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POSTER ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

Outcome of Allogeneic Stem Cell Transplantation in FLT3-TKD-Mutated AML - a Study on Behalf of the Acute Leukemia Working Party of the EBMT

Thomas Heinicke, MD[1], Myriam Labopin[2], Didier Blaise, MD PhD[3], Jaime Sanz, MD PhD[4], Ibrahim Yakoub-Agha, MD PhD[5], Thomas Cluzeau, MDPhD[6], Marco Ladetto[7], Jürgen Finke, MD[8], Eric Deconinck[9], Jurjen Versluis, MD PhD[10], Urpu Salmenniemi, MD PhD[11], Andreas Neubauer, MD[12], Eolia Brissot[13], Ali Bazarbachi, MD PhD[14], Arnon Nagler, MD[15], Jordi Esteve, MD PhD[16], Fabio Ciceri[17], Mohamad Mohty, MDPhD[18]

[1] Department of Hematology and Oncology, University Hospital Magdeburg, Magdeburg, Germany
[2] EBMT Statistical Unit, Sorbonne University, Saint-Antoine Hospital, AP-HP, INSERM UMRs 938, Paris, France
[3] Institut Paoli Calmettes, Marseille, FRA
[4] Hematology Department, Hospital Universitari i Politècnic La Fe, Valencia, España, Valencia, Spain
[5] CHU de Lille, Université de Lille, INSERM U1286, Infinite, 59000, Lille, France
[6] Nice University Hospital, Nice, France
[7] Department of Translational Medicine, Università del Piemonte Orientale SCDU Ematologia SS Antonio e Biagio e Cesare Arrigo, Alessandria, Italy
[8] Department of Hematology, Oncology and Stem Cell Transplantation, Faculty of Medicine, University of Freiburg, Freiburg, Germany
[9] Besançon University Hospital, Besançon, France
[10] Erasmus Medical Center Cancer Institute, Rotterdam, Netherlands
[11] HUCH Comprehensive Cancer Center, Stem Cell Transplantation Unit, Helsinki, Finland
[12] Philipps University, Marburg, DEU
[13] Sorbonne Université Service d' Hématologie Clinique et Thérapie Cellulaire, Hospital Saint-Antoine, Centre de Recherche Saint-Antoine (CRSA), Paris, France
[14] American University of Beirut Dept. of Medicine, Beirut, Lebanon
[15] Division of Hematology and Bone Marrow Transplantation, Chaim Sheba Medical Center, Tel Hashomer, Israel
[16] Hematopoietic Cell Transplantation Unit, Hospital Clínic de Barcelona, ICHMO, Barcelona, Spain
[17] Unit of Hematology and Stem Cell Transplantation, Ospedale San Raffaele, University Vita-Salute San Raffaele, Milan, Italy
[18] department of hematology and cell therapy, hopital Saint-Antoine, EBMT Acute Leukemia Working Party and Registry, Hospital Saint-Antoine, Paris University, Paris, France

Introduction

The overall prognostic impact of point mutations in the tyrosine-kinase domain 1 of FLT3 (FLT3-TKD ^{mut}) in patients (pts) with acute myelogenous leukemia (AML) remains controversial. Furthermore, co-occurrence of FLT3-TKD ^{mut} and mutated nucleophosmin-1 (NPM1 ^{mut}) was shown to have a favorable prognostic impact on AML pts receiving conventional chemotherapy. However, little is known about the outcome of AML pts with FLT3-TKD ^{mut} with or without co-occurring NPM1 ^{mut} treated with allogeneic stem cell transplantation (alloSCT).

Patients and Methods

This is a retrospective study of the acute leukemia working party (ALWP) of the European Society for Blood and Marrow transplantation (EBMT) investigating the outcome of adult AML pts with FLT3-TKD ^{mut} with or without NPM1 ^{mut} after first alloSCT using matched sibling (MSD), unrelated (UD) or haploidentical (haplo) donors between 2005 and 2022. All patients were in first or second complete remission (CR1 of CR2). Information on cytogenetic risk was necessary for inclusion. No *ex-vivo* T-cell depletion (TCD) was allowed. The primary endpoint was leukemia-free survival (LFS) at two years after alloSCT. Secondary endpoints were overall survival (OS), cumulative incidence of relapse (RI), non-relapse mortality (NRM), acute and chronic graft-versus-host disease (GVHD) and GVHD-free, relapse free survival (GRFS).

One hundred and eighty-two adult AML pts with FLT3-TKD ^{mut} were identified, of which 74 (40.7%) had a co-occurring mutation in NPM1. Median age was 55.1 years (range 18.6-79.1) and 46.7% were male. Median follow-up was 21.4 months [IQR 13.6-28.1]. 78% of the pts were in CR1. Cytogentic risk was favorable, intermediate and adverse in 12.6%, 75.3% and 12.1% of pts, respectively. Additional FLT3 internal tandem duplication (FLT3-ITD) was present in 25.8% of pts. Information on measurable residual disease (MRD) was available for 68.7% of pts, being positive in 48% of these. Karnofsky performance score was < 90% in 21.1%, and hematopoietic cell transplantation-specific comorbidity index (HCT-CI) was >=3 in 28.1% of pts. 69.6% of pts were cytomegalovirus (CMV) positive. Conditioning was myeloablative in 52.8% and reduced intensity in 47.2% of pts. Stem cell donors were MSD, UD and haplo in 25.8%, 55.5% and 18.7% of cases. Stem cell source was bone marrow in 10.4%, peripheral blood in 87.4% and both in 2.2%. *In-vivo* TCD was performed in 59.2% of pts. GVHD prophylaxis was calcineurin inhibitor-based in 92.2% of pts.

Results

Engraftment was achieved in 99.4% of pts with a day-60 absolute neutrophil count (ANC) >0.5 x 10 ^{9}/L of 97.7% [95% CI: 93.7-99.2]. Day-180 rates of acute GVHD (aGVHD) grade II-IV and grade III-IV were 26.2% (95% CI:19.9-32.9) and 8.1% (95% CI:4.6-12.8), respectively. At two years, rates of total chronic GVHD (cGVHD) and extensive cGVHD were 30% (95% CI: 22.5-38) and 16.6% (95% CI:10.6-23.7), respectively.

Two-year LFS and OS were 66.1% (95% CI: 57.6-73.2) and 74% (95% CI: 65.4-80.8), respectively. Two-year RI, NRM and GRFS were 22.5% (95% CI:16-29.8), 11.4% (95% CI: 7-17), and 51.1% (95% CI: 42.4-59.1), respectively. Cause of death was original disease in 47.5%, infection in 27.5%, GVHD in 22.5% and non-SCT related in 2.5% of cases.

In univariate analysis the only factor with significant impact on LFS was donor type (haplo [n=34] vs. others, p=0.006). For GRFS, patient CMV negativity (p=0.014) and *in-vivo* TCD (p=0.01) were significant. Interestingly, co-occurring mutations in FLT3 (FLT3-ITD) or NPM1 were not identified as having a significant impact on LFS or GRFS. Moreover, MRD status before alloSCT was also not shown to have a significant impact on these outcomes.

In multivariate analysis of LFS and GRFS, only donor type (haplo [n=34] vs. others) was shown to be significant for both endpoints, hazard ratio (HR) 2.54; 95% CI: 1.4-4.6; p=0.002, and HR 2.01; 95% CI: 1.18-3.41; p=0.01, respectively.

Conclusion

Acknowledging the limitations of our retrospective study in this rare entity results are encouraging given the high-risk population (median age 55.1 years, CR2 in 22%, co-occurring FLT3-ITD in 25.8%, positive MRD in 48%, HCT CI >=3 in 28.1%). LFS, OS and GRFS rates were 66.1%, 74% and 51.1%, respectively, and both RI and NRM were comparably low with rates of 22.5% and 11.4%, respectively. No positive prognostic impact of co-occurring mutations in FLT3-TKD and NPM1 was detected, unlike what was found for conventional chemotherapy.

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