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Allogeneic Hematopoietic Stem Cell Transplantation for Secondary Acute Myeloid Leukemia- a Report from the Acute Leukemia Working Party of the EBMT

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Secondary AML (sAML) has traditionally been considered a devastating disease with inferior outcomes compared to de novo AML, affecting a vulnerable population of heavily pre-treated, especially older patients. No systematic large analysis of allogeneic hematopoietic stem cell transplantation (HCT) for sAML is available to study the risk factors and outcome.

Patients who underwent HLA-identical sibling (n=2290) or unrelated donor (n=1966) peripheral blood (n=3781) or bone marrow transplantation (n=475) from 2000 to 2013 are included in the study. All unrelated donors were Human Leucocyte Antigens (HLA)-matched (10/10) (n=1532) or one locus mismatched (9/10) (n=434). 1901 (45%) patients received ablative (MAC) and 2355 (55%) reduced-intensity conditioning (RIC) regimen. Median age at transplant was 56 years, IQR 48-63 (MAC 51 IQR, 42-58; RIC 60 IQR, 54-64). Median time from diagnosis of sAML to HCT was 6.2 months, IQR 4-12 (MAC 6, IQR 4-10; RIC 7, IQR 4-14; $p<0.0001$). At time of transplant, 2313 (54%) patients were in CR1, 278 (7%) in ≥CR2 and active diseases in 1665 (39%) patients.

Two-year cumulative incidence of relapse (RI) and non-relapse mortality (NRM) were 33% (95% CI, 32–35%) and 25% (95% CI, 24–27%), respectively. The Kaplan-Meier estimate of overall survival (OS) and leukemia-free survival (LFS) at 2-year were 46% (95% CI, 44–48%) and 41% (95% CI, 39–43%), respectively. Acute GVHD (grade II-IV) occurred in 1043 (26%) patients. The 2-year cumulative incidence of chronic GVHD was 54% (95% CI, 51-56). Two-year OS, LFS, RI and NRM of MAC and RIC groups were 48% (95% CI, 46-50) vs. 44% (95% CI, 42-47), p=0.06, 44% (95% CI, 41-46) vs. 39% (95% CI, 37-41), p=0.003, 30% (95% CI, 28-32) vs. 36% (95% CI, 34-38), $p<0.0001$, 26% (95% CI, 24-28) vs. 25% (95% CI, 24-27), p=0.273, respectively. Two-year OS of patients in CR1, ≥CR2 and active disease before HCT was 54% (95% CI, 52-56), 45% (95% CI, 39-52) and 35% (95% CI, 33-38), respectively ($p<0.0001$).

In multivariate analysis adjusted for variable with different distribution between groups, the type of conditioning (RIC vs. MAC) had no impact on OS and LFS, however RIC group had higher RI (HR, 1.3, 95% CI 1.12-1.44, p=0.0001) and lower NRM (HR 0.8, 95% CI 0.72-0.96, p=0.01). Older age at HCT was an independent adverse prognostic factor for OS, LFS and NRM. Time from diagnosis to HCT had no impact on transplant outcome. Patients receiving PB grafts had superior OS (HR 0.84, 95% CI 0.73-0.97, p=0.01), LFS (HR 0.85, 95% CI 0.74-0.97, p=0.02) and lower RI (HR 0.83, 95% CI 0.70-0.99, p=0.049) compared with BM.

In summary, our registry study in the largest cohort of patients studied so far receiving HCT for secondary AML, demonstrated that about 45% of patients with secondary AML can attain long term survival after HCT. Post- transplant pre-emptive therapy to decrease relapse risk might improve outcome further in these high risk populations.

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Stem Cell Transplantation in AML and Socioeconomic Factors: National Cancer Database (NCBD) Analysis

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Introduction: National comprehensive cancer network guidelines recommend considering stem cell transplant (SCT) for intermediate to high-risk acute myeloid leukemia (AML) patients less than 60 years of age after initial induction chemotherapy. Here we report NCDB analysis of factors affecting the probability of patients with AML undergoing SCT.

Methods: Data from 37,820 men and women, between ages 18-64 years diagnosed with AML, registered in the NCDB between 1998 and 2012 was analyzed. The primary predictor variable was payer status and outcome variable was use of SCT. Additional variables addressed and adjusted for included age, sex, race, Charleston comorbidity index (CCI), level of education, income, facility type (academic/community), treatment delay and chemotherapy.

Results: The mean age at diagnoses was 47.3 years. Logistic regression analysis was used and the following results were obtained. Patients aged 50-64 years were 31% less likely to get SCT compared with those aged 18-49. Patients with CCI of 1 and 2 were 29% and 53 % less likely to get SCT compared to those with CCI of 0 respectively. CCI was not available in 29.6 % of patients. Whites were 50.2 % more likely to get SCT than Blacks. Compared to patients with private health care funding, patients with Medicaid, Medicare, unknown and no funding were 29.5, 37.2, 52.1, and 66.6 % less likely to