SSI use was 152 (13-981) days. At 6 months and 1 year, 63% and 83% of patients were off all immunosuppressive therapy, respectively. With a median follow-up of 26 months, cumulative incidence of chronic GVHD was 10%. Only 3 patients have died with refractory GVHD. These results extend our previous observations that post-transplantation Cy is effective single agent strategy for prophylaxis of acute GVHD with both a low rate of grade III-IV and more than half of the patients never requiring additional SSI. The limited use of SSI may be responsible for low infectious rate and excellent immune reconstitution seen in these patients. This approach also provides novel platform to facilitate the use of post-transplant immunotherapy aimed at reducing relapse.

20

HIGH IMPACT OF HUMAN LEUKOCYTE ANTIGEN MATCHING ON OVERALL SURVIVAL AND TRANSPLANT RELATED MORTALITY IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR CLL: LONG-TERM STUDY FROM THE EBMT REGISTRY

Michallet, M.[1], Sobh, M.[1], Morisset, S.[1], Niederwieser, D.[2], Koza, V.[3], Ruutu, T.[4], Russell, N.[5], Verdonck, L.[6], Milligan, D.[7], Dhedin, N.[8], Kozak, T.[9], Boogaerts, M.[10], Finke, J.[11], Dubois, V.[1], Van Biezen, A.[12], Brand, R.[12], De Witte, T.[12], Dreger, P.[13] [1] Lyon, France; [2] Leipzig, Germany; [3] Pilsen, Czech Republic; [4] Helsinki, Finland; [5] Nottingham, UK; [6] Utrecht, Netherlands; [7] Birmingham, UK; [8] Paris, France; [9] Prague, Czech Republic; [10] Leuven, Belgium; [11] Freiburg University Medical Center, Freiburg, Germany; [12] Leiden, Netherlands; [13] Heidelberg, Germany

Objective: To evaluate the impact of HLA matching and difference in matching degree among transplants from unrelated donors (UD) on different outcomes in chronic lymphocytic leukemia (CLL).

Materials & Methods: We have analyzed 370 CLL patients who underwent an allogeneic HSCT reported to the EBMT registry. There were 280 males (75%) and 90 females with a median age of 53 years (24-69). At transplant, 294 among 317 evaluated patients had a good performance status (PS) (93%), 43 patients were in CR (12%), 160 in PR (46%), 44 in SD (13%) and 103 in PD (29%) among 349 evaluated patients. Two hundred and sixty six patients received a reduced intensity conditioning regimen (RIC) and 103 a standard (Std) conditioning; 313 patients received PBSC, 56 BM and 2 cord blood cells from 198 HLA siblings, and 172 unrelated donors (UD).According to the registry, there were 198 HLA siblings, 135 matched UD (MUD) and 37 mismatched UD (MMUD). We focused on UD and re-analyzed all HLA typings for patients and donors, after classification we found: 31 well matched (10/10, 8/8) in high resolution), 30 matched in low resolution and 111 mismatched in high resolution.

We found a high significant difference in term of OS between the siblings, well & partially matched groups versus low & MMUD groups (p = 0.002) (figure2). [OS at 3 & 5 years: Siblings: 68.3% (61.8-75.5) and 57.2% (49.8-65.6); well matched: 60.8% (43.1-85.8) from 3 to 5 years, low resolution & MMUD: 50.5% (43.1-60.1) and 39.6% (29.5-50.2) respectively]. We observed also a high significant difference in term of transplant related mortality (TRM) between the same groups (p = 0.0024) (figure4). The multivariate analysis using Cox model studying age, pre-transplant status, gender, PS, cells source, ABO compatibility, conditioning and different HLA groups, showed a significant impact of 3 factors on OS: age [HR = 1.04 (1.02-1.6) p = 0.001], PS [HR = 2.75 (1.5-5.1) p = 0.001] and HLA MMUD + Low resolution group [HR = 1.43 (1.01-2.01) p = 0.04]. The same factors were also highly significant in multivariate analysis in term of TRM (age: HR = 1.04 (1.001-1.07) p = 0.0033; PS: HR = 2.47 (1.1-5.4) p = 0.009 and HLA MMUD group: HR = 1.8 (1.07-3.37) p = 0.004.

21

REDUCED-INTENSITY CONDITIONING (RIC) ALLOGENEIC STEM CELL TRANSPLANTATION (ALLO-SCT) FOR PATIENTS AGED ≥60 YEARS: A RETROSPECTIVE ANALYSIS OF 629 PATIENTS FROM THE SOCIETE FRANCAISE DE GREFFE DE MOELLE ET DE THERAPIE CELLULAIRE (SFGM-TC)

Mohty, M., Blaise, D., Milpied, N., Michallet, M., Vernant, J.P., Fegueux, N., Guilhot, F., Rio, B., Gratecos, N., Cahn, J.Y., Socie, G., Yakoub-Agha, I., Huynh, A., Francois, S., Bay, J.O., Cordonnier, C., Buzyn, A., Contentin, N., Deconinck, E., Chevallier, P. On behalf of the Societe Francaise de Greffe de Moelle et de Therapie Cellulaire (SFGM-TC), France

This retrospective report assessed the outcome of 629 patients aged ≥60 years and who received RIC allo-SCT, with a special emphasis on the comparison of the outcome of patients aged 60-65 and patients aged >65 y.

The median age for the whole cohort was 62 (range, 60-71) y. 378 patients (55%) had a myeloid malignancy, while 240 (38%) had lymphoid malignancies, and 11 (2%) had other diseases. 386 patients (61%) received allo-SCT from an HLA-matched related donor, while 199 patients (32%) received the graft from a MUD, and 44 (7%) from mismatched donors. The conditioning regimen consisted of Fludarabine and Busulfan in 280 cases (44.5%), Fludarabine and low dose TBI in 150 cases (24%). The remaining 199 patients (32%) received other so-called RIC regimens.

With a median follow-up of 9 (range, 1-90) m., grade II-IV and grade III-IV acute GVHD occurred in 29% (n = 182) and 12% (n = 76) of patients, respectively. Chronic GVHD was observed in 145 patients (23%; limited: n = 67; extensive: n = 72; unknown stage: n = 6). 180 patients died of transplant-related causes (TRM: 29%). The estimates of overall survival (OS) at 1 and 2 years were 57% (95%CI, 53-62%) and 47% (95%CI, 42-52%), respectively.

In order to assess the applicability of RIC allo-SCT to the older age group, we compared the outcome of patients aged from 60 to 65 y. (n = 516) and those aged >65 y. (n = 113). Except for age, in univariate analysis, these 2 groups were not statistically different in terms of demographic, disease or transplant characteristics. The incidences of grade II-IV and grade III-IV acute GVHD were comparable between both groups (29% vs. 30%, p = NS; and 12% vs. 12%; p = NS). The TRM incidence was 29% in the younger group vs. 27% in the older group (p = NS). The estimates of OS at one and 2 years were 58% (95%CI, 53-62%) and 47% (95%CI, 42-52%) in the younger age group and 55% (95%CI, 44-65%) and 48% (95%CI, 37-60%) in the older age group (p = NS). In a Cox multivariate analysis accounting for all relevant factors, age >65 y. was not found to be a statistically significant factor associated with worsened survival.

In all, this data support the use of RIC-allo-SCT in patients >60 y. Outcome of patients aged >65 y. appears to be comparable to that of patients aged 60-65 y. Physiologic aging is likely more important than chronologic aging. With the refinement of comorbidities scoring systems, age per se (at least up to 70 y.) should not be a contraindication to perform RIC allo-SCT.

22

ENGRAFTMENT FAILURE AFTER NONMYELOABLATIVE HEMATOPOIETIC STEM CELL TRANSPLANTATION: DONOR CD4 CELLS INTERFERE WITH RESIDUAL HOST CELLS AND CAN TRIGGER GRAFT REJECTION

Mueller, A.M.S.[1,2], Florek, M.[1], Shizuru, J.A.[1] [1] Stanford School of Medicine, Stanford, CA; [2] University Medical Center, Freiburg i.Br., Germany

While non-myeloablative conditioning significantly reduces morbidity and mortality after allogeneic hematopoietic cell transplantation (HCT), the risk of allograft rejection is increased. Persistent host cells mediate host-vs-graft alloreactivity or occupy niches in the hematopoietic microenvironment. Here we studied engraftment and hematopoietic reconstitution in BALB.K mice given non-myeloablative radiation and purified hematopoietic stem cells (HSC: cKIT + Thy1.1loSca1 + Lin-) +/- T cells (TC) from AKR/J donors, a MHC-identical (H-2 K) model with high barriers to engraftment. Recipients of pure HSC regularly achieved stable mixed chimerism. However, if grafts contained CD4 TC (but not CD8 TC) donor lymphopoiesis was completely abolished in ~80% of hosts, even long-term. This suppression was associated with bone marrow (BM) lymphopenia (<5% vs >40% after HSC alone), and hypocellularity (median 3.8 vs 13.3 x10^6 cells/2 legs; p = 0.0003) at 2 weeks post-HCT. B cell reconstitution was the most severely affected (6% vs 75% of lymphocytes). At this early time point there was expansion of donor and host CD4 TC, each comprising ~6% of BM cells (vs