Which is better in CD19 CAR-T treatment of r/r B-ALL, CD28 or 4-1BB? A parallel trial under the same manufacturing process. First Author: Peihua Lu, Hebei Yanda Lu Daopei Hospital, Langfang, China

Background: Second-generation CARs have been shown to improve the overall functional activity and persistence of CAR-T cells. KYMRIAH and YESCARTA used 4-1BB and CD28 co-stimulatory signaling domains, respectively. Methods: A parallel trial under the same manufacturing process to compare the CD28 and 4-1BB CD19 CAR-T. Results: This study enrolled 47 relapsed or refractory CD19-positive B-cell acute lymphoblastic leukemia (B-ALL) patients, including 19 patients in CD28 group and 28 patients in 4-1BB group. 47 patients who received at least one infusion treatment and one clinical evaluation were available for assessing safety and efficacy. The overall objective response rate (ORR) was 96%. The ORR of 4-1BB group (100%) was higher than that of CD28 group (89%). All of the patients achieving objective response were MRD negative. CAR-T cell expansion in peripheral blood was detected by Flow cytometry, and the peak of CAR-T cells of 4-1BB group was significantly higher than that of CD28 group. Different degrees of cytokine release syndrome (CRS) occurred in 45 of 47 patients (95%). 5 patients who had grade III-IV of CRS were all in CD28 group. Cytokine release peak in CD28 group was significantly higher than that of the 4-1BB group. 9 patients experienced different levels of neurotoxicity (19%). 5 patients who had grade III-IV of neurotoxicity were all in CD28 group, too. All adverse events were effectively controlled within 1 month. Conclusions: The study illustrates that 4-1BB CAR-T cells show enhanced safety, efficacy, and expansion than CD28 CAR-T cells, suggesting a superior therapeutic strategy in the treatment of relapsed or refractory CD19-positive B-ALL patients. Clinical trial information: NCT03173417.