**Purpose**

This study will develop a national cord blood bank for siblings of patients with hemoglobinopathies and thalasemia.

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<th>Condition</th>
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<td>Hematologic Diseases</td>
<td>Drug: Sangstat</td>
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<td>Anemia, Sickle Cell</td>
<td>Drug: Cyclophosphamide</td>
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<td>Beta-Thalassemia</td>
<td>Drug: Busulfan</td>
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<td>Hematopoietic Stem Cell Transplant</td>
<td>Drug: Mycophenolate Mofetil</td>
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<td>Drug: Cyclosporine</td>
<td>Phase 2</td>
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<td>Procedure: Cord Blood Transplantion</td>
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Study Type: Interventional  
Study Design: Primary Purpose: Treatment  
Official Title: Sibling Donor Cord Blood Banking and Transplantation

Resource links provided by NLM:
- Genetics Home Reference related topics: beta thalassemia, sickle cell disease
- MedlinePlus related topics: Anemia, Blood Disorders, Sickle Cell Anemia, Thalassemia
- Drug Information available for: Cyclophosphamide, Busulfan, Mycophenolic acid, Mycophenolate sodium, Cyclosporine, Mycophenolate mofetil hydrochloride, Mycophenolate mofetil

Further study details as provided by National Heart, Lung, and Blood Institute (NHLBI):

Primary Outcome Measures:
- Hematologic parameters
- GVHD

Estimated Enrollment: 30  
Study Start Date: January 1999  
Study Completion Date: August 2006  
Primary Completion Date: August 2006 (Final data collection date for primary outcome measure)
Detailed Description:

BACKGROUND:

During the past decade, a number of advances have been made in the treatment of patients with sickle cell anemia and thalassemia. Among these advances is allogeneic bone marrow transplantation, which is the only current treatment that offers a potential for cure. In sickle cell anemia, transplantation has been performed in patients who have had advanced organ damage. In thalassemia, transplantation has been performed before having any evidence of iron-related tissue damage. Due to concerns over engraftment and graft versus host disease (GVHD), transplants for patients with hemoglobinopathies have been limited to situations in which a human leukocyte antigen (HLA) compatible donor existed. Unfortunately, an HLA-matched related donor is often not available. Umbilical cord blood (UCB), a recently recognized source of hematopoietic stem cells, has been used to successfully transplant bone marrow to over 500 patients. The potential advantage of cord blood over other donor sources of stem cells is the minimal risk of high-grade GVHD (even without complete HLA compatibility).

DESIGN NARRATIVE:

This study will establish a national sibling donor cord blood (SDCB) program, evaluate its use in a multi-center pilot study of transplantation, and develop a Web-based data management system to support these two projects. A multi-center pilot study was conducted on cord blood transplantation in children with either sickle cell disease or thalassemias. The investigators tested the hypothesis that a novel immunosuppressive conditioning regimen (fludarabine, cyclophosphamide, and busulfan) and post transplant therapy (mycophenolate mofetil and cyclosporine) would improve engraftment rates and prevent disease recurrence. The effect of SDCB transplantation on hematologic parameters and GVHD was monitored. Enrollment in the study was suspended on December 29, 2003. The protocol was revised, replacing the previous conditioning regimen of fludarabine, busulfan, and cyclophosphamide with a more conventional regimen of rabbit anti-thymocyte globulin (Sandoglobulin), busulfan, and cyclophosphamide. The revised protocol is open for enrollment.

Eligibility

Ages Eligible for Study: 3 Years to 14 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Suitable UCB collection from an HLA-identical sibling
- Sickle cell anemia (Hb SS or S beta thalassemia) with significant disease manifestations as defined by at least one of the following criteria:
  a. A history of painful events defined as three or more painful events in the 2 years prior to enrollment. Pain may occur in typical sites associated with vaso-occlusive painful events and cannot be explained by causes other than sickle cell disease. The pain must last at least 4 hours and require treatment with either parenteral narcotics, an equianalgesic dose of oral narcotics (if pain is treated in a local facility where parenteral narcotics are not routinely used to treat painful events), or parenteral nonsteroidal anti-inflammatory drugs. Painful events managed at home will be considered only if there is documentation of the event in a clinical record that may be reviewed by an investigator.
  b. Acute chest syndrome (ACS) with two or more episodes of ACS with the development of a new infiltrate on chest radiograph and/or having a perfusion defect demonstrable on a lung radioisotope scan
  c. Any combination of painful events and episodes of ACS that total three events in the 2 years before transplantation
  d. Any clinically significant neurologic event (stroke or hemorrhage) or any neurologic defect lasting more than 24 hours
  e. Abnormal cerebral MRI and abnormal cerebrospinal MRA
  f. An episode of dactylitis in the first year of life with significant anemia (Hbg less than 7 g/dL), or leukocytosis in the second year of life such that the risk of a severe adverse outcome before 18 years of age exceeds 54% (as defined by the cooperative study of sickle cell disease (CSSCD) infant cohort study)
  g. History of positive trans-cranial Doppler studies (average greater than 200 cm/sec)
- Beta thalassemia major with significant disease manifestations as defined by the following criteria: Beta thalassemia genotype consistent with clinical diagnosis of beta thalassemia major (could include patients with E-beta thalassemia genotype) and requiring eight or more red blood cell (RBC) transfusions a year and iron chelation therapy. Younger patients who are at risk of transfusional iron overload but who have not yet initiated iron chelation therapy will be eligible.
- Adequate physical function as measured by the following criteria:
  a. Cardiac: Asymptomatic or, if symptomatic, then left ventricular ejection fraction at rest must be greater than 40% and must improve with exercise, or shortening fraction greater than 26%
  b. Hepatic: Less than 5 times the clinical baseline of AST and less than 2.5 times the clinical baseline mg/dL of total serum bilirubin (clinical baseline is determined from the mean of the four most recent test results)
  c. Renal: Serum creatinine within normal range for age or if serum creatinine is outside normal range for age then renal function (creatinine clearance or GFR) greater than 50% of the lower limit of normal (LLN) for age
  d. Pulmonary: Asymptomatic, or, if symptomatic, DLCO, FEV1, FRC (diffusion capacity) greater than 45% of predicted (corrected for hemoglobin); if unable to obtain PFT, oxygen saturation greater than 85% on room air
Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00029380

Locations

United States, California
- Children's Hospital, Oakland
  Oakland, California, United States, 94609
- Children's Hospital Oakland
  Oakland, California, United States, 94609

United States, District of Columbia
- Children's National Medical Center
  Washington, District of Columbia, United States

United States, Florida
- Nemours Children's Clinic
  Jacksonville, Florida, United States, 32207
- University of Miami Batchelor Children's Research Center
  Miami, Florida, United States, 33136

United States, Illinois
- Children's Memorial Hospital
  Chicago, Illinois, United States, 60614

United States, Louisiana
- Louisiana State University Children's Medical Center
  New Orleans, Louisiana, United States

United States, Michigan
- University of Michigan
  Ann Arbor, Michigan, United States, 48109

United States, New Jersey
- Hackensack University Medical Center
  Hackensack, New Jersey, United States, 07601

United States, North Carolina
- Duke University Medical Center Children's Hospital
  Durham, North Carolina, United States

United States, Pennsylvania
- Children's Hospital Philadelphia
  Philadelphia, Pennsylvania, United States, 19104

United States, South Carolina
- Medical University of South Carolina
  Charleston, South Carolina, United States, 29403

United States, Texas
- University of Texas Southwestern Medical Center - Dallas
  Dallas, Texas, United States, 75235
- Texas Transplant Institute
  San Antonio, Texas, United States, 78229

Canada, Quebec
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  Montreal, Quebec, Canada

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More Information

Publications:


Responsible Party: Bertram H. Lubin, Children's Hospital, Oakland
ClinicalTrials.gov Identifier: NCT00029380 History of Changes
Other Study ID Numbers: 141, U01 HL61877
Study First Received: January 10, 2002
Last Updated: September 30, 2008
Health Authority: United States: Federal Government

Additional relevant MeSH terms:

Anemia, Sickle Cell
Anemia, Hemolytic, Congenital
Beta-Thalassemia
Hematologic Diseases
Thalassemia
Hemoglobinopathies
Genetic Diseases, Inborn
Busulfan
Cyclophosphamide
Cyclosporins
Cyclosporine
Mycophenolate mofetil
Mycophenolic Acid
Immunosuppressive Agents
Immunologic Factors
Physiological Effects of Drugs
Pharmacologic Actions
Antineoplastic Agents, Alkylating
Alkylating Agents
Molecular Mechanisms of Pharmacological Action
Antineoplastic Agents
Therapeutic Uses
Myeloablative Agonists
Antirheumatic Agents
Enzyme Inhibitors
Antifungal Agents
Anti-Infective Agents
Dermatologic Agents