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Blood 142 (2023) 4098–4099

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

508.BONE MARROW FAILURE: ACQUIRED

Haploidentical Stem Cell Transplantation Using Total Body Irradiation (600 cGy) and Fludarabine with ATG in Upfront and Salvage Setting in Adult Patients with Severe Aplastic Anemia

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Background: Haploidentical stem cell transplantation from a related mismatched donor (Haplo-SCT) has extended into adult patients with severe aplastic anemia (SAA) with advances in controlling graft failure and GVHD. However, because of concerns for morbidity and mortality, Haplo-SCT has been used as salvage treatment after the failure of immunosuppressive therapy (IST). In Haplo-SCT for SAA patients, the achievement of successful engraftment without GVHD is fundamental for better long-term survival with good quality of life. We optimized the dose of rabbit ATG and fractionated TBI (fTBI) with fixed dose of fludarabine (Flu, 150mg/m ^{2}/day) using step-by-step dose de-escalation (Lee et al, Am J Hematol, 2018) and reached fTBI 600 cGy/Flu/intermediate-dose ATG (5 mg/kg). This protocol showed an overall survival rate of 91.0% after a median follow-up of 32.3 months in a study of 47 patients (Lee et al, BBMT, 2020). Here, we evaluated the feasibility of this protocol in both upfront and salvage setting for Haplo-SCT in adult patients with SAA.
Methods: We analyzed 68 consecutive patients who underwent Haplo-SCT between Oct. 2014 and Jan. 2023. Fifty-six (82%) patients had salvage Haplo-SCT after the failure of standard IST (ATG + CsA) (n=36) and CsA monotherapy (n=20). Twelve (18%) patients underwent upfront Haplo-SCT. All patients received a conditioning regimen of 600 cGy fTBI (200 cGy, 3 times) and Flu (30 mg/m ^{2}/day) for 5 days. GVHD prophylaxis consisted of ATG/tacrolimus/methotrexate (MTX). ATG (Thymoglobulin ®,2.5 mg/kg/day) was administered on days -2 and -3. All patients received PBSC.
Results: The median age was 34.0 years (17-61) and 30 (44%) patients had very SAA (VSAA) at transplantation. Haploidentical donors are composed of mother (n=10), father (n =8), sibling (n=30), offspring (n=17), and others (n=3). All patients achieved primary engraftment. The cumulative incidence of acute GVHD (grade ≥2) and chronic GVHD (≥ moderate) was 26.5% at 100 days and 9.3% at 4 years, respectively. With a median follow-up of 54 months, the 4-year overall survival (OS) and failure-free survival (FFS) was 93.9% and 92.4%, respectively. 4-year OS of upfront and salvage Haplo-SCT was 100 and 94.7%, respectively (P = 0.352). The 4-year GFFS was 78.9%, and there was no significant difference between upfront and salvage Haplo-SCT (83.3% vs 78.1%, P = 0.709). In the subgroup analysis, 4-year GFFS of patients who failed the standard IST (ATG+CsA) excluding CsA monotherapy also showed no statistical difference compared to the others (85.8% vs 71.3%, P = 0.143). Furthermore, after adjusting for the potential factors affecting GFFS (patient's age, donor type, and comorbidity index), no different GFFS was shown between upfront and salvage Haplo-SCT.
Conclusions: Our results suggest that Haplo-SCT with fTBI 600 cGy/Flu/ATG-5 can be an effective alternative option in both upfront and salvage settings, when fully matched donors are not available.

Disclosures Lee: *Kira:* Consultancy; *Samsung:* Consultancy; *AlloVir:* Consultancy; *Arrowhead:* Consultancy; *Achillion:* Research Funding; *Alexion, AstraZeneca Rare Disease:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding.

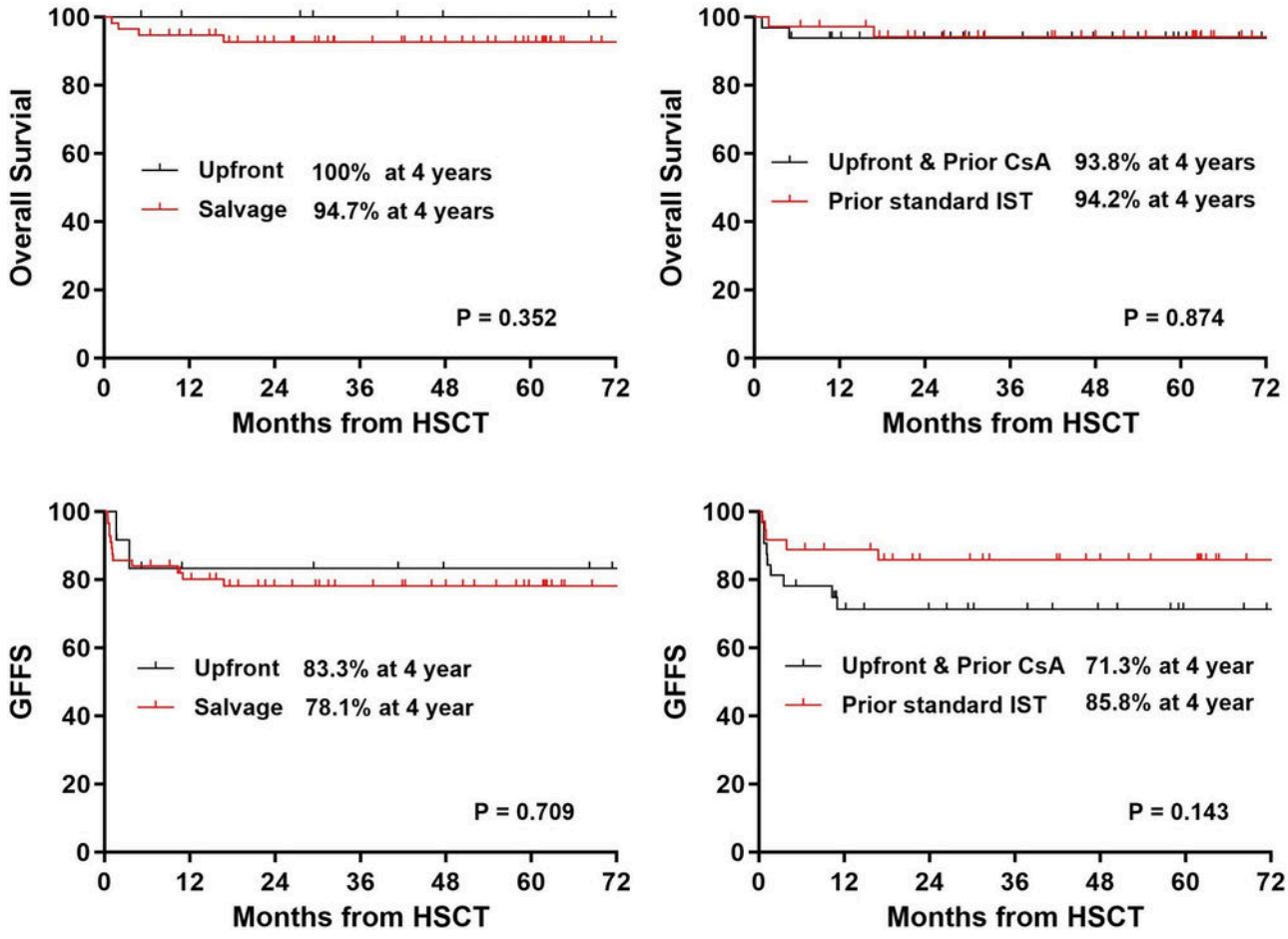

Figure 1

https://doi.org/10.1182/blood-2023-188758