myeloablative in all cases. Overall survival, leukemia free survival (LFS) and relapse incidence (RI) at 3 years were 57±4%, 49±4% and 45±3%, respectively. Only 4 patients (1.9%) had VOD (moderate-2, severe-2) at median day 16 range (10-47). One of the patients died from VOD. Non relapse mortality at 3 years was low 6±1%. In multivariat analysis the only prognostic factor that was found to be significant for OS, LFS, RI and NRM was age >50 vs <50 years with p-value of <0.001, <0.001, <0.006 and <0.001, respectively (47±5%, 38±5%, 52±5%, 10±3% vs 68±5%, 76±4%, 32±5% and 0%, respectively). In summary, these results suggest, that similar to the allogeneic setting, VOD is a very uncommon event after AutoSCT using iv Bu in the conditioning regimen translating into a low NRM incidence.

O345 Intravenous busulfan plus cyclophosphamide (CyT) versus TBI plus Cy conditioning for allogeneic stem cell transplantation from matched unrelated donors. In adult patients with AML in first relapse: a survey from the ALWP of EBMT

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We compared TBI/Cy to i.V Bu/Cy conditioning prior to alloSCT from HLA matched unrelated donors in 169 adult pts with AML in Rel 1. 95 pts were given TBI/Cy and 74 Bu/Cy. Median age was 38 (18-62) and 42 (19-72) years in the TBI/Cy vs. Bu/Cy groups, respectively (P=0.005). FAB classification, cytogenetic risk, time from diagnosis to alloSCT, donor gender and CMV serostatus did not differ between the groups. Median year of alloSCT was 2004 vs. 2007, respectively (P=0.001). ATG was used in 35% vs. 71% in the TBI/Cy and Bu/Cy groups, respectively (P=0.0001). 80% and 78% of the TBI/Cy and Bu/Cy groups received PBSC grafts, while 22% and 20% received BM grafts, respectively (P=0.8). Median follow-up was 23 (range, 1-125) and 27 (1-120) months in the TBI/Cy and Bu/Cy groups, respectively. Engraftment was similar, 17 (10-33) and 16 (6-31) days in the TBI/Cy and Bu/Cy groups, respectively (P=0.23). Similarly, acute GVHD (≥Gr II) incidence did not differ between the 2 groups; 33% vs. 37% for the TBI/Cy vs. Bu/Cy, respectively. Death before day 100 occurred in 38% vs. 25% with TBI/Cy vs. Bu/Cy, respectively (P=0.25). 2y NRM was similar between the 2 groups, 28±5% vs. 19±5%, respectively (P=0.2). 2y relapse rate was 54±5% vs. 50±6%, respectively (P=0.56). Induction of remission post alloSCT was higher with Bu/Cy vs TBI/Cy, 72% vs 54% (P=0.02). 2y LFS was also higher with the Bu/Cy vs TBI/Cy, 82±2% vs. 76±2%, respectively (P=0.045). Similarly, 2y OS was significantly higher with Bu/Cy vs TBI/Cy 37±6% vs. 21±5%, respectively (P=0.013). The main cause of death was disease relapse: 53% and 60%, with TBI/Cy vs. Bu/Cy, respectively (P=0.49). VOD and infection-related deaths did not differ between the groups. In multivariate analysis the interval from diagnosis to transplant (t vs < 16 months) was the most significant prognostic factor for Rel, LFS and OS 25±8% vs 59±4% (P=0.004), 48±9% vs 17±3% (p=0.002) and 41±7% vs 20±4% (P=0.003), respectively. Age, cytogenetic risk groups and use of ATG were not significant prognostic factors for survival. In all, this observational registry based study suggest that in AML pts in first Rel undergoing unrelated transplantation post transplant iv Bu/Cy vs TBI/Cy induced higher remission rate which results in better LFS and OS. This advantage in favor of the iv Bu/Cy regimen is also possibly due to a lower overall toxicity and improved capacity for salvage therapy.


We investigated the impact of occurrence of GVHD on transplant outcomes in a large cohort of AML pts given allogeneic PBSC after RIC conditioning. Data from 1859 AML pts in first (n=1439) or second (n=420) CR transplanted between 2000 and 2009 following a RIC regimens at EBMT affiliated centres were analysed. Pts were given PBSC from HLA-identical sibling (MUD, n=1208), or from HLA-matched unrelated donors (MUD, n=651). ATG was given in 269 (22%) MUD and in 267 (41%) MUD recipients, respectively, while 151 (13%) MUD and 165 (25%) MUD recipients received in-vivo T cell depletion in patients with altemtumab. The impact of chronic GVHD (cGVHD) on outcomes was assessed using time-dependent multivariate Cox models in a landmark analysis at 18 months after transplant. The 3-y cumulative incidence of cGVHD was 47%. Fifty-three percent of patients with cGVHD had extensive cGVHD, while the remaining 47% had limited cGVHD. In multivariate analyses, occurrence of grade II-IV aGVHD was associated with a lower risk of relapse (HR=0.8, P=0.04), a higher risk of chronic (HR=2.2; P<0.001) and extensive chronic GVHD (HR=2.8; P=0.001), a higher risk of NRM (HR=2.4 P<0.001), a worsened LFS (HR=1.3; P=0.01), and a worsened OS (HR=1.5; P<0.001). In multivariate time-dependent analyses, occurrence of limited cGVHD was associated with a lower risk of relapse (HR=0.7; P=0.05), comparable NRM (HR=1.4; P=0.16), comparable LFS (HR=0.9; P=0.29) and better OS (HR=0.5; P<0.001), while occurrence of extensive cGVHD was associated with a lower risk of relapse (HR=0.6; P=0.01), higher NRM (HR=R=3.2; P<0.001), a trend for worsened LFS (HR=1.3; P=0.06) and comparable OS (HR=0.9; P=0.34). In a landmark analysis in patients who were leukemia-free at 18 months after transplantation (n=776), 2-year relapse, NRM, LFS and OS were 16±2%, 2.5±1%, 82±2% and 89±2%, respectively, in patients without cGVHD before the landmark time-point, versus 9±1% (P=0.001), 8±1% (P<0.001), 83±2% (P=0.65) and 86±2% (P=0.38), respectively, in patients with cGVHD before the landmark time-point. In conclusion, in this cohort of AML patients transplanted in remission, occurrence of cGVHD was associated with a lower risk of relapse that translated to better OS in patients with limited cGVHD but not in those with extensive cGVHD who experienced higher long term NRM. These results highlight the role of the GVT effect in RIC allo-SCT, but also the need for improving the prevention of severe cGVHD in pts receiving RIC allo-SCT.
aged 40-60 years, entered in 4 prospective HOVON/SAKK trials, were studied, including 237 pts proceeding to MAB and 144 to RIC allH SCT. 724 pts were consolidated with either a third cycle of CT (n=470) or autoH SCT (n=254). More pts with poor-risk AML proceeded to allH SCT than to autoH SCT/CT. Recipients of MAB or RIC were comparable as regards AML-risk and EBMT-risk-score, but differed with respect to use of T-cell-depletion (TCD) and year of transplant. A trend towards more chronic GVHD was observed among recipients of RIC allH SCT (49% vs 39%, p=0.07). Patients with allH SCT showed better OS (56% vs 33%) than pts receiving alternative consolidation (46% vs 22%), p<0.001, irrespective of leukemia risk, and with no difference between autoH SCT and CT. Relapse Free Survival (RFS) at 5 years estimated 55±5% following RIC allH SCT, determined by 36±4% relapse and 9±3% NRM. RFS at 5 years following MAB allH SCT estimated 47±3% with relapse 29±3% and NRM 24±3% at 5 years. Multivariate analysis including TCD and year of transplant showed no significant differences between RIC and MAB pts, as regards OS (HR=0.89, p=0.05), RFS (HR=0.94, p=0.75), NRM (HR=0.67, p=0.26), and relapse (HR=1.05, p=0.87). In conclusion, consolidation by allH SCT significantly improves outcome as compared to either CT or autoH SCT in AML CR1 pts aged 40-60 years, indicating that allH SCT could be considered standard consolidation therapy in intermediate and poor-risk AML in CR1 up to the age of 60. Since consolidation with RIC allH SCT produces results at least as good as those following MAB allH SCT, a prospective randomized trial of RIC vs MAB, that includes younger pts with AML in CR1 as well, is advocated.

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Improved survival by allogeneic haematopoietic stem cell transplantation versus autologous HSCT or chemotherapy as consolidation therapy in AML CR1 patients aged 40-60 years: the role of reduced-intensity conditioning and leukemia risk category

Results: Within the EBMT registry 139 patients could be identified who underwent alloSCT (n=100) or autoSCT (n=39) for the diagnosis of BPDCN. In 74 patients histology and immunophenotyping reports could be obtained and central review confirmed the diagnosis of BPDC in 39 patients (34 alloSCT, 5 autoSCT). The 34 allografted patients were treated with a reduced intensity conditioning regimen (RIC, n=9) or myeloablative conditioning (MAC, n=25) and 19 of 34 patients were transplanted in CR1. After a median follow up time of 28 months (range: 4-77+ months), 11 patients relapsed of whom 8 died due to disease progression. 9 patients died in the absence of relapse. No relapse occurred later than 27 months after transplant. Median disease free survival (DFS) was 15 months (range: 4-77+ months) and median overall survival (OS) was 22 months (range: 8-77+ months; Figure 1a). However, long-term remissions of up to 77 months after alloSCT could be observed. Patients allografted in CR1 tended to have a superior DFS (p=0.119) and OS (p=0.057; Figure 1b). MAC was associated with a better OS (p=0.001) which was attributable to the significantly higher non-relapse mortality (NRM) rate of patients after RIC (p=0.014), who had been significantly older (age RIC: 56 years, age MAC: 36 years, p=0.0014). The relapse rate was not different in patients after RIC and MAC, respectively. However, there was no survivor after RIC.