Transfusion Medicine and Hemotherapy

Case Report

Transfus Med Hemother
DOI: 10.1159/000531681

Received: November 8, 2022
Accepted: June 21, 2023
Published online: August 22, 2023

Quartic CAR-T Cell Bridging to Twice Allo-HSCT Therapy in a Patient with Acute Lymphoblastic Leukemia

Qing Zhang Yi Dong Zhimin Zhai Qianshan Tao

Department of Hematology, The Second Affiliated Hospital of Anhui Medical University, Hefei, China

Keywords

Acute lymphoblastic leukemia · Relapse · Refractory · CAR-T cell · Hematopoietic stem cell transplantation

Abstract

Introduction: Chimeric antigen receptor T (CAR-T) cell therapy is an effective bridging treatment for allogeneic hematopoietic stem cell transplantation (allo-HSCT) in relapsed or refractory acute lymphoblastic leukemia (ALL). However, repetitive CAR-T cell therapy and allo-HSCT can only be performed in a few patients because of technical difficulties and patients' physical, economic, and social conditions. ***Case Presentation:*** A 23-year-old female patient with second relapsed B-cell ALL (B-ALL) underwent human-murine chimeric CD19 CAR-T cell therapy twice, human-murine chimeric CD22 CAR-T cell therapy once, and humanized CD19 CAR-T cell therapy once. Moreover, she was sequentially bridged to her mother donor allo-HSCT once and cousin donor allo-HSCT once. ***Conclusion:*** Repetitive CAR-T cell therapy bridging to repetitive allo-HSCT is still a safe and active therapeutic strategy for patients with relapsed or refractory ALL.

Introduction

Adult acute lymphoblastic leukemia (ALL) is a rare hematological malignancy with poor prognosis [1]. Patients with relapsed or refractory ALL often undergo allogeneic hematopoietic stem cell transplantation (allo-HSCT) to achieve long-term survival. However, it is difficult to achieve complete remission (CR) and create the right conditions for allo-HSCT only through traditional chemotherapy. Chimeric antigen receptor T (CAR-T) cell therapy is a new type of precise targeted therapy for the treatment of leukemia; moreover, it has been used as a great bridging therapy before allo-HSCT in relapsed or refractory ALL [2]. The conventional structure of CAR consists of three components: a single-chain variable fragment (scFv), a transmembrane domain, and an endodomain. The second and third CAR structures introduce one or two costimulatory signaling domains to the endodomain. Most scFV has been obtained through human-animal immunization, but due to the immunogenicity and drug resistance of human-animal scFv, fully humanized scFvs are now applied in many clinical trials [3, 4]. However, few patients with relapsed or refractory ALL can undergo repetitive CAR-T cell and allo-HSCT because of the technical difficulties and patients' physical, economic, and social conditions. Herein, we report an adult female with second relapsed B-cell ALL (B-ALL) who successfully underwent quartic CAR-T cell bridging to twice allo-HSCT.

Case Presentation

A 23-year-old female patient was admitted to a local hospital due to leukocytosis in August 2017. Routine blood examination showed leukocytosis and anemia. Bone marrow cytology showed 83.5% lymphoblastic leukemia blasts, immunophenotyping showed 83% CD10-and CD19-positive B-ALL, chromosomes showed normal karyotype, 43 fusion genes were all negative, and

karger@karger.com
www.karger.com/tmh

Correspondcence to:
Qianshan Tao, ahmutqs@126.com

Table 1. Clinical characteristics and therapy process of the patient with B-ALL

Time	Disease status	Therapy regiment and dosages	Curative effect	Adverse reaction
August 2017	ND	Initial induction chemotherapy: VDCLP (vincristine 2 mg on day 1, 8, 15, 22, adriamycin 70 mg on day 1–3, cyclophosphamide 1,000 mg on day 1, 15, pegaspargase 3750IU on day 19, prednisone 60 mg on day 1–14 and 40 mg on day 15–28)	CR 1	–
September 2017	CR 1	Consolidation therapy: VDCLP/CAM (VDCLP: same as above; CAM: cyclophosphamide 1,200 mg on day 1, cytarabine 1,600 mg every 12 h on day 2–4, 6-mercaptopurine 80 mg on day 1–7)	CCR	–
August 2018	Relapse 1	Reinduction chemotherapy: VDCP (vincristine 2 mg on day 1, 8, 15, 22, idarubicin 10 mg on day 1, 8, 15, 22, cyclophosphamide 1,000 mg on day 1, 15, dexamethasone on day 1–4, 8–11, 15–18, 22–25)	CR 2	–
September 2018	CR 2	Consolidation therapy: VDCLP (same as above)	CCR	–
November 2018	Relapse 2	Autologous human-murine CD19 CAR-T	CR 3	CRS 1
June 2019	Relapse 3	Re-induction chemotherapy: VDCLP/hyper-CVAD (VDCLP: same as above; hyper-CVAD: cyclophosphamide 450 mg every 12 h on day 1–3, vincristine 2 mg on day 4 and day 11, liposomal doxorubicin 40 mg on day 4, dexamethasone 40 mg on day 1–4, day 11–14)	No remission	–
October 2019	Refractory	Autologous human-murine CD19 CAR-T	No remission	CRS 2
November 2019	Refractory	Autologous human-murine CD22 CAR-T	CR 4	CRS 2
January 2020	CR 4	Mother donor haploidentical allo-HSCT	CCR	GVHD 1
October 2021	Relapse 4	Autologous humanized CD19 CAR-T	CR 5	CRS 2
December 2021	CR 5	Cousin donor haploidentical allo-HSCT	CCR	GVHD 1

ND, newly diagnosed; CR, complete remission; CCR, continuous complete remission; CRS, cytokine release syndrome; GVHD, graft versus host disease.

next-generation sequencing (NGS) showed positive CTCF gene mutation. She was diagnosed with "ALL (common-B, standard risk group)" according to the National Comprehensive Cancer Network guideline. On September 10, 2017, the initial induction chemotherapy, which consisted of a VDCLP regimen, was administered (Table 1). On day 29, routine blood and bone marrow examination showed CR. Two rounds of consolidation chemotherapy, including VDCLP and CAM regimens (Table 1); multiple lumbar punctures and intrathecal injection of chemotherapeutic drugs to prevent central nervous system leukemia were performed in the next 2 months (Fig. 1). However, the patient refused to continue consolidation chemotherapy and allo-HSCT because of her physical, economic, and social conditions.

On August 09, 2018, the patient had a fever, and routine blood examination showed leukocytosis, anemia, and thrombocytopenia. The patient went to our hospital for further treatment. Bone marrow cell morphology showed 89.5% lymphoblastic leukemia blasts, immunophenotyping showed 95% CD10-and CD19-positive B-ALL, chromosomes showed normal karyotype, and 43 fusion genes were all negative, suggesting first early intramedullary relapse. On August 10, 2018, the VDCP regimen was administered (Table 1). On day 28, bone marrow cell morphology and immunophenotyping showed no primitive naive lymphocytes, suggesting that the patient had achieved CR again. In September 2018, one cycle of consolidation chemotherapy (i.e., the VDCLP regimen) was administered, and simultaneously, the patient was actively being prepared for allo-HSCT. Unfortunately, the patient relapsed again in November 2018.

Peripheral blood cells were collected from the patient on November 30, 2018, and human-murine scFv CAR-T cell was cultured in Sinobioway Cell Therapy Co., Ltd. for further treatment [5] (Table 2). In December 2018, cyclophosphamide (1,200 mg) was administered on days 1–2; then, CD19 CAR-T cell (1.89×10^9) was infused. On day 3 after CD19 CAR-T cell infusion, the patient had a low-grade fever and muscle soreness, which was defined as cytokine release syndrome (CRS) 1 according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE V4.0). The treatment efficacy was evaluated as CR on day 28 after CD19 CAR-T cell infusion. In June 2019, the patient was admitted to our hospital for regular examination. Bone marrow cell morphology showed that the proportion of primitive naive lymphocytes was 66%, and immunophenotyping showed 67% CD19-positive abnormal lymphocytes. CAR-T cell could not be detected in peripheral blood or bone marrow. The patient was considered to have relapsed for the

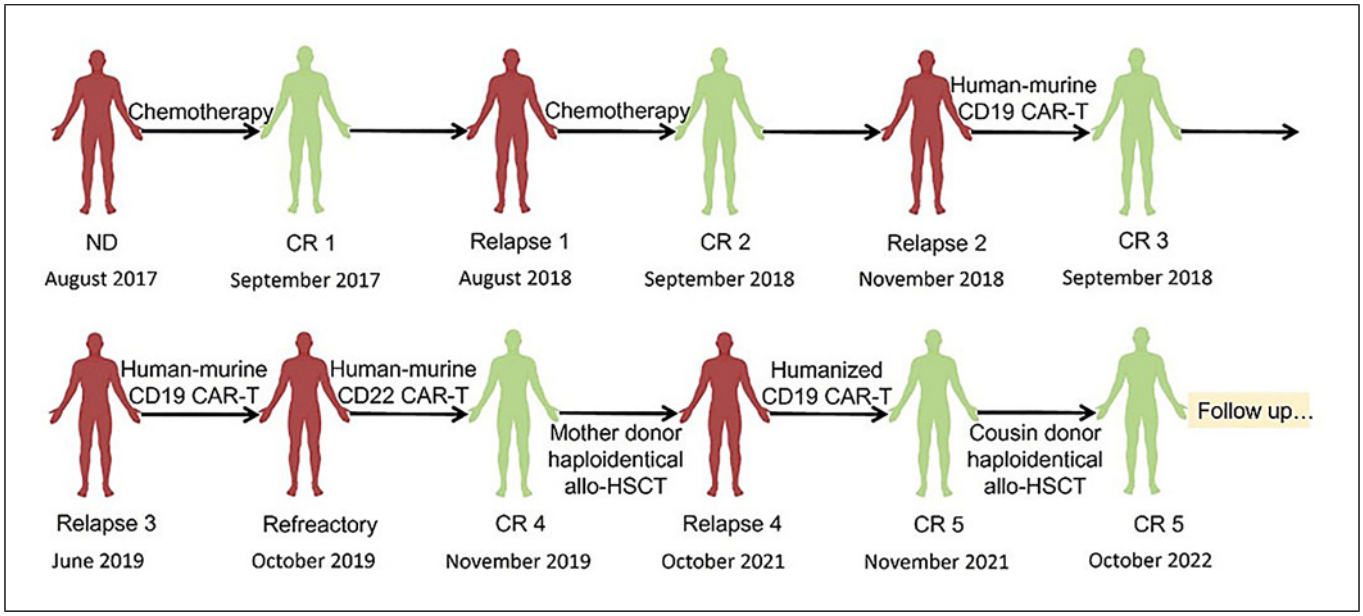

Fig. 1. Therapy process of the patient with B-ALL.

Table 2. Characterization of the four infusions of CAR-T cell and two allo-HSCT

	1st CAR-T	2nd CAR-T	3rd CAR-T	1st allo-HSCT	4th-CAR-T	2nd allo-HSCT
Vector	Lentivirus	Lentivirus	Lentivirus	–	Lentivirus	–
scFV	Human-murine	Human-murine	Human-murine	–	Humanized	–
CAR structure	Anti-CD19 scFV-CD28-4-1BB-CD3ζ	Anti-CD19 scFV-CD28-4-1BB-CD3ζ	Anti-CD22 scFV-CD8a-4-1BB-CD3ζ	–	Anti-CD19 scFV-CD8a-4-1BB-CD3ζ	–
Generation	3	3	3	–	3	–
CAR-T cell dose	1.89×10^9	9.39×10^7	2.00×10^7	–	1.42 × 107	–
Expression of CD19/CD22	CD19+CD22+	CD19+CD22+	CD19+CD22+	–	CD19+CD22+	–
Manufacturer	GenScript (Nanjing) Co., Ltd.	GenScript (Nanjing) Co., Ltd.		–		–
Response	CR	NR	CR	–	CR	–
CRS	1	2	2	–	2	–
Disease state pre-allo-HSCT	–	–	–	CR	–	CR
Donor	–	–	–	Mother	–	Cousin
HLA matches	–	–	–	5/10	–	5/10
Pretreatment regimen	–	–	–	TBI+ARA-C + CY + ATG	–	BU+ARA-C+ATG+TEPA
GVHD onset	–	–	–	1	–	1
GVHD type				skin		skin
Immunosuppression				Pred+MMF		Pred+FK-506

CAR, chimeric antigen receptor; scFV, single-chain fragment variable; CTX, cyclophosphamide; FC, fludarabine, cyclophosphamide; CO., company; CR, complete remission; CRS, cytokine release syndrome; TBI, total body irradiation; ARA-C, cytarabine; CY, cyclophosphamide; ATG, antithymocyte globulin; BU, busulfan; TEPA, tepadina; GVHD, graft versus host disease; Pred, methylprednisolone; MMF, mycophenolate mofetil; FK-506, tacrolimus.

third time with CD19-positive cells. The patient did not achieve CR through reinduction chemotherapy using the VDCLP regimen and hyper-CVAD(A) regimen (Table 1). In July 2019, after pretreatment with the FC regimen (25 mg/m^2 fludarabine on days 1–2 and 250 mg/m^2 cyclophosphamide on days 1–4), the second autologous human-murine chimeric CD19 CAR-T cell (9.39×10^7) was infused. The CRS characterized by high fever and low-flow oxygen was assessed as grade 2. However, CAR-T cells did not expand in vivo, and the disease was not controlled. Subsequently, in October 2019, the patient was pretreated with the FC regimen (same as above) and then infused with autologous human-murine chimeric CD22 CAR-T cell (7.00×10^7). The CRS was assessed as grade 2. CD22 CAR-T cell expanded in vivo, and the patient achieved CR in November 2019. In January 2020, the patient was pretreated with the TBI+ARA-C+CY + ATG regimen (total body irradiation, cytarabine, cyclophosphamide, and antithymocyte globulin) and then underwent her mother donor haploidentical allo-HSCT (5/10 HLA matches, mononuclear cells [MNCs] 7.34×10^8/kg, CD34$^+$ cells 6.09×10^6/kg). According to the Mount Sinai Acute GVHD International Consortium, graft versus host disease (GVHD) was assessed as grade 1 manifested by skin rash covering <25% body surface area [6]. The patient received meprednisone and mycophenolate mofetil to control GVHD. Multiple bone marrow tests showed that the patient had been in continuous CR (CCR). The donor chimerism was more than 98%, but continuous CAR-T cell expansion was not achieved. Unfortunately, in October 2021, the bone marrow test showed that the patient relapsed for the fourth time with CD19-and CD22-positive cells, and the donor chimerism was 10.47%. The patient was then pretreated with the FC regimen (same as above). On October 28, 2021, the patient received the fourth autologous fully humanized CD19 CAR-T cell infusion (5.11×10^7). On the second day after infusion, the patient developed high fever and hypoxia. The CRS was grade 2. On day 28, bone marrow test showed that the patient had achieved CR again. After pretreatment with the BU+ARA-C+FLU+ATG+Tepadina regimen (busulfan, cytarabine, fludarabine, antithymocyte globulin, and tepadina), the patient was bridged to her cousin donor haploidentical allo-HSCT (5/10 HLA matches, MNCs 8.1×10^8/kg, CD34$^+$ cells 7.04×10^6/kg). The GVHD was grade 1 manifested by 15% rash. Low-dose meprednisone and tacrolimus were used to prevent GVHD after allo-HSCT. Finally, at the last follow-up time of writing the present article up to October 2022, the patient had continuously maintained leukemia-free status and CAR-T cell expansion since January 2022.

Discussion and Conclusion

CAR-T cell therapy is a milestone in the immunotherapy of relapsed or refractory B-ALL and has resulted in high remission rates. However, the relatively high relapse rate remains a barrier to making CAR-T cell therapy an excellent treatment option. HSCT is widely used to treat multiple hematological disorders, including B-ALL, but patients who received HSCT in advanced stages of disease have a poor prognosis. Combining CAR-T cell therapy and HSCT is an attractive strategy to further improve the long-term prognosis of relapsed or refractory B-ALL [7, 8]. However, few patients with relapsed or refractory B-ALL who have been exposed to CAR-T cell therapy and HSCT can undergo repetitive CAR-T cell therapy and HSCT because of the technical difficulties and patients' physical, economic, and social conditions.

In this study, the patient relapsed after the first human-murine chimeric CD19 CAR-T cell and was repeatedly treated with the second human-murine chimeric CD19 CAR-T cell. However, the treatment was ineffective. Human-murine chimeric CD19 CAR-T cell therapy is safe, but repeated antigen exposure can lead to T cell exhaustion and induce the emergence of antidrug antibodies, which is related to the failure of CAR-T cell therapy [9, 10]. Interestingly, human-murine chimeric CD22 CAR-T cell has been reported to induce remission in patients with CD22-positive B-ALL who are naive or resistant to CD19 CAR-T cell [11]. Another study suggested that the combination of sequential CD19 CAR-T cell and CD22 CAR-T cell therapy can improve long-term survival in B-ALL [12]. Therefore, the present case was treated with human-murine chimeric CD22 CAR-T cell and prospectively achieved remission, but regrettably, the case relapsed again 2 years later. With the development of CAR-T cell technology, fully humanized CAR-T cell therapy has emerged as a novel treatment option with long-term persistence for patients with B-ALL who relapsed or resisted prior human-murine chimeric CAR-T cell [13, 14]. In the present study, the patient adjusted to humanized CD19 CAR-T cell therapy and fortunately achieved remission again. Patients with relapsed or refractory B-ALL might still benefit from repetitive CAR-T cell therapy, as long as the CAR-T cell was manufactured in different targets or different CAR structures.

While CAR-T cell therapy has become an area of intense focus, CRS remains a significant barrier to the dissemination of promising CAR-T therapies [15, 16]. The present patient was repeatedly treated with quartic infusion of CAR-T cell. Only grade 1 CRS occurred in the first infusion. Grade 2 CRS occurred in the next three infusions, but no severe CRS (grade 3 or above) occurred. This indicated that the repetitive infusion of CAR-T cell was safe and did not increase the severity of CRS.

Recently, some studies have shown that CAR-T cell bridging to HSCT therapy decreases the relapse rate and improves leukemia free survival (LFS) and overall survival (OS) in patients with relapsed or refractory B-ALL [17], while others have reported that CAR-T cell bridging to HSCT therapy does not influence the relapse rate and long-term outcomes [18, 19]. In fact, a systematic review of 19 studies with 690 patients indicated that consolidative HSCT after CAR-T cell therapy can prolong LFS and OS in relapsed or refractory B-ALL, with acceptable incidence rates for adverse events [20]. Another meta-analysis including

18 studies with 758 patients also indicated that CAR-T cell therapy bridging to HSCT decreases the relapse rate and improves long-term survival in relapsed or refractory B-ALL [21], especially for patients with a high proportion of measurable residual disease (MRD) or poor prognostic molecular markers [17, 22, 23]. In our previous study, we also found that allo-HSCT is a protective factor for OS and LFS in patients with relapsed or refractory B-ALL undergoing CD19 CAR-T cell therapy [5]. Hence, the present patient was immediately bridged to her mother donor haploidentical allo-HSCT after achieving remission from being treated with human-murine chimeric CD22 CAR-T cell. The patient maintained remission for 2 years, which far exceeded the previous clinical benefit of CD19 CAR-T cell therapy alone. Furthermore, after the patient relapsed for the fourth time, she was repeatedly bridged to her cousin donor allo-HSCT after achieving remission from being treated with humanized CD19 CAR-T cell. She maintained remission up to October 2022. This finding indicated that repetitive HSCT might still be beneficial for patients with relapsed or refractory B-ALL undergoing different types of CAR-T cell therapy.

Allo-HSCT is a curative option, but its benefits are often compromised by "GVHD" [24]. Thus, caution should be taken when applying allo-HSCT in patients who have experienced CAR-T cell therapy. However, studies have reported that the 100-day cumulative incidence of grade 3–4 acute GVHD and the 2-year cumulative incidence of chronic GVHD do not increase significantly in patients with relapsed or refractory B-ALL undergoing CAR-T cell therapy [17, 25]. Additionally, we have illustrated that patients with B-ALL who have previously undergone allo-HSCT do not develop GVHD after CAR-T cell therapy [5]. Thus, the present patient was sequentially bridged to her mother donor haploidentical allo-HSCT and cousin donor haploidentical allo-HSCT after achieving remission twice with CAR-T cell therapy. However, only grade 1 GVHD occurred after treatment with allo-HSCT twice. This finding indicated that the repetitive application of allo-HSCT in patients with B-ALL who experienced CAR-T cell therapy did not increase the severity of GVHD.

In conclusion, the present case of relapsed B-ALL was successively treated with human-murine chimeric CD19 CAR-T cell twice, human-murine chimeric CD22 CAR-T cell once, humanized CD19 CAR-T cell once, and bridged to mother donor haploidentical allo-HSCT once and cousin donor haploidentical allo-HSCT once. The findings suggest that repetitive CAR-T cell therapy bridging to repetitive allo-HSCT is still a safe therapeutic strategy for patients with relapsed or refractory ALL.

Acknowledgments

The authors thank the patient and all the investigators including the physicians, nurses, and laboratory technicians in this study, especially the patient provided who medical information sourced from the department of Hematology of Beijing Boren Hospital.

Statement of Ethics

This study was approved by the Institutional Review Board at the Second Affiliated Hospital of Anhui Medical University (PJ-YX2019-015 (F1)). The patient has given her written informed consent for publication of this case report.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This work was supported by the Major Subject of Science and Technology of Anhui Province (No. 201903a07020030) and the Natural Science Foundation of Anhui Province (No. 2208085MH217).

Author Contributions

Qianshan Tao designed the study. Qing Zhang collected data, analyzed data, and wrote the paper. Yi Dong and Zhimin Zhai provided the case for the study and performed the data. Qianshan Tao revised and edited the manuscript. All authors contributed to and approved the final version of the manuscript.

Data Availability Statement

Not applicable.

References

1 Medinger M, Heim D, Lengerke C, Halter JP, Passweg JR. Acute lymphoblastic leukemia-diagnosis and therapy. Ther Umsch. 2019; 76(9):510–5.

2 Chen W, Ma Y, Shen Z, Chen H, Ma R, Yan D, et al. Humanized anti-CD19 CAR-T cell therapy and sequential allogeneic hematopoietic stem cell transplantation achieved long-term survival in refractory and relapsed B lymphocytic leukemia: a retrospective study of CAR-T cell therapy. Front Immunol. 2021;12:755549.

3 Mazinani M, Rahbarizadeh F. CAR-T cell potency: from structural elements to vector backbone components. Biomark Res. 2022;10(1):70.
4 Frenzel A, Schirrmann T, Hust M. Phage display-derived human antibodies in clinical development and therapy. MAbs. 2016;8(7):1177–94.
5 An F, Wang H, Liu Z, Wu F, Zhang J, Tao Q, et al. Influence of patient characteristics on chimeric antigen receptor T cell therapy in B-cell acute lymphoblastic leukemia. Nat Commun. 2020;11(1):5928.
6 Harris AC, Young R, Devine S, Hogan WJ, Ayuk F, Bunworasate U, et al. International, multicenter standardization of acute graft-versus-host disease clinical data collection: a report from the Mount Sinai acute GVHD international Consortium. Biol Blood Marrow Transplant. 2016;22(1):4–10.
7 Liu J, Zhang X, Zhong JF, Zhang C. CAR-T cells and allogeneic hematopoietic stem cell transplantation for relapsed/refractory B-cell acute lymphoblastic leukemia. Immunotherapy. 2017;9(13):1115–25.
8 Jacoby E. The role of allogeneic HSCT after CAR T cells for acute lymphoblastic leukemia. Bone Marrow Transplant. 2019;54(Suppl 2):810–4.
9 Shi M, Li L, Wang S, Cheng H, Chen W, Sang W, et al. Safety and efficacy of a humanized CD19 chimeric antigen receptor T cells for relapsed/refractory acute lymphoblastic leukemia. Am J Hematol. 2022;97(6):711–8.
10 Li X, Chen W. Mechanisms of failure of chimeric antigen receptor T-cell therapy. Curr Opin Hematol. 2019;26(6):427–33.
11 Fry TJ, Shah NN, Orentas RJ, Stetler-Stevenson M, Yuan CM, Ramakrishna S, et al. CD22-targeted CAR T cells induce remission in B-ALL that is naive or resistant to CD19-targeted CAR immunotherapy. Nat Med. 2018;24(1):20–8.
12 Liu S, Deng B, Yin Z, Lin Y, An L, Liu D, et al. Combination of CD19 and CD22 CAR-T cell therapy in relapsed B-cell acute lymphoblastic leukemia after allogeneic transplantation. Am J Hematol. 2021;96(6):671–9.
13 An L, Lin Y, Deng B, Yin Z, Zhao D, Ling Z, et al. Humanized CD19 CAR-T cells in relapsed/refractory B-ALL patients who relapsed after or failed murine CD19 CAR-T therapy. BMC Cancer. 2022;22(1):393.
14 Myers RM, Li Y, Barz Leahy A, Barrett DM, Teachey DT, Callahan C, et al. Humanized CD19-targeted chimeric antigen receptor (CAR) T cells in CAR-naive and CAR-exposed children and young adults with relapsed or refractory acute lymphoblastic leukemia. J Clin Oncol. 2021;39(27):3044–55.
15 Brudno JN, Kochenderfer JN. Recent advances in CAR T-cell toxicity: mechanisms, manifestations and management. Blood Rev. 2019;34:45–55.
16 Greenbaum U, Kebriaei P, Srour SA, Olson A, Bashir Q, Neelapu SS, et al. Chimeric antigen receptor T-cell therapy toxicities. Br J Clin Pharmacol. 2021;87(6):2414–24.
17 Zhao H, Wei J, Wei G, Luo Y, Shi J, Cui Q, et al. Pre-transplant MRD negativity predicts favorable outcomes of CAR-T therapy followed by haploidentical HSCT for relapsed/refractory acute lymphoblastic leukemia: a multi-center retrospective study. J Hematol Oncol. 2020;13(1):42.
18 Park JH, Bienenfeld A, Orlow SJ, Nagler AR, Sénéchal B, Curran KJ. The use of hormonal antiandrogen therapy in female patients with acne: a 10-year retrospective study. N Engl J Med. 2018;19(3):449–55.
19 Bouziana S, Bouzianas D. Exploring the dilemma of allogeneic hematopoietic cell transplantation after chimeric antigen receptor T cell therapy: to transplant or not? Biol Blood Marrow Transplant. 2020;26(8):e183–91.
20 Xu X, Chen S, Zhao Z, Xiao X, Huang S, Huo Z, et al. Consolidative hematopoietic stem cell transplantation after CD19 CAR-T Cell therapy for acute lymphoblastic leukemia: a systematic review and meta-analysis. Front Oncol. 2021;11:651944.
21 Hu L, Charwudzi A, Li Q, Zhu W, Tao Q, Xiong S, et al. Anti-CD19 CAR-T cell therapy bridge to HSCT decreases the relapse rate and improves the long-term survival of R/R B-ALL patients: a systematic review and meta-analysis. Ann Hematol. 2021;100(4):1003–12.
22 Jiang H, Li C, Yin P, Guo T, Liu L, Xia L, et al. Anti-CD19 chimeric antigen receptor-modified T-cell therapy bridging to allogeneic hematopoietic stem cell transplantation for relapsed/refractory B-cell acute lymphoblastic leukemia: an open-label pragmatic clinical trial. Am J Hematol. 2019;94(10):1113–22.
23 Yan M, Wu YJ, Chen F, Tang XW, Han Y, Qiu HY, et al. CAR-T cell bridging to allo-HSCT for relapsed/refractory B-cell acute lymphoblastic leukemia: the follow-up outcomes. Zhonghua Xue Ye Xue Za Zhi. 2020;41(9):710–5.
24 Mhandire K, Saggu K, Buxbaum NP. Immunometabolic therapeutic targets of graft-versus-host disease (GvHD). Metabolites. 2021;11(11):736.
25 Zhang Y, Chen H, Song Y, Tan X, Zhao Y, Liu X, et al. Chimeric antigens receptor T cell therapy as a bridge to haematopoietic stem cell transplantation for refractory/relapsed B-cell acute lymphomalastic leukemia. Br J Haematol. 2020;189(1):146–52.