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Conference Abstract A13

Allogeneic Hematopoietic Cell Transplantation in Combination Therapy for Refractory Myeloid Neoplasms

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Introduction

The prognosis after salvage allogeneic hematopoietic cell transplantation in refractory myeloid malignant neoplasms remains unsatisfactory, and no standard therapy is currently available.

Methods

We conducted a prospective single-arm study to evaluate whether the combination of bendamustine and cyclophosphamide administered post-transplantation (PTBCr) could enhance the graft-versus-leukemia effect in this group of patients. Fifty patients with refractory myeloid neoplasms undergoing allogeneic hematopoietic cell transplantation from all donor types were enrolled in this prospective study.

Results

The cumulative engraftment rate was 88%, and 76% of patients achieved undetectable residual disease. Immune toxicity in the form of cytokine release syndrome occurred in 30% of patients. The cumulative incidence of acute graft-versus-host disease of grade II–IV was 20%, and the cumulative incidence of moderate to severe chronic graft-versus-host disease was 34%. Non-relapse mortality was 20%. The relapse rate was 62%, but the median time to relapse reached 245 days. Overall survival was 33%, and event-free survival was 22%. In the multivariate analysis of event-free survival, significant factors were alternative donor (hazard ratio 0.24, 95% confidence interval 0.11–0.52) and adverse genetic characteristics (hazard ratio 2.48, 95% confidence interval 1.26–4.88). The PTBCr was associated with a unique profile of immune reconstitution characterized by high levels of effector memory $CD8^+$ T cells, programmed death ligand-1–positive monocytes, and granulocytes. Compared with the historical control, two-year overall survival increased from 18% to 33% ($p = 0.01$) and progression-free survival from 15% to 22% ($p = 0.07$) with the post-transplant bendamustine plus cyclophosphamide regimen.

Conclusions

Prophylaxis of graft-versus-host disease using the PTBCr represents a promising approach in refractory myeloid neoplasms, delaying relapse after hematopoietic cell transplantation and opening opportunities for post-transplant prophylaxis. Optimization of this regimen is ongoing in partially human leukocyte antigen–matched hematopoietic stem cell transplantation.

Figure. Overall survival (left) and event-free survival (right) comparing results of the post-transplant bendamustine plus cyclophosphamide regimen with historical control.