93 days (range 15 - 674) post HSCT. Fourteen (40%) were determined to have invasive ADV disease (7 on tissue biopsy). ADV viral load evaluation over time revealed the following: HVL at presentation in 18 (51.4%) (median $1.1x10^4$,range $7.4x10^5$ - $6.8x10^9$ copies/ml); 10 (28%) progressed to HVL (median 2 log increase from presentation) at a median of 15 days (range 3 - 56); and LVL-only at any time point in 7 (20%) pts (median 4000 copies/ml, range 600 - 8866). Fifteen pts with HVL were treated with cidovofir intravenously or/and CMX001 a median 7 doses (range 1 - 38). Despite treatment with antiviral therapy 12 pts (92%) with HVL and 7 pts (87.5%) with LVL-HVL died. Mortality was attributable to ADV in 11 (31.4%) pts. All cause 180 day mortality was 74.3% for pts with ADV.

Conclusions: ADV viremia was relatively low (8.7%) in this high risk population and similar to the 5% reported in populations receiving conventional transplants. Determination of viral status in patients with clinical symptoms resulted in a relatively high yield of positivity - 40%. The mortality attributable to ADV of 30% suggests the need for development of better treatment modalities. The 180 day all cause mortality of 74% suggests ADV viremia complicates other medical conditions and complications of transplant.

33

COINFUSION OF HAPLO-IDENTICAL DONOR STEM CELLS WITH AN (UN) RELATED CORD TRANSPLANT PROVED TO BE SUCCESSFUL IN A VERY HIGH RISK GROUP OF PATIENTS

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Introduction: Combining haplo-donor stem cells with a full graft cord blood (CB)-unit has been proposed as a cell support mechanism which can make single CB available as a donor source for allogeneic HSCT to a larger proportion of patients: e.g. patients with only donors available with low NC-counts, or with active infections.

Methods: Since 2009 we have a CB+haplo protocol for this group of patients. Patients (with any indication) with active infection (e.g. fungal) as well as patients with only a CB-unit available below the lower acceptable cut off were offered a CB+Haplo grafting. All patients received myeloablative conditioning (busulfan with therapeutic drug monitoring in combination with either CY or FLU) and serotherapy (ATG 8, Campath 1). Haplo-grafts were CD34+ selected (except 1: CD3/CD19 negative selected). After infusion of the CB, the haplograft containing 5milj/kg CD34+ cells were infused. G-CSF was given from day +7. GvHD prophylaxis: CsA+pred 1mg/kg.

Results.: 9 patients (8 children, 1 adult; 8 with active infection, 1 low cell count CBU). Median age was 12.4 yr (range 0.25-41.2 yr). 7 had a non-malignant disease (5 immunodeficiencies, 1 Osteopetrosis, 1 AA), 2 had a malignant indication. For 2 patients it was their second transplant. All patients except 1 engrafted at a median time of 12 days (range 9-15). Thrombocyte engraftment (TBC50) was 36 days (range14-300). EFS was 33% after a median follow up 249 days (14-1245). Incidence of GvHD gr. 2-4 was 25%. The non-relapse mortality was 2/9 (day 14 and day 24 respectively).The initial donor chimerism at 1 month post SCT showed >80% haplo chimerism in most patients but all 7 reached a full donor cord blood chimerism (>95%) within a median period of 121 days (28-925 days) post SCT.

Conclusion: Coinfusion of Haplo with (unrelated) CB transplantation is a safe and effective option for a group of very high risk patients (including patients with higher non-engraftment risks) to secure early engraftment. Haplo-support leads to early haplo-engraftment switching to full CB donor-chimerism within 4 months, allowing a normal immune recovery and repertoire.

34

CD8-DEPLETED DONOR-LYMPHOCYTE INFUSIONS AFTER T-CELL DEPLETED ALLOGENEIC HEMOPOIETIC STEM CELL TRANSPLANTATION

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In a phase I/II clinical trial, we investigated the prophylactic use of CD8-depleted ($CD8^{depl}$) donor lymphocyte infusions (DLI) in the setting of T-cell depleted allogeneic hematopoietic stem cell transplantation (HSCT). T-cell depletion was carried out by the use of high-dose Alemtuzumab (100 mg or 60 mg for unrelated or sibling donor transplantation, respectively). Here, we provide clinical follow-up data of 101 patients with different hematologic diseases and a median observation time of 1.5 years (range, 6-84 months). Median age was 56 years (range, 20-71). Stem cell source were peripheral blood stem cells of matched siblings (n = 15), matched unrelated (n = 48), or unrelated donors with single HLA mismatches (n = 38). Tapering of Cyclosporin A was started in the 6^{th} week after transplantation. Subsequently, $CD8^{depl}$ DLI were administered prophylactically in escalating doses starting with $1x10^6$ CD4 T cells/kg bodyweight. 39 patients received at least one dose of DLI. Among patients who did not qualify for DLI, 46 patients had primary GVHD. In 16 patients DLI were not administered for other reasons. Following DLI, acute GVHD was the major reason for withholding subsequent DLI-doses (64%) and 30% suffered from acute GVHD $< 2°$. Extensive chronic GVHD was diagnosed in 10% of the patients. The 1 and 3 year overall survival was 63% and 43%, respectively. Survival significantly differed between the DLI and non DLI group after 3 years (62% vs. 27%, p = 0.002). When the DLI group was compard to those patients who did not receive DLI for other reasons than primary GVHD, the difference in overall survival was similar (62% vs. 28%, p = 0.01). The presence of GVHD at any time was associated with a reduced relapse rate (56% vs. 31%, p = 0.013), independent of DLI. We demonstrated that 21 of 24 patients (84%) with decreasing T-cell chimerism (TCC) converted to full donor following $CD8^{depl}$ DLI. In contrast, only 2 of 8 patients (25%) with decreasing TCC in the non-DLI group converted spontaneously.

In summary, we observed that the application of prophylactic $CD8^{depl}$ DLI was associated with a survival benefit – even though the nature of the trial does not argue for a causal relationship. Our data strongly ask for randomized trials either comparing prophylactic application of $CD8^{depl}$ DLI vs. no DLI or $CD8^{depl}$ vs. non-manipulated DLI in a preemptive setting.

35

CORD BLOOD TRANSPLANTATION FOR LONG TERM MANAGEMENT OR POSSIBLE CURE OF HIV INFECTION

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Background: The most important mechanism for natural protection against HIV transmission is a mutation in the *CCR5* gene leading to a 32-base-pair deletion (*CCR5*-delta32) and a non-functional CCR5 protein. Prior to 2001, Chow et al pioneered the concept to screen allogeneic stem cell donors for those homozygous for *CCR5*-delta32 to transplant HIV infected patients (U.S. patent 2003/0099621 A1), as acknowledged by Hutter et al recently (TheScientificWorld Journal, 2011;11:1068-1076). Hutter et al (NEJM 2009;360:692-698) performed a bone marrow transplant in a patient with acute leukemia who was infected with HIV using a donor homozygous for the *CCR5*-delta32 deletion. More than 4 years later the patient does not require antiretrovial therapy and no viral load or proviral DNA can be detected. However, this procedure cannot be generalized using adult donors because the variant allele is quite unusual (<1% of Caucasians, and much lower in other ethnic groups) and a very close HLA match is required between adult donors and patients.

Hypothesis: Cord blood HCT requires HLA matching of only 4 of 6 alleles. Therefore, our hypothesis is that an inventory of cord blood