

# 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.*

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## 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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trial (NCT 03779854; 16-NTCD): a Pediatric Transplantation and Cellular Therapy Consortium (PBMTCC) multicenter randomized controlled trial of naive T-cell-depleted peripheral blood stem cell transplantation for which M.B. serves as the principal investigator. M.B. is also a founder and scientific advisory board member of HighPassBio, and a scientific advisory board member of Orca Bio.

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