Trial record **2 of 100** for: Myelodysplastic syndromes and cord blood
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Combination Chemotherapy Followed By Donor Umbilical Cord Blood Transplant in Treating Infants With High-Risk Acute Leukemia or Myelodysplastic Syndromes

This study is currently recruiting participants.

Verified July 2013 by Masonic Cancer Center, University of Minnesota

Sponsor:
Masonic Cancer Center, University of Minnesota

Information provided by (Responsible Party):
Masonic Cancer Center, University of Minnesota

ClinicalTrials.gov Identifier:
NCT00357565

First received: July 26, 2006
Last updated: July 25, 2013
Last verified: July 2013
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

RATIONALE: Giving chemotherapy, such as busulfan, fludarabine, and melphalan, before a donor umbilical **cord blood** stem cell transplant helps stop the growth of abnormal or cancer cells and prepares the patient's bone marrow for the stem cells. When the healthy stem cells from a donor are infused into the patient they may help the patient's bone marrow make stem cells, red **blood** cells, white **blood** cells, and platelets. Sometimes the transplanted cells from a donor can make an immune response against the body's normal cells. Giving cyclosporine and mycophenolate mofetil may stop this from happening.

PURPOSE: This phase II trial is studying how well combination chemotherapy followed by a donor umbilical **cord blood** transplant works in treating infants with high-risk acute leukemia or **myelodysplastic syndromes**.

Condition	Intervention	Phase
Leukemia **Myelodysplastic Syndromes**	Biological: filgrastim Drug: busulfan Drug: cyclosporine Drug: fludarabine phosphate Drug: melphalan Drug: mycophenolate mofetil Procedure: umbilical **cord blood** transplantation	Phase 2

Study Type: Interventional
Study Design: Allocation: Non-Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Hematopoietic Cell Transplantation in the Treatment of Infant Leukemia Using Double Umbilical **Cord** Transplantation

Resource links provided by NLM:

Genetics Home Reference related topics: familial acute myeloid leukemia with mutated CEBPA

MedlinePlus related topics: Acute Myeloid Leukemia Anemia Cancer Leukemia Myelodysplastic Syndromes

Drug Information available for: Busulfan Melphalan Melphalan hydrochloride Fludarabine Mycophenolic acid Mycophenolate sodium Cyclosporine Fludarabine phosphate Mycophenolate mofetil hydrochloride Filgrastim Mycophenolate mofetil Lenograstim Granulocyte colony-stimulating factor

U.S. FDA Resources

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

Primary Outcome Measures:

- Incidence of Engraftment [Time Frame: Day 42 After Transplant] [Designated as safety issue: Yes]

  Defined as achieving donor derived neutrophil count >500/uL by day 42 in young children with leukemia or myelodysplastic syndrome treated with busulfan, melphalan and fludarabine followed by umbilical cord blood transplantation (UCBT) with two partially HLA matched units.

Secondary Outcome Measures:

- Incidence of transplant-related mortality (TRM) [Time Frame: at 6 months after transplant] [Designated as safety issue: Yes]

  defined as death due to transplant

- Pattern of chimerism [Time Frame: Day 21, Day 100, 6 Months, 1 Year, 2 Years] [Designated as safety issue: No]

  as measured by bone marrow samples (composed of two genetically distinct types of cells)

- Incidence of platelet engraftment [Time Frame: at 1 year after transplant] [Designated as safety issue: No]

  defined as platelet count > 50,000

- Incidence of acute graft-versus-host disease (GVHD) grade II-IV and grade III-IV [Time Frame: Day 100 After Transplant] [Designated as safety issue: No]

  Graft-versus-host disease (GVHD) is a common complication of allogeneic bone marrow transplantation in which functional immune cells in the transplanted marrow recognize the recipient as "foreign" and mount an immunologic attack.

- Incidence of chronic graft-versus-host disease (GVHD) [Time Frame: 1 Year After Transplant] [Designated as safety issue: No]

  Graft-versus-host disease (GVHD) is a common complication of allogeneic bone marrow transplantation in which functional immune cells in the transplanted marrow recognize the recipient as "foreign" and mount an immunologic attack.

- Incidence of relapse [Time Frame: at 1 and 2 years after transplant] [Designated as safety issue: No]

  defined using standard criteria (bone marrow blast count and cytogenetics).

- Overall survival [Time Frame: at 1 and 2 years after transplant] [Designated as safety issue: No]

  Alive after transplant.

- Developmental Outcomes [Time Frame: at 1, 2, and 5 years after transplant] [Designated as safety issue: No]

  Neuropsychological evaluation to assess baseline neurocognitive, adaptive, and behavioral functioning and presence of developmental delays

- Disease-free survival [Time Frame: at 1 and 2 years after transplant] [Designated as safety issue: No]

  defined as patients who are alive and in hematological remission.

Estimated Enrollment:	20
Study Start Date:	December 2005
Estimated Study Completion Date:	August 2015
Estimated Primary Completion Date:	August 2013 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Double Unit UCB Transplantation Patients that receive 2 units of umbilical **cord blood** transplantation (UCBT).	Biological: filgrastim All patients will receive G-CSF 5 mcg/kg/day intravenous (IV) (dose rounded to vial size) based on the actual body weight IV beginning on day +1 after umbilical **cord blood** (UCB) infusion. G-CSF will be administered daily until the absolute neutrophil count (ANC) exceeds 2.5 x 10^9/L for three consecutive days and then discontinued. If the ANC decreases to <1.0 x 10^9/L, G-CSF will be reinstituted. Other Name: G-CSF Drug: busulfan

	Administered 1.1 mg/kg if <12 kg intravenous (IV) every 6 hours (0.8 mg/kg if >12 kg IV every 6 hours on Days -8 through -5. Other Name: Busulfex Drug: cyclosporine Patients will receive cyclosporine (CSA) therapy beginning on day -3 maintaining a level of >200 ng/mL. For children < 40 kg the initial dose will be 2.5 mg/kg intravenous (IV) over 2 hours every 8 hours. Other Name: CSA Drug: fludarabine phosphate Administered 25 mg/m^2 intravenous (IV) over 60 minutes on Days -4 through -2. Other Name: Fludara Drug: melphalan Administered 60 mg/m^2 intravenous (IV) over 30 minutes on Days -4 through -2. Other Name: Alkeran Drug: mycophenolate mofetil All patients will begin mycophenolate mofetil (MMF) on day -3. Patients <45 kilograms will receive MMF at the dose of 15 mg/kg/dose every 8 hours (max dose 1gm/dose) orally or intravenously (PO or IV). Other Name: MMF Procedure: umbilical **cord blood** transplantation The product is infused via IV drip directly into the central line without a needle, pump or filter on Day 0.
Experimental: Single Unit UCB Transplantation Patients that receive one unit of umbilical **cord blood** transplantation (only if 2 adequate size and matched units are not available).	Biological: filgrastim All patients will receive G-CSF 5 mcg/kg/day intravenous (IV) (dose rounded to vial size) based on the actual body weight IV beginning on day +1 after umbilical **cord blood** (UCB) infusion. G-CSF will be administered daily until the absolute neutrophil count (ANC) exceeds 2.5 x 10^9/L for three consecutive days and then discontinued. If the ANC decreases to <1.0 x 10^9/L, G-CSF will be reinstituted. Other Name: G-CSF Drug: busulfan Administered 1.1 mg/kg if <12 kg intravenous (IV) every 6 hours (0.8 mg/kg if >12 kg IV every 6 hours on Days -8 through -5. Other Name: Busulfex Drug: cyclosporine Patients will receive cyclosporine (CSA) therapy beginning on day -3 maintaining a level of >200 ng/mL. For children < 40 kg the initial dose will be 2.5 mg/kg intravenous (IV) over 2 hours every 8 hours. Other Name: CSA Drug: fludarabine phosphate Administered 25 mg/m^2 intravenous (IV) over 60 minutes on Days -4 through -2. Other Name: Fludara Drug: melphalan Administered 60 mg/m^2 intravenous (IV) over 30 minutes on Days -4 through -2. Other Name: Alkeran Drug: mycophenolate mofetil All patients will begin mycophenolate mofetil (MMF) on day -3. Patients <45 kilograms will receive MMF at the dose of 15 mg/kg/dose every 8 hours (max dose 1gm/dose) orally or intravenously (PO or IV). Other Name: MMF Procedure: umbilical **cord blood** transplantation The product is infused via IV drip directly into the central line without a needle, pump or filter on Day 0.

Detailed Description:
OBJECTIVES:

Primary

- Determine the incidence of engraftment, defined as achieving donor-derived neutrophil count > 500/mm³ by day 42, in infants with high-risk acute myeloid leukemia, acute lymphoblastic leukemia, or myelodysplastic syndromes treated with a non-irradiation containing myeloablative conditioning regimen comprising busulfan, fludarabine, and melphalan followed by double umbilical cord blood transplantation (UCBT) with two partially HLA-matched units.

Secondary Objectives

- Determine the incidence of transplant-related mortality (TRM) at 6 months after UCBT
- Evaluate pattern of chimerism after double UCBT
- Determine the incidence of platelet engraftment at 1 year after UCBT
- Determine the incidence of acute graft-versus-host disease (GVHD) grade II-IV and grade III-IV at day 100 after UCBT

- Evaluate the developmental outcome after UCBT

Transplant Related Objectives

- Determine the incidence of chronic GVHD at 1 year after UCBT
- Determine the survival and disease free survival at 1 and 2 years after UCBT
- Determine the incidence relapse at 1 and 2 years after UCBT

Eligibility

Ages Eligible for Study: up to 2 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Patients on this trial will receive two partially HLA matched umbilical cord blood (UCB) units, if available (treatment arm 1). If two units are not available, then single UCB unit transplantation will be allowed (on treatment arm 2).
- UCB units will be selected according to the University Of Minnesota UCB Graft Selection Algorithm. The unrelated cord blood donor(s) must be 4-6/6 HLA-A, B, DRB1 matched with the recipient (HLA matching using molecular techniques: A and B to antigen level resolution and DR to allele level resolution).
- Patients aged ≤ 2 years at diagnosis (not age of transplant) with hematological malignancy as detailed below:
  - Acute myeloid leukemia: high risk CR1 as evidenced by:
    - High risk cytogenetics t(4;11) or other MLL rearrangements; chromosome 5, 7, or 19 abnormalities; complex karyotype (>5 distinct changes); ≥ 2 cycles to obtain complete response (CR); CR2 or higher; Preceding myelodysplastic syndrome (MDS); All patients must be in CR or early relapse (i.e., <15% blasts in BM).
    - Acute lymphocytic leukemia: high risk CR1 as evidenced by: High-risk cytogenetic: t(4;11) or other MLL rearrangements; hypodiploid; t(9;22); >1 cycle to obtain CR; CR2 or higher; All patients must be in CR as defined by hematological recovery, AND <5% blasts by light microscopy within the bone marrow with a cellularity of ≥15%.
  - Myelodysplasia (MDS) IPSS Int-2 or High risk (i.e. RAEB, RAEBt) or refractory anemia with severe pancytopenia or high risk cytogenetics. Blasts must be < 10% by a representative bone marrow aspirate morphology.
  - Minimal Residual Disease (MRD): Patients with evidence of minimal residual disease at the completion of therapy or evidence of rising MRD while on therapy. MRD will be defined by either flow cytometry (>0.1% residual cells in the blast gate with immune phenotype of original leukemic clone), by molecular techniques (PCR or FISH) or conventional cytogenetics (g-banding).
- Recipients must have a Lansky score > or = 50% and have acceptable organ function defined as:
  - Renal: glomerial filtration rate > 60ml/min/1.73m^2
  - Hepatic: bilirubin, AST/ALT, ALP < 5 x upper limit of normal,
  - Pulmonary function: oxygen saturation >92%
  - Cardiac: left ventricular ejection fraction > 45%.
- Voluntary written informed consent before performance of any study-related procedure not part of normal medical care.

Exclusion Criteria:

- Active infection at time of transplantation (including active infection with Aspergillus or other mold within 30 days).
- History of HIV infection
- Prior myeloablative transplant within the last 6 months.
- Evidence of active extramedullary disease (including central nervous system leukemia).

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00357565

Contacts

Contact: Michael R. Verneris, M.D. 612-626-2961 verneris@umn.edu

Locations

United States, Minnesota

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Principal Investigator: Michael R. Verneris, M.D.

Sponsors and Collaborators

Masonic Cancer Center, University of Minnesota

Investigators

Principal Investigator: Michael R. Verneris, MD Masonic Cancer Center, University of Minnesota

More Information

Additional Information:

Clinical trial summary from the National Cancer Institute's PDQ® database

No publications provided

Responsible Party:	Masonic Cancer Center, University of Minnesota
ClinicalTrials.gov Identifier:	NCT00357565 History of Changes
Other Study ID Numbers:	2005LS075, UMN-MT2005-25, UMN-0511M77206
Study First Received:	July 26, 2006
Last Updated:	July 25, 2013
Health Authority:	United States: Institutional Review Board

Keywords provided by Masonic Cancer Center, University of Minnesota:

previously treated **myelodysplastic syndromes**
secondary **myelodysplastic syndromes**
de novo **myelodysplastic syndromes**
childhood **myelodysplastic syndromes**
childhood acute myeloid leukemia in remission
recurrent childhood acute myeloid leukemia
secondary acute myeloid leukemia
childhood acute lymphoblastic leukemia in remission
refractory anemia with excess blasts in transformation
refractory anemia with excess blasts
refractory anemia

Additional relevant MeSH terms:

Myelodysplastic Syndromes
Preleukemia
Leukemia
Neoplasms by Histologic Type
Neoplasms
Bone Marrow Diseases
Hematologic Diseases
Precancerous Conditions
Busulfan
Cyclosporins
Cyclosporine
Melphalan
Mycophenolate mofetil
Fludarabine monophosphate
Fludarabine
Mycophenolic Acid
Lenograstim
Vidarabine
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
Enzyme Inhibitors
Antifungal Agents

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