Secondary AML is an independent risk factor for outcome after SCT in First complete remission: a registry-based comparison to de novo AML on behalf of the EBMT acute leukemia working party

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alloHSCT), and 2 patients derived transient benefit - 1 had an improvement in ANC (0 pre-T cells to >500 at wk8) with concomitant decline in blood and platelet transfusions while another had clearance of peripheral blasts (56% to 0%) with a <50% decline in marrow blasts. Three pts developed PD, failed subsequent lines of therapies and died 4-12mths post-infusion. Clinical responses correlated with the emergence and persistence (>9mths) of "line-exclusive" tumor-reactive T cells, as assessed by longitudinal clonotype tracking using deep sequencing. The expansion of product-derived clones was higher in patients who responded as compared with those that progressed post-infusion as confirmed by both ELIspot and deep sequencing. Notably, no patient had infusion-related CRS, neurotoxicity or GVHD. Thus, mLAA-targeted T cells directed to PRAME, WT1, NYESO1 and Survivin can be safely administered to patients with AML/MDS, in whom they can subsequently be detected long-term and produce sustained responses.

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Secondary AML Is an Independent Risk Factor for Outcome after SCT in First Complete Remission - a Registry-Based Comparison to De Novo AML on Behalf of the EBMT Acute Leukemia Working Party

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Background: Acute myeloid leukemia (AML) secondary to another haematological neoplasia or malignant disease (sAML) is thought to have an inferior prognosis than de novo AML. However, the role of this difference for allogeneic stem cell transplantation (SCT) is unclear. A registry-based analysis was performed to compare results after SCT for sAML versus AML.
Methods: Inclusion criteria were age ≥18y and SCT for de novo or sAML from a matched related, unrelated or T-cell replete haploidentical donor between 2000 and 2016. A multivariate Cox model was performed for risk factors for outcome. It was stratified for different stages at SCT. Further, a matched pair analysis of de novo versus sAML was done, using age (+/-3 years), stage at SCT, Karnofsky performance score (KPS), conditioning, in vivo/ex vivo T cell depletion, donor, donor/recipient sex and CMV-status combination, cytogenetics, and graft source as matching criteria.
Results: 11439 patients (pts) with de novo and 1325 with sAML were identified. Median follow-up was 36 and 33 months. After SCT in first complete remission (CR1), 3Y cumulative incidence of relapse (CIR) and non-relapse mortality (NRM) were 28.5%/16.4% for de novo (n=7691), and 35%/23.4% for sAML (n=909). 3Y overall survival (OS), leukemia-free survival (LFS) and GvHD/relapse free survival (GRFS) were 60.8%, 55.1% and 38.6% for de novo and 46.7%, 41.6% and 28.4% for sAML. In a multivariate Cox model focusing on SCT in CR1, sAML was associated with higher NRM (HR=1.32; $p<10^{-5}$) and CIR (HR=1.28; p=0.0002), and lower LFS (HR=1.30; $p<10^{-5}$), OS (HR=1.32; $p<10^{-5}$) and GRFS (HR=1.20; $p<10^{-5}$). Other factors for OS were age (p=<10-5), cytogenetics (intermediate, p=0.002, poor, p=<10-5), patient/donor sex combination (female/male, p=<10-5), KPS (<>80, p=0.003) and donor (UD 10/10 match, p=0.007; UD 9/10 match, p=10-5; haplo, p=0.002). When focusing on pts transplanted for primary refractory (de novo, n=607, sAML, n=199) or relapsed AML (de novo, n=1009, sAML, n=124), results were generally inferior. However, Cox models did not identify sAML as a relevant factor. Instead, outcome was determined by age, cytogenetics and KPS.
The matched pair analysis was performed on 877 pairs and confirmed the above findings: Over all, sAML was associated with higher NRM (p=0.004), and lower LFS (p=0.004), OS (p=0.008) and GRFS (p=0.04). However, when the analysis was stratified by stage at SCT, again differences were only seen among pts transplanted in CR1, but not after SCT in advanced disease.
Conclusion: Our large-scale, registry-based analysis identified sAML as independent risk factor for outcome after SCT in first CR1. In primary refractory and relapsed AML, other factors such as age, cytogenetics and performance status were of higher relevance. This data may help to improve risk stratification and prognostic estimates after SCT for sAML.

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Radius: Midostaurin (mido) Plus Standard of Care (SOC) after Allogeneic Stem Cell Transplant (alloSCT) in Patients (pts) with *FLT3*-Internal Tandem Duplication (ITD)–Mutated Acute Myeloid Leukemia (AML)

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Introduction: Allogeneic stem cell transplant (alloSCT) provides pts with *FLT3*-ITD+ AML the highest likelihood of