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Title: THE TREATMENT RESPONSE OF A TWO-DOSE REGIMEN OF DOSE-ADJUSTED INOTUZUMAB IN RELAPSED/REFRACTORY B-ALL

Abstract Type: Poster Presentation

Session Title: Acute lymphoblastic leukemia - Clinical

Background:

CD19- or CD22-specific chimeric antigen receptor (CAR) T-cell therapy resulted in promising outcomes in relapsed/refractory B-cell acute lymphoblastic leukemia (r/r B-ALL). However, some patients relapse after CAR-T and usually it's more difficult for them to achieve complete remission (CR); also, a few patients cannot receive CAR-T treatment due to some medical problems such as severe infections or inability to collect lymphocytes for producing CAR-T cells. Under these circumstances, the monoclonal antibodies targeting CD19 or CD22 could be as another treatment options. The CD22 antibody inotuzumab ozogamicin conjugated with calicheamicin toxin has shown superior antileukemic activity, particularly for CD19-negative patients after treatment with CD19 CAR-T or CD19 antibody blinatumomab. Here, we administered inotuzumab to r/r B-ALL patients who failed or relapsed after CAR-T, or those unable to receive CAR-T; the dosage was adjusted based on one vial containing 1mg of inotuzumab and only two doses were given for cost saving.

Aims:

To observe the treatment response of this two-dose regimen of inotuzumab for heavily treated r/r B-ALL patients especially those failed or relapsed after CAR-T therapy.

Methods:

Pediatric and adult patients who received 2 doses of inotuzumab and were evaluated after inotuzumab were included. Antibody infusions were performed between March 2020 and September 2022, the follow-up was as of January 2023. All patients expressed CD22 antigen (>80% leukemic cells displaying CD22) before treatment. For adults, the maximum dosage per dose was 1mg (1mg, twice), for children, the maximum dosage per dose was 0.85mg/m^2, the total dosage administered in each patient was less than the standard dosage of 1.8mg/m^2 (0.8mg/m^2, 0.5mg/m^2, 0.5mg/m^2).

Results:

A total of 21 r/r B-ALL patients were involved, the median age was 29 (range, 4-72) years, including 5 children (<18 years old) and 16 adults. Seventeen patients presented with 5.0%-99.0% leukemic blasts in bone marrow/peripheral blood (4 also with extramedullary disease) and four cases were minimal residual disease (MRD)-positive. Fourteen patients had received both CD19 and CD22 CAR-T therapies, 4 received CD19 CAR-T and 3 received blinatumomab. Eleven cases underwent allogeneic hematopoietic cell transplantation (allo-HCT). Eight patients showed CD19 loss and 2 had CD19 partial expression.

After inotuzumab treatment, 14 of 21 (66.7%) patients achieved CR (1 was MRD+CR) and all of 4 MRD-positive cases turned MRD-negative; importantly, 4 of 6 cases who failed recent CD22 CAR-T therapy achieved CR after subsequent inotuzumab. Seven patients (33.3%) had no response. Among CR patients, 7 proceeded to allo-HCT, 4 of them (57.1%) remained in CR for 2-15 months, 2 relapsed and 1 developed posttransplant lymphoproliferative disorder. Whereas in 7 patients without undergoing allo-HCT, 5 relapsed within 3-6 months after inotuzumab even followed by other consolidations. Grade 1-3 hepatotoxicity occurred in 5 cases (23.8%), one child with no response experienced hepatic veno-occlusive disease (VOD) during salvage transplantation and recovered completely. The VOD rate was 4.8% (1/21) in all patients and 12.5% (1/8) in patients received following allo-HCT.

Summary/Conclusion:

For heavily treated r/r B-ALL patients including those after treatment with both CD19 and CD22 CAR-T cells, our two-dose cost-saving regimen of inotuzumab resulted in a CR rate of 66.7%, and the frequency of hepatotoxicity and VOD was lower. To obtain a longer remission, the subsequent allo-HCT in CR patients was recommended.

Keywords: Immune therapy, Acute lymphoblastic leukemia