Name of project: Efficacy of Blinatumomab sequential donor lymphocyte infusion in patients with relapsed B-cell acute lymphoblastic leukemia after allogeneic hematopoietic stem cell transplantation

Institution Name: The First Affiliated Hospital of Zhengzhou University

Study start date: September 2023

Study deadline: December 2026

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Purpose of the study

Objective To observe and analyze the efficacy and side effects of Blinatumomab followed by donor lymphocyte infusion in patients with relapsed acute B lymphoblastic leukemia after allogeneic hematopoietic stem cell transplantation in our hospital. This study explores the treatment of patients with relapsed B-cell acute lymphoblastic leukemia after allogeneic hematopoietic stem cell transplantation.

Background of Research

Acute lymphoblastic leukemia (ALL) is a malignant blood disease. The traditional treatment mainly includes chemotherapy and hematopoietic stem cell transplantation. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an effective and even the only means to cure ALL and other malignant blood diseases. However, acute lymphoblastic leukemia still has a high recurrence rate after allo-HSCT, and the prognosis of patients with relapse after transplantation is extremely poor, with an average survival time of about 5.5 months. There is no uniform treatment for patients with relapse after allogeneic hematopoietic stem cell transplantation. Donor lymphocyte infusion (DLI) is the main salvage treatment for relapse after transplantation, but in the treatment of relapse after allo-HSCT for ALL patients, the efficacy is often poor, and less than 20% of patients can achieve remission. Relapse after allogeneic hematopoietic stem cell transplantation in ALL is still an urgent clinical problem to be solved.

In recent years, chimeric antigen receptor T cell (CAR-T) therapy targeting CD19 can achieve hematological complete response (CR) in 60% to 90% of patients with refractory and relapsed acute B- lymphoblastic leukemia (B-ALL), creating an opportunity for the long-term survival of such patients. However, the cost of CD19+ CAR-T therapy currently on the market in China is extremely expensive, and the vast majority of patients cannot receive this treatment. Blinatumomab is the first CD19-positive and CD3-positive targeted immunotherapy drug approved by the FDA in the United States and has also been approved for relapsed or refractory B-ALL in adults and children in China. By linking CD3 on T cell receptor complexes with CD19 expressed on B cell line-derived cells, Blinatumomab aggregates T cells with target cells by forming cytolytic synapses, thus activating endogenous T cells and enabling them to solubilize CD19+ cells for tumor cell killing. In an open-label single-arm phase

II study in adults with B-ALL, Blinatumomab achieved a 43% complete response rate (CR) or peripheral blood count (CRh) partial blood recovery rate (CR) over 2 treatment cycles, among 64 patients who relapsed after allo-HSCT, 45% of patients achieved CR/CRh in the first two treatment cycles, and 22 patients had minimal residual disease (MRD) response (including 19 complete MRD response). After 1 year and 3 years of follow-up, the median relapse-free survival of patients who achieved CR/CRh in the first 2 cycles was 7.4 months, and the median overall survival was 8.5 months. Overall survival (Kaplan-Meier estimates) was 36% at 1 year and 18% at 3 years. Grade 3 and 4 adverse events were reported in 20 patients (31%) and 28 patients (44%), respectively, including grade 3 and 4 neurological events in 8 and 2 patients, respectively, and grade 3 cytokine release syndrome in 2 patients. Fatal adverse events occurred in eight patients, including five due to infection. Seven patients developed grade 3 GVHD during the study, none of which resulted in drug withdrawal or hospitalization. The results confirm that Blinatumomab is an effective salvage therapy in refractory B-cell acute lymphoblastic leukemia in this patient population.
In this study, patients with relapsed acute B lymphoblastic leukemia after allogeneic hematopoietic stem cell transplantation (allo-HSCT) were treated with blinatumomab followed by DLI. The overall survival, disease-free survival, complications, adverse reactions, and other indicators of these patients were observed. To investigate the treatment of relapsed B-cell acute lymphoblastic leukemia after allogeneic hematopoietic stem cell transplantation.

Criteria for inclusion of subjects
Patients with acute B lymphoblastic leukemia who relapsed after allogeneic hematopoietic stem cell transplantation in our hospital and received Blinatumomab sequential DLI after relapse. Patients with acute B lymphoblastic leukemia who relapsed after allogeneic hematopoietic stem cell transplantation in our hospital from September 2023, to December 2026, were enrolled. After relapse, patients were treated with Blinatumomab sequential donor lymphocyte infusion (DLI).
1. Age ≤65 years old
2. Stable vital signs
3. No severe infection
4. There was no degree II-IV graft-versus-host disease
5. No organ failure

Criteria of exclusion
1. Age > 65 years old
2. Unstable vital signs
3. Complicated with severe infection
4. Combined with degree II-IV graft-versus-host disease
5. Heart, liver, kidney and other organ failure
6. Complicated with central nervous system leukemia
7. Allergies to medications in the treatment regimen

Treatment plan

B-ALL patients received regular follow-up after allogeneic hematopoietic stem cell transplantation. In case of recurrence, they were treated with Blinatumomab followed by DLI, and the second course of treatment was carried out 1-2 months after DLI.

In MRD-positive patients, Blinatumomab 28μg×5-15 days were given, followed by DLI therapy (infusion of MNC was about 5×10^7/kg~1×10^8/kg).

Patients with hematologic recurrence were given Blinatumomab 9μg D1-4,11.66μg d5-7, 28μg d8 (for a total of 8 to 21 days), followed by DLI therapy (infusion of MNC was about 5×10^7/kg~1×10^8/kg).

The use time of the barstool is determined according to the patient's tolerance, economic situation, and other comprehensive factors.

Main observations and statistical indicators

Overall survival, disease-free survival, cytokine release syndrome (CRS) incidence, acute/chronic graft-versus-host disease (GVHD) incidence, infection incidence, hematological adverse reactions, etc.

Case data collection

The electronic medical record system of our hospital was used to review the data of B-ALL patients who relapsed after allogeneic hematopoietic stem cell therapy and received Blinatumomab followed by DLI after relapse. Pay attention to protect the privacy of patients and ensure that the personal information of patients' case data is not disclosed.

Statistical analysis

SPSS26.0 software was used for statistical analysis. The $\chi 2$ test and Mann-Whitney U test were used to compare qualitative and quantitative data between groups, respectively. The survival rate and survival analysis were estimated by the Kaplan-Meier method, and the Log-rank test was used for comparison between the two groups. $P<0.05$ was considered statistically significant.

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