

LOW-DOSE RATG IMPROVES GRFS AND REDUCES CGVHD IN MSD ALLOGENEIC TRANSPLANTATION: A RETROSPECTIVE ANALYSIS FROM GATMO-TC

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Background: Chronic graft-versus-host disease (cGvHD) is a major cause of morbidity and non-relapse mortality (NRM) after allogeneic hematopoietic stem cell transplantation (allo-HSCT). In matched sibling donor (MSD) transplants, antithymocyte globulin (ATG) reduces cGvHD, with conflicting findings regarding relapse incidence. We retrospectively compared low-dose rabbit ATG (rATG) plus methotrexate (MTX) and calcineurin inhibitor (CNI) vs MTX+CNI in MSD allo-HSCT.

Methods: We included 195 adult MSD recipients from 9 Argentine centers (2017–2023). Primary endpoint was graft-versus-host disease-free, relapse-free survival (GRFS). Secondary endpoints: acute (a) and cGvHD, relapse, NRM, and OS. GRFS/OS were estimated using Kaplan-Meier and log-rank test. Cumulative incidence (CI) was assessed with Gray’s test. Results: GVHD prophylaxis was MTX+CNI in 141 and rATG-based (median 4.4 mg/kg, range 2.5–5) in 54 patients. Median age: 43.4 years (range 17–70), 56.4% male. Diagnoses: AML (45.1%), MDS (16.4%), B-ALL (19.5%), Ph+ ALL (15.4%), T-ALL (3.6%). Peripheral blood was used in 99.5%; 83.1% received myeloablative conditioning. Graft failure: 2 MTX+CNI, 1 rATG. Median follow-up: 24 months. rATG was associated with longer median GRFS (18.1 vs. 10.2 m) and higher 24-m GRFS (47% vs. 28%, $p=0.006$). In MVA, rATG (HR 0.58, $p=0.017$), reduced-intensity conditioning (HR 0.54, $p=0.033$), and melphalan-based (N: 12) regimens (HR 0.29, $p=0.035$) improved GRFS. At 24 m, both total and moderate-severe cGvHD CI was lower with rATG (16.5% vs. 42.6%, $p=0.005$ and 10.3% vs 33.4%, $p=0.001$; respectively). In the Fine–Gray model, rATG (HR 0.41, $p=0.011$), tacrolimus (HR 0.40, $p=0.003$), and male donor sex (HR 0.56, $p=0.019$) were protective for cGvHD. No differences were found in aGvHD, NRM, relapse, and OS.

Conclusion: In MSD transplants, low-dose rATG improved GRFS by reducing cGvHD, without impacting relapses, NRM, or OS in MSD allo-HSCT. The protective effect of RIC and MEL regimens should be interpreted cautiously given small subgroups.