ELSEVIER

Blood 142 (2023) 4987–4988

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

Should the European Leukemia Net 2022 Adverse Risk Classification of *NPM1* mutated Acute Myeloid Leukemia be Revisited? Among Adverse Risk Cytogenetics, Solely Complex Karyotype Is Associated with Worse Post-Transplant Survival: A Study from the EBMT Acute Leukemia Working Party

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Introduction The European LeukemiaNet (ELN) 2022 risk classification has identified acute myeloid leukemia (AML) with *Nucleophosmin 1 (NPM1)* mutation as a distinct entity associated with a favorable prognosis in those with normal cytogenetics (CG) and absent *FLT3 ITD*. Furthermore, the ELN 2022 reclassified AML patients with mutated *NPM1* and high risk CG as adverse risk (AR) regardless of their *FLT3 ITD* status. We performed this analysis to evaluate the impact of the different AR CG aberrations on post-transplant outcomes in that setting.
Methods: In this retrospective registry based analysis from the EBMT, we included adult patients (≥ 18 years) with *NPM1* mutated *de novo* AML, intermediate or AR CG, and known *FLT3 ITD* mutation status, who received their first allogeneic hematopoietic cell transplantation (HCT) in first complete remission between 2005 and 2021. Multivariate analysis adjusting for differences between the groups (according to CG) was performed using a Cox proportional hazards regression model.
Results: We identified a total of 3275 patients (54% females). *FLT3 ITD* was present in 2377 patients (73%); significantly higher in those with normal CG (75% versus 57%). Normal CG was seen in 2782 patients (85%), while CG aberrations were noted in 493 patients, the most common of which was trisomy 8 (141 patients). Adverse risk CG were seen in 160 patients (4.9%) including complex karyotype (CK) in 72 patients and monosomal karyotype (MK) in 66 patients. The median age was 54 [IQR 45-62]. No significant difference was noted between those with normal and those with abnormal CG with regards to baseline patient and transplant characteristics: HCT comorbidity index (CI) was £2 in 79% of patients in both groups, minimal measurable disease

at transplant was positive in 42% and 44%, donor type was matched sibling (MSD) in 32% and 34%, unrelated (UD) in 57% and 58%, or haploidentical in 11% and 9%, stem cell source was peripheral blood in 89% and 89%, conditioning was myeloablative in 52% and 49% respectively.
The median follow up for alive patients was 35 months (IQR 33-36). During this follow up a total of 961 patients died (48.3% due to disease relapse). In univariate analysis, post-transplant outcomes were not significantly affected when comparing normal to abnormal CG, or intermediate versus adverse risk CG. Patients with a normal karyotype had a 2-year relapse rate of 23%, NRM of 13%, LFS 63%, OS of 71%, and GRFS of 51%. Conversely, patients with aberrant CG had a 2-year relapse rate of 27%, NRM 12%, LFS 61%, OS of 68%, and GRFS of 48%. On multivariate analysis, CK as well as *FLT3* ITD was associated with a worse OS with HR of 1.7 (95% CI 1.13-2.56) and 1.18 (95% CI 1.01-1.39), respectively. When analyzed by subgroup by univariate analysis according to *FLT3* ITD status, the impact of CK was maintained for those with *FLT3* wild type: 2-year LFS 39.6% vs. 70.5%; p=0.006, and 2-year OS 49% vs. 75.3%, p=0.012. Similarly for patients with *FLT3* ITD, CK was associated with a higher risk of relapse (45.7% vs. 26.5%, p=0.021), and worse OS (52.7% vs. 67.4%; p=0.047) with no significant effect on other outcomes. Within patients with chromosomal aberrations, CK was the only significant predictor of worse LFS (HR 1.58 [1.06-2.34]), and OS (HR 1.85 [1.22-2.82]). *FLT3* ITD mutation status, CG risk category, as well as the various CG abnormality subgroups had no significant effects (Notably, MK was not associated with a significant impact on LFS [60.9% versus 61.4%; p-value 0.7], OS [67.7% versus 68.2%; p-value 0.97] or GRFS [51.5% versus 47.8%; p-value 0.61].
Conclusion: These data suggest a need to revisit the ELN 2022 risk stratification of AML patients with mutated *NPM1* and CG aberrations. In the transplant setting for patients in first remission, only CK among other AR CG appears to predict worse outcomes, although a significant proportion of patients with CK can still achieve long term post-transplant survival.

Disclosures Versluis: *ExCellThera:* Consultancy; *AbbVie:* Honoraria. **Blaise:** *Jazz Pharmaceuticals:* Honoraria. **Rambaldi:** *Abbvie:* Honoraria. **Kröger:** *Riemser:* Honoraria, Research Funding; *Neovii Biotech:* Honoraria, Research Funding; *Novartis:* Honoraria, Research Funding; *Takeda:* Consultancy; *BMS:* Honoraria, Research Funding; *Pfizer:* Honoraria; *MSD:* Honoraria; *Jazz:* Honoraria; *Kite/Gilead:* Honoraria; *Sanofi:* Honoraria. **Forcade:** *Alexion:* Other: Travel support, Speakers Bureau; *Jazz:* Other: Travel support; *GSK:* Speakers Bureau; *MSD:* Other: Travel support; *Sanofi:* Speakers Bureau; *Astellas:* Speakers Bureau; *Gilead Sciences:* Other: Travel support, Speakers Bureau; *Novartis:* Consultancy, Other: Travel support, Speakers Bureau. **Esteve:** *Jazz Pharmaceuticals:* Consultancy, Research Funding; *Abbvie:* Consultancy; *Kronos Bio:* Research Funding; *Pfizer:* Research Funding; *Gilead:* Consultancy; *Astellas:* Consultancy. **Ciceri:** *ExCellThera:* Other: Scientific Advisory Board . **Mohty:** *JAZZ PHARMACEUTICALS:* Honoraria, Research Funding.

https://doi.org/10.1182/blood-2023-185434