patients received PARPi as maintenance after maintenance therapy. The median PFS (mPFS) was 10.6 months (95% confidence interval [CI], 7.1–12.0) with first PARPi (PARPi1) and 8.6 months (95% CI, 5.3–13.0) with PARPi retreatment (PARPi2). 32.1% (18/56) patients were BRCA1/2 mutated, the PFS were not significantly different from BRCA wild-type or unknown patients (BRCAm vs. BRCAwt or unknown, HR=0.997 [95%CI: 0.480–2.072], P=0.9935). 87.5% (39/56) of patients switched to other PARPi when rechallenging. Patients switched to other PARPi rechallenging had numerically longer mPFS compared with those didn't switch (mPFS: 8.6 vs. 7.7 months; HR=0.820 [95%CI: 0.394–1.707], P=0.5958). Overall, 4.3% (3/70) discontinued PARPi2 due to adverse events, most commonly due to hematologic adverse events.

Abstract #509 Table 1 Patients' characteristics

Patients' Characteristic	Total (N = 70) N (%)
Age, years	
Median (Q1-Q3)	58 (53-63.75)
***BRCA* mutation status, *n* (%)**	
Wild-type or unknown	43 (61.4)
BRCA1/2 mutated	27 (38.6)
Histology, *n* (%)	
High-grade serous carcinoma	68 (97.1)
Endometrioid	1 (1.4)
Others	1 (1.4)
Name of PARPi1	
Olaparib	50 (71.4)
Niraparib	20 (28.6)
Treatment phase of PARPi1	
Neoadjuvant	1 (1.4)
Maintenance therapy	67 (95.7)
Salvage treatment	2 (2.9)
PARPi1 treatment outcomes	
Disease progression	61 (87.2)
Adverse events	5 (7.1)
Others	4 (5.7)
Switch to other PARPi or not after PARPi1	
Switch	48 (68.6)
No switch	22 (31.4)
Treatment phase of PARPi2	
Maintenance therapy	57 (81.4)
Salvage treatment	13 (18.6)
Lines of PARPi2	
1	1 (1.4)
2	18 (25.7)
3	30 (42.9)
≥4	21 (30.0)
Treatment pattern of PARPi rechallenge	
Maintenance after maintenance	56 (80.0)
Treatment after maintenance	11 (15.7)
Treatment after treatment	2 (2.9)
Maintenance after neoadjuvant	1 (1.4)
Name of PARPi2	
Olaparib	23 (32.8)
Niraparib	42 (60.0)
Fuzoloparib	3 (4.3)
Pamiparib	2 (2.9)
PARPi2 treatment outcomes	
Still on treatment	24 (34.3)
Disease progression	43 (61.4)
Adverse events	3 (4.3)

Conclusion Our study is the first multicenter real-world study to evaluate the rechallenge of PARPi in ovarian cancerpatients in China. There is a pressing need to identify biomarkers except BRCA to select appropriate patients for PARPi rechallenge.

Disclosures The authors have no potential conflict of interest to report.

#523 INITIAL EFFICACY AND SAFETY RESULTS FROM ENGOT-OV60/GOG-3052/RAMP 201: A PHASE 2 STUDY OF AVUTOMETINIB (VS-6766) ± DEFACTINIB IN RECURRENT LOW-GRADE SEROUS OVARIAN CANCER (LGSOC)

[1]Susana N Banerjee*, [2]Kari L Ring, [3]Els Van Niewenhuysen, [4]Michel Fabbro, [5]Carol Aghajanian, [6]Ana Oaknin, [7]Nicoletta Colombo, [8]Alessandro D Santin, [9]Andrew R Clamp, [10]Kathleen N Moore, [10]Peter G Rose, [11]O'Malley David M, [12]Hye Sook Chon, [13]Erin A Salinas, [14]Emily N Prendergast, [15]Stephanie Lustgarten, [16]Manuel Rodrigues, [17]Christine Gennigens, [18]Bradley J Monk, [5]Rachel N Grisham. *[1]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, National Cancer Research Institute (NCRI), London, UK; [2]Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, University of Virginia, Charlottesville, USA; [3]University Hospitals Leuven, Leuven, Belgium; [4]ICM Val d'Aurelle Parc Euromedecine, Oncologie médicale, Montpellier, GINECO, Paris, France; [5]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York City, USA; [6]Gynaecologic Cancer Programme;Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [7]Department of Medicine and Surgery, University of Milan-Bicocca, Italy and Gynecologic Oncology Program, European Institute of Oncology IRCCS, Milan, Italy; [8]Department of Obstetrics, Gynecology, and Reproductive Sciences, Division of Gynecologic Oncology, Yale School of Medicine, New Haven, USA; [9]Medical Oncology, The Christie NHS Foundation Trust and University of Manchester, Manchester, UK; [10]Stephenson Oklahoma Cancer Center at the University of Oklahoma Health Sciences Center, Oklahoma City, USA; [11]The Ohio State University, James Comprehensive Cancer Center, Columbus, USA; [12]Department of Gynecologic Oncology, H. Lee Moffitt Cancer Center, Tampa, USA; [13]Compass Oncology, Portland, USA; [14]Gynecologic Oncology, Minnesota Oncology and Metro-Minnesota Community Oncology Research Consortium, Minneapolis, USA; [15]Verastem Inc., Needham, USA; [16]Department of Medical Oncology, INSERM U830, Institut Curie, Paris, France; [17]Department of Medical Oncology, Centre Hospitalier Universitaire de Liège, Liège, Belgium; [18]HonorHealth, University of Arizona, Creighton University, Phoenix, USA*

10.1136/ijgc-2023-ESGO.29

Introduction/Background LGSOC, a RAS/MAPK driven cancer, constitutes ≤10% of ovarian cancer, with no FDA-approved treatments. Avutometinib is a novel small molecule RAF/MEK clamp. Focal adhesion kinase (FAK) activation is a resistance mechanism to RAF/MEK inhibition; defactinib, a small molecule FAK inhibitor, has shown synergistic antitumor activity with avutometinib. Avutometinib + defactinib demonstrated a high confirmed and durable response rate (objective response rate [ORR]=46%) in recurrent LGSOC.

Methodology A phase 2, multicenter, randomized study evaluated avutometinib ± defactinib in patients with KRAS mutant (mt) and KRAS wild-type (wt) recurrent LGSOC to identify an optimal regimen based on confirmed ORR by blinded independent central review (Part A) and determine efficacy (Part B) (NCT04625270). Patients were randomized to avutometinib (mono) or avutometinib + defactinib (combo). Key inclusion criteria: histologically-confirmed recurrent LGSOC, known KRAS status, prior platinum chemotherapy. Unlimited prior therapies, including MEK inhibitor, were permitted. Efficacy results from Part A (evaluable patients, N=64) and safety data from all patients (N=151) are presented (April 2023 data cutoff).

Results In Part A, median number of prior regimens was 3 for mono, 4 for combo. A 45% confirmed ORR was observed

for combo (60% KRAS mt, 29% KRAS wt) and 10% for mono (13% KRAS mt, 6% KRAS wt). Three of 4 patients previously treated with MEK inhibitor showed confirmed partial response on combo arm. Median time to response: 7.3 months (mono) and 5.5 months (combo). Most treatment-related adverse events (AEs) for combo (n=81) were grade 1–2, with a low proportion of dose reductions (17%) and discontinuations due to AEs (12.3%) in the combo arm.

Conclusion Interim data support avutometinib + defactinib as an active go-forward regimen in heavily-pretreated recurrent LGSOC, regardless of KRAS status. No new safety signals were observed; most AEs were mild to moderate.

#528 EFFICACY OF SUBSEQUENT CHEMOTHERAPY FOLLOWED BY PARP INHIBITOR MAINTENANCE IN PATIENTS WITH ADVANCED OVARIAN CANCER IN THE PHASE III PAOLA-1/ENGOT-OV25 TRIAL

[1]Christian Marth*, [2]Marie-Ange Mouret-Reynier, [3]Domenica Lorusso, [4]Claire Cropet, [5]Philipp Harter, [6]Eva Guerra, [7]Takashi Matsumoto, [8]Ignace Vergote, [9]Nicoletta Colombo, [10]Johanna Mäenpää, [11]Coriolan Lebreton, [12,13]Nikolaus De Gregorio, [14]Anna Maria Mosconi, [15]María Jesús Rubio, [16]Hugues Bourgeois, [17]Peter A Fasching, [18]Anne-Claire Hardy-Bessard, [19]Dominik Denschlag, [20]Eric Pujade-Lauraine, [4]Isabelle Ray-Coquard.
[1]Department of Obstetrics and Gynaecology, Medical University of Innsbruck, and AGO-Austria, Innsbruck, Austria; [2]Centre Jean Perrin, and GINECO, Clermont-Ferrand, France; [3]Istituto Tumori Milano + Fondazione Policlinico Universitario A. Gemelli IRCCS and Catholic University of Sacred Heart, and MITO, Rome, Italy; [4]Centre Léon BERARD, and GINECO, Lyon, France; [5]Kliniken Essen-Mitte, and AGO, Essen, Germany; [6]Hospital Universitario Ramón y Cajal, and GEICO, Madrid, Spain; [7]Ehime University Hospital, and GOTIC, Toon, Japan; [8]University Hospital Leuven, Leuven Cancer Institute, and BGOG, Leuven, Belgium; [9]University of Milan-Bicocca and European Institute of Oncology IRCCS, and MANGO, Milan, Italy; [10]Tampere University Hospital, and NSGO, Tampere, Finland; [11]Institut Bergonié, and GINECO, Bordeaux, France; [12]Universitätsklinikum Ulm, Klinik für Frauenheilkunde und Geburtshilfe, and AGO, Ulm, Germany; [13]SLK-Kliniken Heilbronn GmbH, Frauenklinik, and AGO, Heilbronn, Germany; [14]S.C. di Oncologia Medica Osp. S. Maria della Misericordia – AO di Perugia, and MITO, Perugia, Italy; [15]Hospital Reina Sofia, and GEICO, Cordoba, Spain; [16]Centre Jean Bernard – Clinique Victor Hugo, and GINECO, Le Mans, France; [17]Universitätsfrauenklinik Erlangen, and AGO, Erlangen, Germany; [18]Centre CARIO – HPCA, and GINECO, Plérin Sur Mer, France; [19]Hochtaunuskliniken, and AGO, Bad Homburg, Germany; [20]ARCAGY Research, and GINECO, Paris, France

10.1136/ijgc-2023-ESGO.30

Introduction/Background In PAOLA-1/ENGOT-ov25 (NCT02477644), maintenance PARP inhibitor (PARPi) olaparib +bevacizumab improved progression-free survival (PFS) in patients with homologous recombination-deficient (HRD+) advanced ovarian cancer (Ray-Coquard. NEJM 2019;381:2416–28). Post-hoc analysis showed the efficacy of subsequent chemotherapy at relapse was reduced in patients who progressed during versus after olaparib treatment (Harter. Presented at ASCO 2023).

In the OReO/ENGOT-ov38 trial (NCT03106987), olaparib rechallenge conferred a modest but statistically significant PFS benefit in patients with platinum-sensitive ovarian cancer (Pujade-Lauraine. Ann Oncol 2021;32:S1308–9), the majority of whom had received initial PARPi therapy in the relapsed setting and, therefore, were most likely to have progressed under PARPi maintenance. We explored PARPi rechallenge in patients who received platinum-based combination therapy (PBC) followed by PARPi (PBC>PARPi) as first subsequent therapy (FST) after progression on first-line treatment in PAOLA-1.

Methodology To explore the efficacy of PBC>PARPi, median time from FST to second subsequent therapy (SST) was analysed post-hoc by timing of progression (during/after olaparib) and tumour HRD status.

Results 544 patients progressed and received subsequent chemotherapy. Time from FST to SST was longer in patients receiving PBC>PARPi (n=159) as FST than in patients receiving PBC without PARPi maintenance (n=293) and was shortest in patients who progressed during olaparib (table 1).

Myelodysplastic syndrome, acute myeloid leukaemia or aplastic anaemia occurred in 3/82 (3.7%) patients in the control arm and no patients who received olaparib. No unexpected toxicity was observed.

Conclusion In this post-hoc exploratory analysis of PAOLA-1, subsequent PBC>PARPi rechallenge led to better outcomes than PBC alone in patients who received olaparib+bevacizumab. Efficacy appeared to depend on whether progression occurred during or after olaparib treatment. Results build on observations from OReO that PARPi rechallenge could be considered for patients responding to PBC, but are limited by small patient numbers and loss of randomisation, and need to be confirmed in a larger randomised study.

Abstract #528 Table 1 Time from FST to SST, months (median)

FST	Progression during olaparib	Progression after olaparib	Control arm
All PBC	**7.3 (5.7–8.4)** *n=157*	**12.0 (10.3–14.8)** *n=132*	**12.9 (11.8–14.1)** *n=162*
PBC without PARPi maintenance*	**6.0 (4.6–7.3)** *n=135*	**8.1 (5.9–10.2)** *n=77*	**9.9 (7.9–11.7)** *n=80*
Patients with CR/PR/SD after PBC without PARPi maintenance	8.6 (8.1–9.7) *n=64*	10.6 (9.7–13.4) *n=44*	11.8 (10.0–13.1) *n=56*
PBC>PARPi	**13.0 (10.2–14.7)** *n=22*	**18.5 (15.2–21.3)** *n=55*	**17.4 (14.0–20.5)** *n=82*
HRD+	11.7 (8.5–NE) *n=4*	18.8 (15.0–NE) *n=29*	23.3 (17.4–34.2) *n=45*
HRD–	13.7 (10.2–23.6) *n=14*	16.7 (13.0–NE) *n=18*	13.2 (11.5–18.6) *n=23*

*1/293 patients not treated. Kaplan–Meier estimates; median months with 95% confidence intervals. HRD+ defined as tumour *BRCA* mutation and/or genomic instability score ≥42 (Myriad MyChoice HRD Plus assay). *BRCA*, breast cancer gene; CR, complete response; NE, not estimable; PR, partial response; SD, stable disease.

Disclosures This work was supported by ARCAGY Research, AstraZeneca, Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, and F. Hoffmann-La Roche.

#631 GLOBAL VARIATIONS IN THE MANAGEMENT OF LOW-GRADE SEROUS CARCINOMA OF THE OVARY

[1]Biswajit Dash*, [2]Geetu Bhandoria, [1]Seema Gulia, [3]Akshay Patil, [1]Amita Maheshwari. *[1]Tata Memorial Centre, Mumbai, India; [2]Command Hospital, Kolkata, India; [3]Royal Papworth NHS Foundation Trust, Cambridge, UK*

10.1136/ijgc-2023-ESGO.31

Introduction/Background Low-grade serous carcinoma (LGSOC) of the ovary is a rare entity. There are significant regional and individual differences in management. This study is unique and possibly the first survey to focus on global variations in management.