Posttransplant cyclophosphamide after allogeneic hematopoietic cell transplantation mitigates the immune activation induced by previous nivolumab therapy

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Abstract

Patients receiving an allogeneic hematopoietic cell transplantation (allo-HCT) after the use of PD-1 inhibitors seem to be at a higher risk of developing acute graft-versus-host disease (aGHVD) through etiopathogenetic mechanisms not fully elucidated. Herein, we investigated the effect of nivolumab administered prior to allo-HCT on the following early T-cell reconstitution and its modulation by the GVHD prophylaxis (tacrolimus/sirolimus vs. posttransplant cyclophosphamide [PTCY]). In all nivolumab-exposed patients we detected circulating nivolumab in plasma for up to 56 days after allo-HCT. This residual nivolumab was able to bind and block PD-1 on T-cells at day 21 after allo-HCT, inducing a T cell activation that was differentially modulated depending on the GVHD prophylactic regimen. Among patients receiving tacrolimus/sirolimus, nivolumab-exposed patients had a higher incidence of severe aGVHD and a more effector T-cell profile compared with anti-PD-1-naïve patients. Conversely, patients receiving PTCY-based prophylaxis showed a similar risk of aGVHD and T-cell profile irrespective of the previous nivolumab exposure. In conclusion, nivolumab persists in plasma after transplantation, binds to allogeneic T cells and generates an increased T-cell activation. This T-cell activation status can be mitigated with the use of PTCY, thus reducing the risk of aGVHD.