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

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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-naïve 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-naïve patients with EOC.

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

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

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
Hypertension	17 (55)
Fatigue	13 (42)
Hypothyroidism	13 (42)
Decreased appetite	12 (39)
Diarrhea	12 (39)
Proteinuria	10 (32)
	Grade 3
	6 (19)
	3 (10)
	0
	0
	1 (3)
	2 (6)

^aDefined as best overall response of complete or partial response, or stable disease.

^bPercentages are based on the total number of patients in each prior therapy subgroup. ^cOne patient had a serious AE of hypovolemic shock that led to death. ^dAmong 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 end-points 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

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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.