Purpose

RATIONALE: A bone marrow or umbilical cord blood transplant may be able to replace blood-forming cells that were destroyed by chemotherapy. Giving combination chemotherapy before a donor stem cell transplant may make the transplant more likely to work. This may be an effective treatment for patients with high risk Fanconi's anemia.

PURPOSE: This clinical trial is studying how well combination chemotherapy works in treating high risk patients who are undergoing a donor stem cell transplant for Fanconi's anemia.

Condition | Intervention | Phase
--- | --- | ---

Study Type: Interventional
Study Design: Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Hematopoietic Stem Cell Transplantation in High Risk Patients With Fanconi Anemia MT2002-02
Primary Outcome Measures:

- Percent of Graft Failure [ Time Frame: Day 30 ] [ Designated as safety issue: No ]
  - Graft failure = ANC < 5 x 10^8/L by day 30.

Secondary Outcome Measures:

- Incidence of Acute and Chronic Graft-Versus-Host Disease [ Time Frame: Day 42 and 1 Year ] [ Designated as safety issue: No ]
- Incidence of Relapse [ Time Frame: 1 Year ] [ Designated as safety issue: No ]
- Incidence of Major Infections [ Time Frame: Day 1 through End of Treatment ] [ Designated as safety issue: Yes ]
- Transplant-Related Toxicity [ Time Frame: Day 100 ] [ Designated as safety issue: Yes ]
- Overall Survival [ Time Frame: 1 Year ] [ Designated as safety issue: No ]
  - cumulative proportion surviving

- Incidence of Chronic Graft-Versus-Host Disease [ Time Frame: Day 42 and 1 Year ] [ Designated as safety issue: No ]

Estimated Enrollment: 25
Study Start Date: March 2002
Estimated Study Completion Date: July 2015
Estimated Primary Completion Date: July 2014 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
</tr>
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<tbody>
<tr>
<td>Experimental: Transplant in Fanconi Anemia Patients</td>
<td></td>
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<tr>
<td>Hematopoietic stem cell transplantation (HSCT) in high risk patients with Fanconi Anemia (FA)- transplanted with related or unrelated CD34+ selected HSCT after Busulfan, Cytoxan, Fludarabine and Antithymocyte globulin.</td>
<td>Biological: anti-thymocyte globulin</td>
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<tr>
<td></td>
<td>Given 15 mg/kg/day intravenously every 12 hours on Days -5 through -1.</td>
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<td>Other Name: ATG</td>
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<td></td>
<td>Biological: filgrastim</td>
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<td></td>
<td>Given 5 mcg/kg/day intravenously on Day 1 (continue until absolute neutrophil count (ANC) ≥ 2.5 x 10^9/L)</td>
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<td>Other Name: G-CSF</td>
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<td></td>
<td>Drug: busulfan</td>
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<td></td>
<td>Busulfan 0.8 mg/kg intravenously (IV) every 12 hours on Days -7 and -6 (1.0 mg/kg IV if &lt; 4 years old)</td>
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<td>Drug: cyclophosphamide</td>
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<td>10 mg/kg intravenously (IV) on Days -5 through -2.</td>
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<td></td>
<td>Other Name: Cytoxan</td>
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<td></td>
<td>Drug: fludarabine phosphate</td>
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<td></td>
<td>35 mg/m^2 intravenously (IV) on Days -5 through -2.</td>
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<td>Other Name: Fludara</td>
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<td></td>
<td>Drug: methylprednisolone</td>
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<td></td>
<td>1 mg/kg intravenously (IV) every 12 hours on Days -5 through -1.</td>
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<td>Biological: Hematopoietic stem cell transplantation</td>
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<td>Infused on Day 0 - Donor bone marrow or umbilical cord blood will be collected in the usual sterile manner using established parameters determined by the National Marrow Donor Program.</td>
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<td>Other Name: HSCT</td>
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</tbody>
</table>

Detailed Description:

OBJECTIVES:

Primary

- Determine whether the incidence of neutrophil engraftment is acceptable in high-risk patients with Fanconi's anemia treated with busulfan, cyclophosphamide, fludarabine, and antithymocyte globulin followed by allogeneic hematopoietic stem cell transplantation.

Secondary

- Determine the tolerability of mycophenolate mofetil in these patients.
• Determine the incidence of acute and chronic graft-vs-host disease in patients treated with this regimen.
• Determine the incidence of major infections in patients with a history of major infections treated with this regimen.
• Determine the incidence of relapse in patients with refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, or acute myeloid leukemia treated with this regimen.
• Determine the probability of 1-year survival of patients treated with this regimen.

OUTLINE: Patients are stratified according to donor/recipient HLA type (identical vs other).

• Cytoreductive combination chemotherapy: Patients receive busulfan intravenously (IV) over 2 hours twice daily on days -7 and -6 and cyclophosphamide IV over 2 hours and fludarabine IV over 30 minutes once daily on days -5 to -2.
• Graft failure prophylaxis: Patients receive methylprednisolone IV twice daily on days -5 to 30 and anti-thymocyte globulin IV over 4-6 hours twice daily on days -5 to -1.
• Graft-vs-host disease prophylaxis: Patients receive cyclosporine IV over 2 hours twice daily on days -3 to 100 (if patient has a matched sibling donor) or days -3 to 180 (if patient has another donor type). Patients also receive mycophenolate mofetil orally or IV twice daily on days -3 to 45.
• Allogeneic hematopoietic stem cell transplantation (HSCT): Patients undergo allogeneic HSCT (using bone marrow or umbilical cord blood) on day 0. Patients receive filgrastim (G-CSF) subcutaneously beginning on day 1 and continuing until blood counts recover.

After completion of study treatment, patients are followed periodically for 3 years.

Eligibility

Ages Eligible for Study: up to 44 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Inclusion Criteria:

• Patients must be <45 years of age with a diagnosis of Fanconi anemia with:
  o Biallelic BRCA2 mutations, or
  o Aplastic anemia, or advanced myelodysplastic syndrome (MDS) (MDS with ≥5% blasts), or acute leukemia who are ineligible for total body irradiation. Aplastic anemia is defined as having at least one of the following (with or without cytogenetic abnormalities): platelet count <20 * 10^9/L, - absolute neutrophil count (ANC) <5 * 10^9/L, - Hgb <8 g/dL /
• Patients must have an HLA-A, B, DRB1 identical or 1 antigen mismatched related or unrelated BM donor or have an HLA-A, B, DRB1 identical, 1 antigen or 2 antigen mismatched related or unrelated umbilical cord blood (UCB) donor. Patients and donors will be typed for HLA-A and B using serological level typing and for DRB1 using high resolution molecular typing.
• Adequate major organ function including:
  o Cardiac: ejection fraction >45%
  o Hepatic: no clinical evidence of hepatic failure (e.g. coagulopathy, ascites, no cirrhosis)
  o Karnofsky performance status >70% or Lansky >50%
• Women of child bearing potential must be using adequate birth control and have a negative pregnancy test.

Exclusion Criteria:

• Active CNS leukemia at time of HSCT.
• Active uncontrolled infection within one week of hematopoietic stem cell transplant (HSCT).
• Pregnant or lactating female.

Donor Inclusion Criteria:

• Donor must be in good health based on review of systems and results of physical examination.
• Donor must have a normal hemoglobin, white count, platelet count and partial thromboplastin time (PTT), and a negative diepoxybutane (DEB) test.
• HIV-NAT negative, HTLV-1, HTLV-2 negative, Hepatitis B and C negative.
• Female donors of childbearing potential must have a negative pregnancy test.
• Unrelated donors must agree to peripheral blood stem cell (PBSC) donation

Donor Exclusion Criteria:

• Donor is a lactating female.

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00258427
Locations

United States, Minnesota

Masonic Cancer Center, University of Minnesota

Recruiting

Minneapolis, Minnesota, United States, 55455

Contact: Timothy Krepski 612-273-2800 tkrepsk1@fairview.org

Principal Investigator: Margaret MacMillan, M.D.

Sponsors and Collaborators

Masonic Cancer Center, University of Minnesota

Investigators

Principal Investigator: Margaret L. MacMillan, MD Masonic Cancer Center, University of Minnesota

More Information

No publications provided

Responsible Party: Masonic Cancer Center, University of Minnesota

ClinicalTrials.gov Identifier: NCT00258427  History of Changes

Other Study ID Numbers: 2002LS014, MT2002-02, 0202M18741

Study First Received: November 22, 2005

Last Updated: May 29, 2013

Health Authority: United States: Food and Drug Administration

Keywords provided by Masonic Cancer Center, University of Minnesota:

Fanconi anemia

Additional relevant MeSH terms:

Anemia  Busulfan
Fanconi Anemia  Cyclophosphamide
Fanconi Syndrome  Fludarabine monophosphate
Anemia, Hypoplastic, Congenital  Lenograstim
Anemia, Aplastic  Fludarabine
Hematologic Diseases  Methylprednisolone Hemisuccinate
Bone Marrow Diseases  Prednisolone
Genetic Diseases, Inborn  Methylprednisolone acetate
DNA Repair-Deficiency Disorders  Prednisolone acetate
Metabolic Diseases  Methylprednisolone
Kidney Diseases  Prednisolone hemisuccinate
Urologic Diseases  Prednisolone phosphate
Renal Tubular Transport, Inborn Errors  Vidarabine
Metabolism, Inborn Errors  Immunosuppressive Agents
Antilymphocyte Serum  Immunologic Factors

ClinicalTrials.gov processed this record on September 22, 2013