Stem Cell Transplantation for Hurler

Purpose

The purpose of this study is to determine the safety and engraftment of donor hematopoietic cells using this conditioning regimen in patients undergoing a hematopoietic (blood forming) cell transplant for Hurler syndrome, Maroteaux Lamy syndrome, Mannosidosis, or I-cell disease.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
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</thead>
<tbody>
<tr>
<td>Mucopolysaccharidosis I</td>
<td>Procedure: Stem Cell Transplant</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Mucopolysaccharidosis VI</td>
<td>Drug: Busulfan, Cyclophosphamide, ATG</td>
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<tr>
<td>Mannosidosis</td>
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<tr>
<td>Mucolipidosis Type II (I-cell Disease)</td>
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Study Type: Intervventional
Study Design: Endpoint Classification: Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Hematopoietic Stem Cell Transplantation for Hurler Syndrome, Maroteaux Lamy Syndrome (MPS VI), and Alpha Mannosidase Deficiency (Mannosidosis)

Resource links provided by NLM:

Genetics Home Reference related topics: alpha-mannosidosis mucolipidosis II alpha/beta mucopolysaccharidosis type I mucopolysaccharidosis type VI Schindler disease succinic semialdehyde dehydrogenase deficiency

Drug Information available for: Cyclophosphamide Busulfan

U.S. FDA Resources

Further study details as provided by Masonic Cancer Center, University of Minnesota:

Primary Outcome Measures:
- Mean Percentage of Donor Cells in Study Population (Chimerism). [Time Frame: at 21 days, 42 days, 60 days, 100 days, 6 months, and 1 year] [Designated as safety issue: No]
  - Donor-derived engraftment determined by restriction fragment length polymorphism (RFLP).

Secondary Outcome Measures:
- Number of Patients Surviving on Study [Time Frame: at 100 days, 1 year, and 3 years post transplant] [Designated as safety issue: Yes]
Number of patients surviving (alive) at specified timepoints.

- Number of Patients Who Failed Engraftment. [ Time Frame: Day 42 Post Transplant ] [ Designated as safety issue: Yes ]
  Toxicity (undesirable effect) of hematologic donor cell engraftment is determined by failure to engraft at Day 42.

- Number of Patients With Grade III-IV Acute Graft-versus-host Disease (aGVHD). [ Time Frame: Day 100 Post Transplant ]
  [ Designated as safety issue: Yes ]
  Toxicity (undesirable effect) of this stem cell transplant preparative regimen due to acute graft-versus-host disease.

Enrollment:
- 41
- Study Start Date: May 1999
- Study Completion Date: May 2010
- Primary Completion Date: May 2008 (Final data collection date for primary outcome measure)

### Arms

<table>
<thead>
<tr>
<th>Assigned Interventions</th>
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<tbody>
<tr>
<td>Procedure: Stem Cell Transplant</td>
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<tr>
<td>The purpose of hematopoietic cell transplantation is to introduce hematopoietic cells from a normal donor that contains the enzyme able to get rid of the substances that have accumulated in the body of patients with storage diseases. Hematopoietic cells can come from bone marrow, peripheral blood (i.e., the blood circulating in our body's blood vessels) or umbilical cord blood (i.e., blood taken from the umbilical cord after a baby is born and umbilical cord is cut).</td>
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<tr>
<td>Other Name: Bone Marrow Transplant</td>
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<tr>
<td>Drug: Busulfan, Cyclophosphamide, ATG</td>
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<tr>
<td>Prior to transplantation, subjects will receive BUSULFAN intravenously (IV) via the Hickman line twice daily for 4 days, CYCLOPHOSPHAMIDE intravenously via the Hickman line once a day for 4 days, and ANTI-THYMOCYTE GLOBULIN IV via the Hickman line twice daily for three days before the transplant. These three drugs are being given to help the new marrow &quot;take&quot; and grow. METHYLPREDNISOLONE will be given as a pre-medication for the ATG.</td>
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<tr>
<td>Other Name: Busulfex, Cytoxan, Thymoglobulin</td>
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### Detailed Description:

Prior to transplantation, subjects will receive Busulfan intravenously (IV) via the Hickman line four times daily for 4 days, Cyclophosphamide intravenously via the Hickman line once a day for 4 days, and Anti-Thymocyte Globulin IV via the Hickman line twice daily for three days before the transplant. These three drugs are being given to help the new marrow "take" and grow.

On the day of transplantation, the donor's hematopoietic cells will be transfused via central venous catheter.

After hematopoietic cell transplant, subjects will then receive two drugs, cyclosporin and either methylprednisolone or Mycophenolate Mofetil (MMF). Cyclosporin and methylprednisolone or MMF are given to help prevent the complication of graft-versus-host disease and to decrease the chance that the new donor cells will be rejected.

### Eligibility

- Genders Eligible for Study: Both
- Accepts Healthy Volunteers: No

### Criteria

#### Inclusion Criteria:

- Patients with Mucopolysaccharidosis, type I (e.g., Hurler syndrome), Maroteaux-Lamy syndrome (MPS VI), Alpha Mannosidosis, or mucolipidosis type II (I-cell disease) who have an HLA-identical or mismatched (at 1 antigen) related marrow, PBSC, or cord blood donor.
- Patients with Mucopolysaccharidosis, type I, Maroteaux-Lamy syndrome (MPS VI), Alpha Mannosidosis, or mucolipidosis type II (I-cell disease) who have an HLA-identical or HLA-1 antigen mismatched unrelated marrow, PBSC, or HLA-0-2 antigen mismatched umbilical cord blood donor.
- Patients with MPS type I, Maroteaux Lamy Syndrome (MPS VI), or mucopolysaccharidosis type II (I-cell disease) will have a mental developmental index within two standard deviations of the normal mean, as best as can be determined using Bayley scales of infant development or other standardized testing, recognizing that these may be affected by speech and/or hearing impairment.
- Adequate organ function:
  - Cardiac: ejection fraction >40%; no decompensated congestive heart failure or uncontrolled arrhythmia
  - Renal: serum creatinine <2.0 mg/dl
  - Hepatic: total bilirubin <3x Upper limits of normal transaminases < 5.0 x Upper limits of normal
- Signed consent.
Exclusion Criteria:

- Presence of major organ dysfunction (see above)
- Pregnancy
- Evidence of HIV infection or known HIV positive serology
- Patients or parents are psychologically incapable of undergoing BMT with associated strict isolation or documented history of medical non-compliance
- Patients >50 kg may be at risk for having cell doses below the goal of ≥ 10 x 10^6 CD 34 cells/kg and therefore will not be eligible to receive unrelated PBSCs.

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00176917

Locations

United States, Minnesota
Masonic Cancer Center, University of Minnesota
Minneapolis, Minnesota, United States, 55455

Sponsors and Collaborators
Masonic Cancer Center, University of Minnesota

Investigators
Principal Investigator: Paul Orchard, MD Masonic Cancer Center, University of Minnesota

More Information

No publications provided

Responsible Party: Masonic Cancer Center, University of Minnesota
ClinicalTrials.gov Identifier: NCT00176917 History of Changes
Obsolete Identifiers: NCT00005899
Other Study ID Numbers: UMN-MT1999-07, 0104M93821
Study First Received: September 12, 2005
Results First Received: July 28, 2009
Last Updated: November 6, 2012
Health Authority: United States: Institutional Review Board

Keywords provided by Masonic Cancer Center, University of Minnesota:
stem cell transplant
storage disease
ersors of metabolism

Additional relevant MeSH terms:
Mucolipidoses
Mucopolysaccharidosis I
Alpha-Mannosidosis
Mannosidase Deficiency Diseases
Mucopolysaccharidoses
Mucopolysaccharidosis VI
Bone Diseases, Metabolic
Bone Diseases
Musculoskeletal Diseases
Lysoosomal Storage Diseases, Nervous System
Brain Diseases, Metabolic, Inborn
Brain Diseases, Metabolic
Brain Diseases
Central Nervous System Diseases
Nervous System Diseases

Metabolism, Inborn Errors
Genetic Diseases, Inborn
Carbohydrate Metabolism, Inborn Errors
Lysoosomal Storage Diseases
Metabolic Diseases
Mucinoses
Connective Tissue Diseases
Busulfan
Cyclophosphamide
Immunosuppressive Agents
Immunologic Factors
Physiological Effects of Drugs
Pharmacologic Actions
Antineoplastic Agents, Alkylating
Alkylating Agents

ClinicalTrials.gov processed this record on September 22, 2013