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A PHASE 1B MULTI-TUMOR COHORT STUDY OF CABOZANTINIB PLUS ATEZOLIZUMAB IN ADVANCED SOLID TUMORS: RESULTS OF THE TRIPLE-NEGATIVE BREAST CANCER, OVARIAN CANCER, AND ENDOMETRIAL CANCER COHORTS

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Background Cabozantinib, a multiple receptor tyrosine kinase inhibitor, promotes an immune-permissive environment which might enhance the activity of immune checkpoint inhibitors. COSMIC-021 (NCT03170960), a multicenter phase 1b study, is evaluating the combination of cabozantinib with atezolizumab in advanced solid tumors; here we present efficacy and safety results in patients with triple negative breast cancer (TNBC), ovarian cancer (OC), and endometrial cancer (EC).

Methods Eligible patients had locally advanced or metastatic TNBC, OC, or EC and had radiographically progressed on prior systemic anticancer therapy. One or two lines of prior therapy were permitted. Patients with OC were platinum resistant or refractory. Prior treatment with anti-PD-1 or anti-PD-L1 agents was allowed for patients with TNBC. Patients received cabozantinib, 40 mg PO QD, plus atezolizumab, 1200 mg IV Q3W. The primary endpoint was objective response rate (ORR) per RECIST 1.1 as assessed by investigator. Other endpoints included safety, duration of response (DOR), progression free survival (PFS), and overall survival (OS). CT/MRI scans were performed Q6W for the first year and Q12W thereafter.

Results As of February 19, 2021, 30–32 patients were enrolled in each of the cohorts. 47% of patients with TNBC, 47% with OC, and 40% with EC had received 2 lines of prior therapy. Median follow-up was 18.7 months, 20.8 months, and 19.0 months for the TNBC, OC, and EC cohorts, respectively. Grade 3/4 treatment-related adverse events occurred in 33% of patients with TNBC, 56% with OC, and 37% with EC. One Grade 5 treatment-related adverse event of pulmonary hemorrhage occurred in the TNBC cohort and one of encephalitis occurred in the OC cohort. Cabozantinib plus atezolizumab demonstrated clinical activity in all three tumor cohorts (table 1).

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Endpoint	Cohort		
	TNBC (N=30)	OC (N=32)	EC (N=30)
ORR, % (95% CI)*	17 (5.6, 34.7)	19 (7.2, 36.4)	7 (0.8, 22.1)
*Disease Control Rate, %	67	63	53
Median DOR, months (95% CI)	9.2 (1.9, NE)	8.3 (5.6, NE)	NR [‡]
Median PFS, months (95% CI)	4.0 (1.4, 5.8)	3.9 (1.5, 6.1)	2.7 (1.4, 8.4)
Median OS, months (95% CI)	14.8 (9.9, NE)	9.3 (5.1, 23.6)	15.5 (8.3, NE)

*complete response+partial response+stable disease per RECIST 1.1 six months following treatment

[‡]For TNBC, 2 confirmed complete responses and 3 confirmed partial responses; for OC, 6 confirmed partial responses; for EC, 2 confirmed partial responses

[‡]Median not reached

Conclusions Cabozantinib in combination with atezolizumab demonstrated encouraging clinical activity in patients with previously treated advanced cancers.

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Ethics Approval Yes

Consent Yes

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