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**

[1]R Grisham*, [2]B Monk J, [3]S Banerjee, [4]R Coleman L, [5]A Oza M, [6]M Oehler K, [7]E Kalbacher, [8]M Mirza Raza, [9]J del Campo M, [10]C Marth, [11]A Westermann, [12]S Pignata, [13]N Colombo, [14]D Cibula, [15]F Hilpert, [1]C Aghajanian, [1]E Drill, [16]V Sandor, [17]A Boyd P, [18]I Vergote. *[1]Memorial Sloan Kettering Cancer Center, Department of Medicine-Gynecologic Medical Oncology, New York, USA; [2]Arizona Oncology US Oncology Network-University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, USA; [3]Royal Marsden Hospital, Gynaecological Cancers at the Institute of Cancer Research, London, UK; [4]MD Anderson Cancer Center, Gynecologic Oncology and Reproductive Medicine, Houston, USA; [5]Princess Margaret Cancer Centre, Medical Oncology and Hematology, Toronto, Canada; [6]Royal Adelaide Hospital, Gynaecological Oncology, Adelaide- SA, Australia; [7]Centre Hospitalier Régional et Universitaire de Besançon, Oncology, de Besançon, France; [8]NSGO and Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; [9]Vall d'Hebron University Hospital, Medical Oncology, Barcelona, Spain; [10]Innsbruck Medical University, Obstetrics and Gynecology, Innsbruck, Austria; [11]Amsterdam University Medical Centers, Dutch Gynaecological Oncology Group DGOG, Amsterdam, The Netherlands; [12]Istituto Nazionale Tumori Fondazione Pascale IRCCS, Medical Oncology, Naples, Italy; [13]Università Milano-Bicocca Direttore Programma Ginecologia Oncologica Istituto Europeo Oncologia, Dipartimento Medicina e Chirurgia, Milan, Italy; [14]First Faculty of Medicine- Charles University in Prague and General University Hospital in Prague, Obstetrics And Gynecology, Prague, Czech Republic; [15]Onkologisches Therapiezentrum am Krankenhaus, Gynecology, Jerusalem, Israel; [16]Array BioPharma Inc, Array, Boulder, USA; [17]Array BioPharma Inc, Biometrics and Clinical Operations, Boulder, USA; [18]Belgium and Luxemburg Gynaecological Oncology Group, Gynaecologic Oncology, Leuven, Belgium*

10.1136/ijgc-2019-IGCS.1

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 ≥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**

[1]R Coleman*, [2]AM Oza, [3]D Lorusso, [4]C Aghajanian, [5]A Oaknin, [6]A Dean, [7]N Colombo, [8]JI Weberpals, [9]AR Clamp, [3]G Scambia, [10]A Leary, [11]RW Holloway, [12]M Amenedo Gancedo, [13]PC Fong, [14]JC Goh, [15]DM O'Malley, [16]S Goble, [17]T Cameron, [18]J Bedel, [19]JA Ledermann. *[1]The University of Texas MD Anderson Cancer Center, Department of Gynecologic Oncology and Reproductive Medicine, Houston- TX, USA; [2]Princess Margaret Cancer Centre- University Health Network, Division of Medical Oncology and Hematology, Toronto- ON, Canada; [3]Policlinico Universitario A. Gemelli IRCCS, Gynecologic Oncology Unit, Rome, Italy; [4]Memorial Sloan Kettering Cancer Center, Gynecologic Medical Oncology, New York- NY, USA; [5]Vall d'Hebron Institute of Oncology VHIO, Medical Oncology Department, Barcelona, Spain; [6]St John of God Subiaco Hospital, Department of Oncology, Subiaco- WA, Australia; [7]European Institute of Oncology and University of Milan-Bicocca, Gynecologic Cancer Program, Milan, Italy; [8]Ottawa Hospital Research Institute, Division of Gynecologic Oncology, Ottawa- ON, Canada; [9]The Christie NHS Foundation Trust and University of Manchester, Department of Medical Oncology, Manchester, UK; [10]Gustave Roussy Cancer Center- INSERM U981- and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens GINECO, Gynecological Unit, Villejuif, France; [11]Florida Hospital Cancer Institute, Department of Gynecologic Oncology, Orlando- FL, USA; [12]Oncology Center of Galicia, Medical Oncology Department, La Coruña, Spain; [13]Auckland City Hospital, Medical Oncology Department, Grafton- Auckland, New Zealand; [14]Royal Brisbane and Women's Hospital and University of Queensland, Department of Oncology- Cancer Care Services, Herston and St Lucia- QLD, Australia; [15]The Ohio State University- James Cancer Center, Clinical Research Gynecologic Oncology, Columbus- OH, USA; [16]Clovis Oncology-Inc., Biostatistics, Boulder- CO, USA; [17]Clovis Oncology UK Ltd., Clinical Science, Cambridge, UK; [18]Clovis Oncology Switzerland GmBH, Pricing and Market Access – Europe, Zurich, Switzerland; [19]UCL Cancer Institute- University College London and UCL Hospitals, Department of Oncology, London, UK*

10.1136/ijgc-2019-IGCS.2

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).
[a]QA-PFS was calculated as PFS function × EQ-5D index score function.
[b]Q-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.

IGCS19-0575

3

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

[1]P Krämer*, [2]A Talhouk, [3]T Bosse, [4]F Heitz, [5]N Singh, [6]F Kommoss, [1]B Krämer, [1]A Hartkopf, [1]S Brucker, [2]J McAlpine, [7]M Koebel, [2]M Anglesio, [1]S Kommoss. *[1]Tuebingen University Hospital, Department of Women's Health, Tuebingen, Germany; [2]University of British Columbia, Department of Obstetrics and Gynecology, Vancouver, Canada; [3]Leiden University Medical Centre, Department of Pathology, Leiden, The Netherlands; [4]Kliniken Essen Mitte, Department of Gynecology and Gynecologic Oncology, Essen, Germany; [5]Barts Health National Health Service Trust, Department of Pathology, London, UK; [6]Heidelberg University Hospital, Institute of Pathology, Heidelberg, Germany; [7]University of Calgary and Calgary Laboratory Services, Department of Pathology and Laboratory Medicine, Calgary, Canada*

10.1136/ijgc-2019-IGCS.3

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