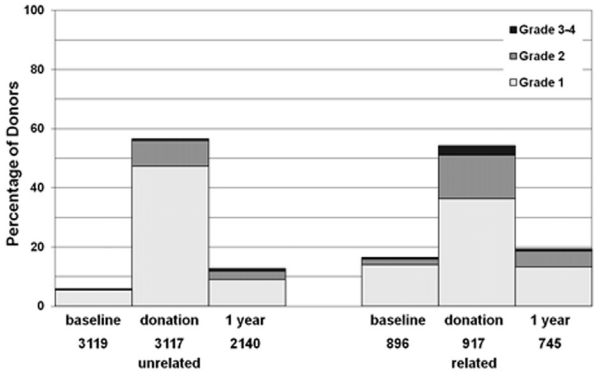

Figure 2. Highest Toxicity Level Across All Body Symptoms (fever in the absence of signs of infection. fatigue, skin rash, local reactions, nausea, vomiting, anorexia, insomnia, dizziness, and syncope) experienced by PBSC donors, by unrelated vs. related donors, at baseline, donation, and 1 year post-donation.

donation-related grade 2-4 pain, grade 3-4 pain, and grade 2-4 MTC (Table 2) compared to URDs of PBSC. In addition, RDs of PBSC were less likely than URDs of PBSC to return to baseline levels of pain and MTC at 1 year. Although only a small fraction of both URDs and RDs reported grade 2-4 pain/MTC 1 year post-donation (Table 1), RDs were 2-3 times more likely to report pain/MTC at 1 year than URDs.

Conclusions: RDs of PBSC have more baseline and donation-related pain/MTC and less complete 1 year recovery than URDs. Ongoing analysis of baseline health status of RDs on the RDSafe trial is underway to further define differences between RDs/URDs that could account for these higher levels of pain/MTC.

21

Beneficial Effects of G-CSF Dosage Adaption in Allogeneic Stem Cell Donors That Are at Risk for Poor Mobilization. Retrospective Dual Center Analysis of 5691 Allogeneic Stem Cell Mobilizations

Michael Punzel [1,2], *Jutta Rox* [2], *Karin Buhrmann* [1], *Helmuth Schmidt* [1], *Anna Kozlova* [1], *Tilo Robitzsch* [2], *Annegret Quade* [3], *Carsten Bartling* [3], *Gerhard Ehninger* [1], *Johannes C. Fischer* [2]. [1] *MediaPark Klinik, Cellex Cologne, Cologne, Germany;* [2] *Institute for Transplantation Diagnostics and Cellular Therapeutics, Medical Faculty Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany;* [3] *MVZ Labor Quade, Cologne, Germany*

Peripheral blood stem cells (PBSC) are the major source for allogeneic stem cell transplantations. It has been shown that treatment with 7.5 μg/kg G-CSF for 5 days is sufficient to mobilize and collect required CD34+ cells for transplantation. However, uncertainty remains in 0.5–5.0% of all donors regarding insufficient mobilization. In this retrospective analysis we evaluated 5691 allogeneic stem cell mobilization regimens (72% male vs. 28% female donors) from two major collection centers focusing on donor risk factors for poor mobilization. According to our historical reciprocal weight and BMI-adapted mobilization protocol low weight/low BMI donors received > 8.3μg/kg/d for 4 days, whereas overweight donors received <7.5 μg/kg. At day 5 all donors received 526μg G-CSF 2 hours before apheresis. In total, a mean G-CSF-dosis of 8.9 ± 1.0μg/kg/d for 5 days has been utilized (min 4.5μg/kg/d – max. 15.9μg/kg/d). Mean CD34+ cell concentration of 95 ± 49/μl could be achieved in the peripheral blood at day 5 before starting apheresis. This enabled us to collect a mean of 9.7 ± 8.0 CD34+ cells/kg body weight recipient corresponding to 658 ± 252 million total CD34+ cells in the product. In 96.3% of all cases one single apheresis was sufficient to collect the requested amount of CD34+ cells. Using logistic regression analysis we defined female sex, low BMI and low platelet (PLT) count at baseline as strongest risk factors for poor mobilization. Low white blood cell (WBC) concentration, low hematocrit and G-CSF-doses < 9μg/kg/d were also significantly associated with poor mobilization. Using the strongest numeric predictors (BMI, PLT) we employed STEPP-analysis to establish a statistically significant cross table risk score, that allows prediction of CD34+ cells in the peripheral blood at day 5 according to baseline PLT and BMI. From lowest cumulative risk score 2 (PLT>290; BMI>34.5) to highest risk score 6 (PLT<170; BMI<20.7) differences between all risk scores were highly significant. Interestingly, subgroup analysis demonstrated that female but not male donors with poor risk score that received > 9μg/kg/d G-CSF could improve significantly mobilization outcome without further side effects. Thus, overall results demonstrated that weight adapted G-CSF dosage for allogeneic donor treatment may improve mobilization outcome, i.e. in poor risk prospect female donors with low BMI and low PLT at baseline. Further genetic analysis may identify factors responsible for mobilization outcome.

22

A Survival Benefit for Reduced Intensity Allogeneic Transplants from Young Unrelated Donors Compared to Older Sibling Donors Depends on the Graft CD8 T-Cell Content

Ran Reshef [1], *Austin P. Huffman* [1], *Amy Gao* [1], *Mary Sell* [2], *Marlise R. Luskin* [1], *Selina Luger* [1], *Alison Loren* [1], *Elizabeth O. Hexner* [1], *Sunita D. Nasta* [1], *Noelle V. Frey* [1], *Saar Gill* [1], *James Mangan* [1], *Lee P. Richman* [3], *Taku Kambayashi* [2], *Edward A. Stadtmauer* [1], *Robert H. Vonderheide* [3], *Rosemarie Mick* [4], *David L. Porter* [1]. [1] *Blood and Marrow Transplantation Program, Abramson Cancer Center, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA;* [2] *Pathology and Laboratory Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA;* [3] *Abramson Family Cancer Research Institute, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA;* [4] *Biostatistics and Epidemiology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA*

Background: Younger donor age is associated with better survival in unrelated donor bone marrow transplants, but young unrelated donors have not shown an overall survival

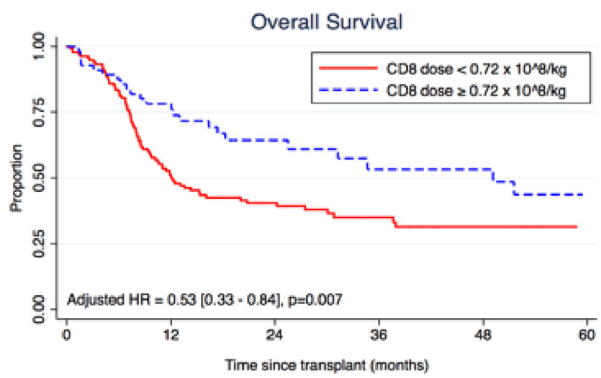

Fig. 1. CD8 cell dose and overall survival.

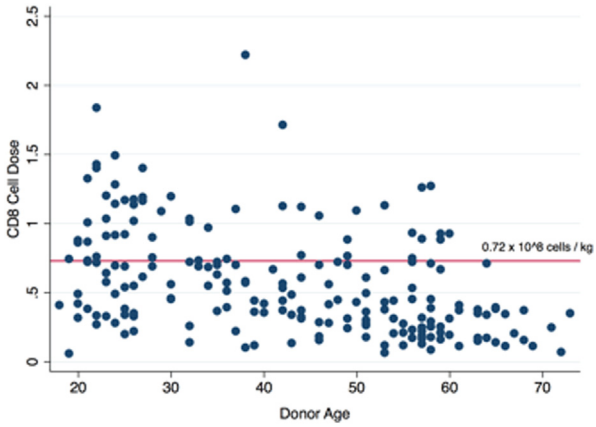

Fig. 2. Donor age and CD8 cell dose.

(OS) advantage over older sibling donors. We previously reported that a high CD8 T-cell content of peripheral blood (PB) stem-cell grafts was associated with improved OS in reduced intensity alloSCT (Reshef et al, Tandem, 2014). In this study we examined whether donor age correlated with graft T-cell content, and whether CD8 T-cell content may inform the selection of an optimal donor.

Methods: We studied 200 patients (pts) who underwent PB alloSCT after Flu/Bu2 conditioning (2007 to 2014). Cumulative incidence and Cox regression analyses were used to evaluate associations between cell doses and outcomes, with adjustment for significant covariates.

Results

Patients

The median age was 62 (range 21-76) and diseases included AML (86), MDS (44), NHL (30), ALL (11), CLL (8) and others (21). Pts were allografted from HLA-matched (86%) or mismatched (14%); sibling (42.5%) or unrelated (57.5%) donors.

Outcomes

A higher CD8 cell dose was associated with a decreased risk of relapse and improved OS. The adjusted hazard ratios (aHR) per 1 x 10^8/kg CD8 cells were: relapse 0.43 (95% CI [0.23 − 0.81]), p = 0.009; OS 0.57 (95% CI [0.33 − 0.97]), p = 0.04. A cutoff of 0.72 x 10^8/kg CD8 cells optimally dichotomized pts with differing OS. Pts who received a CD8hi (>=0.72) graft had significantly improved OS (aHR = 0.53, p = 0.007; Fig 1). The 1-year survival rates were 77.1% for CD8hi grafts and 50.2% for CD8lo grafts (p = 0.0002). CD3, CD4 and CD8 doses were not associated with GvHD or NRM.

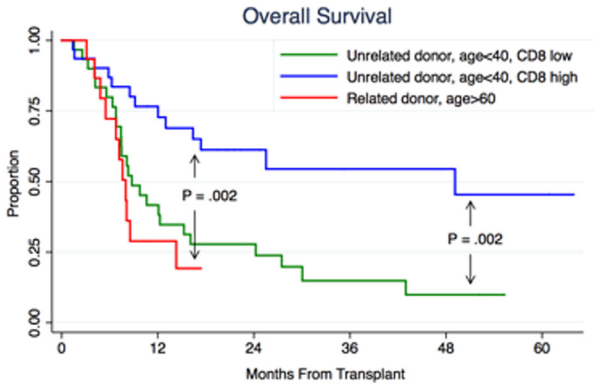

Fig. 3. Survival of recipients (age>60) is better with young unrelated donors and a CD8hi graft.

Donors

Donor age inversely correlated with CD8 cell doses (r = -0.44, p < 0.0001; Fig 2). All donors over age 60 provided a CD8lo graft while 45% of donors under age 40 provided a CD8hi graft. In recipients over age 60 (n=118; Fig 3), OS was better for patients allografted from young unrelated donors with a CD8hi graft compared to older sibling donors (p = 0.002) or young unrelated donors with a CD8lo graft (p = 0.002). The OS benefit was driven by a reduction in relapse risk without significant differences in GVHD or NRM. We then investigated whether a high CD8 cell dose could be predicted during donor screening. We found that donors (n=23) whose grafts contained a higher CD8 cell dose had higher %CD8 cells (r = 0.69, p = 0.0004) and lower CD4/8 ratio (r = -0.55, p = 0.007) in a screening blood sample.

Conclusion: A higher CD8 cell dose is associated with improved survival after reduced intensity alloSCT. Young unrelated donors with CD8hi grafts lead to better survival compared to older sibling donors. Donor selection based on predicted CD8 cell dose should be considered in prospective trials of reduced intensity alloSCT.

23

Double-Unit Cord Blood (CB) Transplantation (DCBT) Combined with Haplo-Identical Peripheral Blood CD34+ Cells (HaploCD34+) Is Associated with Enhanced Neutrophil Recovery, Universal Haplo Rejection, and Frequent Pre-Engraftment Syndrome

Matias E. Sanchez [1], *Doris M. Ponce* [1], *Emily Lauer* [1], *Marissa Lubin* [1], *Jonathan Barone* [2], *Courtney Byam* [3], *Parastoo Dahi* [1], *Richard Meagher* [4], *Hugo Castro-Malaspina* [1], *Ann A. Jakubowski* [1], *Guenther Koehne* [5], *Esperanza Papadopoulos* [1], *Miguel-Angel Perales* [1], *Craig Sauter* [1], *Roni Tamari* [1], *James W. Young* [1], *Andromachi Scaradavou* [3], *Nancy A. Kernan* [3], *Sergio Giralt* [1], *Richard J. O'Reilly* [3], *Juliet Barker* [1]. [1] *Department of Medicine, Adult Bone Marrow Transplant Service, Memorial Sloan Kettering Cancer Center, New York, NY;* [2] *American Red Cross, Philadelphia, PA;* [3] *Department of Pediatrics, Bone Marrow Transplant Service, Memorial Sloan Kettering Cancer Center, New York, NY;* [4] *Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, NY;* [5] *Department of Medicine, Adult Bone Marrow Transplant Service, Memorial Sloan Kettering Cancer Center, New York, NY*

Introduction: Delayed neutrophil recovery after myeloablative DCBT (median 25 days in adults) is frequent & associated with prolonged hospitalization & increased transplant-related mortality.

Methods: We investigated DCBT combined with haploCD34+ cells to speed myeloid recovery.

Results: Between 9/2012-8/2014 16/55 (29%) eligible patients (pts) could not receive DCBT-haplo as they had no haplo (n = 10) or had no CB ± no haplo graft (n = 6). 39 pts (median 48 years, range 15-68) with high-risk hematologic malignancies [30 acute leukemias (25 morphologic CR or aplasia, 5 not in CR) & 9 advanced lymphomas] underwent DCBT-haploCD34+ after myeloablation (2 high-dose Cy/Flu/TBI-1375, 37 reduced intensity Cy/Flu/Thio/TBI-400) with CSA/MMF & no ATG. CB units had a median infused TNC x 10^7/kg of 2.30 (larger unit) & 1.86 (smaller unit), & a median donor-recipient HLA-allele match of 5/8 (range 2-7/8). Haplo-donors (median 37 years, range 15-71) had a median 4/8 (range 4-6/8) donor-recipient HLA-match. The median infused haploCD34+ cell dose was