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Letter-to-the-Editor

Impressive Graft-versus-Host Disease-Free, Relapse-Free Survival in Matched Unrelated Donor Allogeneic Hematopoietic Stem Cell Transplantation Using Reduced-Intensity Conditioning and a Combination of Antithymocyte Globulin and Post-Transplantation Cyclophosphamide

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To the Editor:

We read with interest the recent article by Efebera et al [1]. The curative effect of reduced-intensity conditioning (RIC) allogeneic hematopoietic stem cell transplantation (allo-HSCT) relies mainly on a graft-versus-leukemia effect, and the safety of in vivo T cell depletion in this setting is not well established [2,3]. Unfortunately, there have been no randomized controlled trials addressing the role of antithymocyte globulin (ATG) in RIC allo-HSCT. Retrospective analyses of Center for International Blood and Marrow Transplant Research and European Society for Blood and Marrow Transplantation data examining the role of ATG in RIC are conflicting [2,3]. Despite the limitations of a retrospective analysis, we agree that a total ATG dose of 4.5 mg/kg is reasonable in RIC allo-HSCT. The very low rates of cytomegalovirus and Epstein-Barr virus reactivation reported by Efebera et al are surprising, given the higher rates reported by others [2,3]. Did the authors only include those cases requiring preemptive treatment in their analysis?

We would like to share our institutional experience using a combination of ATG and post-transplantation cyclophosphamide (PTCy) for graft-versus-host disease (GVHD) prophylaxis. At Princess Margaret Cancer Center, an RIC regimen composed of fludarabine, busulfan, and 200 cGy of total body irradiation became the institutional standard of care for peripheral blood allo-HSCT in October 2015. For GVHD prophylaxis, rabbit ATG (total dose 4.5 mg/kg from day -3 to day -1) has been combined with PTCy (50 mg/kg/day on days +3 and +4) and cyclosporine (from day +5). The safety and efficacy of this combination has been reported in different patient cohorts [4,5].

To compare our results with those reported by Efebera et al [1], we performed a retrospective subanalysis of 121 consecutive patients who underwent 10/10 matched unrelated donor allo-HSCT under the described protocol. The median patient age was 59 years (range, 18 to 74 years). The cumulative incidence of CMV reactivation was 46%, that of EBV reactivation was 51.5%, and that of BK viruria was 16.2%. The cumulative incidences of grade II-IV and grade III-IV acute GVHD at day +180 were 17.8% and 3.2%, respectively, and the cumulative incidence of moderate to severe chronic GVHD at 1 year was 9.1%. With a median follow-up of 16.1 months (range, 0.5 to 42 months), 37 patients (29.8%) died and 27 (21.7%) relapsed. Main causes of death were infections and relapse, with only 1 death secondary to GVHD. Our cohort had a higher 2-year overall survival of 66% and relapse-free survival of 63%, albeit with a shorter follow-up. In addition, nonrelapse mortality at 1 year was 12%.

The very low rates of GVHD seen in our subanalysis support the efficacy of dual T cell depletion. Furthermore, the GVHD-free, relapse-free survival was 55% at 2 years. This is especially important when considering long-term complications secondary to chronic GVHD and their impact on quality of life. We suggest that the combination of ATG and PTCy for GVHD prophylaxis merits further studies to refine post-transplantation results.

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