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POSTER ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

A Parallel Comparison of the Safety and Efficacy of Allogeneic Hematopoietic Stem Cell Transplantation for Refractory and Relapsed T-ALL/Lbl Patients Who Achieved Complete Remission with CD7 CAR-T Versus Patients Who Achieved First Complete Remission with Chemotherapy before Transplantation

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Introduction

We have developed a fratricide-resistant CD7 CAR-T cells from bulk T cells transduced with CD7 CAR without gene editing or additional gene transfer, named
naturally selected CD7 CAR-T (NS7CAR-T). NS7 CAR-T therapy has shown a robust complete remission (CR) rate in patients with refractory or relapsed (R/R) T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma (T-ALL/LBL). Nonetheless, the risk of relapse remains a challenge post-CD7 CAR-T therapy alone, suggesting the potential benefits of consolidation allogeneic hematopoietic stem cell transplantation (allo-HSCT). The question remains whether CD7 CAR-T therapy could increase the incidence of post-transplant complications. Here we conduct a parallel study to compare the safety and efficacy of allo-HSCT in R/R T-ALL/LBL patients who achieved CR with NS7 CAR-T therapy vs those who reached first CR (CR1) using chemotherapy prior to transplantation.

Methods

Between November 2020 and January 2023, a total of 223 consecutive patients with T-ALL/LBL who underwent allo-HSCT at our center were retrospectively analyzed. Patients who met the following criteria were included in this parallel study: 1) underwent the first allo-HSCT in our hospital, 2) achieved CR before transplantation either from NS7CAR-T therapy or CR1 from chemotherapy (Fig. 1). A total of 139 patients met the criteria for analysis and underwent allo-HSCT after achieving CR either from NS7CAR-T therapy (n=43) or chemotherapy (CR1=96). The median patient age at the time of transplantation was 15 years (range: 1-51 years). The median follow-up time was 370 days (2-941 days). CD7 CAR-T patients were from two clinical trials registered at www.clinicaltrials.gov NCT04572308, NCT04916860. Transplant donor types included sibling identical (n=12), haploidentical (n=110), and unrelated donors (n=17). We used total body irradiation (TBI)-based conditioning regimens (n=128) or Busulfan/Melphalan-based regimens (n=11). To prevent graft-versus-host disease (GVHD), we used ATG along with a short-term regimen combining methotrexate, cyclosporine/tacrolimus, and mycophenolate mofetil.

Results

The characteristics of patients from both groups are detailed in Table 1. The median interval between CD7 CAR-T treatment and transplantation was 59 (39-131) days. Within the CAR-T group, 16 patients had primary refractory disease, 18 had relapsed disease and 9 in minimal residual disease (MRD)-positive status in bone marrow before CD7 CAR-T therapy. Prior to CAR-T therapy, 55.8% (24 patients) had extramedullary lesions. In comparing the CAR-T and chemotherapy CR1 groups, we observed no significant differences in long-term efficacy post-allo-HSCT. The 2-year leukemia-free survival (LFS) rates were 64.9 (95% CI, 49.1-79.2)% and 69.8 (95% CI, 59.0-79.6)% (p=0.340); the 2-year overall survival (OS) rates were 64.1 (95%CI, 48.0-78.6)% and 71.8 (95%CI, 60.5-81.9)% (p=0.107); the 2-year relapse incidence (RI) rates were 9.3 (95%CI, 3.7-23.7)% and 11.5 (95%CI, 6.4-20.7)% (p=0.873); and the 2-year non-relapsed mortality (NRM) rates were 28.3 (95% CI, 16.9-47.4)% and 21.6 (95% CI, 13.9-33.4)% (p=0.244), for the CD7 CAR-T and non-CAR-T groups, respectively. The incidence of all grades of acute GVHD (aGVHD) 37.2 (95%CI, 25.2-54.9)% vs. 42.1 (95%CI, 33.3-53.3)% did not significantly differ between the CAR-T and non-CAR-T groups. A trend toward an increased rate but no P significance was observed in Grade 3-4 aGVHD incidence of 20.93 (95%CI, 11.7-37.4)% vs. 9.5 (95%CI, 5.1-17.6)% (p=0.139). One-year incidences of moderate to severe chronic GVHD (cGVHD) were 12.2 (95%CI, 5.4-28.0)% and 18.0 (95%CI, 11.5-28.0)% (p=0.357) in the CD7CAR-T and non-CAR-T groups, respectively (Table 2).

No statistically significant differences were detected in the occurrences of transplant-associated thrombotic microangiopathy (TA-TMA), CMV, EBV, and HHV-6 infections between the two groups. Upon analyzing, we found that r/r patients who received allo-HSCT after achieving remission with NS7 CAR-T had a similar OS to CR1 patients (Fig. 2).

Conclusions

Our parallel study showed that T-ALL/LBL patients, who achieved CR via CD7 CAR-T therapy followed by a consolidation allo-HSCT, had similar favorable OS and LFS compared to patients who underwent allo-HSCT in the CR1 state induced by chemotherapy. This was achieved without increasing the incidence of GVHD, infections, or TA-TMA.

Disclosures No relevant conflicts of interest to declare.

Table 1. Characteristics of patients in the CD 7 CAR-T and chemotherapy CR1 groups

Variables	CD7 CAR-T group No.(%) n=43	Chemotherapy CR1 group No.(%) n=96	*P value*
Age, median(range)years	17	14.5	0.067
Gender, male/female	33/10	76/20	0.748
Time from diagnosis to HSCT; median(range) days	270	153	0.000
Diagnosis; n (%)			0.125
T-ALL	35	87	
T-LBL	8	9	
MRD status before transplant			0.176
MRD-negative	38	91	
MRD-positive	5	5	
Conditioning regimens			0.784
TBI	40	88	
Bu/Mel	3	8	
Donor age, median(range)years	33		
Donor source			0.085
Sibling-identical	1	11	
Haplo	34	76	
URD	8	9	
Stem cell source; n (%)			0.083
BM+PB	32	83	
PB	11	13	
Infused MNC count; median(range)×10^8/kg	8.8	10.4	0.012
Infused CD34+ cells count; median(range)×10^6/kg	5.0	5.0	0.489
Infused CD3+ cells count; median(range)×10^8/kg	1.5	2.0	0.058
DLI after HSCT; n (%)			
Follow-up time, median(range)days	300.0	436.5	0.029

Table 2. Clinical outcomes and complications after allo-HSCT in the CD7 CAR-T and chemotherapy groups

Variables	CD7 CAR-T-group Median (range) (n=43)	Chemotherapy CR1 group Median(range) (n=96)	*P value*
Time to neutrophil>500/ μ L, days	15	13	0.067
Time to platelet>20×10^9/L, days	14	13	0.024
Day 30 neutrophil engraftment(95%CI)	97.7(93.3-100)%	97.9(95.1-100)%	0.189
Day 100 platelet engraftment(95%CI)	86.1(76.3-97.1)%	92.7(87.7-98.1)%	0.087
2-year LFS (95%CI)	64.9(49.1-79.2)%	69.8(59.0-79.6)%	0.340
2-year OS (95%CI)	64.1(48.0-78.6)%	71.8(60.5-81.9)%	0.107
2-year RI (95%CI)	9.3(3.7-23.7)%	11.5(6.4-20.7)%	0.873
2-year NRM (95%CI)	28.3(16.9-47.4)%	21.6(13.9-33.4)%	0.244
Day 100 aGVHD all grades (95%CI)	37.2(25.2-54.9)%	42.1(33.3-53.3)%	0.661
Day 100 grade 3-4 aGVHD (95%CI)	20.9(11.7-37.4)%	9.5(5.1-17.6)%	0.139
1-year all grades cGVHD (95%CI)	30.2(18.7-48.8)%	27.4(19.6-38.3)%	0.899
1-year moderate to severe cGVHD (95%CI)	12.2(5.35-28.0)%	18.0(11.5-28.0)%	0.357
Day 100 CMV reactivation (95%CI)	55.8(42.8-72.8)%	53.2(44.0-64.1)%	0.781
Day 100 EBV reactivation (95%CI)	20.9(11.7-37.4)%	20.8(14.1-30.8)%	0.577
2-year PTLD	2.3(0.3-16.1)%	2.5(0.6-10.1)%	0.915
2-year TA-TMA	11.6(5.1-26.5)%	12.2(6.2-23.9)%	0.585
Day 100 HHV-6 infection	4.7(1.2-18.0)%	2.1(0.5-8.2)%	0.179

Figure 1: Patients enrollment diagram

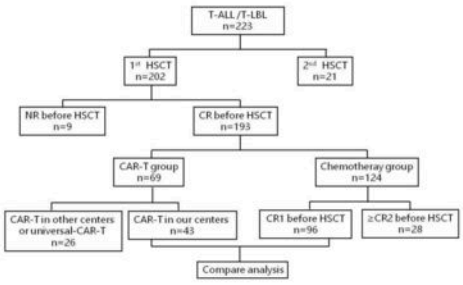

Figure 2: Overall survival among the total, CR1 induced by chemotherapy and CD7 CAR-T groups after allo-transplantation

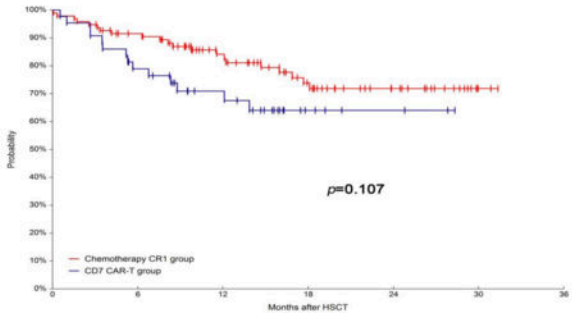

Figure 1

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