

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 multivariate 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, groups: 23 ± 6% vs. 18±4%, 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 (> 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 incuded 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.

#### O346

##### **Impact of chronic graft-versus-host disease after reduced-intensity conditioning allogeneic stem cell transplantation for acute myeloid leukaemia: A report from the Acute Leukaemia Working Party of the European Group for Blood and Marrow Transplantation**

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We investigated the impact of occurrence of GVHD on transplantation 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 regimen at EBMT affiliated centres were analyzed. Pts were given PBSC from HLA-identical sibling (MRD, n=1208), or from HLA-matched unrelated donors (MUD, n=651). ATG was given in 269 (22%) MRD and in 267 (41%) MUD recipients, respectively, while 151 (13%) MRD and 165 (25%) MUD recipients received in-vivo T cell depletion with alemtuzumab. The impact of chronic GVHD (cGVHD) on outcomes was assessed using time-dependent multivariate Cox models and 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=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.

#### O347

##### **Impact of alemtuzumab versus anti-thymocyte globulin after unrelated allogeneic stem cell transplantation with reduced-intensity conditioning as treatment for AML in CR1: a survey from the Acute Leukaemia Working Party of the EBMT**

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In vivo T cell depletion of the graft with anti-thymocyte globulin (ATG) or with alemtuzumab has been frequently used in the

setting of RIC allo-SCT from unrelated donors. This survey compared allo-SCT outcomes between 364 AML patients in first CR given unrelated PBSC after chemotherapy-based RIC and given either ATG (n=213) or alemtuzumab (n=151) in the conditioning regimen. Alemtuzumab patients were more frequently given grafts from HLA-mismatched donors (30% versus 16% having at least 1/10 HLA-mismatch with their donor, P=0.005), and were conditioned more often with melphalan-based RIC (62%), while ATG recipients were more frequently conditioned with busulfan-based RIC (84%). Median time to neutrophil engraftment (>500 ANC) was 16 days in ATG recipients, versus 12 days in alemtuzumab recipients (P<0.001). The incidence of grade II-IV acute GVHD was 28% in ATG recipients (9 patients with grade IV) and 24% (NS) in alemtuzumab recipients (2 patients with grade IV). Two-year incidences of chronic GVHD, relapse and NRM were 45%, 23% and 14%, respectively, in ATG recipients, and 47% (NS), 25% (NS) and 25% (P=0.008), respectively, in alemtuzumab recipients. Two-year OS and LFS were 69% and 63%, respectively, in ATG recipients, versus 55% (P=0.003) and 51% (P=0.02), respectively, in alemtuzumab recipients. Death from infection occurred in 7% of ATG recipients, versus 12% of alemtuzumab recipients. When the analysis was restricted to the 210 patients given grafts from 10/10 HLA-matched unrelated donors, the use of alemtuzumab (n=64) remained significantly associated with higher NRM (22% vs 9%, P=0.007), lower LFS (58% vs 69%, P=0.07), and lower OS (62% vs 74%, P=0.04). In multivariate analyses (performed in patients given grafts from 10/10 HLA-matched donors), in comparison to the use of ATG, the use of alemtuzumab was associated with higher NRM (HR=2.5, P=0.025), a statistically non-significant but higher relapse rate (HR=1.7, P=0.18), and significantly worse LFS (HR=0.5, P=0.013) and OS (HR=0.4, P=0.002). In summary, this homogeneous cohort of AML patients transplanted in first CR and given PBSC grafts from unrelated donors, the use of alemtuzumab in comparison with ATG was associated with worse LFS and OS.

#### O348

##### **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 leukaemia risk category**

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Patients (pts) with AML in CR1 currently qualify for alloHSCT in case of intermediate or poor-risk AML. Earlier, we showed limited benefit by alloHSCT in pts >40 yrs, due to increased non-relapse mortality (NRM) (Blood 2007; 109:3658). Since, transplant outcome has improved and reduced intensity conditioning (RIC) regimen were introduced in this age category by several centers. The HOVON/SAKK group set out to address the question whether alloHSCT would result in better outcome as compared to autoHSCT or chemotherapy (CT) with integrated comparison of myeloablative (MAB) versus RIC and of autoHSCT versus CT. Patients (n=1105) with AML in CR1,

aged 40-60 years, entered in 4 prospective HOVON/SAKK trials, were studied, including 237 pts proceeding to MAB and 144 to RIC alloHSCT. 724 pts were consolidated with either a third cycle of CT (n=470) or autoHSCT (n=254). More pts with poor-risk AML proceeded to alloHSCT than to autoHSCT/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 alloHSCT (49% vs 39%, p=0.07). Patients with alloHSCT showed better OS (56%±3) than pts receiving alternative consolidation (46% ±2), p<0.001, irrespective of leukemia risk, and with no difference between autoHSCT and CT. Relapse Free Survival (RFS) at 5 years estimated 55±5% following RIC alloHSCT, as determined by 36±4% relapse and 9±3% NRM. RFS at 5 years following MAB alloHSCT 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=0.55), 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 alloHSCT significantly improves outcome as compared to either CT or autoHSCT in AML CR1 pts aged 40-60 years, indicating that alloHSCT should be considered standard consolidation therapy in intermediate and poor-risk AML in CR1 up to the age of 60. Since consolidation with RIC alloHSCT produces results at least as good as those following MAB alloHSCT, a prospective randomized trial of RIC vs MAB, that includes younger pts with AML in CR1 as well, is advocated.

#### O349

##### **Stem cell transplantation can provide durable disease control in blastic plasmacytoid dendritic cell neoplasia: a retrospective study from the European Group for Blood and Marrow Transplantation**

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Blastic plasmacytoid dendritic cell neoplasm (BPDC), formerly known as blastic NK cell lymphoma, is a rare hematopoietic malignancy preferentially involving the skin, bone marrow and lymph nodes. Most patients relapse very soon after aggressive acute leukaemia like chemotherapy but anecdotal long term remissions after consolidating myeloablative allogeneic stem cell transplantation have been reported.

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.