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POSTER ABSTRACTS

722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

Improved Gvhd-Relapse Free Survival of *Ex Vivo* αβtcr/CD19 Depleted Allo-Sct Combined with *In Vivo* T Cell Depletion with ATG When Compared to T Cell Replete Transplantations with or without the Addition of ATG

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Introduction

The aim of allogeneic stem cell transplantation (allo-SCT) is to reach graft-versus-host disease, relapse free survival (GRFS). To reduce the incidence of graft-versus-host disease (GVHD), we have developed an allo-SCT platform combining *ex vivo* αβTCR/CD19 depletion with *in vivo* T-cell depletion through administration of antithymoglobulin (ATG). Here we compare GRFS to historical cohorts of T-cell replete allo-SCT.

Methods

Adults with hematological malignancies and transplanted between 2011 and 2022 were included in this retrospective analysis. Written informed consent was obtained in accordance with the JACIE guidelines. Clinical data was extracted from the EBMT registry. 3 cohorts were identified. Cohort A: Allo-SCT of unmanipulated peripheral blood derived mononuclear cells (PBMCs) of matched related donors (MRD) after non-myeloablative (NMA) or myeloablative (MA) conditioning without ATG. Cohort B: Allo-SCT of unmanipulated PBMCs of 10/10 or 9/10 matched unrelated donors (MUD) after NMA or MA conditioning with ATG. Patients in cohorts A & B received dual immunosuppression with cyclosporin (CsA) and mycophenolic acid (MMF). Cohort C: Allo-SCT of αβTCR/CD19 depleted PBMCs of MRD and MUD (10/10 and 9/10) after ATG and a myeloablative conditioning as previously described[1]. Patients in cohort C received 28 days of MMF. Cumulative incidence (CI) of GVHD was defined as time to onset of GVHD, with relapse and death as competing events. Overall survival (OS) was defined as time to death from any cause. CI of relapse was defined as time to relapse, with death as a competing event. Non-relapse mortality (NRM) was defined as time to death, without relapse or progression. Event free survival (EFS) was defined as the time to relapse, graft failure or death. GRFS was defined as the time to relapse, aGVHD 3-4 or extensive cGVHD, graft failure or death. CI of CMV and EBV reactivations were calculated with relapse and death as competing events.

Results

341 patients were included (cohort A: N=63; cohort B: N=150; cohort C: N=128) (table 1). In T cell replete allo-SCT (A&B) ATG was administered to recipients of MUD and MA conditioning was administered to patients < 40 years with acute leukemia. In cohort C, all patients received ATG and an MA conditioning, regardless of age or underlying malignancy. This explains differences donor types and intensity of conditioning between the cohorts (table 1). Other clinical characteristics were comparable. Two year OS (A=66.7%; B=58.7%; C=63.8%) and EFS (A=57.1%; B=52%; C=55.7%) was comparable between the cohorts. Two year CI of relapse was also comparable (A=30%; B=23%; C=28%). Two year NRM appeared higher in B, but this difference did not reach significance (A= 9.8%; B=24%; C=15%). The CI of aGVHD grade 2-4 and 3-4 at day 100 was significantly higher in T cell replete allo-SCT with MUD (2-4; A=23%; B=37%; C=20% (p=0.002); 3-4: A=5%; B=16%; C=4.7% (p=0.043)). The incidence of extensive cGVHD was significantly higher in T cell replete allo-SCT of MRD. (A= 25%; B=13%; C= 2.3%

(p=< 0.001)). The low incidence of grade 3-4 aGVHD and extensive cGVHD without an increase in relapse or NRM, translated into a superior 2 year GRFS in patients receiving ATG combined with an $\alpha\beta$TCR/CD19 allograft (C=55.6%) as compared to T cell replete allo-HSCT of MRD (A=38.1%) and MUD (B=40.8%) (Figure 1, p=0.04). This difference remained significant in a multivariate analysis.

Conclusion

We demonstrate that $\alpha\beta$TCR/CD19 depletion combined with ATG, with a myeloablative conditioning and a very short course of immunosuppression results in very low incidences of life-threatening GVHD and an improved GRFS as compared to T cell replete allo-SCT for adult patients up to the age of 70. This is likely to positively impact the long term quality of life in survivors of allo-SCT[2]. In addition, this platform provides a window for additional early post allo-interventions to further improve the control of underlying hematological malignancies.

1. de Witte, M.A., et al., alphabeta T-cell graft depletion for allogeneic HSCT in adults with hematological malignancies. Blood Adv, 2021. 5(1): p. 240-249.

2. Oerlemans, S., et al. Relapse and severe Graft-versus-Host Disease have a negative impact on long-term symptoms and quality of life of patients three years after allogeneic haematopoietic stem cell transplantation. Annual meeting EBMT 2022.

Disclosures No relevant conflicts of interest to declare.

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