Rabbit anti-T-lymphocyte globulin nullifies differences in clinical outcomes of patients transplanted from HLA-mismatched unrelated donors

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INTRODUCTION

Rabbit anti-T-lymphocyte globulin (ATLG) is recommended for unrelated donor (UD) allogeneic hematopoietic cell transplantation (HCT) in malignant diseases to prevent graft-versus-host disease (GVHD) (1,2). This study aimed to compare the outcomes of adult patients with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML) who underwent HCT from 10/10 HLA-matched UD (MUD) vs. mismatched UD (MMUD) with low-dose ATLG, between 2010-2023.

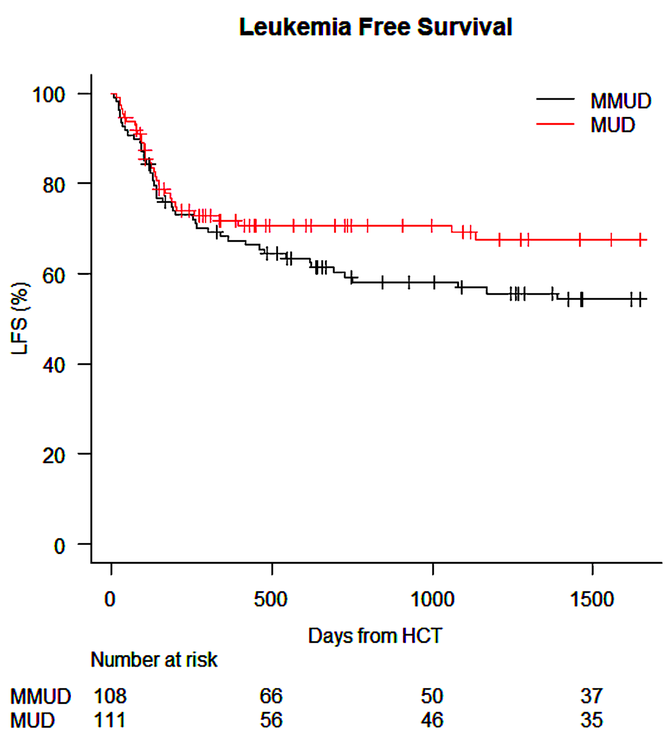
RESULTS

The study cohort included 219 patients, median age 55 years (18-71). Donors were MUD (n=111) and MMUD (n=108). Graft sources were peripheral blood stem cells (PBSCs) in 175 patients and bone marrow (BM) in 44. All patients received low-dose ATLG (15 to 30 mg/kg) during conditioning in combination with calcineurin inhibitor (CNI) and methotrexate (MTX, 92%) or mycophenolate mofetil (MMF, 8%). BM was used more frequently in MMUD group vs. MUD (28% vs. 13%; p=0.005); MMF was used more frequently in MUD group vs. MMUD patients (13% vs. 4%; p=0.016); more patients had Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI) ≥3 in MUD group vs. MMUD (33% vs. 19%; p=0.019) (**Table 1**).

Table 1. Baseline characteristics of patients

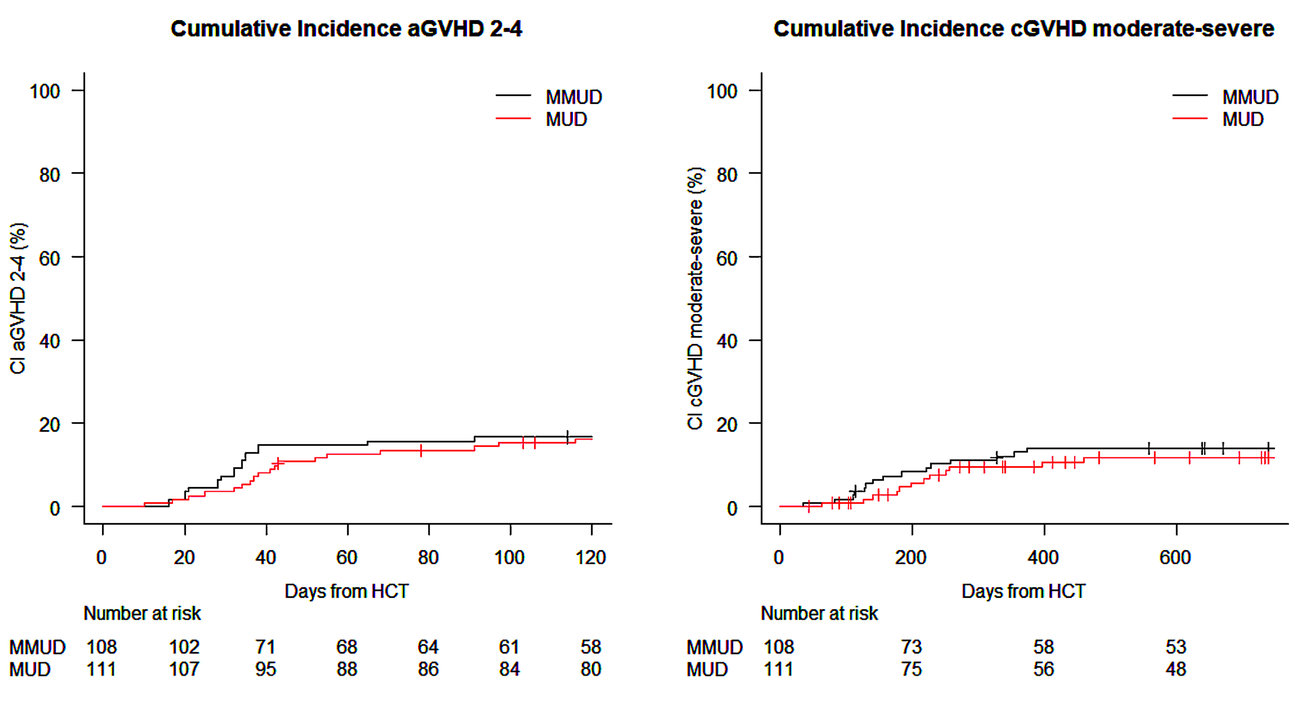
	Total (n=219)	MUD (n=111)	MMUD (n=108)
Median recipient age, years (range)	55 (18-71)	56 (19-71)	55 (18-71)
Recipient sex, n (%)			
Male	124 (57)	66 (59)	58 (54)
HTC-CI, n (%)			
< 3	**161 (74)**	**74 (67)**	**87 (81)**
≥ 3	**58 (26)**	**37 (33)**	**21 (19)**
Diagnosis, n (%)			
AML	185 (84)	94 (85)	91 (84)
MDS	34 (16)	17 (15)	17 (16)
Phase at HCT, n (%)			
CR1	134 (61)	65 (59)	69 (64)
CR2	19 (9)	12 (11)	7 (6)
Active disease	66 (30)	34 (30)	32 (30)
HLA matching, n (%)			
HLA 10/10	111 (51)	111 (100)	0 (0)
HLA 9/10	95 (43)	0 (0)	95 (88)
HLA 8/10	13 (6)	0 (0)	13 (12)
Stem cell source, n (%)			
PBSCs	**175 (80)**	**97 (87)**	**78 (72)**
BM	**44 (20)**	**14 (13)**	**30 (28)**
Female donor-male recipient pairs, n (%)	21 (10)	12 (10)	9 (8)
CMV IgG-positive recipients, n (%)	170 (78)	87 (78)	83 (77)
Conditioning, n (%)			
Myeloablative	137 (63)	69 (62)	68 (63)
GVHD prophylaxis			
CNI-MTX-ATLG	**201 (92)**	**97 (87)**	**104 (96)**
CNI-MMF-ATLG	**18 (8)**	**14 (13)**	**4 (4)**

Figure 1. Leukemia Free Survival (LFS)



At median follow up of 4.6 years, overall survival, leukemia-free survival (LFS) (**Figure 1**), non-relapse mortality (NRM) and relapse incidence, were 69.4% vs. 57.1% (p=0.086), 67.5% vs. 54.3% (p=0.129), 10.3% vs. 28.3% (p=0.002) and 22.2% vs. 17.4% (p=0.257), for MUD and MMUD, respectively. HLA-matching was the only factor influencing NRM (MUD HR: 0.358; CI 95%: 0.180-0.714; p=0.004). Day-100 incidence of 2-4 and 3-4 acute GVHD (aGVHD) were 15.4% vs. 16.7% (p=0.862), and 5.4% vs. 7.4% (p=0.396); 2-y cumulative incidence of chronic GVHD (cGVHD) and moderate-severe cGVHD were 17.8% vs. 16.8% (p=0.396), and 11.9% vs. 14.0% (p=0.995) in MUD vs MMUD, respectively (**Figure 2**). Graft source and antimetabolite (MTX/MMF) were not associated with GVHD development.

Figure 2. Cumulative Incidence of 2-4 aGVHD and moderate-severe cGVHD



CONCLUSION

Low-dose ATLG for GVHD prophylaxis resulted in superimposable acute and chronic GVHD incidence and overall clinical outcomes for MUD and MMUD in AML and MDS.

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ACKNOWLEDGEMENTS

The work reported in this publication was funded by the Italian Ministry of Health, RC-2022-2773290 to FB: "Ottimizzazione dell'outcome del trapianto allogenico tramite l'applicazione di regimi profilattici e terapeutici che riducano le complicanze post-trapianto". The authors thank AIL Bologna ODV, the Italian Association for research on leukemia, lymphoma and myeloma, for the support of the Laboratory of Immunobiology of Transplant and Cellular Therapies, IRCCS AOU di Bologna, Bologna, Italy, led by FB, MD, PhD.