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POSTER ABSTRACTS

721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Comparable Survival for Fludarabine and Treosulfan Vs. Fludarabine and TBI As Conditioning Regimens in Patients with AML and MDS Undergoing Allogeneic Stem Cell Transplantation

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Introduction

Allogeneic stem cell transplantation (alloSCT) is a standard treatment option for patients (pts) with acute myeloid leukemia (AML) and myelodysplastic neoplasia (MDS) with relapse remaining the main cause of treatment failure. For AML pts transplanted in complete remission (CR) or MDS pts, the combination of fludarabin with fractionated total body irradiation (8 GyTBI, "FluTBI") is an established conditioning regimen. Based on the favorable outcome data reported for fludarabine/treosulfan ("FluTreo"), especially for older and/or comorbid pts, this regimen has become a reliable dose reduced conditioning therapy prior to alloSCT and a valuable alternative to other TBI or chemotherapy-based regimens.

Methods

We conducted a retrospective analysis of 215 pts with AML in CR and 96 pts with MDS who underwent first alloSCT between 2010 and 2022 with a median follow-up (FU) of survivors of 34 months (range: 1 - 124 months). After conditioning therapy with FluTreo (150mg/m ^{2} fludarabin, 30g/m ^{2} treosulfan) or FluTBI (120mg/m ^{2} fludarabin, 4x2Gy TBI) pts were allografted from matched related (MRD; n=65), 10/10 human leukocyte antigen (HLA)-matched unrelated (MUD; n=200), or 9/10 HLA-matched unrelated donors (MMUD; n=46). For AML pts, any detectable molecular/cytogenetic alteration prior to alloSCT was classified as potentially measurable residual disease. Propensity score matching allowed us to identify 55 pair-matched FluTBI and FluTreo pts (nearest matching for age at alloSCT, sex, disease, HCT-CI score, ECOG, with a caliper distance of 0.5).

Results

Before matching, pts characteristics differed significantly between FluTreo and FluTBI in terms of age at alloSCT (median 64 vs. 47 yr), underlying disease (AML: 59% vs. 88%), ECOG (≥2 15% vs. 6%) and HCT-CI-Score (≥3 50% vs. 25%). In the AML subgroup, pts with measurable residual disease prior to alloSCT were significantly more frequent in the FluTreo group (68% vs. 48%, $p<.001$). GvHD prophylaxis consisted of calcineurin inhibitor and methotrexate/MMF in all pts. In addition, pts transplanted from unrelated donors received ATLG (Neovii). In the FluTreo group, more patients were transplanted from MRDs (24% vs. 14%, $p.013$). After matching, patient characteristics were well balanced with respect to age (median 57 vs. 55 yr, $p.11$), disease (AML/MDS) (p .8), HCT-CI score (p .24), sex (p .85), donor types (MRD: 25.5% vs. 14.5%, MUD: 58.2% vs. 67.3%, MMUD: 16.4% vs. 18.2%, p .36) and measurable residual disease prior to alloSCT (p .58). Risk groups for AML and MDS pts at diagnosis were comparable across both groups (ELN for AML and IPSS-R for MDS).

Relapse incidences (RI) at 3 yrs were similar for FluTreo and FluTBI pts in the unmatched (25% vs. 25%, $p.8$) and matched cohorts (28% vs. 28% p .7). The non-relapse mortality (NRM) rate was <10% trending towards a lower NRM rate for the FluTBI group in the unmatched cohorts (at 1 yr: 8% vs. 5%, p .07) and a significant difference after matching (at 1 year 2% vs. 9% p .03). Overall survival (OS) for the whole cohort showed a trend towards an inferior outcome for FluTreo (3 yr: 71% vs. 79% p .06), after matching, no difference could be observed (3 yr: 80% vs. 71% p .54). Leukemia-free survival (LFS) was comparable across conditionings in the unmatched (59% vs. 66% p .42) and the matched cohorts (70% vs. 59% p .42).

Irrespective of conditioning therapy, pts with measurable residual disease prior to alloSCT had comparable OS and LFS. However, for the matched cohort, pts with measurable disease treated with FluTreo showed a trend towards an inferior OS and LFS after 3 yr in contrast to FluTBI pts (OS: 66% vs. 80%, p .13; PFS: 58% vs. 67%, p .3).

No significant differences could be observed in the incidence of acute onset graft versus host disease (GvHD) grade 2-4 at day 100 after alloSCT. Similarly, occurrence of chronic GvHD at 3 yr did not differ in the matched cohorts (32% vs. 43%, p .4).

Conclusion

With a meaningful median follow up of 34 months, our data for dose-reduced conditioning with either FluTreo or FluTBI highlight favorable and comparable survival rates of >70%. RI and NRM were low for both regimens. For pts with AML, who received FluTBI, measurable residual disease prior to alloSCT seemed to have no effect on outcome, while for the FluTreo cohort measurable residual disease prior to alloSCT showed a trend towards lower survival rates. This finding should be evaluated in a prospective trial comparing TBI and treosulfan based conditioning.

Disclosures Mikesch: *Pfizer:* Honoraria, Other: Advisory Boards; *Daiichi Sankyo:* Honoraria, Other: Advisory Boards; *Celgene:* Honoraria, Other: Congress Support; *Novartis:* Honoraria; *BeiGene:* Honoraria; *Jazz Pharmaceutics:* Honoraria. **Schliemann:** *Boehringer Ingelheim:* Research Funding; *AngioBiomed:* Research Funding; *Pfizer:* Honoraria, Other; *Roche:* Honoraria; *Novartis AG:* Honoraria; *Jazz Pharmaceuticals:* Honoraria, Other, Research Funding; *Bristol Myers Squibb:* Honoraria, Other; *AstraZeneca:* Honoraria; *Astellas Pharma Inc.:* Honoraria; *Laboratoires Delbert:* Honoraria; *AbbVie Inc.:* Honoraria, Other. **Lenz:** *Genmab:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Karyopharm:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Morphosys:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Incyte:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Constellation:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *ADC Therapeutics:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Miltenyi:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *PentixPharm:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Sobi:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Immagene:* Consultancy; *Genase:* Consultancy; *Hexal/Sandoz:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Lilly:* Consultancy; *University Hospital Munster:* Current Employment; *Celgene:* Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *NanoString:* Membership on an entity's Board of Directors or advisory committees; *BeiGene:* Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *BMS:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *AstraZeneca:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Novartis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Bayer:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Janssen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Gilead:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *F. Hoffmann-La Roche Ltd:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau. **Stelljes:** *Pfizer:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *abbvie:* Speakers Bureau; *MSD:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Amgen:* Membership on an entity's Board of Directors or advisory committees; *Jazz:* Speakers Bureau; *Novartis:* Speakers Bureau; *Gilead:* Speakers Bureau; *medac:* Other: Editorial and statistical support , Speakers Bureau.

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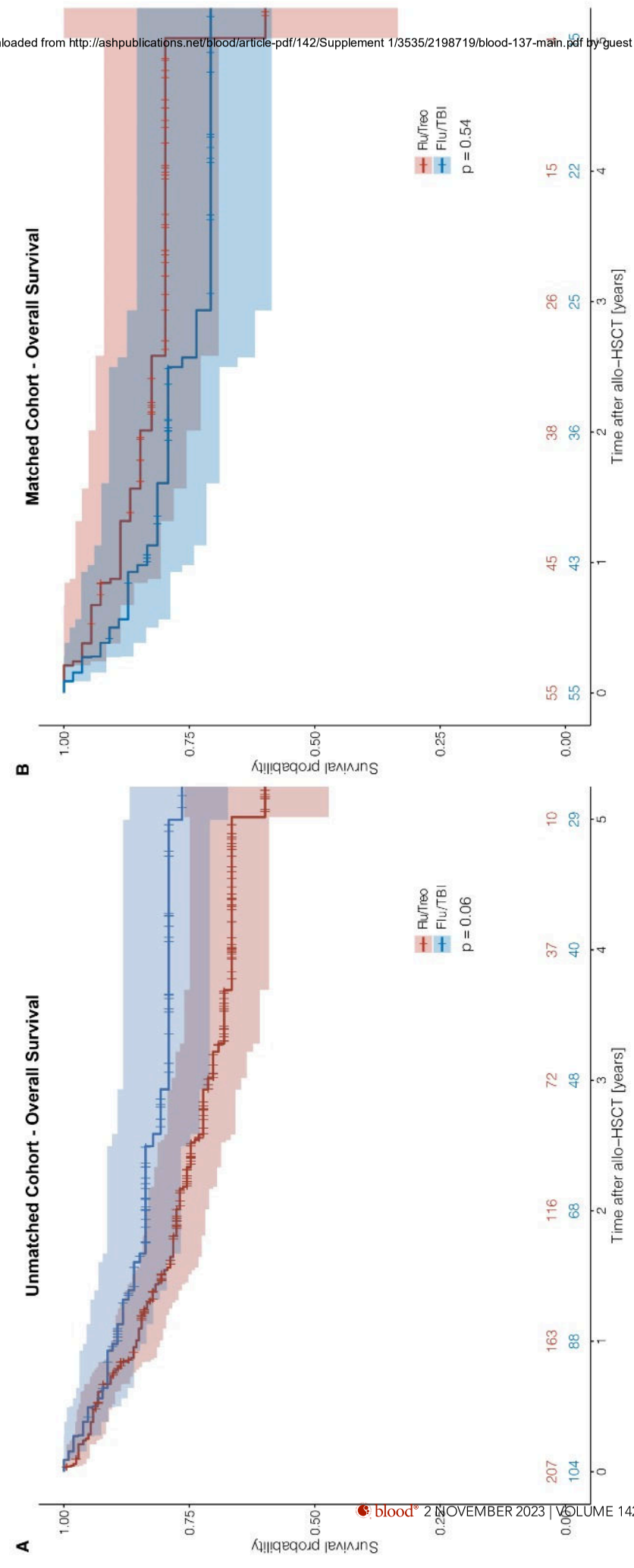

Figure 1