CTX130 ALLOGENEIC CRISPR-CA9–ENGINEERED CHIMERIC ANTIGEN RECEPTOR (CAR) T CELLS IN PATIENTS WITH ADVANCED CLEAR CELL RENAL CELL CARCINOMA: RESULTS FROM THE PHASE 1 COBALT-RCC STUDY


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Background Clear cell renal cell carcinoma (ccRCC) is the most common subtype of renal tumors. Patients with ccRCC who fail checkpoint inhibitors (CPIs) and tyrosine kinase inhibitors (TKIs) have a poor prognosis. Preclinical studies identified substantial expression of CD70 in ccRCC tumor samples. Here, we report results from the Phase 1 dose-escalation study of CTX130™, a CD70-targeting allogeneic CAR T cell therapy in patients with ccRCC.

Methods COBALT-RCC (NCT04438083) is a Phase 1, open-label, multicenter, global study evaluating safety and efficacy of CTX130 in patients 18y with advanced (unresectable or metastatic), relapsed, or refractory (R/R) ccRCC and prior exposure to both CPIs and TKIs. Patients received standard lymphodepleting chemotherapy with fludarabine 30mg/m² and cyclophosphamide 500mg/m² for 3 days, followed by CTX130 infusion.

Results As of May 2, 2022, 14 patients with a median age of 64.5y (range, 54-77) were treated with CTX130. All patients had stage IV disease, and received a median of 3 (range, 1-6) prior treatments. Six patients had documented refractory disease at study entry. Median CD70 expression level on the tumors was 100% (range, 1-100%). Patients received CTX130 at dose levels (DLs) ranging from 3x10⁷ to 9x10⁸ CAR T cells. Overall, expansion occurred across all DLs. An emerging relationship between higher CAR T exposure and disease control was observed. CTX130 had an acceptable safety profile; there were no dose-limiting toxicities across all DLs. Seven (50%) patients experienced grade (Gr) 1-2 cytokine release syndrome (CRS); there was no Gr≥3 CRS. Three patients experienced serious adverse events (SAEs) related to CTX130; all were episodes of CRS. Three patients had SAEs of infections, all unrelated to CTX130, including a Gr5 pneumonia with Gr4 dyspnea resulting in death. No patients experienced immune effector cell associated neurotoxicity syndrome, graft versus host disease, or hemophagocytic lymphohistiocytosis. One patient (7.7%) had a durable complete remission (CR) maintained at 18+ months and 9 (69.2%) patients had stable disease (SD) with 4 patients (30.8%) in SD at 4 months. The disease control rate (CR + partial response + SD) was 76.9%.

Conclusions This first-in-human clinical trial exploring CD70 CAR T-cell therapy in ccRCC showed an excellent safety profile with no unexpected on-target off-tumor toxicities and encouraging antitumor activity. To our knowledge, this durable CR is the first to be achieved with allogeneic CAR T cell therapy in patients with R/R solid tumors and represents a proof-of-concept for further exploration of CD70-targeted CAR T cells in ccRCC and other CD70+ malignancies.