Oral Plenary

Plenary I

IGCS20_1256

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

IGCS20_1255

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

Abstract 2 Table 1

	Lenvatinib + Pembrolizumab (n=31)
Efficacy	
Confirmed ORR, % (95% CI)	32 (17–51)
Disease control rate,[a] % (95% CI)	74 (55–88)
Duration of response, median (range) months	NR (1.5+ to 7.9+)
Progression-free survival, median (95% CI) months	4.4 (4.0–8.5)
Responders by prior therapy, n (%)[b]	
Platinum refractory/resistant (n=25)	6 (24)
Bevacizumab exposed (n=19)	4 (21)
Treatment-related AEs, n (%)	29 (94)
Grade 3–5 treatment-related AEs	21 (68)
Treatment-related AEs leading to death	1 (3)[c]
Treatment-related AEs resulting in treatment discontinuation	4 (13)
Treatment-related AEs occurring in ≥10 patients	
	Any Grade[d] / Grade 3
Hypertension	17 (55) / 6 (19)
Fatigue	13 (42) / 3 (10)
Hypothyroidism	13 (42) / 0
Decreased appetite	12 (39) / 0
Diarrhea	12 (39) / 1 (3)
Proteinuria	10 (32) / 2 (6)

[a]Defined as best overall response of complete or partial response, or stable disease. [b]Percentages are based on the total number of patients in each prior therapy subgroup. [c]One patient had a serious AE of hypovolemic shock that led to death. [d]Among treatment-related AEs occurring in ≥10 patients, none were grade 4/5. AE, adverse event; NR, not reached; ORR, objective response rate.

central review per RECIST v1.1) and safety. Secondary endpoints included disease control rate, duration of response, and progression-free survival.

Results 31 patients with ovarian cancer received ≥1 dose of lenvatinib plus pembrolizumab in LEAP-005 (median age 62 years [range 40–76]); median study follow-up was 7.8 months (range, 4.6–12.4) as of April 10, 2020. ORR was 32% (95% CI, 17–51); other efficacy endpoints were also favorable (table 1). Treatment-related adverse events occurred in 29 (94%) patients (table 1).

Conclusion Lenvatinib plus pembrolizumab demonstrated encouraging efficacy and manageable safety in patients with heavily pretreated ovarian cancer, including those with prior platinum failure and those with previous bevacizumab exposure.

IGCS20_1268

3 POSTPROGRESSION EFFICACY OUTCOMES FROM THE PHASE 3 ARIEL3 STUDY OF RUCAPARIB IN PATIENTS WITH PLATINUM-SENSITIVE RECURRENT OVARIAN CARCINOMA ASSOCIATED WITH EITHER BRCA1 OR BRCA2 MUTATIONS

[1]J Weberpals*, [2]A Oza, [3]D Lorusso, [3]G Scambia, [4]C Aghajanian, [5]A Oaknin, [6]A Dean, [7]N Colombo, [8]AR Clamp, [9]A Leary, [10]RW Holloway, [11]M Amenedo Gancedo, [12]PC Fong, [13]JC Goh, [14]DM O'Malley, [15]DK Armstrong, [16]S Banerjee, [17]J García-Donas, [18]EM Swisher, [19]T Cameron, [20]L Maloney, [20]S Goble, [21]RL Coleman, [22]JA Ledermann. *[1]Ottawa Hospital Research Institute, Canada; [2]Princess Margaret Cancer Centre, University Health Network, Canada; [3]Fondazione Policlinico Universitario A. Gemelli IRCCS, Italy; [4]Memorial Sloan Kettering Cancer Center, USA; [5]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Spain; [6]St John of God Subiaco Hospital, Australia; [7]European Institute of Oncology IRCCS and University of Milan-Bicocca, Italy; [8]The Christie NHS Foundation Trust and University of Manchester, UK; [9]Gustave Roussy Cancer Center, INSERM U981, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO), France; [10]AdventHealth Cancer Institute Orlando, USA; [11]Oncology Center of Galicia, Spain; [12]Auckland City Hospital and University of Auckland, New Zealand; [13]Royal Brisbane and Women's Hospital, Herston and University of Queensland, Australia; [14]The Ohio State University, James Cancer Center, USA; [15]Johns Hopkins University School of Medicine, USA; [16]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, UK; [17]HM Hospitales—Centro Integral Oncológico Hospital de Madrid Clara Campal, Spain; [18]University of Washington, USA; [19]Clovis Oncology UK Ltd., UK; [20]Clovis Oncology, Inc., USA; [21]US Oncology Research, USA; [22]UCL Cancer Institute, University College London and UCL Hospitals, UK*

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Abstract 3 Table 1

	BRCA1		*BRCA2*	
	Rucaparib (n=80)	Placebo (n=37)	Rucaparib (n=50)	Placebo (n=29)
TFST				
Median, mo	16.8	8.1	30.4	7.1
HR (95% CI)	0.41 (0.27–0.64)		0.17 (0.09–0.33)	
CFI				
Median, mo	18.4	9.4	36.1	8.7
HR (95% CI)	0.40 (0.26–0.62)		0.16 (0.08–0.32)	
PFS2				
Median, mo	25.1	21.8	34.1	18.4
HR (95% CI)	0.84 (0.53–1.32)		0.51 (0.29–0.91)	
TSST				
Median, mo	25.9	18.5	34.2	19.4
HR (95% CI)	0.65 (0.41–1.04)		0.55 (0.31–0.96)	

Visit cutoff date: 31 Dec 2019.
CFI, chemotherapy-free interval; CI, confidence interval; HR, hazard ratio; PFS2, time to disease progression on subsequent therapy or death; TFST, time to first subsequent therapy; TSST, time to second subsequent therapy.