

# Confirmation of Unrelated Cord Blood Transplant as a Treatment Strategy for Severe Aplastic Anemia

Jonathan Wofford, Donna Regan, Jennifer Sander, and Deepika Bhatla, MD  
Saint Louis Cord Blood Bank, SSM Cardinal Glennon Children's Medical Center

## Abstract

The St. Louis Cord Blood Bank (SLCBB) serves to collect, process, cryopreserve, and distribute umbilical cord blood for human transplantation. To date, nearly 1,600 units have been distributed globally for the treatment of more than 70 diseases with a notable recent increase in utilization for Severe Aplastic Anemia (SAA). Recent data, although limited, has suggested that unrelated cord blood transplantation can be a successful treatment strategy for patients with SAA lacking a well-matched adult donor. A retrospective analysis was performed as a means to compare the SLCBB experience (n=42) with published results. Outcomes data was available and evaluated for 16 singleton cord transplants. This population included 11 pediatric and 5 adult patients. The mean age was 15.4 years (1.7-45.2). Donor/recipient HLA matching was six of six (n=2), five of six (n=8), four of six (n=6). Median total nucleated cell dose was  $7.2 \times 10^7/\text{kg}$ . Fourteen patients received myeloablative conditioning regimens while two received non-myeloablative conditioning. Thirteen patients achieved neutrophil engraftment with a median time to recovery of 21 days (9-46). The seven patients who received a total nucleated cell dose (TNC)  $> 5.0 \times 10^7/\text{kg}$  had a median time to engraftment of 20 days as compared to 27 days for patients receiving a TNC dose  $\leq 5.0 \times 10^7/\text{kg}$ . There was one instance of graft failure and one patient censored due to early death. Ten patients are alive and three have expired from infectious complications. Acute GVHD occurred in nine patients and chronic GVHD developed in six. Outcomes for dual cord transplants (n=11) were available for three patients. All three patients engrafted with a median time to absolute neutrophil recovery of 25 days (22-28). These findings support that unrelated cord blood transplant is a feasible treatment strategy for Severe Aplastic Anemia. The SLCBB will continue to track and report outcomes for this population.

## Materials & Methods

- A retrospective analysis was performed on outcomes data for patients undergoing singleton cord blood unit transplant with products provided by The St. Louis Cord Blood Bank.
- Outcomes data used for this analysis was provided through one of two methods:
  - Direct report to the SLCBB via the transplant center
  - Through the Center for International Blood and Marrow Transplant Research (CIBMTR)
- Patients for whom engraftment data was not available were excluded from this analysis
- Study populations were divided based on total nucleated cell dose /kg

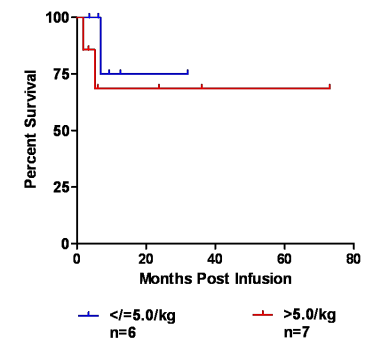
## Results (continued)

**Table 1: Demographic and Clinical Characteristics**

Variable	$\leq 5.0/\text{kg}$	$> 5.0/\text{kg}$
Age (y)		
Mean	26.4	3.4
Median	33.1	3.3
Gender		
Female	5	7
Male	2	2
HLA Match /6		
6/6	1	1
5/6	2	4
4/6	4	4
Conditioning Regimen		
Myeloablative	5	8
Non-Myeloablative	2	1

## Results (continued)

**Figure 2: Overall Survival by Cell Dose Group**



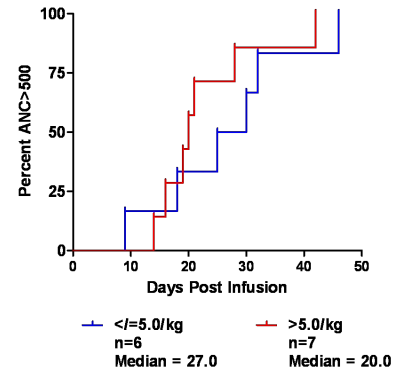
## Background

Severe Aplastic Anemia (SAA) is an uncommon life-threatening bone marrow failure syndrome. Until a few decades ago, this disease carried a dismal prognosis. Currently the standard of care for patients is hematopoietic stem cell transplant from a matched related donor and this strategy is able to cure 80-90% of patients with SAA. However, a matched related donor is available in only 20-30% of patients with SAA. Patients without a matched related donor are typically treated with immune suppressive therapy (IST). Though the majority of patients (up to 70%) show an initial response to IST, disease recurrence is seen in up to 50% of patients long-term. Hence, alternative donor sources have been sought in an effort to increase the cure rate. Outcomes with unrelated donor transplantation have improved significantly over the last 25 years with long-term survival approaching 75%. This improvement is due in part to better HLA-matching and to significant changes in conditioning regimens. Outcomes with HLA-mismatched unrelated donor transplantation remain significantly inferior with survival rates of 34-40%. Even with the expansion of donor registries, finding well matched unrelated donors is challenging for ethnic minorities, underscoring the need to look for alternative donor sources. Umbilical cord blood has been used very successfully as a source of hematopoietic stem cells in patients with leukemia. However, data for use of umbilical cord blood (UCB) in SAA is limited to case series or anecdotal reports. Historically, concerns for delayed/poor engraftment and limitations of cell dose for adult patients have been the disadvantages to utilizing UCB. With the recent data on the successful use of double cord transplants in leukemia patients, there may be renewed interest in the use of UCB in SAA patients. UCB transplants also have the advantage of a lower incidence of graft-versus-host disease (GVHD).

## Results

- 7 patients who received a TNC dose  $> 5.0 \times 10^7/\text{kg}$  had a median time to engraftment of 20 days (Figure 1)
- This was an improvement of 7 days over patients receiving a TNC dose of  $\leq 5.0 \times 10^7/\text{kg}$  (Figure 1)
- Ten patients are alive (5 in each group) and 3 patients have expired due to infectious complications (Figure 2)
- Incidence of Acute Graft vs. Host Disease (AGVHD) was similar between the the two groups with 4 cases reported in the lower cell dose group and 5 in the higher cell dose category.
- Chronic GVHD was more prevalent in the low dose cell group with 4 patients diagnosed as compared to 2 in the higher cell dose category.

**Figure 1: Overall Neutrophil Recovery by Cell Dose Group**



## Discussion

- The SLCBB has been exporting cord blood units for various disease and disorders since 1997
- During this time, 47 units have been exported for Severe Aplastic Anemia
- Of these 47 units,  $\sim 40\%$  have been exported between 2007 and 2009, marking a significant increase in utilization
- This increase is due in part to the success of dual cord blood transplantation as a means of overcoming cell dose limitations
- The SLCBB's findings support the idea of unrelated cord blood transplant as a feasible treatment strategy for Severe Aplastic Anemia
- A major limitation to this study has been the lack of available outcomes data – the SLCBB will be working with transplant centers to publish an updated data set