

RESULTS FROM A PHASE 1 STUDY OF CDX-1140, A FULLY HUMAN ANTI-CD40 AGONIST MONOCLONAL ANTIBODY (MAB), IN COMBINATION WITH PEMBROLIZUMAB

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Background CD40 agonist mAbs can enhance the efficacy of checkpoint blockade in preclinical models and can functionally revive PD-1^{hi} exhausted T cells. This Phase 1 study examined safety, clinical activity, and pharmacodynamics of CDX-1140 as monotherapy or in combination with other agents (NCT03329950). We now report the completed results from Part 3 of the study, combination with anti-PD-1 mAb pembrolizumab.

Methods Patients with advanced solid tumors and documented disease progression on a single prior anti-PD-1/L1 based regimen were enrolled. In dose-escalation (DE) cohorts, CDX-1140 was administered at 0.72 mg/kg and 1.5 mg/kg. Expansion cohorts (EX) in non-small cell lung cancer (NSCLC) and squamous cell carcinoma of head and neck (SCCHN) evaluated CDX-1140 1.5 mg/kg. Treatment was q3w co-administered with pembrolizumab 200 mg in both DE and EX.

Results 10 patients were treated in DE (renal cell carcinoma n=2, SCCHN n=2, n=1 for NSCLC, endometrial cancer, MSI^{hi}-CRC, ocular melanoma, esophageal adenocarcinoma, MSI^{hi}-cholangiocarcinoma) and 15 patients treated in EX; NSCLC (n=9) and SCCHN (n=6). The median number of prior regimens was 3. Treatment was generally well tolerated, with most treatment-related AEs (TRAE) being grade 1 or 2. The most frequent TRAE at the CDX-1140 1.5 mg/kg dose level (n=21) were arthralgia (62%), fatigue (62%), nausea (48%), diarrhea (48%), vomiting (43%), myalgia (43%), fever (38%), chills (38%), AST increase (38%), bilirubin increase (24%), ALT increase (19%), and cytokine release syndrome (CRS) (19%). Across Part 3, there was 1 complete response (CR) in a patient with oropharyngeal cancer (HPV⁺ and PD-L1 status unknown); 9 additional patients had stable disease (SD), including 4 with SCCHN and 4 with NSCLC. The patient achieving CR received 4 prior regimens (including chemotherapy, pembrolizumab, and cetuximab), discontinued study therapy after 2 doses due to arthralgia (grade 3) and CRS (grade 2), and initially demonstrated a partial response that evolved into CR, with the response ongoing at 12+ months without further anti-tumor treatment. Of the 4 SCCHN with SD, 2 had target lesions shrinkage (-15% and -18%) and 2 had no change. One NSCLC patient has SD for 10+ months with a nadir in target lesions of -15%. Part 3 biomarker data will be presented.

Conclusions CDX-1140 in combination with pembrolizumab had an acceptable safety profile. Evidence of clinical benefit was most evident in patients with SCCHN, all of whom had progressive disease on prior anti-PD-1/L1 based therapies. Further studies are warranted.

Trial Registration NCT03329950

Ethics Approval The study was reviewed and approved by the following institutional review boards:

Providence Health & Services Institutional Review Board for Earle A. Chiles Research Institute/Providence Cancer Institute; approval number/ID: PHS IRB #2017000532

WCG-IRB for Gabrail Cancer Center, Georgia Cancer Specialists, HonorHealth Research Institute, and Nebraska Cancer Specialists; approval number/ID: 20172645

Rhode Island Hospital IIRB#1 for Legorreta Cancer Center at Brown University/Rhode Island Hospital/Lifespan Cancer Center; approval number/ID: LS-P-Camp

Office of Regulatory Affairs of the University of Pennsylvania for Hospital of the University of Pennsylvania; approval number/ID: UPCC 18917

Memorial Sloan Kettering Cancer Center Institutional Review Board/Privacy Board; approval number/ID: 18-225

Participants gave informed consent before taking part in the study.

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