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Blood 142 (2023) 2234–2235

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

How Much Have Post-Transplant Outcomes Improved Since 2000 for Patients with Philadelphia-Positive Acute Lymphoblastic Leukemia in First Remission? a Study from the EBMT Acute Leukemia Working Party

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Background

Allogeneic hematopoietic cell transplantation (allo-HCT) remains an important curative modality for patients with Philadelphia-positive acute lymphoblastic leukemia (Ph+ ALL) in first complete remission (CR1). Recent years have witnessed an improvement in transplant techniques and increased use of post-transplant pharmacological interventions aimed at reducing the risk of relapse. However, recent results using the combination of blinatumomab and second or third-generation tyrosine kinase inhibitors (TKI) have challenged the role of allo-HCT in CR1. To address these challenges, we assessed real-world changes over time in transplant characteristics and post-transplant outcomes in adult patients with Ph+ ALL in CR1, using a large dataset from the European Society for Blood and Marrow Transplantation (EBMT) registry.

Methods

We identified 3292 adult patients (45% female; median age 45 years, range 18-76) with Ph+ ALL allografted between 2001 and 2020 in CR1 from a matched sibling (38%), unrelated (54%) or haploidentical donor (8%).At transplant, 41% of patients were measurable disease (MRD) positive (pos). The comorbidity index (CI) was zero in 63% of patients with available data. Conditioning was myeloablative (MAC) in 77% of patients, and included total body irradiation (TBI) in 64% of patients. *In vivo* T cell depletion (TCD) and peripheral blood stem cells (PBSC) were given to 52% and 86% of patients, respectively. Most

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patients (66%) and donors (55%) were cytomegalovirus (CMV) positive. Median follow-up for live patients was 56 months (interquartile range [IQR] 28-32).

Results

We compared changes in patient and transplant characteristics over time in 245 patients transplanted in 2001-2005, 679 patients transplanted in 2006-2010, 1035 patients transplanted in 2011-2015, and 1333 patients transplanted in 2016-2020. Patients transplanted in recent years were older, were less likely to be MRDpos, and more likely to receive PBSC and TCD. The 3-year cumulative incidence of relapse (CIR) gradually and significantly decreased from 41% to 32%, 27%, and 19% over the 4 time periods (p=0.001), and non-relapse mortality (NRM) significantly decreased as well from 25% to 24%, 23% and 17% (p=0.001). The 3-year leukemia-free survival (LFS) and overall survival (OS) gradually and significantly improved over time from 34% to 44%, 50%, and 64% (p=0.001) and from 47% to 56%, 65%, and 75% (p=0.001), respectively. Finally, graft-versus-host disease (GVHD)-free, relapse-free survival (GRFS) improved from 26% to 34%, 37%, and 49% (p=0.001). In a Cox regression multivariate analysis (MVA), a progressive and significant improvement in all transplant outcomes was noted including reduced acute and chronic GVHD, reduced CIR and NRM, and increased LFS, OS, and GRFS. LFS was also negatively affected by older age, male gender of both patients and donors, MRDpos pretransplant, and the use of reduced intensity conditioning while positively affected by the use of TBI. OS was also positively affected by younger age, female gender of patients, matched sibling donor, TBI, and TCD. This improvement in post-transplant outcomes over time was observed both in MRDpos but also in MRD negative (neg) patients. In MRDneg patients, 3-year CIR decreased from 34% to 30%, 24%, and 17% (p=0.001) over the 4 time periods whereas LFS improved from 41% to 46%, 52%, and 66% (p=0.001). Similarly, in MRD-positive patients, CIR decreased from 48% to 34%, 32%, and 23% (p=0.001) over the 4 time periods whereas LFS improved from 27% to 42%, 47% and 60% (p=0.001).

Conclusion

In patients with Ph+ ALL, we observed an impressive improvement over time in post-transplant outcomes with decreased CIR and NRM and improved LFS, OS, and GRFS, both in MRDpos and MRDneg patients. These large-scale, real-world data can serve as a benchmark for future studies in this setting, including those testing the combination of TKI and blinatumomab as an alternative to transplant.

Disclosures Yakoub-Agha: *Novartis:* Consultancy, Honoraria; *Janssen:* Honoraria; *Bristol-Myers Squibb:* Honoraria; *Kite, a Gilead Company:* Consultancy, Honoraria, Other: Travel Support. **Peffault De Latour:** *Jazz Pharmaceuticals:* Honoraria. **Kröger:** *MSD:* Honoraria; *Neovii Biotech:* Honoraria, Research Funding; *Jazz:* Honoraria; *Takeda:* Consultancy; *BMS:* Honoraria, Research Funding; *Kite/Gilead:* Honoraria; *Novartis:* Honoraria, Research Funding; *Riemser:* Honoraria, Research Funding; *Pfizer:* Honoraria; *Sanofi:* Honoraria. **Giebel:** *Abbvie:* Consultancy, Honoraria, Speakers Bureau; *Gilead:* Consultancy, Honoraria, Speakers Bureau; *Janssen:* Consultancy, Honoraria, Speakers Bureau; *Amgen:* Consultancy, Honoraria, Speakers Bureau; *AstraZeneca:* Consultancy, Honoraria, Speakers Bureau; *Roche:* Consultancy, Honoraria, Speakers Bureau; *Pfizer:* Consultancy, Honoraria, Speakers Bureau; *Novartis:* Consultancy, Honoraria, Speakers Bureau; *Servier:* Honoraria, Speakers Bureau; *Swixx:* Honoraria, Speakers Bureau; *Angelini:* Honoraria, Speakers Bureau; *BMS:* Honoraria, Speakers Bureau; *Zentiva:* Consultancy, Honoraria. **Ciceri:** *ExCellThera:* Other: Scientific Advisory Board . **Mohty:** *JAZZ PHARMACEUTICALS:* Honoraria, Research Funding.

https://doi.org/10.1182/blood-2023-179578

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