BLOOD ADVANCES TALK

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Naive T-cell depletion in stem cell transplantation

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The audio version of this* Blood Advances *Talk is available on the full-text article page.

Abstract

Allogeneic hematopoietic stem cell transplantation (HCT) is curative in many patients with advanced hematopoietic malignancies. Donor T cells not only facilitate engraftment and protect against opportunistic pathogens and residual disease, but can also cause graft-versus-host disease (GVHD), with significant morbidity and mortality. Complete T-cell depletion can not only substantially reduce GVHD rates but can also delay immune reconstitution and increase rates of opportunistic infections and relapse. Murine models have shown that naive T cells (T_Ns) consistently cause severe GVHD, whereas memory T cells cause milder or no GVHD and have critical graft-versus-tumor function. Informed by experiments performed in murine models of HCT, clinical trials are being conducted to evaluate T_N-depleted peripheral blood stem cell (PBSC) grafts. These trials are showing very low rates of chronic GVHD and of serious acute GVHD in the HLA-matched HCT setting, with lower frequencies of opportunistic infections than after fully T-cell–depleted HCT and no apparent increase in relapse rates. Randomized clinical trials are ongoing, comparing standard unselected HCT with T_N-depleted PBSCs and other promising GVHD-reduction strategies. Correlative laboratory studies will clarify how antitumor function is retained in T_N-depleted HCT and inform strategies to further augment graft-versus-leukemia in patients at a high risk of relapse. T_N depletion of donor lymphocyte infusions and of haploidentical stem cell grafts is also being investigated.

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The complete text of this *Blood Advances* Talk is available as a data supplement.

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