Secondary AML (sAML) has traditionally been considered a devastating disease with inferior outcomes compared to de novo AML, affecting a vulnerable population of heavily pretreated, 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=1632) 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 HR (RI, 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.