



## 2012 COUNCIL MEETING

# E4: Cord Blood Transplantation for Non-Malignant Disease

Saturday, November 10, 2012

3:30 - 4:45 p.m.

### Presented by

Mary Eapen, MD, MS  
Naynesh Kamani, MD  
Annalisa Ruggeri, MD

### Objectives

At the conclusion of this session, the attendee will be able to:

1. Describe the use of umbilical cord blood transplant (UCBT) for the treatment of non-malignant diseases, specifically sickle cell anemia and hemoglobinopathies.
2. Explain the challenges of UCBT for the treatment of non-malignant diseases, specifically sickle cell anemia and hemoglobinopathies.

### Conflict of Interest/Financial Disclosure

The Speaker(s) voluntarily disclosed the following pertinent financial relationships and/or conflicts of interest:

- *None – The speaker(s) in this session have disclosed NO conflicts*

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Attendee Signature

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Date

## **Unrelated donor cord blood transplantation for children with severe sickle cell disease: results of one cohort from the phase II study from the Blood and Marrow Transplant Clinical Trials Network (BMT CTN).**

Kamani NR, Walters MC, Carter S, Aquino V, Brochstein JA, Chaudhury S, Eapen M, Freed BM, Grimley M, Levine JE, Logan B, Moore T, Panepinto J, Parikh S, Pulsipher MA, Sande J, Schultz KR, Spellman S, Shenoy S.

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The Sickle Cell Unrelated Donor Transplant Trial (SCURT trial) of the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) is a phase II study of the toxicity and efficacy of unrelated donor hematopoietic cell transplantation in children with severe sickle cell disease (SCD) using a reduced-intensity conditioning regimen. Here we report the results for the cord blood cohort of this trial. Eight children with severe SCD underwent unrelated donor cord blood transplantation (CBT) following alemtuzumab, fludarabine, and melphalan. Cyclosporine or tacrolimus and mycophenolate mofetil were administered for graft-versus-host disease (GVHD) prophylaxis. Donor/recipient HLA match status was 6 of 6 ( $n = 1$ ) or 5 of 6 ( $n = 7$ ), based on low/intermediate-resolution molecular typing at HLA -A, -B, and high-resolution typing at -DRB1. Median recipient age was 13.7 years (range: 7.4-16.2 years), and median weight was 35.0 kg (range: 25.2-90.2 kg). The median pre-cryopreservation total nucleated cell dose was  $6.4 \times 10^7$  /kg (range: 3.1-7.6), and the median postthaw infused CD34 cell dose was  $1.5 \times 10^5$  /kg (range: 0.2-2.3). All patients achieved neutrophil recovery (absolute neutrophil count  $>500/\text{mm}^3$ ) by day 33 (median: 22 days). Three patients who engrafted had 100% donor cells by day 100, which was sustained, and 5 patients had autologous hematopoietic recovery. Six of 8 patients had a platelet recovery to  $>50,000/\text{mm}^3$  by day 100. Two patients developed grade II acute GVHD. Of these, 1 developed extensive chronic GVHD and died of respiratory failure 14 months posttransplantation. With a median follow-up of 1.8 years (range: 1-2.6), 7 patients are alive with a 1-year survival of 100%, and 3 of 8 are alive without graft failure or disease recurrence. Based upon the high incidence of graft rejection after unrelated donor CBT, enrollment onto the cord blood arm of the SCURT trial was suspended. However, because this reduced-intensity regimen has demonstrated a favorable safety profile, this trial remains open to enrollment for unrelated marrow donor transplants. Novel approaches aimed at improving engraftment will be needed before unrelated CBT can be widely adopted for transplanting patients with severe SCD.

## **Umbilical cord blood transplantation for children with thalassemia and sickle cell disease.**

Ruggeri A, Eapen M, Scaravadou A, Cairo MS, Bhatia M, Kurtzberg J, Wingard JR, Fasth A, Lo Nigro L, Ayas M, Purtill D, Boudjedir K, Chaves W, Walters MC, Wagner J, Gluckman E, Rocha V; Eurocord Registry; Center for International Blood and Marrow Transplant Research; New York Blood Center.

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We examined the efficacy of unrelated cord blood (CB) transplantation in children with thalassemia (n = 35) and sickle cell disease (n = 16), using data reported to 3 registries. Donor-recipient pairs were matched at HLA-A and -B (antigen level) and DRB1 (allele level) in 7 or HLA mismatched at 1 (n = 18), 2 (n = 25), or 3 loci (n = 1). Transplant conditioning was myeloablative (n = 39) or reduced intensity (n = 12). Neutrophil recovery with donor chimerism was documented in 24 patients; 11 patients developed grade II-IV acute graft-versus-host disease (aGVHD) and 10 patients, chronic GVHD (cGVHD). Overall survival (OS) and disease-free survival (DFS) were 62% and 21% for thalassemia and 94% and 50% for sickle cell disease (SCD), respectively. In multivariate analysis, engraftment rate (hazard ratio [HR] 2.2, P = .05) and DFS (HR 0.4, P = .01) were higher with cell dose  $>5 \times 10^7$ /kg. The 2-year probability of DFS was 45% in patients who received grafts with cell dose  $>5 \times 10^7$ /kg and 13% with lower cell dose. Primary graft failure was the predominant cause of treatment failure occurring in 20 patients with thalassemia and 7 patients with SCD. Primary graft failure was fatal in 5 patients with thalassemia. These results suggest that only CB units containing an expected infused cell dose  $>5 \times 10^7$ /kg should be considered for transplantation for hemoglobinopathy.

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Biol Blood Marrow Transplant. 2011 Sep;17(9):1375-82. Epub 2011 Jan 28.

## A multicentric comparative analysis of outcomes of HLA identical related cord blood and bone marrow transplantation in patients with beta-thalassemia or sickle cell disease

N. Kabbara\*, F. Locatelli, V. Rocha, S. Grafakos, A. Ghavamzadeh, I. Roberts, C.K. Li, F. Bernaudin, C. Vermynen, J.H. Dalle, J. Stein, R. Wynn, P. Lutz, C. Cordonnier, F. Pinto, E. Angelucci, G. Socié, E. Gluckman, M. Walters (Paris, FR; Pavia, IT; Athens, GR; Tehran, IR; London, UK; Shatin, HK; Créteil, FR; Brussels, BE; Petach-Tikva, IL; Manchester, UK; Strasbourg, FR; Calgiari, IT; Oakland, US)

Most patients with beta thalassemia major (TM) or sickle cell disease (SCD) can be cured by hematopoietic stem cell transplantation (HSCT) from either cord blood (CB) or bone marrow (BM). One advantage of CB is the absence of risk associated with donation. In order to compare outcomes after HSCT with CB or BM, we studied 388 patients with TM or SCD who received HLA identical sibling CB (n=72) or BM (n=316) allografts between 1994 and 2005. In order to avoid center and period effect, only centers that performed both types of HSCT during the same period were included. We compared the incidence of hematopoietic recovery, acute and chronic graft-versus-host disease (GvHD), disease-free survival (DFS) and overall survival (OS) after CB and BM transplantation. Compared to BM, CB recipients were significantly younger (median of 6.2 y versus 7.2 y), smaller (19 kg vs 24 kg), and were transplanted more recently (in 2001 vs 1998). The BM group consisted of 127 (40%) SCD and 189 (60%) TM patients, and the CB group, 26 (36%) SCD and 46 (64%) TM patients. The indications for transplantation in SCD were not statistically different between CB and BM groups. More TM patients belonging to Pesaro II-III risk classes received BM (65%) compared to CB (36%) (p=0.004). There were also differences in the conditioning regimen (more frequent use of ATG/ALG in the BM group and of Fludarabine and Thiotepea in the CB group) and GVHD prophylaxis (more methotrexate-containing therapy in the BM group compared to the CB group). In addition, the nucleated cell content was 10 times higher in BM compared to CB. The table below shows the non-adjusted univariate analysis for outcomes for all patients according to the stem cell source used. In TM patients, the 5 year-DFS rates were 87% and 83% for BM and CB recipients, respectively, and in SCD patients, 92% and 85%, respectively. In a multivariate analysis adjusted for age and type of hemoglobinopathy, DFS was not statistically different between CB and BM recipients (RR=1.4, p=0.34). In conclusion, patients with TM or SCD had excellent outcomes after HSCT whether they received stem cells of CB or of BM from an HLA identical sibling. These results strongly suggest that CB transplantation from HLA identical siblings should be pursued when possible to avoid the discomfort and risks of a bone marrow harvest.

Source	Neutrophil recovery	Acute GVHD II-IV	Chronic GVHD	5y DFS	5y OS
CB	93%	9%	8%	84	95%
BM	92%	14%	9%	89%	95%
p value	0.02	0.41	0.61	0.44	0.97