Post-Transplant Cyclophosphamide and Tacrolimus–Mycophenolate Mofetil Combination Prevents Graft-versus-Host Disease in Allogeneic Peripheral Blood Hematopoietic Cell Transplantation from HLA-Matched Donors

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ABSTRACT

Allogeneic hematopoietic cell transplant (HCT) remains the only curative therapy for many hematologic malignancies but it is limited by high nonrelapse mortality (NRM), primarily from unpredictable control of graft-versus-host disease (GVHD). Recently, post-transplant cyclophosphamide demonstrated improved GVHD control in allogeneic bone marrow HCT. Here we explore cyclophosphamide in allogeneic peripheral blood stem cell transplantation (alloPBSCT). Patients with high-risk hematologic malignancies received alloPBSCT from HLA-matched unrelated/related donors. GVHD prophylaxis included combination post-HCT cyclophosphamide 50 mg/kg (days +3 and +4) and tacrolimus/mofetil mycophenolate (T/MMF) (day +5 forward). The primary objective was the cumulative incidence of acute and chronic GVHD. Between March 2011 and May 2015, 35 consecutive patients received the proposed regimen. MMF was stopped in all patients at day +28: the median discontinuation of tacrolimus was day +112. Acute and chronic GVHD cumulative incidences were 17% and 7%, respectively, with no grade IV GVHD events, only 2 patients requiring chronic GVHD immunosuppression control, and no deaths from GVHD. Two year NRM, overall survival, event-free survival, and chronic GVHD event-free survival rates were 3%, 77%, 54%, and 49%, respectively. The graft-versus-tumor effect was maintained as 5 of 15 patients (33%) who received HCT with evidence of disease experienced further disease response. A post-transplant cyclophosphamide + T/MMF combination strategy effectively prevented acute and chronic GVHD after alloPBSCT from HLA-matched donors and achieved an unprecedented low NRM without losing efficacy in disease control or impaired development of the graft-versus-tumor effect. This trial is registered at clinicaltrials.gov as NCT02300571.

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INTRODUCTION

Allogeneic hematopoietic cell transplant (HCT) remains the only curative therapy for many hematologic malignancies [1–3]. However, broad application of the procedure has been limited by the difficult control of graft-versus-host disease (GVHD), the principal complication and cause of mortality in allogeneic HCT [1,2]. The GVHD prophylaxis used most