OFF-THE-SHELF CD33 CAR-NK CELL THERAPY FOR RELAPSE/REFRACTORY AML: FIRST-IN-HUMAN, PHASE I TRIAL

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Background

The primary results of CAR-T therapy for patients with R/R AML has shown limited efficacy and severe side-effect. One of the main challenges is that current targets for myeloid malignancies are either widely expressed on healthy hemopoietic stem cells such as CD33 or specific for a group of tumor cells presented as Lewis Y antigen, which could cause lasting bone marrow depression induced by “on target off tumor” side-effect or target negative relapse. Therefore, to receive a balance, we designed a CD33 CAR to recognize AML cells and using NK cells to replace T cells as the carrier to eliminate tumor cells. The CD33 CAR NK cells have combined the wide-expression advantage of CD33 target and the safety of NK cells.

Aims

To evaluate the safety and primary efficacy of CD33 CAR NK cells

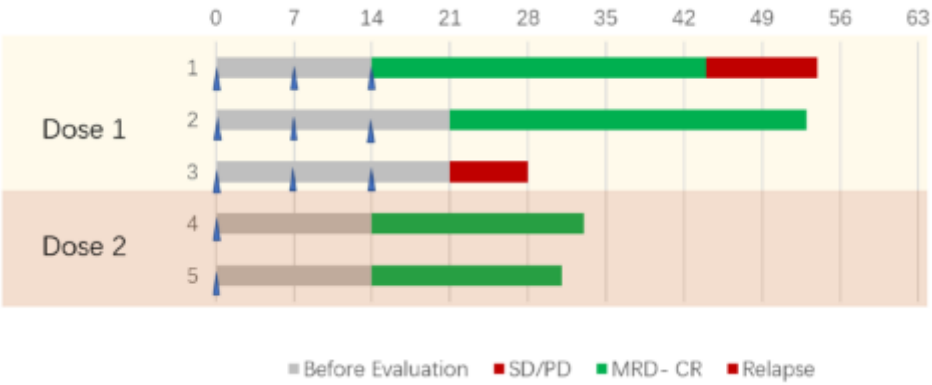
Methods

5 qualified subjects with R/R AML aged between 18 and 65 years-old were enrolled and received round(s) of infusion of anti-CD33 CAR NK cells (6×10^8, 1.2×10^9 or 1.8×10^9 cells per round after the precondition with Fludarabine ($30mg/m^2$) and Cytoxan 300-500mg/m^2 for 3 days to 5 days, determined by tumor burden at baseline. We investigated the response rate at D28 and treatment related side-effect after the CAR NK cell infusion and the long-term efficacy.

Results

As of data cut (February 26, 2021), 5 pts have finished CAR NK cells infusion. The median age was 43 (18-65) years-old and the median tumor burden before infusion is 31% (21%-77.5%). 4 of 5 patients have received MRD negetive CR at day 28 assessment. In dose group one, three patients have received 3 rounds of CAR NK cells (6×10^8, 1.2×10^9 and 1.8×10^9 cells) with the interval of 7 days after last round, and only patient 1 developed grade 1 CRS represented as fever after the infusion of 1.8×10^9 CAR NK cells and alleviated within 24h after symptomatic treatment. Patient 1 and patient 2 received MRD negetive CR at day 14 and 21, but patient 2 relapsed at day 43 after first round infusion. In dosage group 2, patient 4 and patient 5 both received one dose of 1.8×10^9 cells CD33 CAR NK cells after precondition, patient 5 developed grade 2 CRS presenting as lasting fever for 6 days after infusion and alleviated after 5mg

Dexamethasone I.V., both patient 4 and patient 5 recieved MRD negetive CR at day 28 after infusion. At the time of this abstract being uploaded, three patients remain MRD negetive CR.



Conclusion

Our primary data of the phase I trial have proved the primary efficacy and safety of CD33 CAR NK cells for patients with R/R AML. The efficacy needs expanded samples and longer follow up.

Keyword(s): Acute myeloid leukemia, CAR-T, Refractory