Introduction Avutometinib is a novel small molecule RAF/MEK clamp. 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 45% ORR and a mild to moderate, manageable/reversible safety profile in heavily pretreated (mLoT=4) recurrent LGSOC (KRAS mt + wt) (ENGOT-ov60/GOG-3052/RAMP 201, NCT04625270).

Methods This post-hoc analysis of the phase 2 ENGOT-ov60/GOG-3052/RAMP 201 study in recurrent LGSOC (06Apr2023 data cutoff) was performed to assess efficacy (Part A; confirmed ORR via blinded independent central review) and safety (all treated patients) in the context of 1) lines of prior systemic therapy (1–3 LoT, ≥4 LoT) and 2) best response to most recent prior treatment in the metastatic/recurrent setting (PR/CR, no PR/CR; as assessed by treating investigator).

Results In the combination arm, similar ORRs were observed in patients that were treated with 1–3 (5/11, 45.5%) and ≥4 LoT (8/18, 44.4%) (table 1). Prior to enrollment in RAMP 201, only 2/23 (8.7%) patients responded to their last prior treatment, whereas the combination of avutometinib + defactinib yielded an ORR of 43.5% (10/23) in this subgroup (table 2). The safety profiles of avutometinib + defactinib were similar in the less and more heavily pretreated subgroups, and both analyses were consistent with previously reported safety data. The majority of TRAEs were mild to moderate, manageable/reversible.

Conclusion/Implications Avutometinib + defactinib demonstrated robust efficacy (ORR) in recurrent LGSOC irrespective of the number of prior therapies, and for most of which, response to previous therapy was poor.

PO005LBA/#1579

A RANDOMIZED, PHASE II/III STUDY OF PEGYLATED-LIPOSOMAL-DOXORUBICIN AND ATEZOLIZUMAB (IND #134427) VERSUS PEGYLATED-LIPOSOMAL-DOXORUBICIN, BEVACIZUMAB AND ATEZOLIZUMAB VERSUS PEGYLATED-LIPOSOMAL-DOXORUBICIN AND BEVACIZUMAB IN PLATINUM-RESISTANT OVARIAN CANCER (NRG-GY009)

[1]Roisin O'Cearbhaill*, [2]Michael Sill, [3]Hoa Duong, [4]Steven Waggoner, [1]Rachel Grisham, [5]Floor Backes, [6]Robert Mannel, [7]Janos Tanyi, [8]Matthew Powell, [9]Cara Mathews, [10]Sharad Ghamande, [11]Leah Mcnally, [12]Alexander Olawaiye, [13]David Bender, [14]Linda Duska, [15]Heather Lankes, [16]Dmitriy Zamarin, [17]Russell Schilder, [18]Michael Bookman, [1]Carol Aghajanian. *[1]Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, Medicine, New York, USA; [2]NRG Oncology Statistics and Data Management Center, Biostatistics and Bioinformatics Department, Buffalo, USA; [3]Kaiser-Permanente Sacramento, Hematology/oncology, Sacramento, USA; [4]CWRU Case Comprehensive Cancer Center, Gynecologic Oncology, Cleveland, USA; [5]Ohio State University Comprehensive Cancer Center, Gynecologic Oncology, Ohio, USA; [6]University of Oklahoma Health Sciences Center, Obstetrics and Gynecology, Oklahoma, USA; [7]University of Pennsylvania/Abramson Cancer Center, Obstetrics and Gynecology, Philadelphia, USA; [8]Washington University, Gynecologic Oncology, St. Louis, USA; [9]Women and Infants Hospital, Obstetrics and Gynecology, Providence, USA; [10]Georgia Cares Minority Underserved NCORP, Gynecologic Oncology, Augusta, USA; [11]Duke Cancer Institute, Gynecologic Oncology, Durham, USA; [12]UPMC Hillman Cancer Center, Gynecologic Oncology, Pittsburgh, USA; [13]University of Iowa, Obstetrics and Gynecology, Iowa City, USA; [14]University of Virginia Cancer Center, Gynecologic Oncology, Charlottesville, USA; [15]NRG Oncology Biospecimen Bank-Columbus, Translational Science Operations, Columbus, USA; [16]Icahn School of Medicine at Mount Sinai, Hematology/oncology, New York, USA; [17]Thomas Jefferson University, Gynecologic Medical Oncology, Philadelphia, USA; [18]Kaiser Permanente Northern California, Gynecologic Oncology, San Francisco, USA*

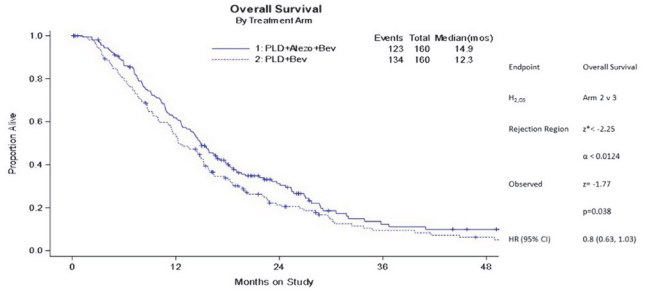
10.1136/ijgc-2023-IGCS.5

Introduction In this multicentre randomized, phase II/III trial, we sought to examine if the 1) combination of anti-programmed death ligand 1 (PD-L1) monoclonal antibody atezolizumab (ATEZO) with pegylated-liposomal- doxorubicin (PLD) [Arm 1] and/or 2) addition of ATEZO to PLD and bevacizumab (BEV) [Arm 2] result in an improvement in survival for patients with platinum resistant ovarian cancer (PROC) compared to the standard PLD/BEV [Arm 3].

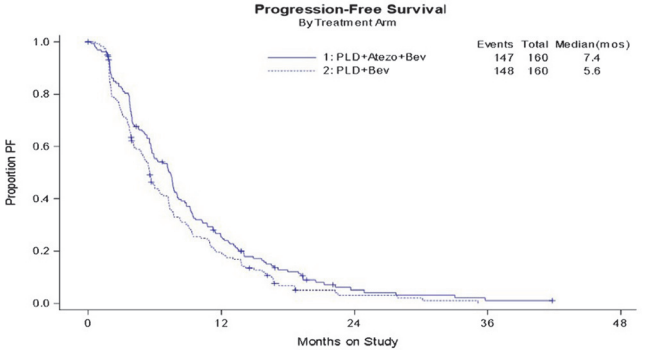
Methods Patients were randomly assigned 1:1:1 to PLD/ATEZO, PLD/BEV/ATEZO or PLD/BEV (IV PLD 40 mg/m^2 q4weeks; BEV 10 mg/kg q2weeks; ATEZO 800 mg q2weeks). Key eligibility: 1–2 prior lines of therapy (no PLD), ECOG 0–2, and RECIST measurable/evaluable PROC. No stratification by PD-L1 status. The phase II primary endpoint was PFS. The phase III coprimary endpoints were PFS/OS.

Results From 05/2017–10/2021 444 patients with PROC were enrolled. The median age was 63 yrs (35–86). All had received prior chemotherapy; 434 (97.7%) prior surgery and 9 (2%) prior biological therapy. At the phase III interim analysis Arm 1 (PLD/ATEZO) was discontinued for futility. The phase III OS/PFS analysis included accruals to Arms 2 (PLD/BEV/ATEZO) and 3 (PLD/BEV) from all phases. With median follow-up of 47 months, median PFS was 7.4 months and 5.6 months (HR 0.79 with 99.99% 1-sided CI 0.0–1.21), and median OS was 14.9 months and 12.3 months (HR 0.80; 98.78% 1-sided CI 0.00–1.06; 1-sided p=0.038) for Arms 2 and 3, respectively. Adverse events were as expected.

Conclusion/Implications The addition of ATEZO to PLD/BEV did not result in a statistically significant longer OS than PLD/BEV in PROC. Subset analysis are planned to evaluate survival outcomes with high PD-L1 expression (NRG-GY009/NCT02839707).



Abstract PO005LBA/#1579 Figure 1



Abstract PO005LBA/#1579 Figure 2