ELSEVIER

Blood 142 (2023) 4843

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Efficacy and Safety of CD19-Specific CAR-T Cell Therapy Following Immunochemotherapy in Newly Diagnosed B-Cell Lymphoma Associated Hemophagocytic Lymphohistiocytosis

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Hemophagocytic lymphohistiocytosis (HLH) represents a grave and potentially fatal systemic inflammatory condition. Lymphoma associated hemophagocytic lymphohistiocytosis (LAHS), as a common type in secondary HLH, suffers the worst outcome among sHLH. B cell Lymphoma associated hemophagocytic lymphohistiocytosis (B-LAHS) typically presents as high-risk lymphoma and is associated with a poorer prognosis compared to B cell lymphoma without HLH with standard first-line chemoimmunotherapy. As a result, there is an urgent need for more effective therapeutic strategies. Recent advancements in chimeric antigen receptor (CAR) T-cell therapy have demonstrated remarkable responses in relapsed or refractory B-cell non-Hodgkin lymphoma (B-NHL), as well as in some high-risk newly diagnosed B-cell lymphoma. However, There have been no clinical reports regarding the application of CAR-T cell treatment as part of first-line therapy in B-LAHS. We assessed the effectiveness and safety of autologous anti-CD19 CAR-T cell therapy following an immunochemotherapeutic regimen based on R-DEP (Rituximab-doxorubicin-etoposide-methylprednisolone) as a first-line treatment option for patients with B-LAHS. As of 1 July 2023, a cohort of 13 patients diagnosed with B-LAHS(with 3 cases enrolled before registration for clinical trials)was recruited for evaluation and met the criteria for assessing treatment efficacy at our institution. The overall response rate (ORR) for HLH was 100% (with 7 cases achieving complete response and 6 cases achieving partial response) prior to infuse CAR-T cells and the ORR for lymphoma also was 100% (with 10 cases achieving complete response and 3 cases achieving partial response) on the time of a month after CAR-T cell infusion. As of the follow-up date on 1 July 2023 (with a median follow-up time of 14 months), all 13 patients were still alive, 12 cases maintained sustained remission, while 1 case experienced relapse at 16 months after CAR-T cell infusion. The median overall survival (OS) has not been reached, and the median progression-free survival (PFS) was 31.5 months. To provide comparison, we included a group of 26 patients diagnosed with B-LAHS who did not receive CAR-T cell therapy during the same period. The non-CAR-T group demonstrated a significantly lower median OS of 5.93 months and a median PFS of 4.43 months, highlighting the superior prognosis of the CAR-T group ($p < 0.001$). Regarding adverse events, the CAR-T group exhibited a cytokine release syndrome (CRS) incidence of 53.8% (7/13) and an immune effector cell-associated neurotoxicity syndrome (ICANS) incidence of 30.7% (4 /13), all of which were classified as grade 1. None of the patients experienced non-hematologic toxicity of grade $\geq$3. While all 13 patients developed cytopenias, hematologic toxicity reactions $\geq$ grade 3 were observed in 76.9% (10 /13) of patients, but blood cell counts recovered within 3 weeks. Robust expansion of CAR T-cells occurred in all patients, with a median time to peak expansion of 8 days. Importantly, no exacerbation of hemophagocytic syndrome occurred following CAR-T cell infusion, and no patients succumbed to adverse events. In conclusion, our findings suggest that CD19 CAR-T cell treatment exhibits high efficacy as part of first-line therapy for B-LAHS, with a manageable safety profile.

Disclosures No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-189192