ELSEVIER

Blood 142 (2023) 3515–3516

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

CAR T-Cell Therapy Combined with PD-1 Inhibitors Significantly Improve the Efficacy and Prognosis of r/r DLBCL with TP53 Alterations

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More than 40% of patients diagnosed with diffuse large B-cell lymphoma (DLBCL) eventually develop relapsed or refractory (r/r) disease and typically have poor outcomes. Autologous chimeric antigen receptor T-cell therapy (CART) has emerged as a crucial second line treatment option for r/r DLBCL, but 60-70% of patients still relapse or are refractory. Recent research has shed light on the role of TP53 alterations (mutation or deletion) in r/r DLBCL patients who do not respond well to CART cell therapy. The findings in this study will show that the combination of CART with PD-1 inhibitors (ICIs) had a significant impact on the efficacy and prognosis of r/r DLBCL patients with TP53 alterations.

This retrospective analysis included adult DLBCL patients who were treated at Shanghai Tongji Hospital of Tongji University with autologous CD19 (N=20) or CD20 (N=2, patient 6 and 7, Fig.1 A) CART-cell therapy between January 1, 2019, and September 30, 2022. All enrolled patients provided their informed consent to participate in the study. The protocol of the study was reviewed and approved by the Institutional Review Board of the National Cancer Institute, ensuring ethical practices were followed. A total of 22 patients with TP53 alterations undergoing CD19-CART therapy were included, of which 2 patients received CD20 CART cell after recurrence of CD19 CART cell therapy. The total dose of CD19 or CD20-CAR T-cell is between 1- 3x10^6/kg. Sintilimab/Tislelizumab was used as PD-1 inhibitors (3 mg/kg in patients weighing <60 kg or 200 mg in patients weighing ≥60 kg) every three weeks within 6 weeks after CAR-T infusion. 1 case had grade 3-4 Cytokine Release Syndrome (CRS) and no case had CART-cell-related encephalopathy syndrome (CRES).

In Table 1, the patients are divided into two groups. One group received CART cells combined with PD-1 inhibitors (ICI+), while the other group received CART cells only (ICI-). The median ICIs treatment time after CART infusion was 17 days (IQR 11-38 days). Baseline factors such as age, gender, disease severity, previous treatment history and etc. had no substantial differences between the groups.

Treatment regimen and the subsequent response were shown in Fig.1 A and B. Patient 1-9 received ICIs treatment after CART cell therapy, of which 8 cases (88.9%) showed the best objective response rate (ORR) at day 90 after CART infusion (Fig.1B) and 6 cases (66.7%) achieved complete remission (CR). In comparison, among the 13 individuals who were treated with CART alone, only 3 cases (23.1%) showed the best ORR at day 90 after CART infusion and only 1 case (7.7%) achieved complete remission. We found a significant difference between the two treatment groups by performing a Chi-square test (P=0.009). Our results suggest that the addition of PD-1 inhibitors to the CART regimen significantly improves the treatment outcome in patients with TP53 alterations.

In Fig.1 C and D, we show that the median progression-free survival (PFS) was NR (not reached) vs. 1.7 months (95% CI:1.0 month-2.3 months) and the median overall survival (OS) was NR vs.10.9 months (95% CI: 3.8 months-18.1 months) in the ICI+ and the ICI- groups. The p-values for PFS and OS was 0.001 (HR=0.18, 95% CI: 0.07-0.47) and 0.003 (HR=0.15, 95% CI: 0.05-0.42) between the two groups. These results suggest that patients in the combination treatment group experienced less disease progression and were more likely to survive longer.

Overall, our study demonstrates the potential benefits of combining immunotherapies, specifically CART with PD-1 inhibitors, in the treatment of relapsed or refractory DLBCL patients with TP53 alterations.

Disclosures No relevant conflicts of interest to declare.

Patients' characteristics

Characteristics	TP53 Altered N=22 (%)	ICI- N=13 (%)	ICI+ N=9 (%)	P
Gender				0.47
Male	13 (59.1)	9 (69.2)	4 (44.4)	
Female	9 (40.9)	4 (30.8)	5 (55.6)	
Age at enrollment				1
<60y	14 (63.6)	8 (61.5)	6 (66.7)	
≥60y	8 (36.4)	5 (38.5)	3 (33.3)	
Hans classification				1
GCB	4 (18.2)	2 (15.4)	2 (22.2)	
N-GCB	18 (81.8)	11 (84.6)	7 (77.8)	
Double expression				1
Yes	9 (40.9)	5 (38.5)	4 (44.4)	
No	13 (59.1)	8 (61.5)	5 (55.6)	
Double hit				1
Yes	1 (4.5)	1 (7.7)	0 (0)	
No	21 (95.5)	12 (92.3)	9 (100)	
Stage at enrollment				1
I-II	2 (9.1)	1 (7.7)	1 (11.1)	
III-IV	20 (90.9)	12 (92.3)	8 (88.9)	
ECOG at enrollment				0.61
0-1	12 (54.5)	6 (46.2)	6 (66.7)	
2-	10 (45.5)	7 (53.8)	3 (33.3)	
IPI score				1
0-2	11 (50)	6 (46.2)	5 (55.6)	
3-4	11 (50)	7 (53.8)	4 (44.4)	
LDH at enrollment				0.61
Low-Normal	10 (45.5)	7 (53.8)	3 (33.3)	
High	12 (54.5)	6 (46.2)	6 (66.7)	
Extra-nodual disease				0.27
0-2	15 (68.1)	10 (76.9)	5 (55.6)	
≥3 organs	7 (31.8)	3 (23.1)	4 (44.4)	
Prior lines of therapy				0.16
1-3	2 (9.1)	0 (0)	2 (22.2)	
≥4 lines	20 (90.9)	13 (100)	7 (77.8)	
Prior ASCT				1
Yes	2 (9.1)	1 (7.7)	1 (11.1)	
No	20 (90.9)	12 (92.3)	8 (88.9)	
Prior CART				0.16
Yes	1 (4.5)	0 (0)	2 (22.2)	
No	21 (95.5)	13 (100)	7 (77.8)	
Response at enrollment				1
PR	2 (9.1)	1 (7.7)	1 (0)	
PD/SD	20 (90.9)	12 (92.3)	8 (100)	
TP53 alterations				-
Mutations	10 (45.5)	7 (53.8)	3 (33.3)	
Deletions	8 (36.4)	5 (38.5)	3 (33.3)	
Mutations and Deletions	4 (18.2)	1 (7.7)	3 (33.3)	

Table1 Baseline characteristics of the patients.

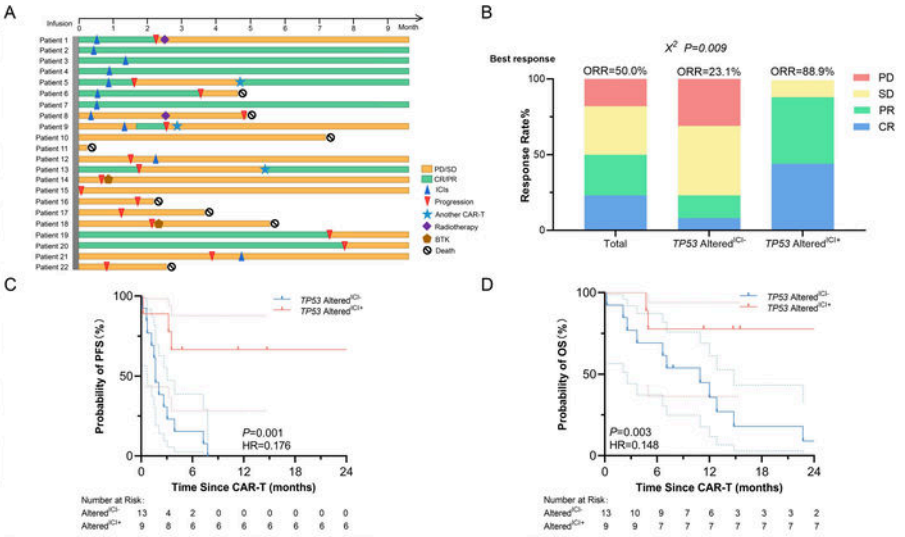

Figure1 Outcomes of r/r DLBCL individuals with TP53 alterations after CART infusion alone or combined with PD-L1/PD-1 inhibitors.
(A) Swimmer plot with the response of each individual patient after CART infusion (n=22). Data cutoff was 24 months or death. (B) Best responses after CART infusion alone or combined with PD-L1/PD-1 inhibitors at day 90. Kaplan-Meier analysis of PFS (C) and OS (D) is shown.

Figure 1

https://doi.org/10.1182/blood-2023-180500