuation in only 2.7%, 1.6%, and 2.7% of rucaparib-treated patients.

Conclusions Rucaparib significantly improved clinically meaningful postprogression outcomes vs placebo in the BRCA-mutant cohort and ITT population. The quality-adjusted analyses, which incorporated patient-centered perspectives during rucaparib maintenance treatment, confirmed the benefit of rucaparib vs placebo. The updated safety profile of rucaparib in ARIEL3 was consistent with prior reports.

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3 TRANSLATING ENDOMETRIAL MOLECULAR RISK STRATIFICATION TO ENDOMETRIOID OVARIAN CARCINOMA: A NOVEL APPLICATION OF PRECISION MEDICINE

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Objectives Endometrioid ovarian carcinoma (ENOC) is generally associated with a more favorable prognosis compared to other ovarian carcinoma histotypes. Nonetheless, patients are