CAR-T CELL THERAPY IN THE TREATMENT OF RELAPSED/REFRACTORY AGGRESSIVE B-CELL LYMPHOMAS

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Introduction

The current standard of treatment for patients with relapsed/refractory B-cell non-Hodgkin lymphoma (r/rB-NHL) are high-dose chemotherapy followed by auto-HSCT and targeted therapy. However, the prognosis for this group of patients remains extremely unfavorable. The most promising treatment method is CAR-T cell therapy.

Aim

To present a single institute experience of CAR-T therapy for patients with r/r B-NHL.

Methods

From September 2018 to October 2023, 11 patients with r/r B-NHL received CAR-T cell therapy: DLBCL-3, BL-2, HGBL transformation from FL-1, PML-1, FL3A – 3, MZL -1. Median age 49 (32-65); M/F=7/4; 6 (54%) of 11 had a mutations in the TP53 gene; median number of lines of therapy 3 (1-4); 4 patients underwent auto-HSCT; 6 received targeted therapy; 4 patients - intensive R-mNHL-BFM-90 program as the first line. Disease status before CAR-T therapy: complete remission - 1, partial remission - 1, relapse - 4 (including with damage to the central nervous system - 1), progression - 5. Characteristics of pts and the therapy performed are presented in Table 1.

Results

7 pts received anti-CD19 CAR-T therapy; anti-CD19/22 – 1, anti-CD19/20/22 -1, CD19/22/GD2 – 1, CD19/CD30/CD22/PSMA – 1. All 11 pts underwent standard lymphodepletion (fludarabine, cyclophosphamide). On the day of CAR-T cell administration, cytokine release syndrome (CRS) prophylaxis was administered with tocilizumab. CRS, grade 1 on the CTCAE 5.0 scale, developed in 2 patients. Neurotoxicity was observed in 1 patient with neuroleukemia. No grade 3-4 hematological toxicity was recorded in any patient.

Analysis of treatment results was carried out in 11 pts; 10 pts achieved CR, 1 patient showed PR. With a median follow-up of 11 months (2-60), relapse developed in 2 (1%) patient with BL (number 7 and 10) with a mutTP53 gene (Fig1); 1 (10%) died from SARS Cov2 at +11 months.

Fig.1 Patients with mutTP53.

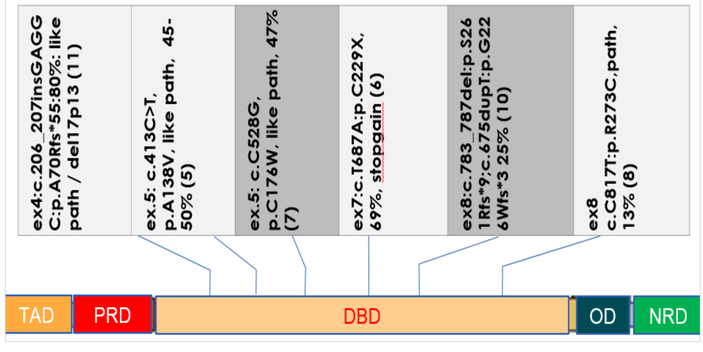


Table1. Patients characteristics.

№	Gender, age	Diagnosis	TP53	Number of prior courses	Previous therapy	Results	CAR-T	Results, months
1	F, 32	PMBL, IIIst	wt	1	R-EPOCH №5	Rel	CD19/CD30/CD22/PSMA	CR +60
2	F, 56	FL 2, IVst	wt	3	GB №6, R-CHOP №4, R-DHAP №2, auto-HSCT, Lena №2	Rel	CD19/CD22 GD2	CR +54
3	M, 55	DLBCL, non-GCB, IIIst	wt	3	R-mNHL-BFM-90 №6, R-DHAPN№2, auto-HSCT	Rel	CD19 CD22	CR +36
4	F, 65	FL 3A IIIst	wt	4	R-CHOPN№4,R-DHAPN№2, R-mNHL-BFM-90 auto-HSCT, PEPCN№1, Ibr+Ven №2	Rel	CD19/CD22 CD19/CD20	CR +11, Death from Cov2
5	M, 38	DLBCL non-GCB, IIIst	mut	2	R-mNHL-BFM-90+Lena №2, DHAP+Benda +Ibr+Lena №1	Progr	CD19	CR +24
6	M, 64	FL3A transformation to DLBCL IIst	mut	3	R-CHOPN№4,DHAPN№2,auto-HSCT, R2N№1	Rel	CD19	CR +18
7	M, 35	BL, IVst CNS involvement,	mut	2	R-mNHL-BFM-90 № 4 Pola+NivoN№3	Progr	CD19	CR +10 Relapse, death from tumor progression
8	F, 54	MZL IIIst transformation to DLBCL	mut	1	R-EPOCH №2, R-HMAN№2	PR	CD19	CR +10
9	M, 65	DLBCL IIE st, single MYC	wt	3	R-CHOPN№4, R-DHAPN№2, CMED	Progr	CD19	CR +7
10	M, 40	BL, III st	mut	2	R-mNHL-BFM-90N№4	Progr	CD19	CR+2 Relapse, death from tumor progression
11	M, 34	HGBL IV st transformation from FL	del17p/ mut	1	R-mNHL-BFM-90+Ven №2	Progr	CD19	PR +20

Summary

Our own experience has demonstrated the high effectiveness of CAR-T cell therapy in the treatment of r/r B-NHL, including those with mutations in the TP53 gene. In the future, it is rational to identify a group at high risk of developing relapse to integrate CAR-T therapy into the 1st line of treatment.