737MO EpCAM-targeted CAR-T cell therapy in patients with advanced colorectal and gastric cancers

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Background: EpCAM is highly expressed in various cancer types of the digestive system and represent an interesting molecular therapeutic target. IMC001, an EpCAM targeted CAR-T cell therapy, showed promising anti-tumor activities in preclinical studies. Here we reported the initial dosage group in advanced GI cancers.

Methods: This first-in-human, open label, multi-centers trial involves a classic 3+3 design with separate EpCAM CAR-T cell dose escalations for monotherapy (Stage 1) and the combination with radiofrequency or microwave ablation (Stage 2) with dosage recommended by stage 1. EpCAM+ patients with relapsed or refractory digestive tumors who have no further standard treatment options and ECOG 0 or 1 are eligible to receive IMC001 at doses of 0.3, 1 or 3 million CAR-T cells/kg after lymphodepletion chemotherapy. The primary objective was to assess the safety, efficacy and cytokinetic profile of IMC001.

Results: As of 29 Apr 2022, a total of 7 patients with 4 colorectal cancers and 3 gastric cancers, received IMC001 infusion of 3×10^{5} cells/kg. 5 patients completed the 4 weeks of DLT follow-up visits. All patients experienced $\geq$G3 hematologic toxicity while no DLT was observed. The most common grade $\geq$3 AEs were decreases in lymphocyte, leukocyte and platelet count. One patient had a SAE of immune hepatitis occurred around 11 days after infusion of CAR-T cells and prolonged the hospitalization duration, resolved after symptomatic treatment. Grade 1 to 2 CRS were observed in 1 colorectal cancer patient and 1 gastric cancer patient. No ICANS was observed. Other adverse events related to the cell therapy were grade 1-2 of nausea, vomit, asthenia or pruritus and recovered quickly. CTC in the blood all decreased to 0 from 7 days to 4 weeks after infusion. Robust engraftment of CAR T cells and significant elevations of cytokines levels in all patients. Preliminary efficacy data showed that 4 out of 5 evaluable patients remain SD and 1 patient evaluated as PD at this lowest dosage.

Conclusions: This is the first CAR T product ever tested in human with the EpCAM target. IMC001 shows a favorable safety profile and reasonable anti-tumor activities at the initial dosage level in patients with refractory EpCAM+ cancers of digestive system. Updated data from open cohorts will be presented.

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abstracts

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