Single Agent of posttransplant cyclophosphamide without calcineurin inhibitor controls severity of experimental chronic GVHD

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Abstract

Chronic graft-versus-host disease (GVHD) is a major cause of late death and morbidity following allogeneic hematopoietic cell transplantation (HCT), but its pathogenesis remains unclear. Recently, haplo-identical HCT with post-transplant cyclophosphamide (Haplo-HCT with PTCY) revealed the low incidence rate of acute GVHD and chronic GVHD. The pathogenesis of acute GVHD in Haplo-HCT with PTCY is well investigated but chronic GVHD still needs to be elucidated, especially in HLA-matched HCT with PTCY. Based on its safety profile, PTCY is currently applied for the HLA-matched HCT setting. Here, we investigated the mechanisms of chronic GVHD in HLA-matched HCT with PTCY using a well-defined mouse chronic GVHD model. PTCY attenuated clinical and pathological chronic GVHD by suppressing effector T-cells and preserving regulatory T-cells compared with a control group. Additionally, we demonstrated that cyclosporine A (CsA) did not show any additional positive effects on attenuation of GVHD in PTCY treated recipients. These results suggest that a single agent of PTCY without CsA could be a promising strategy for the prevention of chronic GVHD in HLA-matched HCT.