Paediatrics Section
Tuesday, March 28th
14:30-16:00
Ped 4: Oral Session - Paediatric transplantation

EWOG-MDS study SCT RC RIC 06: Reduced intensity conditioning for children and adolescents with refractory cytopenia of childhood

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Abstract

EWOG-MDS study SCT RC RIC 06: Reduced intensity conditioning for children and adolescents with refractory cytopenia of childhood Objective: Refractory cytopenia of childhood (RCC) is the most common subtype of myelodysplastic syndrome (MDS) in this age group. According to the EWOG-MDS policy, patients with RCC without chromosomal aberrations were eligible for hematopoietic stem cell transplantation (HSCT) with a reduced intensity conditioning regimen (RIC) consisting of fludarabine and thiotepa. Here, we report the outcome of children with RCC included in the prospective EWOG-MDS study SCT RC RIC 06. Patients and transplantations procedure: One-hundred-and-sixty-nine patients (89 males/80 females) were diagnosed with RCC at a median age of 9.8 (0.8-21.4) years. Prior to HSCT, patients were transfusion-dependent for platelets (107) and/or red blood cells (125) and/or had neutropenia (156). None of them had an abnormal karyotype. Forty-one patients received immunosuppressive therapy consisting of anti-thymocyte globuline (ATG) and cyclosporine-A (CSA) prior to HSCT. The median time from diagnosis to HSCT was 166 days (18 days-6 years). Patients were grafted from a matched sibling donor (MSD) (51), an alternative family donor (3) or an unrelated donor (UD) (115). UD were matched in 9/10 (33) or 10/10 (81) HLA antigens. Stem cell source was bone marrow (147) or peripheral blood (22). All patients were prepared with thiotepa (15 mg/kg) and fludarabine (160 mg/m2). Prophylaxis for graft-versus-host-disease (GVHD) was CSA +/- MTX/MMF +/- ATG for MSD, and CSA, MTX/MMF and ATG for patients transplanted from an UD. Results: After a median follow-up of 2.1 (0.3-9.4) years, 161 patients are alive, resulting in a probability of overall survival of 0.94 (0.90-0.98). Graft failure or delayed hematopoietic recovery was the main cause of treatment failure, including primary and secondary graft failure (GF) in 9 patients (5%) each and delayed platelet engraftment in 5 patients (3%). Twenty-one patients (12%) received a second allograft (17) or a stem cell boost (4). Sixteen patients were successfully rescued, whereas five died following the second procedure. An additional three patients died due to GVHD (2) or EBV associated lymphoproliferative disease. The cumulative incidence of grade II-IV and grade III-IV acute GVHD was 19% and 10%, respectively. Twenty-six of 152 patients (17%) at risk developed chronic GVHD, which was mild (14), moderate (6) or severe (6).
Event-free survival was significantly worse for patients transplanted from a 9/10 UD compared to patients receiving an allograft from a MSD or a completely matched UD (0.69 [0.53-0.85] versus 0.88 [0.78-0.98] and 0.86 [0.78-0.94]; p=0.02) due to an increased risk of GF. Unexpectedly, the only other patient, disease or transplantation variable associated with an inferior outcome was male sex of the recipient. Conclusion: In summary, the conditioning regimen with thiotepa and fludarabine offered an excellent survival despite a considerable incidence of graft failure. The risk of graft failure needs to be assessed in the light of an expected reduced risk of long term sequels, such as infertility with this preparation.

**Disclosure of conflict of interest**

None
Second allogeneic stem cell transplantation for children and adolescents following relapse after first transplantation for MDS with excess of blasts - A Study of the European Working Group of MDS in childhood (EWOG-MDS)

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Abstract

Objective: Allogeneic stem cell transplantation is the only curative treatment for myelodysplastic syndromes with excess of blasts (MDS-EB). It is associated with a risk of relapse in the order of 15-30%. We report the outcome of MDS-EB patients who received a second HSCT (HSCT2) for disease recurrence following first HSCT (HSCT1). Patients and transplantation procedure: Fifty-two patients (pts) registered in the EWOG-MDS 98 and 2006 studies relapsed after HSCT1 for MDS-EB (38 with primary MDS, 14 with therapy-related MDS). Preparative regimen of HSCT1 consisted of busulfan (Bu), cyclophosphamide and melphalan in 38 patients, other Bu-based regimens in 8 and other schemes in 10 pts. Median time to relapse after HSCT1 was 14.6 months (3.3-92.5), median time from relapse to HSCT2 3.5 months (0.6-90.7) and median age at HSCT2 13.3 years (5.4–25.3). Nine patients were transplanted from a matched sibling donor, 32 from a 9/10 or 10/10 matched unrelated donor (MUD), 2 from an 8/10 MUD and 9 from an alternative family donor. Stem cell source was peripheral blood (PB) (n = 33), bone marrow (BM) (n = 18) or cord blood (n = 1). Second conditioning regimen was based on the use of TBI in 23 pts, on treosulfan in 13 pts. The remaining 16 other pts received different regimens. Outcome: With a median follow-up time for survivors of 4.1 years (0.3-10.6) after HSCT2, the probability of overall survival (OS) and event-free survival (EFS) at 5 years were 0.29 (0.15-0.43) and 0.27 (0.14-0.40), respectively. The 5-year cumulative incidence of relapse was 0.49 (0.37-0.65), while that of transplant-related mortality (TRM) was 0.24 (0.15-0.40). Thirteen patients died due to TRM, 6 of them because of GvHD-related complications. A second relapse was recorded in 25 pts; 3 of them are alive with disease. All but one patient engrafted. Grade III–IV acute and chronic GvHD (cGvHD) was observed in in 12 pts each; cGvHD was extensive in
three pts. Patients with a structural complex karyotype or a blast count above 20% at second HSCT had a trend towards worse 5-year EFS (0.13 and 0.09, respectively). There was no difference in EFS according to the type of donor employed and age at second HSCT. Patients with an early relapse before 12 months after HSCT1 had a higher risk for TRM at 5 yrs. (0.42 vs 0.15, p=0.05). The cumulative incidence of relapse at 5 years was significantly lower in pts receiving PBSC in comparison with pts receiving BM (0.34 vs. 0.78, p < 0.01), as well as in patients experiencing cGvHD in contrast to pts without cGvHD (0.08 vs. 0.66, p<0.01). Stem cell source and presence of cGvHD were highly correlated (no cGvHD was observed in BMT recipients). In a multivariate COX-analysis the absence of chronic GvHD remained a predictive variable for an increased risk of relapse (RR=9.2). Conclusion: We conclude that HSCT2 can cure one out of four patients with MDS-EB relapsing after HSCT1. The association of cGVHD with a lower risk of relapse indicates the importance of a Graft-versus-leukemia effect. PBSC as stem cell source for HSCT2 might be privileged in case of adult donors.

Disclosure of conflict of interest

None
Outcomes of hematopoietic stem cell transplantation for acute lymphoblastic leukemia: a comparative study between adolescents-young adults and children. A study on behalf of the SFGM-TC

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Abstract

Introduction: Overall survival (OS) after Hematopoietic Stem Cell Transplantation (HSCT) for Acute Lymphoblastic Leukemia (ALL) is lower in Adolescent and Young Adults (AYAs) than in children (1,2). AYAs seem to have higher risk diseases but same relapse rates than children (3), whereas Transplantation Related Mortality (TRM) seems to be higher in AYAs (2). This study compare, in a large cohort, OS after HSCT for ALL between AYA and children to determine factors influencing survival and TRM differences. Patients and method: Patients aged between 1 and 25 years who received HSCT for ALL between 2005 and 2012, reported in the SFGM-TC registry were included. 5-years OS and DFS and cumulative incidence of relapse and TRM were compared between AYAs (15-25 years old) and pediatric patients (1-15 years old). Results: 891 patients, 494 children (1-15 years) and 397 AYAs (15-25 years) were included. Median follow-up was 45,67 months. T phenotype was found in 29,8% of AYAs and 25,1% of children, and high risk cytogenetic was more frequent in AYAs (29,8% versus 26,7% in children) but without any significant difference. HSCT was commonly done in first Complete Remission (CR) in AYAs (56,8%) and later (2nd CR or more) in children (57,5%). Peripheral stem cells (PBSC) were more used in AYAs than in children (28% versus 10,3%), and cord blood were used more often in children (29,4% versus 16,4%) p<0,0001. AYAs had a significantly lower 5 years-OS than children (Figure1), and lower 5 years-DFS than children. Those differences were confirmed in multivariate analysis. AYAs had greater risk of TRM than younger (18% versus 13%, p =0,04) (Figure 1), whereas incidence of relapse was similar in both group (32% in AYAs and 27% in children, p=0,1663). In univariate analysis, TRM was higher in case of transplantation with PBSC, but this result was not confirmed in multivariate analysis. Regarding causes of transplantation related deaths, chronic GVHD related mortality was significantly higher in AYAs (34,3% versus 23%, p < 0,0001), whereas organ toxicity mortality was higher in children (74,4% versus 60%, p = 0,02). Frequency of death due to acute GVHD or infections are similar in both group. Incidence of Chronic GVHD was higher in AYAs (32% versus 18% in younger, p=<0,0001), whereas cumulative incidence of acute GVHD are similar in both group (61% in children, 62% in AYAs, p=0,6488). Use of PBSC increased the incidence of chronic GVHD (HR: 1.67 [ 1.21; 2.32 ], p=0,0072) in univariate analysis. Conclusion: AYAs patients also seem to have greater risk of TRM after HSCT due to chronic GVHD. Choice of stem cell source or treatment adhesion should be questioned in further studies. Figure 1 : A:OS for AYAs (AJA) and pediatrics (PED) patients (p=0,0012) B: Cumulative incidence of TRM in AYAs(AJA) and children (PED) p=0,0413.
Table 1: Results of HSCT in pediatric patients and AYA. Univariate analysis:

<table>
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<th></th>
<th>Pediatric</th>
<th>AYAs</th>
<th>p</th>
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<tbody>
<tr>
<td>2 years OS</td>
<td>64%</td>
<td>53%</td>
<td>0.0012</td>
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<tr>
<td>2 years DFS</td>
<td>60%</td>
<td>49%</td>
<td>0.0074</td>
</tr>
<tr>
<td>Relapse incidence</td>
<td>27%</td>
<td>32%</td>
<td>0.1663</td>
</tr>
<tr>
<td>TRM cumulative incidence</td>
<td>13%</td>
<td>18%</td>
<td>0.0413</td>
</tr>
<tr>
<td>Acute GVHD</td>
<td>61%</td>
<td>62%</td>
<td>0.6488</td>
</tr>
<tr>
<td>Chronic GVHD</td>
<td>18%</td>
<td>32%</td>
<td>&lt;0.0001</td>
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Causes of death (n=132)

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<th></th>
<th>Pediatric</th>
<th>AYAs</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Acute GVHD</td>
<td>59.70%</td>
<td>76.80%</td>
<td>0.503</td>
</tr>
<tr>
<td>Chronic GVHD</td>
<td>23%</td>
<td>34.30%</td>
<td>&lt;0.0001</td>
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<tr>
<td>Infection</td>
<td>84.70%</td>
<td>89.20%</td>
<td>0.6348</td>
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<tr>
<td>Organ toxicity</td>
<td>74.40%</td>
<td>60%</td>
<td>0.0205</td>
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Disclosure of conflict of interest

None
Long-term results for children with high-risk neuroblastoma treated on the randomized high-dose therapy trial of busulphan-melphalan versus carboplatin-etoposide-melphalan: A Siopen study

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Abstract

Background: High-dose chemotherapy and autologous stem cell rescue (HDT/SCR) was shown to improve outcome for patients with high-risk neuroblastoma (HR-NBL), however it is unknown which regimen has the greatest patient benefit. We tested the hypothesis that HDT/SCR with busulphan and melphalan (BuMel) results in a superior 5-year event-free and overall survival (EFS, OS) than HDT/SCR with carboplatin, etoposide, melphalan (CEM). Methods Patients (<21 years) with metastatic neuroblastoma over the age of one or INSS stage 2–4 with MYCN amplification (MNA) were randomly assigned just prior HDT/SCR to BuMel or CEM taking into account age, stage, MYCNA and national group. Eligibility criteria were based on metastatic response requiring a complete bone marrow response and at least a partial response at skeletal sites, with three or less abnormal areas on 123iodine-metaiodobenzylguanidine scintigraphy. Induction treatments included Rapid Cojec chemotherapy, two additional courses of TVD in case of inadequate metastatic response and attempt of gross resection of the primary tumour. Further treatments after HDT/SCR were radiotherapy (21 Gray) to the primary site and 13-cis-retinoic acid. Findings 676 patients were eligible, of whom 598 (88%) were randomized. EFS(+/−SE) and OS (+/−SE) was 45±3% and 54%±3% in 296 patients in the BuMel group versus 33±3% and 41%±3% in 302 patients in the CEM group (p=0.001). The cumulative incidence of relapse was significantly lower with BuMel (52%±3) compared to CEM (63%±3) (p=0.003). Severe toxicities (need for intensive care and toxic deaths) were lower with BuMel (4%) compared to CEM (10%) (p=0.012). BuMel had fewer grade 3&4 non-haematological toxicities, but had 22% veno-occlusive disease Bearman grades 1–3 (but only 4% grade 3) versus 9% with CEM (1%
grade 3). Conclusion After Rapid Cojec induction, BuMel showed significantly improved EFS and OS in long-term outcome observation. An interaction of platinum based induction with CEM must be considered.

Disclosure of conflict of interest

The funding of the European Commission 5th Frame Work Grant (SIOPEN-R-NET EC grant No. QLRI-CT-2002-01768, www.siopen-r-net.org is disclosed as funding source.
Haematopoietic Cell Transplant (HCT) in Pediatric Acute Myeloid Leukemia (AML) after Similar Upfront Therapy with AML-Nopho; A Comparison of Conditioning Regimens

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Abstract

Background Severe toxicity, treatment related mortality (TRM) and relapse after HCT remain unmet needs in HCT for pediatric AML. Conditioning regimen is suggested to influence these outcomes. We compared the outcomes of pediatric AML patients treated with the same upfront AML-NOPHO protocols but transplanted with different conditioning regimens. Methods We retrospectively analysed pediatric AML patients treated with NOPHO2004/DB01 or NOPHO/DBH AML2012, transplanted between 2005-2015 in the Netherlands, Belgium and the Nordic countries. 3 Busulfan-based conditioning strategies were compared; CloFluBu: Busulfan (dosing with therapeutic drug monitoring; TDM), Fludarabin (40 mg/m2), Clofarabin (120 mg/m2), BuCy: Busulfan (TDM or 16 mg/kg), Cyclofosfamide (120 mg/kg) and BuCyMel: Busulfan (TDM or 16 mg/kg, Melphalan (140 mg/m2), Cyclofosfamide (120 mg/kg). TDM target was a cumulative Bu-exposure of 90 mg*h/l. Main outcome of interest was leukemia free survival (LFS). Other endpoints were occurrence of veno occlusive disease (VOD), acute and chronic Graft-Versus-Host-Disease (GVHD), relapse and TRM. Predictor analysis was performed using Cox Proportional Hazard Models. Risk factors considered were age, conditioning, cells source, gender and CR-status. Results 106 children were included (80 CR2, 24 CR1, 2 refractory), 57% male, median age 9.1 (0.8-21.5) years, transplanted with matched family donor 30 (28%), mismatchFD 3 (2.8%), MUD 54 (51%) and unrelated cord blood 18 (17%). In 69 (65%) patients Busulfan TDM was done. Median follow up was 1.9 (0.1–10) years. 37 received CloFluBu, 38 BuCyMel and 31BuCy. Estimated 3 years LFS was 64% (±5). Conditioning was the only predictor for LFS: compared to CloFluBu no difference was found with BuCyMel (HR1.3, 95%CI 0.5-3.5, p=0.5), but BuCy compared worse (HR 2.6, 95%CI 1.1-6.3, p=0.03; fig 1). The estimated TRM at 2 years was 10%(±3), non-significantly higher in BuCyMel (15%±6) compared to CloFluBu (6%±5) and BuCy (8%±5); fig 2. Relapse rate was 24% (±5) with conditioning regimen being the only predictor: compared to CloFluBu there was no difference with BuCyMel (HR 1.0, 95%CI 0.3-3.3, p=0.99), but BuCy compared worse (HR 3.1, 95%CI 1.1-8.6, p=0.03; fig 3). Probability for aGVHD grade 2-4 was lowest after CloFluBu 18.9%, compared to 32.3% and 47.4% in BuCy and BuCyMel respectively (p=0.032). For cGVHD no differences were found between groups. No VOD was noted in the CloBuFlu and the BuCy group while in the BuCyMel group, where almost 30% received VOD prophylaxis, VOD occurred twice. Conclusion LFS after BuCyMel and CloFluBu were similar, but BuCyMel was associated with increased toxicity (aGvHD, VOD). BuCy was associated with lower survival due to higher relapse probability. CloFluBu holds promise as low toxic and effective conditioning in pediatric AML-patients. Longer follow up and prospective studies are needed to confirm these results.
Figures abstract titled Haematopoietic Cell Transplant (HCT) in Pediatric Acute Myeloid Leukemia (AML) after Similar Upfront Therapy with AML-Nopho; A Comparison of Conditioning Regimens

Figure 1. LFS according to conditioning

Figure 2. TRM according to conditioning

Figure 3. Relapse according to conditioning

Disclosure of conflict of interest

NA
Donor age matters in T-cell depleted haploidentical hematopoietic stem cell transplantation in pediatric patients

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Abstract

Nowadays, T-cell depleted (TCD) haploidentical transplantation is increasingly used in paediatric patients with haematological malignancies otherwise incurable. For many years, donor selection has been based on KIR mismatch and KIR genotype. In unrelated and sibling transplantation setting, donor age has been associated to poor overall survival due to increased NRM. We analyzed the impact on outcome of donor age in TCD haploidentical transplantation. Ninety-four high-risk leukaemia patients that underwent first haploidential HSCT since 2007 to 2016 have been included in the study. Graft manipulation consisted on CD3/CD19 depletion in 69 cases and TCRαβ+/CD19 depletion in the remainder cases. Both procedures were performed with a CliniMACS device (Miltenyi Biotec, Germany). Conditioning consisted on high doses of fludarabine, busulfan and thiotepa. The median time to neutrophil (>0.5 x 10^9/L) and platelet recovery (>20 x 10^9/L) were 13 and 10 days, respectively. Cumulative incidence of NRM was 22±5% at a median time of 89 days (30-1391 days). None patient in 1st CR died because toxicity. Univariate analysis showed that donor age was the main risk factor associated with NRM (donor ≥40 years: 43±10% vs. donor <40 years: 13±5%, p=0.006). Twenty-five patients relapsed at a median time of 160 days (range: 23-617 days). Cumulative incidence of relapse was 28±5%. Cox analysis showed that the main prognostic factors of relapse were: disease status (non remission, HR: 2.86, 95% CI: 1.21-6.75, p=0.02), KIR genotype (genotype A, HR: 3.05, 95% CI: 1.3-7.12, p=0.01) and chronic GvHD (non chronic GvHD, HR: 3.99, 95% CI: 1.16-13.75, p=0.03). The probability of DFS was 50±6%. The median follow-up for survivors was 4 years (9 months-11 years). Donor age (< 40 years: 59±7% vs. ≥ 40 years: 35±8%, p=0.02), KIR genotype (genotype B: 59±6%, vs. genotype A: 13±8%; p=0.0001), disease status (remission: 57±6% vs. not in remission: 26±9%, p=0.001), disease phase (1st CR: 96±4% vs. ≥1st CR: 35±6%, p=0.0001), chronic GvHD (yes: 70±10% vs. no: 43±6%, p=0.005) and the number of NK cells at day +30 after transplant (above median: 70±8%, vs. below median: 31±8%; p=0.004) were found associated to DFS in univariate analysis. In conclusion, simple criteria such as donor age should be considered as donor selection criteria also in depleted haploidentical setting.

Disclosure of conflict of interest

No disclosures
Solid organ transplantation (SOT) after Haematopoietic Stem Cell Transplantation (HSCT) in pediatric patients. A multicentric retrospective EBMT study; on behalf of Paediatric Disease Working Party (PDWP)

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Abstract

Introduction. Solid organ transplantation (SOT) is a rare possible therapeutic approach to cure severe complications that may occur after hematopoietic stem cell transplantation (HSCT). Aim of this retrospective multicentric EBMT study is to analyze the incidence of SOTs performed after either allogeneic or autologous HSCT in pediatric patients (pts). Material and Methods. A questionnaire including information about HSCT and SOT procedures has been sent to 249 pediatric EBMT centers. 78 centers (31%) answered and 20 (25.6%) accepted to participate, carrying out the data. We evaluated SOTs performed in HSCT recipients between 1984 and 2016. Results. In this survey, a total number of 44 SOTs was collected: 20 were liver, 12 lung, 6 heart and 6 kidney. HSCT characteristics of children given SOT after HSCT are reported in Table 1. The majority of pts (n=15) received SOT 4-12 years (yrs) after HSCT, while 13, 8 and 7 underwent SOT 12-18, 18 and 1-4 yrs later, respectively. The indications for SOT were Graft versus Host disease (GvHD) in 13 pts (29.5%), underlying disease in 10 (22.7%), either acute (n=2), chronic (n=13) or acute/chronic (n=1) toxicity in 16 pts (36.3%). Three of these latter children underwent SOT due to toxicity combined with GvHD. Organ failure resulted in SOT in 4 pts (9%), while in 1 patient (2.2%) the reason is unknown. In 30 (68.1%) cases the donor of the
solid organ was a cadaver, while in 4 cases the donor was the same of the HSCT. Overall, 39 pts received immunosuppressive therapies (IST) after SOT and, at last follow-up, IST are still ongoing in 95% of them. Details about indications and outcome of different SOTs are reported in Table 2.

Conclusion. To the best of our knowledge, this is the first survey collecting SOTs performed in pediatric patients receiving HSCT. In comparison to recent published studies1, 2, we collected a large number of SOT evaluating only EBMT pediatric centers (44 SOT in 20 centers). In our experience, GvHD and toxicity represent the major indications for SOT. Cardio-toxicity secondary to radiotherapy is the major indication for heart transplantation, while lung transplantation, as reported in adults, is mostly offered to patients experiencing chronic GvHD (obliterans bronchiolitis). Considering an overall survival at last follow-up (> 10 yrs) of 75% (100% for kidney, 83% for lung, 67% for heart, 65% for liver transplantation), our data indicate that SOT may be a therapeutic option in very selected patients given HSCT, also during pediatric age.

References


Disclosure of conflict of interest

The authors declare that there are no competing financial interests in relation to the work described herein.
Results of a Prospective Multicenter Phase I/II Clinical Trial with TCR-Alpha/Beta and CD19 Depleted Haploidentical Stem Cell Transplantation Following Reduced Intensity Conditioning in Children

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Abstract

Background We report the first prospective, multi-center, open-label, single-arm phase I/II clinical trial that assesses the safety and feasibility of TCRalpha/beta and CD19-depleted peripheral haploidentical stem cells in combination with a reduced-intensity conditioning in pediatric patients (www.clinicaltrialregister.org; 2011-005562-38). Methods The CliniMACS plus System (Miltenyi Biotec, Germany) was used for cell depletion. Single agent MMF was given as short-term GVHD prophylaxis (40mg/kg/day for 30 days). Immune reconstitution was measured in two core labs using standardized methods and the MACSQuant flow cytometry device (Miltenyi Biotec, Germany). Results 30 patients from 6 hospitals were treated (median age 7 years, range 1 – 17). Diagnoses were: ALL (8) AML (6), solid tumors (6), MDS/MPS (3), lysosomal storage disorder (1), SCID (1), and Wiskott Aldrich syndrome (1). Disease status in acute leukemias/MDS was: CR1 (n=4), relapsed/refractory (n=17). 5/6 patients with solid tumors had relapsed metastatic disease. The conditioning regimen consisted of 15 or 30 mg ATG (Fresenius/Grafalon) or 7 Gy total nodal irradiation, 160 mg/m² fludarabine, 10 mg/kg thiotepa, and 140 mg/m² melphalan. The median number of CD34+ cells, TCRAlpha/beta+ cells and CD20+ cells infused was 14.6 x 106 (range, 4 – 54.9), 14 x 103 (range, 0.62 – 40.6) and 0.55 x 105 (range, 0.04 – 1.85), respectively. In addition, significant numbers of NK and TCRgd+ cells/kg were infused: 6.67 x 107 (0.68 – 18.2) and 1.58 x 107 (0.13 – 4.7), respectively. 25 patients had primary engraftment of ANC > 500 cells/µL at a median of 12 days (range, 10 – 18) and PLT > 20,000 cells/µL at a median of 15 days (range, 11 – 27). Five patients experienced primary and 2 had secondary graft failure. All except of one were successfully re-transplanted. Thus, final engraftment occurred in 29/30 patients. No aGVHD grades III – IV occurred. Only one patient had aGVHD grade II, 96.7% experienced no or only aGVHD grade I. Samples from 24/25 patients with primary engraftment were evaluable for immune reconstitution. On day 28, the majority of cells were NK cells (median 309 cells/µL; range, 64 – 1026), followed by CD3+ cells (151 cells/µL; 9 – 953), mostly TCRgd+ (87 cells/µL; 7 – 891). At day 100, TCRab+ cells equalized TCRgd+ cells (108 vs.116 cells/µL). B cells recovered slower, with a median of 255.5 cells/µL (1 – 1218) on day 63. ADV reactivation contributed most to infectious complications. In total, 16/30 patients had ADV DNAemia or were positive in stool. Additionally, seven patients were tested positive for CMV (blood or throat or urine). No EBV reactivation was observed. No fatal viral infection occurred within 100 days. Two patients died within 100 days after transplantation: 1 patient due to bacterial sepsis following graft failure (TRM) and 1 due to relapse. One molecular relapse was
observed. On day 100, chimerism was completely donor in 20 patients and mixed in two. Conclusions Depletion of TCRalpha/beta+/ CD19+ cells yielded a large number of CD34+ cells, NK cells and TCRgd+ cells, that could be infused safely with minimal risk of severe acute GVHD. The immune reconstitution was rapid and there was no TRM associated with viral or fungal infections. Longer follow up will provide essential information on chronic GVHD and survival outcomes.

**Disclosure of conflict of interest**