P1452 THE PRELIMINARY SAFETY AND EFFICACY STUDY OF SC-U02, A NON-VIRAL GENOME TARGETING, ANTI-CD19 UNIVERSAL CAR-T PRODUCT, IN RELAPSED/REFRACTORY (R/R) DIFFUSE LARGE B-CELL LYMPHOMA PATIENTS

Topic: 25. Gene therapy, cellular immunotherapy and vaccination - Clinical

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Background: Allogeneic CAR-T therapy has made exciting progresses and represents the future trend of this T cell therapy. However, the classic way of using CD52 antibody for lymphodepletion, which aim to overcome Host versus Graft reaction (HvG), would put patients at risk of infection and longer in-patient care duration. In this study, we conducted a Non-viral Genome Targeting approach for producing the allogeneic anti-CD19 CAR-T cells (nvGT UCART19), SC-U02. To avoid Graft versus Host Disease (GvHD), TCR gene was knocked-out. And to prevent T cell rejection, B2M gene was disrupted. Meanwhile, the anti-CD19 CAR gene together with an artificial B2M-HLA-E gene were inserted at the same TRAC locus (Figure 1), which prevents NK cell rejection triggered by the loss of surface expression of HLA class I due to B2M gene knock-out (Figure 2). Thus, it prolongs the persistence of SC-U02 in patients’ body without the aid of CD52 antibody, which reduces the infection risk of patients in UCAR-T treatment process. The efficacy of SC-U02 had been demonstrated in our previous pre-clinical studies. In this single-arm, single center, dose-finding, investigator initiated trial (IIT) (ChiCTR2100051028), its safety and efficacy in relapsed/refractory diffuse large B-cell lymphoma (r/r DLBCL) patients were explored.

Aims: The primary objective of this trial is to assess safety profile of SC-U02, including evaluation of adverse events (AEs) and AEs of special interests, such as Cytokine Release Syndrome (CRS), neurotoxicity, GvHD and infection. Secondary objective is to evaluate efficacy as measured by the ratio of overall response (ORR) and complete response (CR). The persistence of SC-U02 in human body is observed as an exploratory endpoint.

Methods: The primary objective of this trial is to assess safety profile of SC-U02, including evaluation of adverse events (AEs) and AEs of special interests, such as Cytokine Release Syndrome (CRS), neurotoxicity, GvHD and infection. Secondary objective is to evaluate efficacy as measured by the ratio of overall response (ORR) and complete response (CR). The persistence of SC-U02 in human body is observed as an exploratory endpoint.

Results: Up to December 1st 2021, two patients with r/r DLBCL had been enrolled in this study and completed their treatment. The median age was 56 years (range, 52 to 59), and the number of previous treatment course is from 3 to 13. They all went through at least 2 lines of systematic chemotherapcy, and both were refractory to last therapy. Baseline characteristics refer to Table 1.

CRS occurred in one patients (50%) with grade 2 CRS. Tocilizumab was administered during CRS for this patient, and the symptom was reversed afterwards. The time of CRS onset was D8 and it lasted for 11 days. Data including body temperature (Figure 3), Interleukin-6 (IL-6) (Figure 4) are in accordance with the trend of CRS. Neither of them developed neurotoxicity and infection. No GvHD was observed.

Until D56 post nvGT UCART19 cell infusion, 1/2 (50%) cases achieved PR (Figure 5) and the other subject did not response (Table 1). CAR-positive T cell percentage showed a peak around D14 (Figure 6) for the responded patient.

Image:
Summary/Conclusion: In this trial, we see patient responded to this novel allogeneic CAR-T therapy which probably shows promise of the approach. However, due to limited cases reported, SC-U02’s safety and efficacy profile still needs to be decided. The research is ongoing and 6×10^8 cell dose level will be assessed later on.