Allogeneic transplant for mixed phenotype acute leukemia (MPAL): characteristics and outcome in the ALWP-EBMT Database

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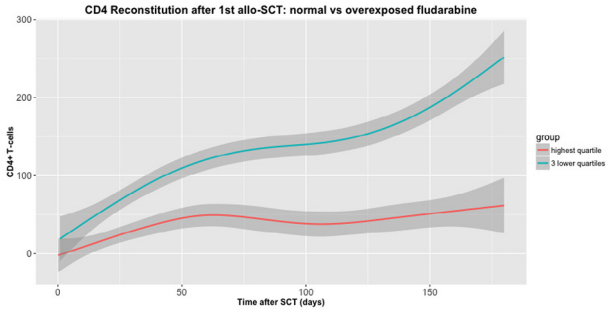

Figure 2. CD4+ T-cell reconstitution after allo HCT in patients receiving busulfan (targeted to optimal exposure) and fludarabine (160mg/m2). Groups consist of patients in the highest quartile of F-ara-A AUC exposure (red) and the lower three quartiles (green).

Conclusions: High exposure to Flu significantly impairs CD4+ T-cell reconstitution and reduces survival chances after HCT. This is the first step in the definition of a target exposure for Flu in this setting. Dose individualization and/or TDM-based corrections towards the Flu target may reduce overexposure and improve survival chances after HCT.

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Allogeneic Transplant for Mixed Phenotype Acute Leukemia (MPAL): Characteristics and Outcome in the ALWP-EBMT Database

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Mixed phenotype acute leukemias (bearing markers of both myeloid and lymphoid lineages, MPAL) are rare (2- 3% of all acute leukemias) and considered puzzling due to their cell of origin. In the past, MPAL was considered as poor risk leukemia. The diagnostic criteria for MPAL were revised by the World Health Organization (WHO) in 2008 and accepted by most centers. The recommended treatment strategy involves induction regimens similar to acute lymphoblastic leukemia and consolidation by allogeneic transplant. Until recently, limited data were available validating this approach. The Center for International Blood and Marrow Transplant Research (CIBMTR) published a series of 95 cases of MPAL (median age 20 years) who underwent allogeneic transplant and found an encouraging long-term survival.
In the present study, the Acute Leukemia Working Party (ALWP) of the EBMT database was queried for all consecutive patients with MPAL who received an allogeneic transplant for MPAL between 2000 and 2014 and were transplanted in complete remission (CR1; total of 519 patients). Cytogenetics were available in 203 patients.
The median age was 38.1 years (range 18- 75). 54.5% of the patients were transplanted from a matched sibling donor, 45.5% were transplanted from a matched unrelated donor. Myeloablative conditioning (MAC) was used in 500 patients (77.1%, 140 chemotherapy-only, 260 chemotherapy with total body-irradiation [TBI]), reduced intensity in the remaining patients (22.9%). Bone marrow was used in 26.4%, peripheral blood stem cells (PBSC) in 73.3%. 32.5% developed acute GVHD grade II- IV.
With a median follow-up of 32 months, the treatment outcomes at 3 years are:

Incidence of cGVHD 37.5% (95% conf. int. [CI] 32.6 – 42.3)
Non-Relapse-Mortality (NRM) 22.1% (CI 18.4 -26.1)
Overall survival (OS) 56.3% (CI 51.5- 61.2)
Leukemia-Free-Survival (LFS) 46.5% (CI 41.7- 51.4)
Relapse Incidence (RI) 31.4% (CI 26.9- 35.9)

In univariate analysis, the age at transplant strongly impacted on LFS, NRM, RI and OS, with the age group 18- 35 having the best outcomes. Transplants done in the more recent period (2005- 2014 vs 2000-2004) had a lower NRM (20% vs 33.2%, $P = .01$) and a better OS (58.3 vs 44.7%, $P = .04$). No differences in outcomes were found between related and unrelated donors. Female donors for male recipients, no in vivo T cell depletion and PBSC were associated with more cGVHD. Use of MAC-TBI correlated with a lower RI and better LFS compared both to MAC-chemo and to RIC. In multivariate analysis, younger age and more recent year of transplant were statistically associated with a better LFS ($P = .03$ and $P = .013$) and OS ($P = .006$ and $P = .004$). MAC-TBI was associated with better LFS and a trend for higher OS.
In conclusion, we confirm and extend the previous CIBMTR study in a large international database. Allogeneic transplant is a valid treatment option for MPAL (with a potential for cure) if a matched donor is available.

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Follistatin and Endoglin: Potential Biomarkers of Endothelial Damage and Non-Relapse Mortality after Myeloablative Allogeneic Hematopoietic Cell Transplantation in Blood and Marrow Transplant Clinical Trials Network (BMT CTN) 0402

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Introduction: Inflammation and tissue repair are linked processes influencing aGVHD after allogeneic HCT. In aGVHD, the balance between angiogenic factors (AF) contributing to tissue healing/repair (epidermal growth factor [EGF]) versus those associated with tissue damage/inflammation (follistatin [FS]) is dysregulated. Given that regimen-related tissue injury plays a role in NRM, we hypothesized that elevated levels of inflammation-associated AF would be associated with NRM even in patients without aGVHD.
Methods: Levels of angiopoietin-2 (Ang2), EGF, FS, vascular endothelial growth factor (VEGF)-A and -B, endoglin (sEng), placental growth factor (PlGF), and soluble VEGF receptor (sVEGFR)-1 and -2 were quantified by MILLIPLEX magnetic bead panels, using plasma samples from patients enrolled on