Adoptive transfer of Epstein-Barr virus (EBV) nuclear antigen 1-specific T cells as treatment for EBV reactivation and lymphoproliferative disorders after allogeneic stem-cell transplantation.

Abstract:
Reactivation of Epstein-Barr virus (EBV) after allogeneic stem-cell transplantation (SCT) can lead to severe life-threatening infections and trigger post-transplantation lymphoproliferative disease (PTLD). Since EBV-specific T cells could prevent PTLD, cellular immunotherapy has been a promising treatment option. However, generation of antigen-specific T-cell populations has been difficult within a short time frame. To improve availability in urgent clinical conditions, we developed a rapid protocol for isolation of polyclonal EBV nuclear antigen 1 (EBNA-1)-specific T cells by using an interferon gamma (IFN-γ) capture technique. We report on the use of adoptive transfer of EBNA-1-specific T cells in 10 pediatric and adult patients with EBV viremia and/or PTLD after SCT. No acute toxicity or graft-versus-host disease (GVHD) of more than grade 2 occurred as a result of adoptive T-cell transfer. In vivo expansion of transferred EBNA-1-specific T cells was observed in eight of 10 patients after a median of 16 days following adoptive transfer that was associated with clinical and virologic response in seven of them (70%). None of the responders had
EBV-associated mortality. Within clinical responders, three patients were disease free by the day of last follow-up (2 to 36 months), three patients died of other infectious complications, and one patient died as a result of relapse of malignancy. EBV-related mortality was observed in two of 10 patients, and another patient had ongoing viremia without clinical symptoms at last follow-up. Adoptive ex vivo transfer of EBNA-1-specific T cells is a feasible and well-tolerated therapeutic option, representing a fast and efficient procedure to achieve reconstitution of antiviral T-cell immunity after SCT.