

A PHASE 1 DOSE ESCALATION STUDY OF GCC19CART – A NOVEL COUPLED CAR[®] THERAPY FOR SUBJECTS WITH METASTATIC COLORECTAL CANCER

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Background GCC19CART, the first clinical candidate from the CoupledCAR[®] solid tumor platform, targets guanylate cyclase-C (GCC) which is expressed in colorectal cancers. Coupled-CAR utilizes multiple vectors to make both solid tumor targeting CAR-T and CD19 CAR-T in a single manufacturing step. An investigator-initiated dose escalation trial in China for patients with relapsed or refractory metastatic colorectal cancer (R/R mCRC) is reported here.

Methods Subjects are screened for GCC expression by immunohistochemistry. Eligible subjects undergo leukapheresis, a single dose of lymphodepleting chemotherapy (fludarabine 30mg/m² and cyclophosphamide 300mg/m²) 3 days prior to infusion, and then administration of a single infusion of GCC19CART at one of two preassigned doses: 1x10⁶ or 2x10⁶ CAR T-cells/kg. Endpoints are safety and preliminary evidence of efficacy as determined by CT or PET/CT per RECIST 1.1 or PERCIST 1.0. All responses were confirmed by an independent third-party imaging contract research organization (CRO).

Results 13 subjects have been enrolled to dose level 1 (1x10⁶ cells/kg) and 8 subjects have been enrolled to dose level 2 (2x10⁶ cells/kg). The most common adverse events were cytokine release syndrome (CRS) in 21/21 subjects (Grade 1 19/21 (90.48%) or Grade 2 2/21 (9.52%)) and diarrhea in 21/21 subjects (Grade 1 6/21 (28.57%) Grade 2 5/21 (23.81%) Grade 3 9/21 (42.86%) or Grade 4 1/21 (4.76%)). All patients with grade 3 and higher side effects were well managed. Immune effector cell-associated neurotoxicity syndrome (ICANS) was observed in 2/21 (9.52%) subjects at Grade 3 or 4 and resolved with corticosteroids. The combined overall response rate (ORR) for both dose levels was 28.6% (6/21). For dose level 1, the overall response rate (ORR) per RECIST 1.1 was 15.4% (2/13). Two subjects demonstrated a partial response (PR) while 3 additional subjects had partial metabolic response (PMR) on PET/CT with stable disease (SD) or progressive disease (PD) per RECIST 1.1. For dose level 2, The ORR per RECIST 1.1 was 50% (4/8). 4 subjects demonstrated a PR (3 at month 1, 1 at month 3 after being SD at month 1) and 2 additional subjects had PMR on PET/CT with SD per RECIST 1.1.

Conclusions Preliminary results demonstrate that GCC19CART has meaningful dose-dependent clinical activity and an acceptable safety profile in relapsed or refractory metastatic colorectal cancer. This trial is ongoing and updated data will be presented. A Phase 1 trial of GCC19CART in the US has opened for accrual and is expected to enroll patients in mid-2022.

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