PRELIMINARY CLINICAL EXPERIENCE WITH XMAB20717, A PD-1 X CTLA-4 BISPECIFIC ANTIBODY, IN PATIENTS WITH ADVANCED SOLID TUMORS

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Background XmAb20717 is a humanized bispecific monoclonal antibody that simultaneously targets PD-1 and CTLA-4. We report updated data on patients treated at the recommended expansion dose from an ongoing, multicenter, Phase 1, dose-escalation and -expansion study of intravenous XmAb20717 in patients with selected advanced solid tumors that progressed after treatment with all standard therapies or with no standard therapeutic options.

Methods A maximum tolerated dose was not reached in dose escalation. XmAb20717 10 mg/kg every 2 weeks (Q2W) was selected as the expansion dose, based on consistent T-cell proliferation in peripheral blood indicative of dual PD-1/CTLA-4 checkpoint blockade, and response to treatment (RECIST [1.1]).¹ Parallel expansion cohorts included ~20 patients each with melanoma, renal cell carcinoma (RCC), non-small cell lung cancer (NSCLC), castration-resistant prostate cancer (CRPC), and a basket of tumor types without an FDA-approved checkpoint inhibitor (CI). Patients treated with 10 mg/kg in dose escalation were pooled with expansion cohorts for analysis of clinical activity and safety.

Results As of 9 June 2021, 110 patients, ranging in age from 39 to 89 years and 66.4% male, were treated, and 5 were continuing treatment. Patients had received a median of 4 prior systemic treatment regimens, including CI therapy for 64.5%. The objective response rate was 13.0% (10/77 patients evaluable for efficacy), including 1 complete response (melanoma [confirmed]) and 9 partial responses (confirmed: 1 melanoma, 2 RCC, 2 CRPC, 1 ovarian cancer; unconfirmed: 1 melanoma, 2 NSCLC). The CRPC responders (2/7 with RECIST-measurable disease) had confirmed PSA decreases $\geq$ 50% from baseline (to 0.02 and 0.3 ng/mL); neither had progression on bone scans. All responders had prior CI exposure, except those with CRPC. Robust CD4 and CD8 T-cell activation was seen. Low baseline tumoral expression of myeloid recruitment genes, including *IL-8*, was associated with clinical benefit. Grade $\geq$ 3 immunotherapy-related adverse events in $\geq$ 3 patients included rash (16.4%), transaminase elevations (9.1%), hyperglycemia (4.5%), acute kidney injury (3.6%), amylase and lipase increased (2.7%), and lipase increased (2.7%).

Conclusions Preliminary data indicate 10 mg/kg XmAb20717 Q2W was associated with complete and partial responses in multiple tumor types and was generally well-tolerated in these heavily pretreated patients with advanced cancer. Changes in T-cell populations in the periphery and tumor are consistent with robust dual checkpoint blockade. These findings support

further development of XmAb20717 in advanced solid tumors, including metastatic prostate cancer.

Trial Registration NCT03517488

REFERENCES

1. Shum E, Daud A, Reilly M, et al. Preliminary safety, pharmacokinetics/pharmacodynamics, and antitumor activity of XmAb20717, a PD-1 x CTLA-4 bispecific antibody, in patients with advanced solid tumors. *JITC* 2020;**8**(3):A247-8.

Ethics Approval The study was approved by each institution's IRB.

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