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Conference Abstract A4

Evaluation of the Effectiveness of Additional Infusion of Hematopoietic Stem Cells ("Boost") as a Treatment for Graft Failure After Allogeneic Hematopoietic Stem Cell Transplantation

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Background

Severe hypofunction of graft is a life-threatening complication following allogeneic hematopoietic stem cell transplantation. One of the therapeutic options is the additional infusion of hematopoietic stem cells from the original donor ("boost").

Aim

To evaluate the effectiveness, overall survival and event-free survival after the administration of a hematopoietic stem cell boost in patients with severe graft hypofunction.

Materials and Methods

Thirty-two consecutive hematopoietic stem cell boosts performed at the R.M. Gorbacheva Research Institute of Pediatric Oncology, Hematology and Transplantation, Pavlov First Saint Petersburg State Medical University during 2009–2024.

The patients' ages ranged from 18 to 69 years (median 38 years); there were 21 men and 11 women with acute lymphoblastic leukemia (n = 7), acute myeloid leukemia (n = 8), myeloproliferative diseases (n = 4), myelodysplastic syndrome (n = 4), chronic myeloid leukemia (n = 4), non-Hodgkin's lymphoma (n = 2), severe aplastic anemia (n = 2), and chronic lymphocytic leukemia (n = 1).

Allogeneic hematopoietic stem cell transplantation had been performed from unrelated fully HLA–matched donors (n = 11), partially matched donors (n = 5), related matched donors (n = 9), and haploidentical donors (n = 7).

The indication for the boost were severe graft hypofunction in 25 cases and severe graft hypofunction with mixed chimerism in 7 cases.

The median interval between the initial allogeneic hematopoietic stem cell transplantation and the boost was 105 days (range 35–545). The source of hematopoietic stem cells was bone marrow in 9 cases and peripheral blood stem cells in 23 cases. $CD34^+$ cell selection was performed for two patients. The median $CD34^+$ cell dose was 3.3 (0.6–11) × 10^6/kg.

Most patients received prophylaxis for graft-versus-host disease with methylprednisolone 5 mg/kg combined with calcineurin inhibitors (CNIs) and mycophenolate mofetil (MMF) (n = 13), CNIs plus MMF (n = 7), ruxolitinib combined with MMF and CNI/sirolimus (n = 5), or post-transplant cyclophosphamide (n = 1); 6 patients received no graft-versus-host disease prophylaxis.

Results and Discussion

The number of boosts performed per year ranged from one to three. Hematopoietic recovery after the boost was achieved in 18 patients (56%), with a median time to recovery of 22 days (range 8–105).

Twelve patients had grade 2–4 acute graft-versus-host disease between the first transplantation and the boost. All patients experienced cytomegalovirus infection or reactivation of human herpesvirus 6 during this period.

Graft rejection occurred in two cases (at 29 and 118 days), and relapse occurred in three patients.

Acute graft-versus-host disease after the boost occurred in eight cases with a cumulative incidence of 26% (95% confidence interval 12–50). Two-year relapse incidence was 9% (95% confidence interval 2–23), with the time from boost to relapse ranging from 14 to 30 days. Non-relapse mortality was 33% (95% confidence interval 17–50).

In total, 19 patients died: infection (n = 12), graft-versus-host disease combined with infection (n = 4), and relapse (n = 3). Two-year overall survival was 53% (95% confidence interval 37–75).

This study has clear limitations due to its retrospective nature and the small, heterogeneous cohort. Notably, prolonged use of hematopoietic stem cells occurred in the historical cohort (2009–2016).

Conclusion

A hematopoietic stem cell boost can be a life-saving procedure for patients with severe graft hypofunction. Further studies are needed to develop protocols for this intervention aimed at reducing the incidence of graft-versus-host disease and infectious complications in this category of patients.