Oral Plenary

Plenary I

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1 AVELUMAB IN COMBINATION WITH AND/OR FOLLOWING CHEMOTHERAPY VS CHEMOTHERAPY IN TREATMENT-NAIVE PATIENTS WITH OVARIAN CANCER: BIOMARKER ANALYSES FROM THE PHASE 3 JAVELIN OVARIAN 100 TRIAL

[1]J Ledermann*, [2]N Colombo, [3]A Oza, [4]K Fujiwara, [5]MJ Birrer, [6]L Randall, [7]E Poddubskaya, [8]G Scambia, [9]YV Shparyk, [10]MC Lim, [11]MC Lim, [12]J Sohn, [13]K Yonemori, [14]RA Stewart, [14]X Zhang, [14]J Perkins Smith, [15]C Linn, [16]BJ Monk. *[1]UCL Cancer Institute and UCL Hospitals NHS Foundation Trust, UK; [2]University of Milan-Bicocca and Istituto Europeo di Oncologia, IRCCS, Italy; [3]Princess Margaret Cancer Centre, Canada; [4]Saitama Medical University International Medical Center, Japan; [5]O'Neal Comprehensive Cancer Center, The University of Alabama at Birmingham, USA; [6]Virginia Commonwealth University, Massey Cancer Center, USA; [7]I.M. Sechenov First Moscow State Medical University and Clinical Center Vitamed, Russia; [8]Gynecologic Oncology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Italy; [9]Lviv State Oncological Regional Treatment and Diagnostic Center, Ukraine; [10]Research Institute and Hospital, National Cancer Center, South Korea; [11]Arizona Oncology Associates, PC – HAL, USA; [12]Severance Hospital, Yonsei University Health System, South Korea; [13]Department of Breast and Medical Oncology, National Cancer Center Hospital, Japan; [14]Pfizer Oncology, Pfizer Inc, USA; [15]Global Product Development, Pfizer Inc, Taiwan; [16]Arizona Oncology (US Oncology Network), University of Arizona and Creighton University, USA*

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Introduction In the JAVELIN Ovarian 100 trial (NCT02718417), avelumab (anti–PD-L1) in combination with chemotherapy or as maintenance did not improve progression-free survival (PFS) vs chemotherapy followed by observation in treatment-naive patients with epithelial ovarian cancer (EOC; hazard ratios [95% CI] were 1.14 [0.832, 1.565] and 1.43 [1.051, 1.946], respectively). The trial was terminated when prespecified futility boundaries were crossed at the interim analysis, and study treatment was subsequently discontinued. Here we report biomarker analyses.

Methods Women with stage III-IV EOC (post debulking/cytoreductive surgery or candidates for neoadjuvant chemotherapy) were randomized 1:1:1 to receive carboplatin/paclitaxel chemotherapy (6 cycles) followed by avelumab every 2 weeks as maintenance (CTx→Ave), chemotherapy + avelumab (10 mg/kg every 3 weeks) followed by avelumab every 2 weeks as maintenance (CTx+Ave→Ave), or chemotherapy followed by observation (CTx→O; control arm). The primary endpoint was PFS by blinded independent central review per RECIST version 1.1. Pretreatment tumor tissue was analyzed by immunohistochemistry (CD8 and PD-L1) and next-generation DNA and RNA sequencing.

Results 998 patients were randomized. Subgroup analyses based on PD-L1, CD8, and germline BRCA1/2 status did not identify subsets with clear PFS benefit in either avelumab arm vs control (table 1). Whole-exome and RNA sequencing analyses will be presented.

Conclusions In the JAVELIN Ovarian 100 trial, PD-L1, CD8, and germline BRCA1/2 status did not predict differential clinical benefit with the addition of avelumab to chemotherapy in treatment-naive patients with EOC.

Abstract 1 Table 1

PFS in biomarker-defined subgroups			
	CTx→Ave (N=332)	CTx+Ave→Ave (N=331)	CTx→O (N=335)
PD-L1+ subgroup	**N=158**	**N=160**	**N=169**
Median, months (95% CI)	NE (12.9, NE)	NE (16.4, NE)	NE (17.5, NE)
HR vs control (95% CI)	1.23 (0.790, 1.924)	0.98 (0.618, 1.541)	–
PD-L1– subgroup	**N=112**	**N=103**	**N=111**
Median, months (95% CI)	16.8 (12.8, NE)	13.9 (12.5, 18.1)	NE (12.6, NE)
HR vs control (95% CI)	1.02 (0.607, 1.704)	1.36 (0.819, 2.269)	–
CD8+ subgroup	**N=107**	**N=107**	**N=118**
Median, months (95% CI)	14.3 (12.8, NE)	NE (15.0, NE)	NE (18.2, NE)
HR vs control (95% CI)	1.64 (0.946, 2.850)	1.25 (0.705, 2.218)	–
CD8– subgroup	**N=143**	**N=143**	**N=139**
Median, months (95% CI)	NE (15.2, NE)	15.0 (13.2, NE)	NE (14.4, NE)
HR vs control (95% CI)	0.94 (0.594, 1.498)	1.11 (0.708, 1.740)	–
***BRCA1/2*-mutated subgroup**	**N=31**	**N=32**	**N=30**
Median, months (95% CI)	NE (18.0, NE)	NE (16.4, NE)	NE (15.3, NE)
HR vs control (95% CI)	1.98 (0.470, 8.315)	2.51 (0.570, 11.09)	–
***BRCA1/2*–wild-type subgroup**	**N=277**	**N=289**	**N=281**
Median, months (95% CI)	15.7 (12.9, NE)	18.1 (14.6, NE)	NE (17.5, NE)
HR vs control (95% CI)	1.32 (0.956, 1.835)	1.14 (0.823, 1.593)	–

HR, hazard ratio; NE, not estimable
Because the trial was terminated at the interim analysis, the duration of available follow-up for PFS was not long enough for the median durations to be reached

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2 EFFICACY AND SAFETY OF LENVATINIB PLUS PEMBROLIZUMAB IN PATIENTS WITH PREVIOUSLY TREATED OVARIAN CANCER IN THE MULTICOHORT PHASE 2 LEAP-005 STUDY

[1]A González-Martín*, [2]H Chung, [3]E Saada-Bouzid, [4]E Yanez, [5]H Senellart, [6]PA Cassier, [7]B Basu, [8]R Ghori, [9]P Kubiak, [10]A Smith, [8]K Norwood, [11]Z Lwin. *[1]Clínica Universidad de Navarra, Spain; [2]Yonsei Cancer Center, Yonsei University College of Medicine, South Korea; [3]Department of Medical Oncology, Centre de Lutte Contre le Cancer Antoine Lacassagne, France; [4]Oncology-Hematology Unit, Department of Internal Medicine, School of Medicine, Universidad de la Frontera, Chile; [5]Institut de Cancérologie de l'Ouest, Centre René Gauducheau ICO, France; [6]Department of Medical Oncology, Centre Léon Bérard, France; [7]Department of Oncology, University of Cambridge, UK; [8]Merck and Co., Inc., USA; [9]Eisai Inc., USA; [10]Eisai Ltd., UK; [11]Royal Brisbane and Women's Hospital, Australia*

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Introduction Lenvatinib, an antiangiogenic multiple receptor tyrosine kinase inhibitor, plus pembrolizumab, a programmed death-1 immune checkpoint inhibitor, demonstrated promising clinical benefit in a previous phase Ib/II trial across several cancer types (ClinicalTrials.gov, NCT02501096). We assessed clinical outcomes with lenvatinib plus pembrolizumab in patients with ovarian cancer in the ongoing, open-label, multicohort, phase 2 LEAP-005 study (ClinicalTrials.gov, NCT03797326).

Methods Female patients aged ≥18 years with histologically/cytologically confirmed, metastatic/unresectable ovarian cancer, measurable disease per RECIST v1.1, ECOG performance status 0/1, and 3 prior lines of therapy were enrolled. Patients received lenvatinib 20 mg daily plus pembrolizumab 200 mg every 3 weeks for 35 cycles, or until confirmed disease progression or unacceptable toxicity. Primary endpoints were objective response rate (ORR; response assessed every 9 weeks for 54 weeks, then every 12 weeks, by blinded independent