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POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Efficacy and Safety of Chimeric Antigen Receptor T Cells Therapy Strategy with Dual Targeting of CD19 and CD70 to Treat Relapsed/Refractory Diffuse Large B-Cell Lymphoma

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Background: Chimeric antigen receptor (CAR) T cells therapy is highly effective in the treatment of B-cell lymphoma, providing alternative therapeutic options for patients who failed to respond to conventional treatment or relapse. Despite impressive progress, more than 30-50% of patients treated with CD19 CAR-T cells experienced progressive disease. Antigen escape is one of the common causes of relapse, especially CD19-negative relapse. Absent or decreased cell surface CD19 as a mechanism of resistance after CD19 CAR-T cells treatment. CD70 is a novel and promising therapeutic target due to the restricted expression pattern in normal tissues and over expression in some lymphoma tissues. Our center explored the efficacy and safety of CAR-T cells therapy with dual targeting of CD19 and CD70 in the treatment of r/r lymphoma.
Patients and Methods: The study included 8 relapsed/refractory diffuse large B-cell lymphoma patients, all patients have exhausted all available treatment options with progressive or stable disease and life expectancy >2 months were enrolled in the study. All patients expressed strong positivity of CD19 and CD70, all of patient details can be found in the table (Fig.1). Autologous T cells were apheresis collected and transduced with an apoptosis-inducible, safety-engineered lentiviral CAR with the following intracellular signaling domains: CD28/CD27/CD3z-iCasp9. All patients received cyclophosphamide/fludarabine chemotherapy conditioning 1-2 days before infusions of CAR-T cells. The quality of apheresis cells, efficiencies of gene transfer and T cell proliferation, CAR-T infusion dose and blood CAR copies were quantitatively documented.
Results: In the first months after CAR-T cells infusion, 75.0% (6/8) of patients achieved complete response (CR), while 12.5% (1/8) of patients evaluated as partial response (PR) and 12.5% (1/8) of patients as progressive disease (PD), overall response rate (ORR) is 87.5% (7/8). In the evaluation of safety, 37.5% (3/8) of patients experienced cytokine release syndrome (CRS), and 25% (2/8) of patients experienced grade 1 CRS and 12.5% (1/8) of patients experienced grade 2 CRS, no case of severe CRS defined as≥grade 3 and no immune effector cell-associated neurotoxicity syndrome (ICANS) occurred. After a median follow-up of 19.9 months, 50% (4/8) of patients maintained CR, while 37.5% (3/8) of patients were relapsed, with a duration of response (DOR) of 50% (4/8), median DFS was 10.5 months and median OS was not reached (Fig.2).
Conclusions: In summary, our research data confirms that the efficacy and safety of CD19/CD70 dual targeted CAR-T cells infusion, continued follow-up will determine whether the CD19/CD70 CAR-T cells therapy can obtain long term overall survival in our study. How to further improve the efficacy and safety of dual target CAR-T is still worth exploring. It's needed to optimize multi-specific targeting by CAR-T cells to improve the efficacy both in B cell malignancies and other hematological malignancies.

Disclosures No relevant conflicts of interest to declare.

No.	Gender	Age	Diagnosis	Pathologic subtype	Molecular genetics changes	Disease status	No.of previous theraples	Disease burden LDH(IU/L)	Tumor mass diameter(cm)	Target	Dose infused of CAR19($x10^6$)	Dose infused of CAR70($x10^6$)	1 month	Last follow-up	Relapsed or not	Relapsed date	Death or not	Lost date
1	Women	47	DLBCL	non-GCB	NOTCH2、KTMT2D	Relapse	4	714.4	0.8	CD19+CD70	1.7	1.5	CR	Relapse	Yes	2022-2-23	No	\
2	Male	44	DLBCL	non-GCB	NOTCH2、B2M	Relapse/Refractory	4	307.2	1.2	CD19+CD70	2.2	1.7	CR	Relapse	Yes	2022-2-28	No	\
3	Male	65	DLBCL	GCB	\	Primary refractory	2	221.7	5.3	CD19+CD70	1.17	1	CR	CR	No	2023-7-31	No	2022-6-27
4	Women	61	DLBCL	non-GCB	TP53 del、KTMT2D、CD79B	Primary refractory	6	285.6	20.6	CD19+CD70	1.97	1.65	PR	CR	No	2023-7-31	No	\
5	Male	63	DLBCL	non-GCB	KMT2D、BCL-6、TP53、ARID1B、CD79B、DTX1、INDD5P、MEF2B、XPO1	Relapse/Refractory	2	\	3.5	CD19+CD70	1.39	1.08	CR	CR	No	2019-4-10	No	\
6	Male	50	DLBCL	non-GCB	\	Relapse	3	\	1.4	CD19+CD70	1.71	1.23	CR	CR	No	2023-7-31	No	\
7	Women	48	DLBCL	non-GCB	NOTCH1、TP53	Primary refractory	3	150.3	3	CD19+CD70	1.6	1.56	PD	Relapse	Yes	2022-5-26	No	\
8	Women	61	DLBCL	non-GCB	CMY-C、BCL2、PAX5	Relapse/Refractory	3	183.4	5	CD19+CD70	2.2	2.9	CR	Relapse	Yes	2022-11-20	No	\

Fig.1 Patient details list

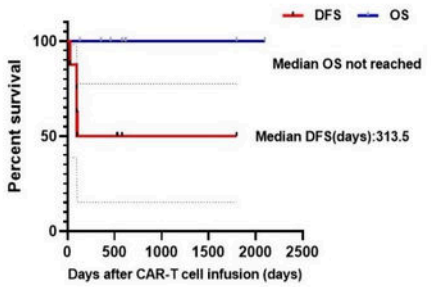

Fig.2 Survival of CAR-T treated patients disease free survival period and overall survival of all the enrolled patients were shown. The dashed lines indicate the 95% confidential interval.

Figure 1

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