Study Objectives

- Assessment of the acute toxicity associated with the infusion of NiCord®, within 24 hours post-infusion
- Assessment of cumulative incidence of donor-derived neutrophil engraftment by day 42 following co-transplantation of NiCord® and unmanipulated cord blood grafts

SECONDARY OBJECTIVES

- Treatment related mortality at 180 days
- Event-free survival at 100 days
- Overall survival at 180 days

EXPLORATORY OBJECTIVES

- Donor chimerism
- Pace of neutrophil, platelet and immune recovery
- GVHD, regimen-related toxicity, infections

Background

• Patients with severe sickle cell disease (SCD) experience organ damage, poor quality of life and premature mortality
• Allogeneic hematopoietic stem cell transplant (HSCT) from a matched related bone marrow donor is the only established curative therapy to date
• Most patients in need of HSCT do not have a matched related or unrelated donors
• Umbilical cord blood is easily available, and transplants (UCBT), using partially mismatched grafts are feasible, thus increasing access to transplant
• However, UCBT is associated with increased graft failure risk in patients with hemoglobinopathies: inadequate cell dose in the graft has been noted to be an important variable associated with graft failure
• NiCord® is an ex vivo expanded product made from a cord blood unit (CBU) using nicotinamide-based technology

NiCord®, in combination with an unmanipulated CBU (pilot study at Duke University; Horwitz et al. JCI 124:7, 2016) or as a standalone graft (Phase III multicenter study; Horwitz et al. 2016 ASCO Annual Meeting), has shown rapid and sustained engraftment in adults with high-risk hematologic malignancies.

Demographics & Transplant Outcomes

<table>
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<tr>
<th>Pt</th>
<th>Age (yrs)</th>
<th>Indication</th>
<th>NiCord® Cultured Fraction INFUSED</th>
<th>Engraftment (day)</th>
<th>Maximum GvHD Acute/ Chronic</th>
<th>GvHD at last F/U</th>
<th>Chimerism Day 7</th>
<th>Chimerism Last F/U</th>
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Median 12.9 yrs 6.6 93.7 7 55

Hypothsis

Co-transplantation of NiCord® & an unmanipulated CBU will be safe and improve engraftment in patients with sickle cell disease undergoing myeloablative HSCT

RESULTS

- NiCord® dose appears to overcome the engraftment barriers of UCB in SCD patients in a myeloablative setting. Sustained donor cell engraftment was achieved in 8/9 transplant, despite 4/6 matched UCB units and in 6 patients without ATG
- Rapid engraftment was achieved consistently with NiCord® approach, most of the patients engrafting within 7-8 days
- Patients consistently achieve transfusion independence normal and hemoglobin profile post-transplant
- Factors influencing one graft to dominate over another need further study
- None of the survivors have active GvHD at the last follow up. However, GvHD is a challenge and further optimization of this approach with strategies to decrease further GvHD is warranted
- NiCord® has the potential to increase access to curative transplantation for SCD patients by enabling the successful use of unrelated UCB donors

CONCLUSIONS

Successful Engraftment and Cure of Sickle Cell Disease after Co-transplantation of NiCord® (Ex Vivo Expanded UCB Progenitor Cells with Nicotinamide) and a Unmanipulated Cord Blood Unit after Myeloablative Chemotherapy in Children with Severe Sickle Cell Disease

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OBJECTIVES

- Myeloablative acute GvHD was not observed in patients with matched related or unrelated donors
- NiCord® grafts were able to support rapid neutrophil engraftment in patients with myeloablative conditioning
- Median neutrophil recovery was observed at day 10 (range: 6-20 days) in all patients
- Platelet recovery was also observed at day 51 (range: 31-94 days)
- No patient had secondary graft failure
- Acute GvHD grade IV; 0
- Chronic extensive GvHD: 0
- No patients died; 1 from infectious complications after second transplant (Pt #2); 1 from liver GVHD (Pt #7)
- Transfusion independence: 7 patients (1 patient too early)
- Hemoglobin profile (post-transplant): Normal in 7 patients
- Survival: 7/9 patients are alive at a median follow-up of 36 months (0.7 – 48 months)

Data represent median ± range unless otherwise indicated.

N = number; M = median; F/U = Follow up; SI = immunosuppressive agents; UM = unmanipulated

NiCord® Shipped to Cryopreserved Product Ready to receive infusion

NiCord® Product Manufacturing

OBJECTIVES

- Evaluated the acute toxicity associated with the infusion of NiCord®, within 24 hours post-infusion
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SECONDARY OBJECTIVES

- Treatment related mortality at 180 days
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EXPLORATORY OBJECTIVES

- Donor chimerism
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- GVHD, regimen-related toxicity, infections

Results

- N = 8; M = 4.5
- Median age 12.9 years (3.3 – 16.9 yrs)
- HLA match of patient with:
  - NiCord® unit 4/6 (n=6); 5/6 (n=1)
  - UM unit 4/6 (n=3); 5/6 (n=3)
- Initial Engraftment noted in all 9 patients:
  - Median time to engraftment:
    - Neutrophils 7 days (range: 6-20 days)
    - Platelets 51 days (range: 31-94 days)
  - 1 patient had secondary graft failure
- Acute GvHD grade IV; 0
- Chronic extensive GvHD: 0
- 2 patients died: 1 from infectious complications after second transplant (Pt #2); 1 from liver GVHD (Pt #7)
- Transfusion independence: 7 patients (1 patient too early)
- Hemoglobin profile (post-transplant): Normal in 7 patients
- Survival: 7/9 patients are alive at a median follow-up of 36 months (0.7 – 48 months)