and inferior RFS and OS at 24 and 60 months. More aggressive therapy may be considered in this subgroup.

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Early Versus Late Allogeneic Hematopoietic Cell Transplantation in Patients with AML - Results From the Randomized AML 2003 Trial

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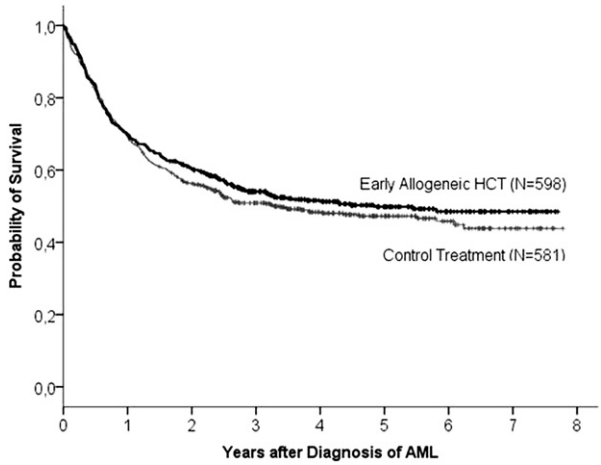
The optimal timing of hematopoietic cell transplantation (HCT) in AML is still under debate. We addressed this question in the AML 2003 study, a large, multicenter, open-label, randomized study of the German SAL group. All patients received one cycle of induction therapy (IT). Upfront molecular characterization, HLA typing and donor search were performed. The transplant strategy was tailored to AML risk and to donor availability. Patients aged 18-60 years were randomly assigned upfront 1:1 to either one of two transplant strategies: In the control arm HLA-identical sibling HCT was scheduled in first complete remission for patients with intermediate cytogenetic risk AML and related or unrelated compatible HCT for patients with a complex karyotype (CK). In the experimental arm the indication for allogeneic HCT was extended to patients with an FLT3-ITD allelic ratio >0.8 (mutant/wild type), >10% marrow blasts on day 15 after IT1 and patients with adverse karyotypes, including: -7, -5, del(5q), inv(3q), t(3;3), t(6;9), t(6;11), t(11;19) (q23;p13.1). Furthermore, HCT was scheduled earlier, i.e. in aplasia after the first or the second cycle of IT.

Between December 1st, 2003 and November 26th, 2009 1179 patients were assigned randomly either to the experimental (N=598) or the control intervention (N=581). The median age was 48 years (range, 18 to 60 years) and the median observation time now is 52 months. In the intent-to-treat analysis the hazard ratio of the treatment effect (experimental versus control) was 0.92 (95% CI, 0.75 to 1.14; $P = .45$) for the primary endpoint overall survival (OS) and 0.85 (95% CI, 0.71 to 1.02; $P = .08$) for the secondary endpoint event-free survival (EFS). However, the rate of patients who received allogeneic HCT as first post-remission therapy was only 39% in the experimental arm and 20% in the control arm. Thus, the analysis according to the intent-to-treat could not discriminate appropriately between the two treatment strategies. In an exploratory analysis, we therefore analyzed the effect of allogeneic HCT as a time-dependent covariate in a Cox-regression model. We adjusted for the cytogenetic risk, age, ECOG performance status, white blood cell count, and LDH at diagnosis. In this as-treated analysis the adjusted hazard ratio for the treatment (allogeneic HCT versus chemotherapy) was 0.73 (95% CI, 0.59 - 0.89; $P = .002$) for OS and 0.67 (95% CI, 0.55 - 0.82; $P < .001$) for EFS. This analysis corrects appropriately for a classical time-selections bias. However, a patient selection based on comorbidity or fitness cannot be ruled out.

In conclusion, a survival benefit from early compared to late allogeneic HCT could not be shown in the intent-to-treat analysis of this large randomized trial using a risk-adapted transplant strategy. However, the results of the as-treated analysis suggest a substantial benefit from allogeneic HCT in first remission versus chemotherapy.



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Mixed Phenotype Acute Leukemia: Patient Outcomes According to the WHO 2008 Classification

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Mixed phenotype acute leukemia (MPAL) is a rare leukemia with features of both myeloid and lymphoid lineage. The 2008 World Health Organization (WHO) definition of MPAL is based on the expression of strictly specific T-lymphoid (cytoplasmic CD3) and myeloid (myeloperoxidase) antigens, and B-cell lineage assignment relies on the expression of CD19 together with other B cell–associated markers (Borowitz et al. World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues. 2008). In this retrospective review, we analyzed the clinical features and treatment outcomes of patients treated at MDACC between 5/2004 and 6/2012 who fulfilled the diagnostic criteria for MPAL. We identified a total of 41 patients with a median age of 47 years (range 9 – 82; 63% male) with characteristics described in the table below. Twenty one (51%) patients had leukemia with myeloid plus B-lymphoid (M/B) markers, 18 (44%) with myeloid plus T-lymphoid (M/T) markers, and 2 (5%) with B-lymphoid plus T-lymphoid (B/T) markers. Cytogenetic analysis showed 31 patients (76%) had an abnormal