



## OPEN ACCESS

## EDITED BY

Yulai Zhou,  
Yale University, United States

## REVIEWED BY

Lipei Shao,  
National Institutes of Health (NIH),  
United States  
Alexander Joshue Acosta,  
University Eloy Alfaro of Manabí, Ecuador  
Silvana Novelli,  
Catalan Institute of Oncology, Spain

## \*CORRESPONDENCE

Xiaoyan Ke  
✉ kexy@gobroadhealthcare.com  
Kai Hu  
✉ huk@gobroadhealthcare.com

RECEIVED 24 October 2025

REVISED 28 November 2025

ACCEPTED 18 December 2025

PUBLISHED 13 January 2026

## CITATION

Li D, Liu R, Fu Z, Yang F, Ma L, Cao M, Guo Y,  
Deng B, Chang AH, Zheng Q, Ke X and  
Hu K (2026) CAR-T cell therapy in  
TP53-mutated CNS lymphoma: overcoming a  
high-risk genetic barrier.  
*Front. Med.* 12:1731589.  
doi: 10.3389/fmed.2025.1731589

## COPYRIGHT

© 2026 Li, Liu, Fu, Yang, Ma, Cao, Guo, Deng,  
Chang, Zheng, Ke and Hu. This is an  
open-access article distributed under the  
terms of the [Creative Commons Attribution  
License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or  
reproduction in other forums is permitted,  
provided the original author(s) and the  
copyright owner(s) are credited and that the  
original publication in this journal is cited, in  
accordance with accepted academic  
practice. No use, distribution or reproduction  
is permitted which does not comply with  
these terms.

# CAR-T cell therapy in TP53-mutated CNS lymphoma: overcoming a high-risk genetic barrier

Danyang Li<sup>1</sup>, Rui Liu<sup>1</sup>, Zhonghua Fu<sup>1</sup>, Fan Yang<sup>1</sup>, Lixia Ma<sup>1</sup>,  
Miaomiao Cao<sup>1</sup>, Yuelu Guo<sup>1</sup>, Biping Deng<sup>1</sup>, Alex H. Chang<sup>2,3</sup>,  
Qinlong Zheng<sup>4</sup>, Xiaoyan Ke<sup>1,5\*</sup> and Kai Hu<sup>1\*</sup>

<sup>1</sup>Department of Lymphoma and Myeloma Research Center, Beijing GoBroad Hospital, Beijing, China,

<sup>2</sup>Engineering Research Center of Gene Technology, Ministry of Education, Institute of Genetics,  
School of Life Sciences, Fudan University, Shanghai, China, <sup>3</sup>Shanghai YaKe Biotechnology Ltd.,  
Shanghai, China, <sup>4</sup>Department of Medical Laboratory, Beijing GoBroad Boren Hospital, Beijing, China,

<sup>5</sup>Department of Hematology, Peking University Third Hospital, Beijing, China

**Background:** Central nervous system lymphoma (CNSL) is a rare but aggressive subtype of lymphoma that presents significant therapeutic challenges. The prognosis for patients with CNSL varies significantly based on several genetic factors, including TP53 mutations, which are among the most critical determinants of treatment outcomes. Chimeric antigen receptor T (CAR-T) cell therapy has shown promising results in several hematological malignancies, including B-cell lymphomas. However, its efficacy in CNSL, particularly in patients with TP53 mutations, requires further investigation.

**Methods:** A retrospective cohort study was conducted on 61 CNSL patients who had been treated at our institution from 2020 to 2024. The median follow-up time was 14.5 months. A total of 43 patients received CAR-T cell infusion therapy. The overall survival (OS) and progression-free survival (PFS) of patients harboring TP53 mutations (TP53+) and those with wild-type TP53 (TP53-) were compared. In addition, factors associated with patient prognosis were also identified.

**Results:** Among the 43 patients who received CAR-T cell therapy, 17 harbored TP53 mutations. The median age of the cohort was 51.5 years, and 51.2% of the patients (22/43) were male. The overall response rate (ORR) and the complete response rate (CRR) in the TP53+ CAR-T+ group were both 64.5% (11/17), the median OS duration was 14.07 months (95% CI 12.63–∞), and the median PFS duration was 12.77 months (95% CI 6.33–∞). In the TP53-CAR-T+ group, the ORR was 73.3% (19/26), the CRR was 69.2% (18/26), the median OS duration was 33.47 months (95% CI 11.23–∞), and the median PFS duration was 22.4 months (95% CI 6.13–∞). In the subgroup analysis, the cell-of-origin (COO) classification was a key factor influencing the long-term survival of CNSL patients; in the TP53+ group, patients with non-germinal center B-cell-like (GCB) classification had longer OS compared to the GCB subtype ( $p = 0.003$ ).

**Conclusion:** CAR-T cell therapy is an effective treatment for CNSL patients harboring TP53 mutations and has the same efficacy as traditional treatment methods. Additionally, CAR-T cells may be more effective for TP53+ CNSL patients with a non-GCB classification.

## KEYWORDS

CAR-T, cell therapy, CNSL, TME, TP53

## Introduction

Central nervous system (CNS) lymphoma includes primary CNS lymphoma (PCNSL) and secondary CNS involvement in systemic lymphoma (1). The first-line treatment for PCNSL is chemotherapy based on high-dose methotrexate (HD-MTX), with or without rituximab and radiotherapy (2). However, these conventional regimens are associated with severe side effects such as delayed neurotoxicity, which can lead to cognitive impairment. While there is no established standard treatment for PCNSL recurrence, temsirolimus, lenalidomide, temozolomide, and the Bruton's tyrosine kinase (BTK) inhibitor ibrutinib are potential options for refractory patients. Over the past few decades, the prognosis of PCNSL patients has improved significantly (median OS: 26 months, 5-year survival rate: 31%) (3).

Histo-genetic and molecular analyses of PCNSL have identified ATM, TP53 (4), PTEN (5), PIK3CA (6), JAK3, CTNNA1, PTPN11, and KRAS as major determinants of pathogenesis, survival, and recurrence (7). TP53 alterations are established markers of poor prognosis in various cancers. P53 regulates apoptosis (8) and may also play a role in immune evasion and the induction of an immunosuppressive tumor microenvironment (TME) (9, 10), factors that can influence the cytotoxicity of chimeric antigen receptor (CAR)-T cells against large-cell B-cell lymphoma (LBCL). However, the impact of TP53 mutations on the efficacy of CAR-T cell therapy in CNSL patients remains unclear. In this observational study, we explored the influence of TP53 mutations on the efficacy of CAR-T cell therapy in CNSL patients.

## Methods

### Patients

Sixty-one patients diagnosed with CNSL from 2020 to 2024 at Beijing GoBroad Hospital were enrolled. All patients were diagnosed with CNSL according to the current diagnostic criteria and had failed first-line treatment. According to the Lugano lymphoma efficacy evaluation criteria, treatment failure includes failure to achieve complete

remission (CR)/partial remission (PR) after the first-line treatment, progression within 6 months after CR/PR, stable disease (SD) lasting for  $\geq 6$  months, or progressive disease (PD). Forty-three patients, including 22 men and 21 women, received CAR-T cell infusion therapy (designated as CAR-T+ in the study). The median age of the cohort was 51.5 years (range, 32–71 years). All patients who did not respond to first-line treatment or experienced a relapse received further treatment at our hospital. We conducted biopsies of the patients' tumor masses and performed next-generation sequencing on the samples, and TP53 mutations were detected. As shown in Figure 1, 17 CAR-T+ patients harbored TP53 mutations (TP53+ CAR-T+), whereas the remaining 26 patients were negative for TP53 mutations (TP53-CAR-T+).

The baseline clinical characteristics of the patients are listed in Table 1. Survival time was defined as the period from the infusion of CAR-T cell therapy to the last follow-up, relapse, or death. This study was approved by the Ethics Committee of Beijing GoBroad Hospital. All patients participated in the clinical trial using the CAR-T cell product (11) from Shanghai YaKe Biotechnology Co., Ltd., in China (clinical registration number ChiCTR2100055062). Written informed consent was obtained from all participants or their families prior to obtaining samples.

### CD19 CAR-T product

A lentiviral vector encoding a CD19 CAR with a 4-1BB costimulatory domain and a CD3-zeta signaling domain was constructed. The CD19 recognition domain consisted of a single-chain fragment variable region derived from the FMC63 monoclonal antibody. This CD19 CAR-T cell was available as an investigational new drug (IND) product from Shanghai YaKe Biotechnology Co., Ltd.

### Endpoints

The primary endpoints were overall response rate (ORR), complete response rate (CRR), overall survival (OS), progression-free

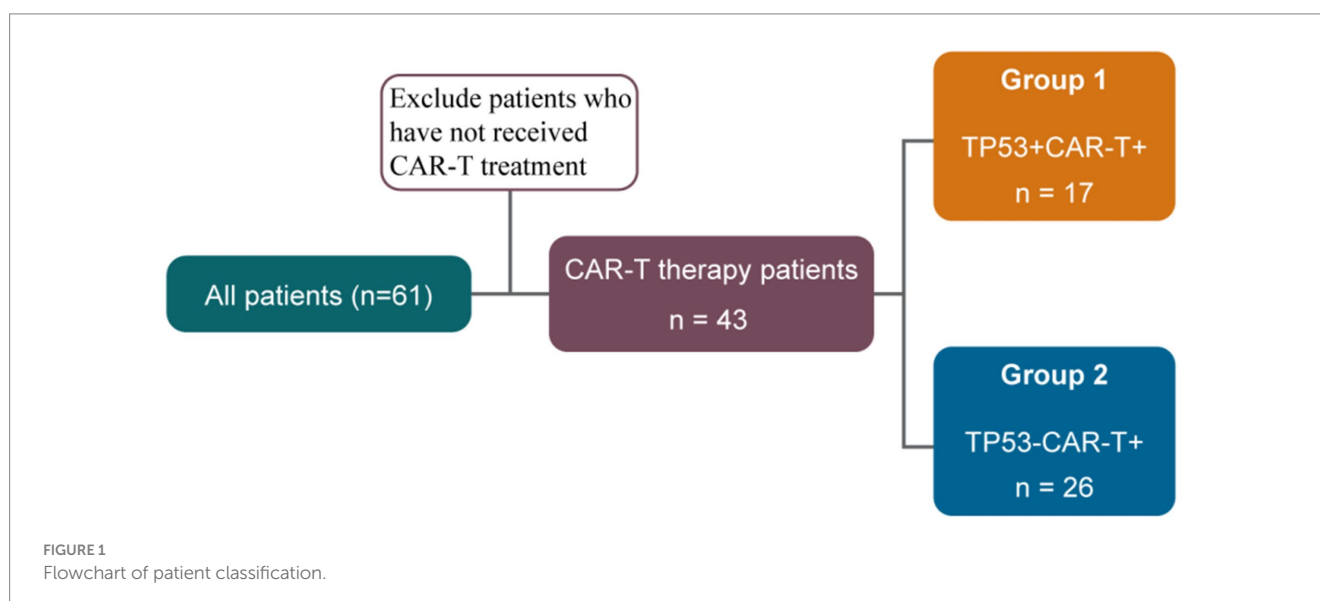


TABLE 1 Patients' characteristics.

Characteristics	Whole cohort		TP53 mutation ( <i>n</i> = 17)		TP53 WT ( <i>n</i> = 26)		<i>p</i> -value <sup>a</sup>
	No.	%	No.	%	No.	%	
	43	100	17	39.5	26	60.5	
Age							
Median (range)	51.5 (32–71)		51 (32–70)		52 (32–71)		
≥60 years, <i>n</i> (%)	12	27.91	7	41.18	5	19.23	0.859
Sex							0.289
Female, <i>n</i> (%)	21	48.84	11	64.71	10	38.46	
Male, <i>n</i> (%)	22	51.16	15	88.24	7	26.92	
Diagnosis							0.722
PCNSL	29	67.44	12	70.59	17	65.38	
SCNSL	14	32.56	5	29.41	9	34.62	
Previous treatment lines							0.021
≥3	22	51.16	5	29.41	17	65.38	
<3	21	48.84	12	70.59	9	34.62	
ECOG score							0.502
≥3	8	18.60	4	23.53	4	15.38	
<3	35	81.40	13	76.47	22	84.62	
COO							0.055
GCB	25	58.14	10	58.82	15	57.69	
Non-GCB	9	20.93	6	35.29	3	11.54	
Unknown	9	20.93	1	5.88	8	30.77	
IPI score							0.973
≥3	10	23.26	4	23.53	6	23.08	
<3	33	76.74	13	76.47	20	76.92	
MYC rearrangement							0.851
Yes	8	18.60	3	17.65	5	19.23	
No	18	41.86	8	47.06	10	38.46	
Unknown	17	39.53	6	35.29	11	42.31	
BCL-2 rearrangement							0.851
Yes	7	16.28	3	17.65	4	15.38	
No	16	37.21	7	41.18	9	34.62	
Unknown	20	46.51	7	41.18	13	50.00	
BCL-6 rearrangement							0.622
Yes	10	23.26	3	17.65	7	26.92	
No	12	27.91	6	35.29	6	23.08	
Unknown	21	48.84	8	47.06	13	50.00	
Pre-treatment efficacy of CAR-T therapy							0.464
CR	21	48.84	7	41.18	14	53.85	
PR	9	20.93	3	17.65	6	23.08	
SD	7	16.28	1	5.88	0	0.00	
PD	12	27.91	6	35.29	6	23.08	
The site of tumor invasion							0.255
Brain parenchyma	23	53.49	9	52.94	14	53.85	

(Continued)

TABLE 1 (Continued)

Characteristics	Whole cohort		TP53 mutation ( <i>n</i> = 17)		TP53 WT ( <i>n</i> = 26)		<i>p</i> -value <sup>a</sup>
	No.	%	No.	%	No.	%	
	43	100	17	39.5	26	60.5	
Secondary brain parenchyma	5	11.63	1	5.88	4	15.38	
Secondary cerebrospinal fluid	2	4.65	0	0.00	2	7.69	
Cerebrospinal fluid and brain parenchyma	11	25.58	5	29.41	6	23.08	
Secondary spinal canal	2	4.65	2	11.76	0	0.00	

COO, cell of origin; GCB, germinal center B cell; Pearson's chi-squared test.

survival (PFS), and adverse events. OS was measured from the date of CAR-T cell therapy to the date of death or the last follow-up. PFS was measured from the initiation of CAR-T therapy to the date of disease progression or death due to the disease. Treatment efficacy was assessed according to the Lugano 2014 criteria. The exploratory endpoint was to evaluate the impact of TP53 mutation status and other factors on clinical outcomes.

## Statistical analysis

The demographic and other baseline data have been presented as frequencies and percentages. The probabilities of OS and PFS were calculated using the Kaplan–Meier method and compared using the log-rank test. The 95% CI for survival was calculated using GraphPad Prism V.9.0 software. SPSS version 26.0 and GraphPad Prism version 9.0 were used for data analysis. A two-sided *p*-value of <0.05 was considered statistically significant.

## Results

### CAR-T therapy is effective in patients with TP53 mutations

Of the 43 CNSL patients included in the study, 17 harbored TP53 mutations. The median age was 51.5 years, and 22 patients (51.2%) were male. Table 2 provides a detailed description of the TP53 mutation types. Before the CAR-T treatment, the tumor burden of the patients and the efficacy of the before CAR-T treatment were evaluated. Among TP53– patients, 18 (69.2%) achieved complete response (CR), and 10 patients (38.5%) underwent CAR-T treatment with tumor mass. Among TP53+ patients, 7 (41.2%) achieved CR, and 9 (52.9%) underwent CAR-T treatment with tumor mass (Table 3).

The ORR and CRR of TP53+ CAR-T+ patients were both 64.5% (11/17). The median OS duration was 14.07 months (95% CI 12.63–∞), and the median PFS was 12.77 months (95% CI 6.33–∞). In the TP53-CAR-T+ group, the ORR was 73.3% (19/26), the CRR was 69.2% (18/26), the median OS duration was 33.47 months (95% CI 11.23–∞), and the median PFS duration was 22.4 months (95% CI 6.13–∞) (Figure 2 and Table 4). Compared with patients with TP53 mutations, those with wild-type TP53 had longer OS and PFS after CAR-T cell therapy. However, there was no statistically significant

difference between the two groups of patients. Although it is unclear whether TP53 affects the prognosis of patients with central nervous system lymphoma, our research suggests that CAR-T therapy is also effective in CNSL patients with TP53 mutations (12, 13).

### Adverse events

Among the TP53+ CAR-T+ patients, 41.2% (7/17) did not experience cytokine release syndrome (CRS), 52.9% (9/17) experienced grade 1–2 CRS, and only 1 (5.9%) experienced grade 3–4 CRS. The reactions were controllable for all patients. Furthermore, one patient had grade 3–4 immune effector cell-associated neurotoxicity syndrome (ICANS). In the TP53-CAR-T+ group, 46.2% of the patients (12/26) did not experience CRS, 46.2% (12/26) experienced grade 1–2 CRS, and only 7.7% (2/26) experienced grade 3–4 CRS. Two patients had grade 3–4 ICANS (Table 5). Based on these results, no conclusion could be drawn regarding the impact of TP53 mutations on the safety of CAR-T cell therapy. No other hematological-related toxicities were observed.

### Subgroup analysis

The impact of patient age, sex, prior treatment regimen, Eastern Cooperative Oncology Group score, first-line efficacy, International Prognostic Index score, and previous ASCT was analyzed by univariate and multivariate Cox regression analyses. All 61 patients were included in the analyses. We identified cell-of-origin (COO) as a key factor influencing the OS (Figure 3). TP53+ patients with the non-germinal center B-cell-like (GCB) subtype had longer survival compared to patients with the GCB lymphoma subtype. In contrast, no significant difference was observed in the prognosis of the GCB and non-GCB subgroups in patients with wild-type TP53 (Figure 4). Interestingly, patients with TP53 mutations exhibited shorter OS after conventional therapies (such as chemotherapy and stem cell transplantation) when compared to those without TP53 mutations, suggesting that the mutation may confer resistance to standard treatments.

## Discussion

The results of this study indicate that CAR-T therapy is effective for CNSL patients with TP53 mutations. While significant ORR and

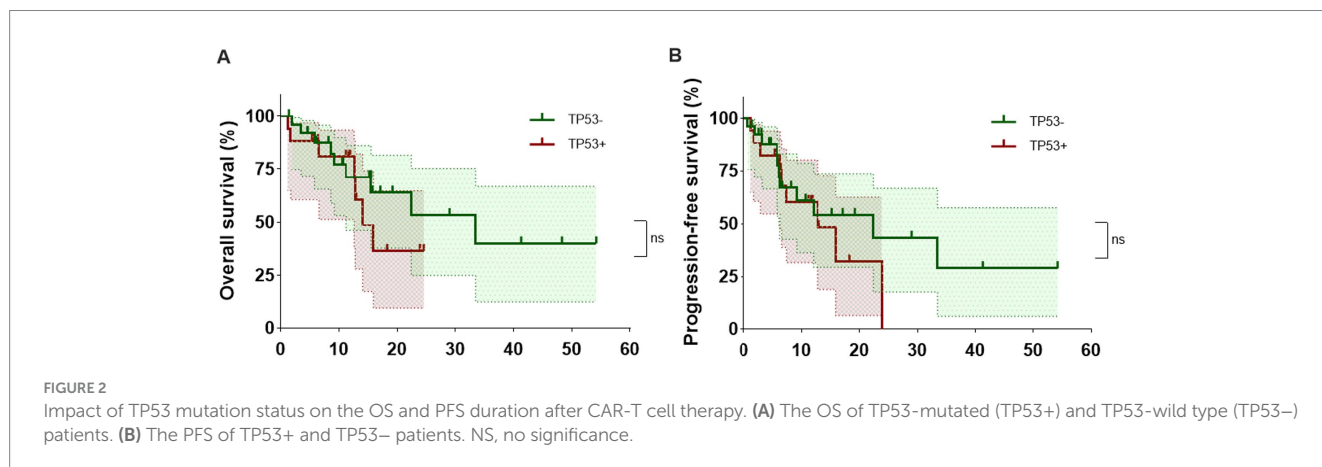
TABLE 2 The type of TP53 mutation in patients.

Patients No.	cDNA level	Protein level	Patients No.	cDNA level	Protein level
1	c.650T>G	p.V217G	10	c.215C>G	p.Pro72Arg
2	c.604C>T	p.R202C	11	c.916C>T/c.743G>A	—
3	c.437G>A	p.W146X	12	—	—
4	c.391A>T	p.N131Y	13	c.742C>G/c.641A>G	p.R248G/p.H214R
5	c.733G>A	p.G245S	14	c.404G>A	p.C135Y
6	c.408A>C	p.Q136H	15	—	—
7	—	—	16	c.215C>G	p.Pro72Arg
8	c.535C>T	p.H179Y	17	c.524G>A	p.Arg175His
9	c.581T>G	p.L194R			

Data of patient 7, patient 12, and patient 15 were lost because they were obtained through a next-generation sequencing conducted outside the hospital.

TABLE 3 Tumor burden and efficacy before CAR-T therapy.

Characteristics	TP53 mutation (n = 17)	TP53 WT (n = 26)	p-value
	No. (%)	No. (%)	
Tumor burden before CAR-T			0.35
Yes	9 (52.9)	10 (38.5)	
No	8 (47.1)	16 (61.5)	
Efficacy before CAR-T			0.119
CR	7 (41.2)	18 (69.2)	
PR	4 (23.5)	5 (19.2)	
PD	6 (35.3)	3 (11.5)	



CRR were observed in the TP53+ CAR-T+ group, the median OS and median PFS were longer in the TP53-CAR-T+ group. Nevertheless, the presence of TP53 mutations did not significantly impact the PFS in patients treated with CAR-T cells. In addition, the frequency of adverse events, particularly CRS, was also similar in the TP53+ and TP53- groups. We also identified COO classification as a key factor influencing patient survival. Furthermore, patients harboring TP53 mutations had shorter OS after conventional therapies, which suggests that TP53 mutations may confer resistance to standard treatments.

Although TP53 mutations are not established prognostic factors for CNSL, they have been reported in patients with CNSL (12, 13). In

a prospective study on patients with diffuse large B-cell lymphoma (DLBCL), mutations in the MYD88 and TP53 genes were identified as sensitive, specific, and accurate predictors of overall mortality and disease progression (14). In the majority of patients with anaplastic lymphoma kinase (ALK)-positive anaplastic large-cell lymphoma (ALCL), long-term survival can be achieved with CHOP chemotherapy. However, TP53 deletion is a risk factor in ALK+ALCL patients treated with the CHOP-based regimens (15). A large retrospective study of patients with refractory/relapsed aggressive B-cell non-Hodgkin's lymphoma (r/r B-NHL) reported that CAR-T cell therapy achieved an ORR of 87.1% and a CRR of 45.2%. The

TABLE 4 Efficacy of CAR-T cell therapy in TP53+ and TP53- patients.

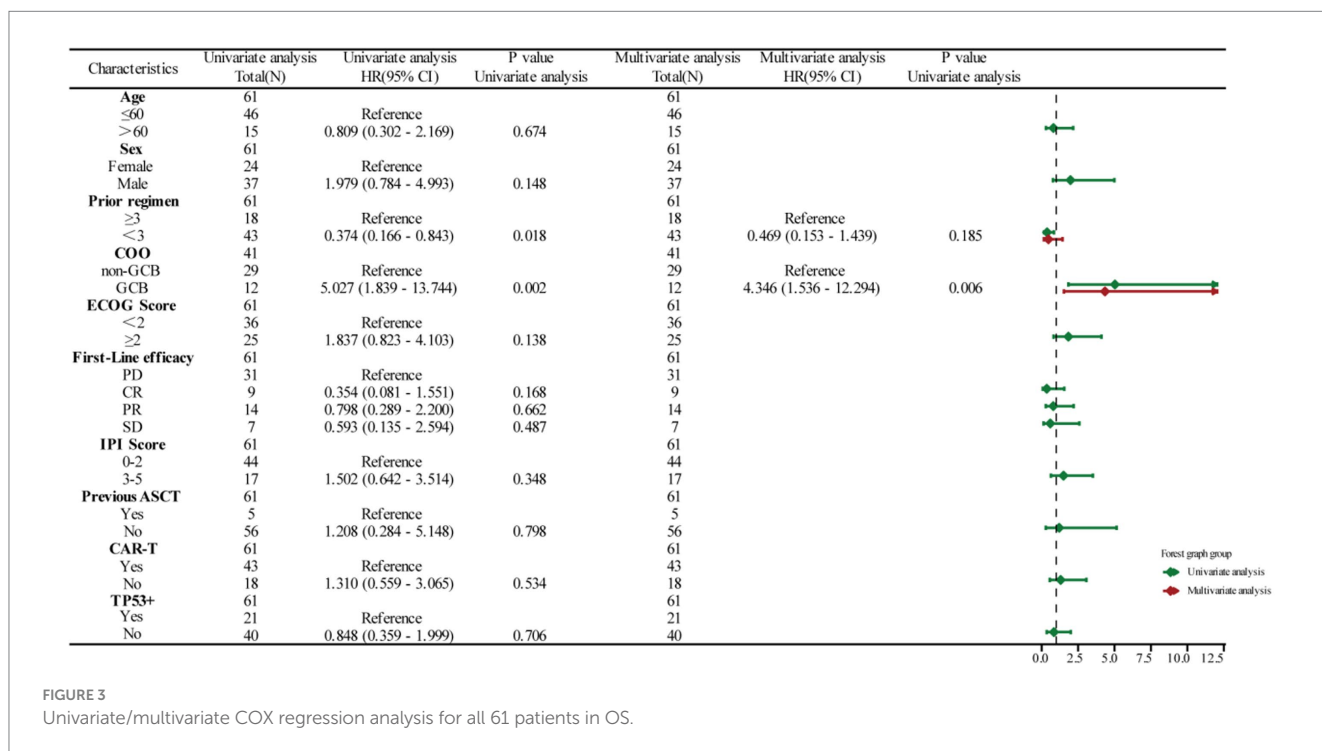
n (95% CI)	CAR-T therapy (n = 43)			
	ORR	CRR	OS	PFS
TP53+ (n = 17)	11/17 (64.5%)	11/17 (64.5%)	14.07 (12.63-∞)	12.77 (6.33-∞)
TP53- (n = 26)	19/26 (73.3%)	18/26 (69.2%)	33.47 (11.23-∞)	22.4 (6.13-∞)

ORR, overall response rate; CRR, complete response rate; OS, overall survival; PFS, progressive-free survival; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; TP53+, presence of TP53 mutation; TP53-, TP53 wild-type. ∞, upper bound not estimable, due to the insufficient follow-up time for some patients, it is impossible to estimate the upper limit of the confidence interval.

TABLE 5 Adverse events in TP53+ and TP53- patients after CAR-T cell therapy.

Adverse events	CRS			ICANS		
	Grade 0	Grades 1-2	Grades 3-4	Grade 0	Grades 1-2	Grades 3-4
Group 1	7/17 (41.2%)	9/17 (52.9%)	1/17 (5.9%)	15/17 (88.2%)	1/17 (5.9%)	1/17 (5.9%)
Group 2	12/26 (46.2%)	12/26 (46.2%)	2/26 (7.7%)	24/26 (92.3%)	0	2 (7.7%)
Total	19/43 (44.2%)	21/43 (48.8%)	3/43 (7.0%)	39/43 (90.7%)	17/43 (39.5%)	3/43 (7.0%)

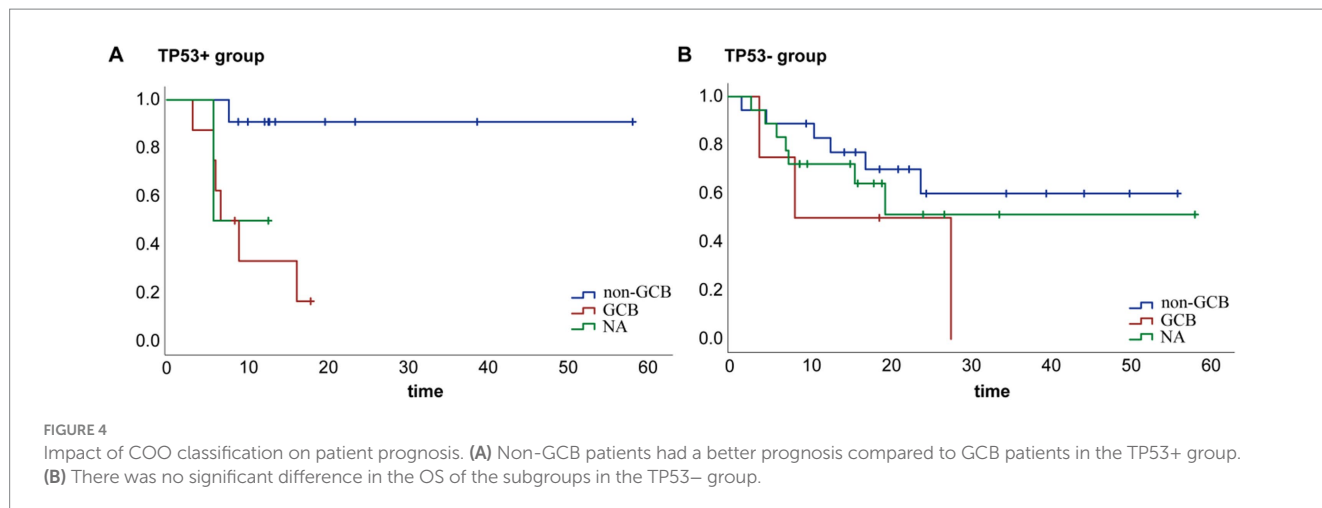
Group 1, TP53 mutation with CAR-T therapy; Group 2, TP53 no mutation with CAR-T therapy.



median PFS was 14.8 months for patients harboring TP53 mutations, and the 24-month OS was 56.3% (16), indicating that CAR-T cell therapy is effective regardless of TP53 mutations. Du et al. (17) constructed a TP53 missense mutation-based risk model for DLBCL using bioinformatics analysis and machine learning, and confirmed that patients with TP53 mutations had a worse prognosis. In addition, multiple studies have shown that CAR-T cell therapy is effective in non-Hodgkin lymphoma patients with TP53 mutations (18-21).

Although our findings provide constructive guidance on the efficacy of CAR-T therapy for CNSL with TP53 mutations, there are

still some limitations to our study. First, this study was conducted at a single center, which may limit the general applicability of the results. Second, the sample size was relatively small, and only 17 patients had TP53 mutations, which may lead to insufficient statistical power and make it difficult to draw highly representative conclusions. Therefore, future multi-center and large-sample studies are needed to enhance the reliability and validity of the results. Nevertheless, this study provides a basis for the future treatment of CNSL, such as the use of combination therapy (22), targeted treatments (23, 24), and new delivery systems such as nanomaterial delivery systems (25-27).



## Conclusion

Our study indicated that CAR-T cell therapy is an effective treatment for CNSL with TP53 mutations and has comparable efficacy to traditional treatment methods in patients without TP53 mutations. However, due to relatively lower efficacy in TP53+ patients, it may be necessary to adopt alternative or combination therapies. Apart from the TP53 mutation status, the COO classification should also be considered when choosing the most appropriate treatment plan for CNSL. CAR-T cell therapy may have better efficacy in patients with TP53 mutations and non-GCB classification.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

The studies involving humans were approved by Ethics Committee at Beijing GoBroad Hospital in Beijing. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

## Author contributions

DL: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. RL: Conceptualization, Writing – original draft, Writing – review & editing. ZF: Investigation, Writing – original draft, Writing – review & editing. FY: Conceptualization, Writing – original draft, Writing – review & editing. LM: Software, Writing – original draft, Writing – review & editing. MC: Methodology, Writing – original draft, Writing – review & editing. YG: Data curation, Writing – original draft,

Writing – review & editing. BD: Supervision, Writing – original draft, Writing – review & editing. AC: Methodology, Writing – original draft, Writing – review & editing. QZ: Formal analysis, Writing – original draft, Writing – review & editing. XK: Project administration, Writing – original draft, Writing – review & editing. KH: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

## Funding

The author(s) declared that financial support was not received for this work and/or its publication.

## Acknowledgments

We express our gratitude to the Cell Biology Department and FCM Core of Beijing GoBroad Hospital.

## Conflict of interest

AC was employed by Shanghai YaKe Biotechnology Ltd. The remaining author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Generative AI statement

The author(s) declared that Generative AI was not used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

## Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated

organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

## References

- Do, J, Yenwongfai, LN, Do, SI, Kim, SW, and Na, K. Comparative study on the clinicopathologic and molecular characteristics of primary and secondary diffuse large B-cell lymphoma in the central nervous system. *Anticancer Res.* (2024) 44:2953–60. doi: 10.21873/anticancer.17107
- Schaff, LR, and Grommes, C. Primary central nervous system lymphoma. *Blood.* (2022) 140:971–9. doi: 10.1182/blood.2020008377
- Schaff, L, Nayak, L, and Grommes, C. Bruton's tyrosine kinase (BTK) inhibitors for the treatment of primary central nervous system lymphoma (PCNSL): current progress and latest advances. *Leuk Lymphoma.* (2024) 65:882–94. doi: 10.1080/10428194.2024.2333985
- Munch-Petersen, HD, Asmar, F, Dimopoulos, K, Areškevičiūtė, A, Brown, P, Girkov, MS, et al. TP53 hotspot mutations are predictive of survival in primary central nervous system lymphoma patients treated with combination chemotherapy. *Acta Neuropathol Commun.* (2016) 4:40. doi: 10.1186/s40478-016-0307-6
- Zhang, X, Wu, Y, Sun, X, Cui, Q, Bai, X, Dong, G, et al. The PI3K/AKT/mTOR signaling pathway is aberrantly activated in primary central nervous system lymphoma and correlated with a poor prognosis. *BMC Cancer.* (2022) 22:190. doi: 10.1186/s12885-022-09275-z
- Lakshmanan, A, and Byrd, JC. Spotlight on ibrutinib in PCNSL: adding another feather to its cap. *Cancer Discov.* (2017) 7:940–2. doi: 10.1158/2159-8290.CD-17-0714
- Yokogami, K, Azuma, M, Takeshima, H, and Hirai, T. Lymphomas of central nervous system. *Adv Exp Med Biol.* (2023) 1405:527–43. doi: 10.1007/978-3-031-23705-8\_20
- Thomas, AF, Kelly, GL, and Strasser, A. Of the many cellular responses activated by TP53, which ones are critical for tumour suppression? *Cell Death Differ.* (2022) 29:961–71. doi: 10.1038/s41418-022-00996-z
- Blagih, J, Buck, MD, and Vousden, KH. p53, cancer and the immune response. *J Cell Sci.* (2020) 133:jcs237453. doi: 10.1242/jcs.237453
- Munoz-Fontela, C, Mandinova, A, Aaronson, SA, and Lee, SW. Emerging roles of p53 and other tumour-suppressor genes in immune regulation. *Nat Rev Immunol.* (2016) 16:741–50. doi: 10.1038/nri.2016.99
- Pan, J, Tang, K, Luo, Y, Seery, S, Tan, Y, Deng, B, et al. Sequential CD19 and CD22 chimeric antigen receptor T-cell therapy for childhood refractory or relapsed B-cell acute lymphocytic leukaemia: a single-arm, phase 2 study. *Lancet Oncol.* (2023) 24:1229–41. doi: 10.1016/S1470-2045(23)00436-9
- Geng, H, Mo, S, Chen, L, Ballapuram, A, Tsang, M, Lu, M, et al. Identification of genomic biomarkers of disease progression and survival in primary CNS lymphoma. *Blood Adv.* (2025) 9:1117–31. doi: 10.1182/bloodadvances.2024014460
- Severson, EA, Haberberger, J, Hemmerich, A, Huang, RSP, Edgerly, C, Schiavone, K, et al. Genomic profiling reveals differences in primary central nervous system lymphoma and large B-cell lymphoma, with subtyping suggesting sensitivity to BTK inhibition. *Oncologist.* (2023) 28:e26–35. doi: 10.1093/oncolo/oyac190
- Ebid, OAEH, Ezz El Arab, LR, Saad, AS, Ezz El Din, M, Mostafa, N, Swellam, M, et al. Prognostic impact of MYD88 and TP53 mutations in diffuse large B cell lymphoma. *Ann Hematol.* (2023) 102:3477–88. doi: 10.1007/s00277-023-05420-1
- Katagiri, S, Akahane, D, Takeyama, K, Sato, N, Takayama, N, Ando, J, et al. TP53 deletion is associated with poor survival of adult ALK-positive ALCL patients receiving CHOP-based chemotherapy. *Ann Hematol.* (2025) 104:1801–6. doi: 10.1007/s00277-025-06297-y
- Wei, J, Xiao, M, Mao, Z, Wang, N, Cao, Y, Xiao, Y, et al. Outcome of aggressive B-cell lymphoma with TP53 alterations administered with CAR T-cell cocktail alone or in combination with ASCT. *Signal Transduct Target Ther.* (2022) 7:101. doi: 10.1038/s41392-022-00924-0
- Du, KX, Wu, Y-F, Hua, W, Duan, Z-W, Gao, R, Liang, J-H, et al. Identify truly high-risk TP53-mutated diffuse large B cell lymphoma patients and explore the underlying biological mechanisms. *Cell Commun Signal.* (2024) 22:401. doi: 10.1186/s12964-024-01765-w
- Shouval, R, Alarcon Tomas, A, Fein, JA, Flynn, JR, Markovits, E, Mayer, S, et al. Impact of TP53 genomic alterations in large B-cell lymphoma treated with CD19-chimeric antigen receptor T-cell therapy. *J Clin Oncol.* (2022) 40:369–81. doi: 10.1200/JCO.21.02143
- Porpaczy, E, Wohlfarth, P, Königsbrügge, O, Rabitsch, W, Skrab, C, Staber, P, et al. Influence of TP53 mutation on survival of diffuse large B-cell lymphoma in the CAR T-cell era. *Cancers.* (2021) 13:5592. doi: 10.3390/cancers13225592
- Xu-Monette, ZY, Wu, L, Visco, C, Tai, YC, Tzankov, A, Liu, WM, et al. Mutational profile and prognostic significance of TP53 in diffuse large B-cell lymphoma patients treated with R-CHOP: report from an international DLBCL rituximab-CHOP consortium program study. *Blood.* (2012) 120:3986–96. doi: 10.1182/blood-2012-05-433334
- Wen, W, Zhang, WL, Tan, R, Zhong, TT, Zhang, MR, and Fang, XS. Progress in deciphering the role of p53 in diffuse large B-cell lymphoma: mechanisms and therapeutic targets. *Am J Cancer Res.* (2024) 14:3280–93. doi: 10.62347/LHIO8294
- Li, D, Liu, R, Fu, Z, Yang, F, Ma, L, Guo, Y, et al. Combination autologous stem cell transplantation with chimeric antigen receptor T-cell therapy for refractory/relapsed B-cell lymphoma: a single-arm clinical study. *Front Immunol.* (2025) 16:1532460. doi: 10.3389/fimmu.2025.1532460
- Chen, X, Zhang, T, Su, W, Dou, Z, Zhao, D, Jin, X, et al. Mutant p53 in cancer: from molecular mechanism to therapeutic modulation. *Cell Death Dis.* (2022) 13:974. doi: 10.1038/s41419-022-05408-1
- Liu, R, Yang, F, Ma, L, Guo, Y, Cao, M, Fu, Z, et al. CAR T-cell therapy provides an opportunity for further consolidation treatment for relapsed or refractory adult Burkitt lymphoma patients. *Front Oncol.* (2025) 15:1566938. doi: 10.3389/fonc.2025.1566938
- Kang, X, Li, D, and Sun, R. Nanotechnology and natural killer cell immunotherapy: synergistic approaches for precise immune system adjustment and targeted cancer treatment in gastrointestinal tumors. *Front Med.* (2025) 12:1647737. doi: 10.3389/fmed.2025.1647737
- Zhao, X, Xiong, J, Li, D, and Zhang, Y. Clinical trials of nanoparticle-enhanced CAR-T and NK cell therapies in oncology: overcoming translational and clinical challenges—a mini review. *Front Med.* (2025) 12:1655693. doi: 10.3389/fmed.2025.1655693
- Zhu, T, Li, Y, Wang, Y, and Li, D. The application of dendritic cells vaccines in tumor therapy and their combination with biomimetic nanoparticles. *Vaccines.* (2025) 13:337. doi: 10.3390/vaccines13040337