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## CLDN 18.2-targeted CAR-T cell therapy in patients with cancers of the digestive system

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### Background

Efficacy of chimeric antigen receptor-engineered T (CAR-T) cell therapy against solid tumors is still limited. CLDN18.2 is a promising target highly expressed in various cancer types of the digestive system. CT041, an anti-CLDN18.2 CAR-T cell therapy, showed promising anti-tumor activities in preclinical studies and an investigator-initiated study (CT041-CG4003 NCT03159819). This newly initiated phase I study was conducted to assess the safety and efficacy of CT041 produced with a modified manufacturing process.

### Methods

Patients with CLDN18.2+ cancers of digestive system received CT041 at doses of  $2.5 \times 10^8$ ,  $3.75 \times 10^8$  or  $5 \times 10^8$  CAR-T cells after preconditioning chemotherapy. The objective was to assess the safety, efficacy and cytokinetic profile of CT041.

### Results

As of April 8, 2021, a total of 37 patients with cancer of digestive system, including 28 with gastric cancer (GC), 5 with pancreatic ductal adenocarcinoma (PDAC) and 4 with other cancer types, received CT041 infusion and completed at least 12 weeks of follow-up after the first infusion for the last subject. Cell doses of  $2.5 \times 10^8$ ,  $3.75 \times 10^8$  and  $5 \times 10^8$  were administered in 28, 6 and 3 patients, respectively. With a median follow-up of 7.6 months (95%CI 5.6, 8.6), all patients experienced  $\geq G3$  hematologic toxicity while no DLT was observed. Immune effector cell-associated neurotoxicity syndrome, treatment-related death and  $\geq G3$  cytokine release syndrome was not observed. The overall ORR for all patients and patients with GC were 48.6% (95%CI, 31.9%, 65.6%) and 57.1% (95%CI, 37.2, 75.5) respectively. At the dose level of  $2.5 \times 10^8$ , 18 patients with GC who have failed at least 2 prior lines of therapy including 44% (8/18) exposure to anti-PD-(L)1 antibody, the overall ORR, median PFS and OS was 61.1% (11/18), 5.4 months (95%CI, 2.6, NE) and 9.5 months (95%CI, 5.2, NE) respectively.

### Conclusions

CT041 showed acceptable safety profile and promising anti-tumor activities in patients with refractory CLDN18.2+ cancers of digestive system. In patients with GC who have failed at least 2 prior lines of therapy, CT041 displayed a significantly improved efficacy compared to historical data.

### Clinical trial identification

NCT03874897, first posted March 14, 2019.

### Legal entity responsible for the study

Peking University Cancer Hospital & Institute.

### Funding

CARsgen Therapeutics Co., Ltd.

### Disclosure

C. Qi: Other, Personal and Institutional, Other, sub-investigator: CARsgen Therapeutics. Y. Qin: Other, Personal and Institutional, Principal Investigator: CARsgen Therapeutics. D. Liu: Other, Personal and Institutional, Other, sub-investigator: CARsgen Therapeutics. J. Gong: Other, Personal and Institutional, Other, sub-investigator: CARsgen Therapeutics. X. Peng: Financial Interests, Personal, Full or part-time Employment: CARsgen Therapeutics. H. Wang: Financial Interests, Personal, Full

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