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POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

A Phase 1 Study of RJMty19: Anti-CD19 Humanized CAR-Engineered Allogeneic Double Negative T Cells in Adults with B-Cell Non-Hodgkin's Lymphoma

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Introduction:
Autologous CAR-T cell therapies has been shown to benefit patients with relapsed/refractory B-cell non-Hodgkin's lymphoma (B-NHL). However, the intrinsic characteristics of autologous CAR-T cell products such as preparation failure, high cost, long production cycle, and bridging therapy required for some patients make it less accessible for a wide range of patients. RJMty19 is a first-in-class humanized anti-CD19 CAR-engineered allogeneic double negative T cells (DNTs). RJMty19 exhibits the advantages of both adaptive and natural immunity and has a high proportion of stem cell-like memory T cells (Tscm). Furthermore, RJMty19 fulfills the requirements of an off-the-shelf cellular immunotherapy, including not causing graft-versus-host disease (GvHD), resistance to host-versus-graft (HvG) rejection, scalability, and storability (WYZE 2022). Preclinical studies had shown that CD19-CAR-DNT has a better safety profile compared to conventional CD19-CAR-T (Zhang 2022). Hence, the first-in-human clinical evaluation of RJMty19 is being undertaken in this Phase 1 study in patients with B-NHL.
Methods:
This is a first-in-class, open-label, single-dose, phase 1 study of CD19-CAR-DNT cells. The study is designed to evaluate five dose levels (DL) of RJMty19 in a 3+3 dose-escalation scheme: 1×10^6, 3×10^6, 9×10^6, 2×10^7 and 3×10^7 viable CAR $^+$ DNT cells per kilogram of body weight. Eligibility criteria included the presence of measurable lesions, at least 2 lines of prior therapy, ECOG score of 0 to 1. All patients received lymphodepleting chemotherapy with fludarabine and cyclophosphamide. The primary endpoint is dose-limiting toxicities, incidence of adverse events and clinically significant laboratory abnormalities. Secondary endpoints include evaluation of standard cellular PK parameters, PD, immunogenicity, objective response rates (ORR) and disease control rate (DCR) per Lugano 2014 Criteria. This phase 1 study is registered on clinicaltrials.gov (NCT05453669).
Results :
As of July 31 2023, 15 patients with B-NHL were enrolled and 12 patients were evaluable (including one subject finished infusion for just 10 days). Of the 11 patients who had completed DLT evaluations at Day 28, five (45.5%) were male, and the average age was 59.7 years (range 45-74). At baseline, 73% of patients with IPI score $\geq$ 3 (range 0-4); the median volume of target lesion was 169,000 (4520-513,688) mm ^{3}. The median number of prior therapies was three (range2-9). Furthermore, five patients had prior BTKi therapy and four patients had prior lenalidomide/venetoclax therapy before recruiting into the trial. No patients had been treated with autologous CD19-CART products.
Following single RJMty19 infusion, there was no cases of GvHD, ICANS and SAEs. Only one patient developed a grade 2 CRS which was resolved within 24 hours. Except for fever, all of $\geq$grade 3 adverse events were hematologic disorders including leukopenia, lymphocytopenia, neutropenia, reduced platelet count and anemia (Table 1). Among patients who received $\geq 9\times10^6$ CAR-DNT cells/kg (DL $\geq$3; N=5), best DCR and ORR were 100% (5/5) and 40% (2/5) respectively at Day 28 with B-ultrasound imaging. One of patients in DL4 achieved 87% reduction of tumor lesions (SPD) at Day 31 and Day 61. CD19-CAR-DNT cell kinetics improved in a dose-dependent manner with peak cell expansion occurring between Day 5 and 7 at DL4 based on flow cytometry. Additionally, the mean of C_{max} in DL4 is 384 CAR $^+$ DNT cells per microliter (μl) blood (N=3), and the highest peak value of 936 CAR $^+$ DNT cells/μl was detected in the recent enrolled patient.

Disclosures No relevant conflicts of interest to declare.

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