Title: Anti-GPC3 Chimeric Antigen Receptor Modified T cells (CAR-GPC3 T) in Chinese Patients with Refractory or Relapsed GPC3+ Hepatocellular Carcinoma (r/r GPC3+ HCC)

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Background: HCC was commonly diagnosed and identified as leading causes of cancer death in China. Using a 10% cutoff score, GPC3 was detected in 63.6% of HCCs. Safety and preliminary efficacy of second, third, and fourth generation of CAR-GPC3 T cell therapies were evaluated in 15 Chinese patients (pts) with r/r GPC3+ HCC in a Phase I trial.
Methods: Pts between 18 and 70 years old with histopathological confirmed r/r GPC3+ HCC, Child-Pugh score≤B7, ECOG≤1, lymphocyte ≥0.7 x10^9/L, post-transduction positive T cells ≥10%, amplification by α CD3/CD28 ≥5, and without ascites requiring treatments and HIV infection were enrolled. Eligible pts undergo leukapheresis or whole blood collection, which further developed into CAR-GPC3 T via lentiviral transduction. Standard release tests were conducted before administering CAR-GPC3 T in patients. Adverse events were graded per NCI CTCAE v.4.03. Efficacy was evaluated per RECIST and modified RECIST. Refer to Huiping Gao et al[4] for details of CAR-GPC3 T manufacture. Clinical Trial Information: NCT 02395250 and NCT 03146234
Results:
Per preliminary data analysis with data cut-off date as of 7Aug2017, all 15 patients with r/r HCC, who received at least one infusion of CAR-GPC3 T cell therapy, tolerated the treatment well. No dose-limiting toxicity (DLT) was identified. Preliminary analysis compared the clinical outcomes in patients who received different generations of CAR-GPC3 T cells with or without baseline lymphodepleting conditioning (BLDC). In patients who received 2nd generation of CAR-GPC3 T III cells with BLDC (N = 7), ranging from 6.96x10^8 to 9.25 x10^9 cells, except two non-evaluable patients, the best response for the rest 5 pts are 1 PR, 2 SD, 2 PD. Median survival has not been reached. As of 7Aug2017, the PR patient remains alive for 18.7 months; 2 SD patients remain alive for 24.9 months and 18.7 months, respectively; and one PD patient deceased at 12 months, and one PD patient remains alive for 15.2 months. Two newly enrolled patients treated with 4th generation of CAR-GPC3 T IV cells remain stable disease for 4.5 months and 5 months at the cut-off date.
Conclusions: CAR-GPC3 T cell therapy is feasible and safe for Chinese pts with r/r GPC3+ HCC, and holds promising antitumor potential when LDC is applied along with CAR-GPC3 T cell therapy.