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POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Safety and Efficacy of CD22/ CD19 CAR-T and Auto-HSCT "Sandwich" Strategy As Consolidation Therapy for Ph Negative B Cell Acute Lymphoblastic Leukemia

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Introduction: Chimeric antigen receptor T-cell (CAR-T) therapy has a high relapse rate in B cell acute lymphoblastic leukemia (B-ALL). CAR T-cells target multi-antigen or CAR-T combined with other strategy may reduce the relapse post CAR-T. The main purpose of this study is to observe the safety and efficacy of CD22/CD19 CAR-T and Auto-HSCT "Sandwich" strategy in Ph negative (Ph $^{-}$) B-ALL patients.
Methods: A total of 19 newly diagnosed Ph $^{-}$ B-ALL patients were enrolled in this study (NCT05470777). These patients received induction and consolidation chemotherapy according to standard protocols. Autologous lymphocytes were collected at week 4 after induction chemotherapy. Afterwards, autologous CAR T-cells targeting CD22 and CD19 (CAR-T 1, co-stimulatory molecule was 4-1BB and infusion dose was 5×10^{6}/kg, respectively) were sequential infused after lymphodepletion chemotherapy with fludarabine and cytophosphamide. Autologous stem cells mobilization and collection were performed at 6-8 weeks after CAR T-cells infusion. After conditioned with modified BuCy regimen, autologous stem cells transplantation (auto-HSCT) was conducted. Sequential infusion of CD22 and CD19 CAR-T cells was performed on the second day after transplantation (CAR-T 2, co-stimulatory molecules and dose as CAR-T 1). No maintenance therapy was performed after auto-HSCT. Measurable detectable disease (MRD) was monitored by flow cytometry and IGHV leader-based next generation sequencing. Persistence of CAR T-cells were detected using real time quantitative RT-PCR (qPCR).
Results: Three of the enrolled patients were Ph-like B-ALL. 10 (52.6%) patients had poor risk factors according to NCCN guidelines. Grade 1-2 cytokine release syndrome (CRS) occurred in four (21.1%) and seven (36.8%) patients after CAR-T 1 and CAR-T 2, respectively. No grade 3-4 CRS and immune effector cell associated neurotoxicity syndrome (ICANS) occurred. After CAR-T therapy, all patients achieved MRDnegative complete remission (MRD $^{-}$CR). Until the last follow-up on July 1 st, 2023, the median follow-up was 16 months (range, 7 - 32 months). 84.2% of enrolled patients remain MRD $^{-}$CR. Duration of continuous MRD $^{-}$CR was detected in 2 patients for more than 2 years and in 9 patients for more than 1 year. The median overall survival (OS) and leukemia-free survival (LFS) in all 19 patients are not reached. Three (3/19, 15.8%) patients experienced antigen-positive relapse. One Ph-like B-ALL patient relapsed at 10 months after auto-HSCT and underwent allogeneic HSCT. Two patients with Ph $^{-}$ B-ALL relapsed at 5 and 6 months after auto-HSCT and were treated with blinatumomab. All of them achieved MRD $^{-}$CR again after treatment. All patients are alive and CAR-T cells are detectable in all patients at the last follow-up (range, 5-28 months).
Conclusions: Our preliminary study demonstrated that CD22/CD19 CAR-T and Auto-HSCT "Sandwich" strategy as a consolidation strategy showed favorable safety and efficacy in Ph $^{-}$ B-ALL. CD22/CD19 CAR-T resulted in deeper remission before transplantation. The new strategy may benefit patients from LFS and OS.

Disclosures No relevant conflicts of interest to declare.

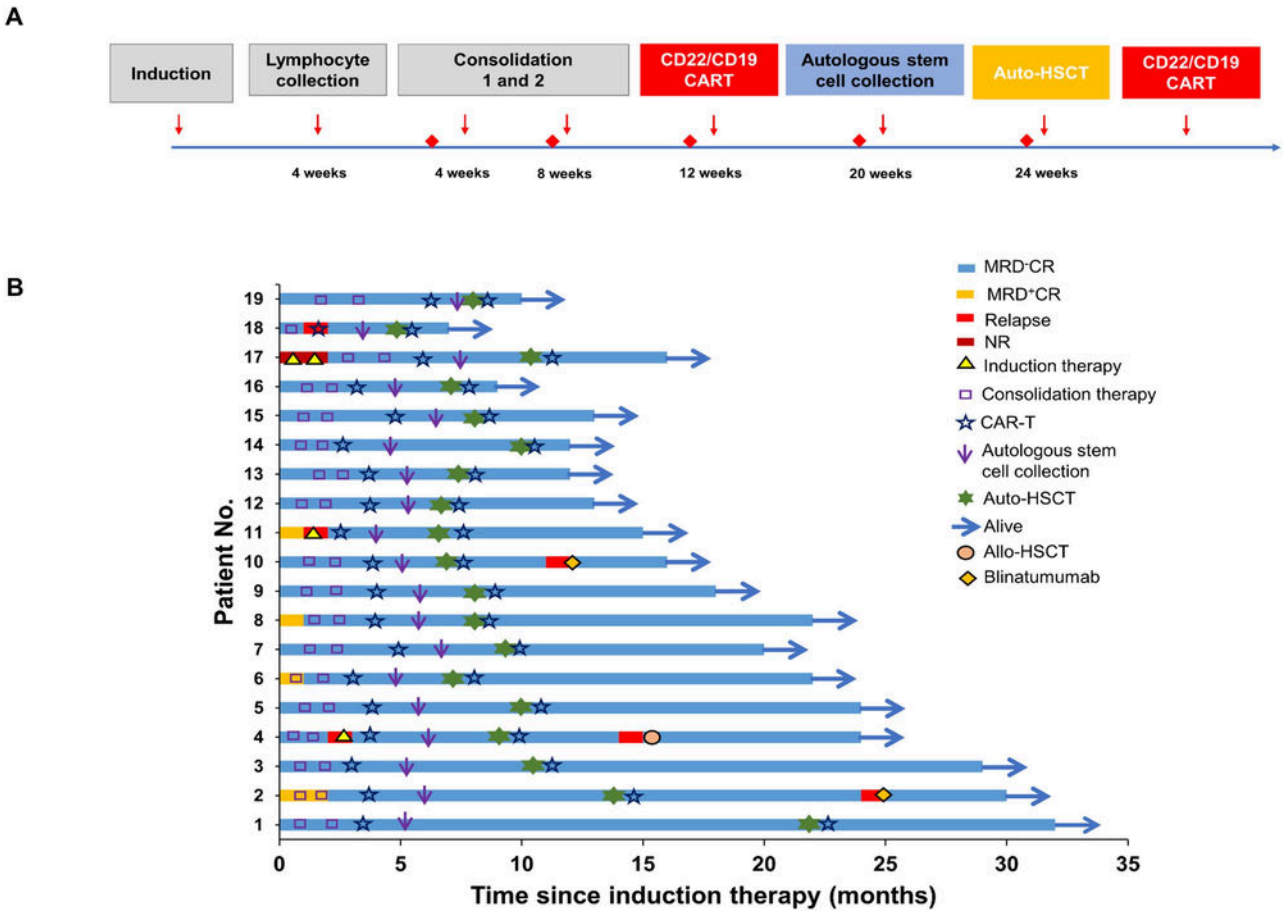

Figure 1

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