Table 1
Patient Characteristics

Sex	
Female	701 (41.0%)
Male	1008 (59.0%)
Age	
Median years (range)	52.7 (0.5 - 77.3)
<18 years	226 (13.2%)
Primary Disease	
Acute Myelogenous Leukemia	620 (36.3%)
Acute Lymphoblastic Leukemia	216 (12.6%)
Chronic Myelogenous Leukemia	69 (4.0%)
Myelodysplastic Syndrome	283 (16.6%)
Multiple Myeloma	40 (2.3%)
Non-Hodgkin Lymphoma	116 (6.8%)
Hodgkin Lymphoma	23 (1.3%)
Severe Aplastic Anemia	48 (2.8%)
Other	294 (17.2%)
Donor Age – median years (range)	31.7 (0.2 - 76.2)
Source of Donor Cells	
Bone Marrow	394 (23.1%)
Peripheral Blood	1233 (72.1%)
Umbilical Cord Blood	82 (4.8%)
Type of Donor	
Related Donor	676 (39.6%)
Unrelated Donor	1033 (60.4%)
Conditioning Regimen Intensity	
Myeloablative	988 (57.8%)
Reduced Intensity	557 (32.6%)
Non-Myeloablative	164 (9.6%)
GVHD Prophylaxis	
T cell depletion strategies	195 (11.4%)
TAC alone or + other(s) (except post-CY)	281 (74.5%)
CSA alone or + other(s) (except post-CY)	212 (12.4%)
Other or Unknown	28 (1.6%)
ATG/Alemtuzumab Use	
ATG alone	433 (25.3%)
Alemtuzumab alone	98 (5.7%)
No ATG/Alemtuzumab	1176 (68.8%)
Unknown	2 (0.1%)
Overall Survival at 1 Year – estimate (95% CI)	70.5% (68.4%, 72.7%)
Non-relapse Mortality at 1 Year – estimate (95% CI)	14.9% (13.2%, 16.7%)
Follow-up Time for Survivors – median months (range)	20.4 (3.2, 38.8)

SESSION J - CONSIDER THE SOURCE - STEM CELL GRAFTS AND DONORS

69

Rapid and Robust CD4+ and CD8+ T-, NK-, B-Cell, Dendritic Cell, and Monocyte Reconstitution after Nicotinamide-Expanded Cord Blood Transplantation

Coco de Koning MSc[1], *Mitchell E. Horwitz MD*[2], *Guillermo Sanz MD*[3], *Madan Jagasia MD, MS*[4], *John E. Wagner MD*[5], *Patrick J. Stiff*[6], *Rabi Hanna MD*[7], *Daniela Cilloni*[8], *Stefan Nierkens PhD*[1,9], *Jaap-Jan Boelens MD PhD*[10]. [1] *Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands;* [2] *Adult Stem Cell Transplant Program, Division of Cellular Therapy, Department of Medicine, Duke University Medical Center, Durham, NC;* [3] *Servicio de Hematología, Hospital Universitari i politècnic La Fe, Valencia, Spain;* [4] *Division of Hematology/Oncology, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN;* [5] *Blood and Marrow Transplantation, Department of Pediatrics, University of Minnesota, Minneapolis, MN;* [6] *Loyola University Medical Center, Maywood, IL;* [7] *Department of Pediatric Hematology Oncology and Bone Marrow Transplantation, Cleveland Clinic Children's Hospital, Cleveland, OH;* [8] *University of Turin, Turin, Italy;* [9] *Medical Immunology, Princess Maxima Centre for Pediatric Oncology, Utrecht, Netherlands;* [10] *Department of Pediatrics, Bone Marrow Transplant Service, Memorial Sloan Kettering Cancer Center, New York, NY*

Introduction: Nicotinamide-expanded cord blood (NiCord) is a potential alternative source for allogeneic hematopoietic cell transplantation (HCT) when an HLA-id donor is lacking. A phase 1/2 trial with standalone NiCord HCT showed rapid neutrophil- (11 days) and platelet engraftment (34 days). We previously reported that successful CD4+ immune reconstitution (IR) is crucial for infectious and relapse control associated with favorable survival (JACI 2017) and is a better predictor for event-free survival than neutrophil reconstitution. We performed unique in-depth immune monitoring to evaluate and compare IR after NiCord and conventional HCT.

Methods: In this phase1/2 international multicenter trial, we compared IR after NiCord HCT to cohorts of adolescent and young adult (AYA) patients receiving either unmanipulated cord blood transplantation (unCBT) or T-repleted-unrelated bone marrow transplantation (BMT). All patients received HCT for a hematologic malignancy with myeloablative conditioning without serotherapy. Immune monitoring was performed (harmonized sampling, handling and analyses) in a central lab. The primary endpoint was probability of achieving CD4+ IR ($>50^{*}10^{6}$/L within 100 days). Secondary endpoints were IR of B-cells, CD4+ and CD8+ T-cells, natural killer (NK)-cells, monocytes, and dendritic cells (DC) 7-365 days after HCT. In addition, TREC analyses were performed on CD3+ MACs-sorted cells. Linear-mixed effects modelling in LOESS-regression curves and two-sided log-rank test for univariate comparisons in cumulative incidence plots were used.

Results: 27 NiCord recipients (median 41.5; 13.4-61.7yrs) were included. NiCord cell dose consisted of median $6.4^{*}10^{6}$ CD34+/kg, and $2.3^{*}10^{6}$ CD3+T-cells/kg of the co-infused negative fraction (following CD133+ selection). Of these patients, 91% achieved successful CD4+ IR, which was comparable (p=0.76, Figure 1) to the 27 unCBT (median 15.4; 12.2-22.1 yrs) and 20 BMT (median 14.3; 12.1-19.7 yrs) recipients included in this study. We observed similar reconstitution of T-cells (p=0.15), monocytes (p=0.94), conventional DCs (p=0.41), and plasmacytoid DCs (p=0.52). Interestingly, reconstitution of NK-cells ($p<0.001$); especially na•ve NK-cells, and B-cells (p=0.02); both follicular B-cells (p=0.04), memory B-cells (p=0.003), and plasma cells (p=0.003), was much faster after NiCord HCT, compared to the unCBT and BMT cohorts (Figure 2).

Conclusions: In-depth immune monitoring reveals fast and full IR after NiCord HCT in adult patients, which is equal or even faster to IR after unCBT or BMT, despite the younger age of the AYA cohorts (expected to reconstitute faster). This may be explained by the higher stem cell dose and higher proliferative capacity of the NiCord-expanded product. Optimal comparison of IR in NiCord vs. unCBT in a randomized phase 3 trial is underway.

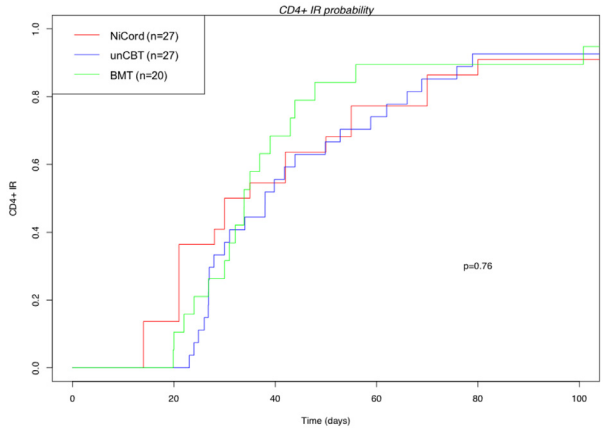

Figure 1. CD4+ T-cell reconstitution probability in NiCord, unCBT, and BMT recipients.