PB2208 CAR-T TREATMENT POST FIRST ALLO-HSCT FAILURE MAY HAVE DIFFERENT PROCESSION COMPARING TO CAR-T BEFORE ALLO-HSCT

**Topic:** 24. Gene therapy, cellular immunotherapy and vaccination - Biology & Translational Research

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**Background:** Chimeric antigen receptor (CAR) T cell therapy achieved a great success in the treatment of B cell acute lymphoblastic leukemia (B-ALL). However, CAR-T post first allogeneic hematopoietic stem cell transplantation (allo-HSCT), donor cells would involve to patients’ immune system, even if same donors’ lymphocytes were used to produce CAR-T cells. To analyze the potential influence of first allo-HSCT, the expansion of CAR-T cells, the clearance of CD19+ cell, and expression of 24 cytokines related to T cell life cycle and graft versus host disease (GVHD) were measured in this study.

**Aims:** To figure out the promising biomarkers may influence the process of CAR-T treatment of HSCT relapsed patients.

**Methods:** 60 patients with B-ALL received CD19-CAR-T treatment in Hebei Yanda Lu Daopei Hospital in 2020 were randomly selected. For 30 patients, CAR-T therapy was performed after the first allo-HSCT failure (group1), and another 30 cases who received CAR-T before allo-HSCT (group2). 22 were females, and 38 were males, with median age 17 (from 2 to 61). All the patients were collected EDTA anti-coagulated PB samples to test CAR-T cells expansion and CD19+ cells clearance by flow cytometer (FCM), and non-anti-coagulated serum to detect 24 kinds of cytokines by FCM microbeads on before CAR-T (d0+), d4, d7, d11, d15, d20, and d30 after CAR-T.

**Results:** As showed in Figure 1A and 1B, CAR-T cells expanded on d4 and reached the peak on d11, and then decreased and went to smooth from d15 in both group. However, a difference was observed between two groups. The peak was higher and the decrease curve was sharp in group2, and the peak was lower and a plateau was formed from d7 to d15 in group1. CD19+ cells clearance formed similar tracking lines in both groups. The CD19+ cells could not be detected on d14 in both group. The clearance rate might be smoother in group2 than that in group1. However, there were no significant differences based on statistic analyze which might result the bigger variable coefficient and less cases. In Figure 1C, within 24 kinds of cytokines, IL-6, sCD25, MCP-1, REG3a, Elafin, ST-2 and TNFRI were observed higher in group1 than group2 with statistic differences. To avoid the effects of allogeneic cells, all the patients in group2 were treated with autologous CD19 CAR-T cells, and patients in group1 with CD19-CAR-T cells from the same donor. Even though CAR-T expansion and target clearance between two groups were lack of statistic differences, the cytokines related to GVHD were higher in group1 as expected, which might be the results of absent of anti-rejection drugs for CAR-T expansion. Furthermore, general markers, skin related markers, and GI tract related markers were all increased in group1, which might be partially explain why higher rate of unexpected erythra or gastrointestinal hemorrhage in group1 after CAR-T.

**Image:**
Summary/Conclusion: Most CAR-T clinical trials were targeting refractory or relapsed patients, and more markers should be observed not only related to CRS or inflammation, but also related to GVHD during CAR-T treatment especially for those who relapsed after first HSCT. Based on our data, clinicians should be alert about GVHD markers while treating HCT relapsed patients with CAR-T therapy.