Trial record **1 of 100** for: Myelodysplastic syndromes and cord blood
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Donor Umbilical Cord Blood Transplant With or Without Ex-Vivo Expanded Cord Blood Progenitor Cells in Treating Patients With Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia, Chronic Myelogenous Leukemia, or Myelodysplastic Syndromes

This study is currently recruiting participants.

Verified July 2013 by Fred Hutchinson Cancer Research Center

Sponsor:
Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium

Collaborators:
National Heart, Lung, and **Blood** Institute (NHLBI)
National Cancer Institute (NCI)

Information provided by:
Fred Hutchinson Cancer Research Center

ClinicalTrials.gov Identifier:
NCT01690520

First received: September 19, 2012
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Last verified: July 2013
History of Changes

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

Purpose

This randomized phase II trial studies how well giving donor umbilical **cord blood** transplant with or without ex-vivo expanded **cord blood** progenitor cells works in treating patients with acute myeloid leukemia, acute lymphoblastic leukemia, chronic myelogenous leukemia, or **myelodysplastic syndromes**. Giving chemotherapy and total-body irradiation before a donor umbilical **cord blood** transplant helps stop the growth of cancer cells. It may also stop the patient's immune system from rejecting the donor's cells. When the healthy stem cells and ex-vivo expanded **cord blood** progenitor cells are infused into the patient they may help the patient's bone marrow make stem cells, red **blood** cells, white **blood** cells, and platelets. It is not yet known whether giving donor umbilical **cord blood** transplant plus ex-vivo expanded **cord blood** progenitor cells is more effective than giving a donor umbilical **cord blood** transplant alone.

Condition	Intervention	F
Accelerated Phase Chronic Myelogenous Leukemia Acute Myeloid Leukemia With Multilineage Dysplasia Following **Myelodysplastic Syndrome** Adult Acute Lymphoblastic Leukemia in Remission Adult Acute Myeloid Leukemia in Remission Adult Acute Myeloid Leukemia With 11q23 (MLL) Abnormalities Adult Acute Myeloid Leukemia With Del(5q) Adult Acute Myeloid Leukemia With Inv(16)(p13;q22) Adult Acute Myeloid Leukemia With t(15;17)(q22;q12) Adult Acute Myeloid Leukemia With t(16;16)(p13;q22) Adult Acute Myeloid Leukemia With t(8;21)(q22;q22) Childhood Acute Lymphoblastic Leukemia in Remission Childhood Acute Myeloid Leukemia in Remission Childhood Chronic Myelogenous Leukemia Chronic Phase Chronic Myelogenous Leukemia de Novo **Myelodysplastic Syndromes** Previously Treated **Myelodysplastic Syndromes** Refractory Anemia Refractory Anemia With Excess Blasts Refractory Anemia With Excess Blasts in Transformation Relapsing Chronic Myelogenous Leukemia Secondary Acute Myeloid Leukemia	Procedure: ex vivo-expanded **cord blood** progenitor cell infusion Procedure: umbilical **cord blood** transplantation Procedure: double-unit umbilical **cord blood** transplantation Drug: fludarabine phosphate Drug: cyclophosphamide Radiation: total-body irradiation Drug: cyclosporine Drug: mycophenolate mofetil	F

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

Official Title: Multi-center, Open-label Randomized Study of Single or Double Myeloablative **Cord Blood** Transplantation With or Without Infusion of Off-The-shelf ex Vivo Expanded Cryopreserved **Cord Blood** Progenitor Cells in Patients With Hematologic Malignancies

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 Chronic Lymphocytic Leukemia Chronic Myeloid Leukemia Leukemia Myelodysplastic Syndromes

Drug Information available for: Cyclophosphamide Fludarabine Mycophenolic acid Mycophenolate sodium Cyclosporine Fludarabine phosphate Mycophenolate mofetil hydrochloride Mycophenolate mofetil

U.S. FDA Resources

Further study details as provided by Fred Hutchinson Cancer Research Center:

Primary Outcome Measures:

- Time to engraftment (ANC greater than or equal to 500) in both arms (standard myeloablative CBT with and without off-the-shelf expanded **cord blood** progenitors) [Time Frame: Up to 2 years] [Designated as safety issue: No]

  The log-rank test will be used. Groups will be compared using Gray's test.

Secondary Outcome Measures:

- Time to engraftment, defined as the first of 2 consecutive days in which ANC is at least 500 [Time Frame: Up to 2 years] [Designated as safety issue: No]

  Groups will be compared using Gray's test.

- Relative contribution to engraftment of the expanded **cord blood** product and the unmanipulated **cord blood** unit(s) in early and long-term engraftment, determined by frequent determination of donor chimerism in the peripheral **blood** [Time Frame: Up to 2 years] [Designated as safety issue: No]

  Groups will be compared using Gray's test.

- Time to ANC greater than or equal to 100 [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Time to ANC greater than or equal to 500 [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Time to platelet engraftment (20k and 50k) [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Duration of initial hospitalization [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Incidence of infectious complications [Time Frame: Up to 100 days post transplant] [Designated as safety issue: No]
- Non-relapse mortality (NRM) [Time Frame: Up to 1 year] [Designated as safety issue: No]
- Incidence and severity of acute and chronic GVHD [Time Frame: Up to 2 years] [Designated as safety issue: Yes]
- Infusional toxicity greater than or equal to grade 3 [Time Frame: Day 0 (day of transplant)] [Designated as safety issue: Yes]

  Toxicities will be graded using the NCI Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0.

- Graft failure (primary and secondary) [Time Frame: Up to 2 years] [Designated as safety issue: Yes]
- Kinetics of immune system recovery as measured by T and B cell subsets, T cell receptor excision circles (TREC), spectratyping and T cell receptor (TCR) sequencing [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Death without engraftment [Time Frame: Up to 2 years] [Designated as safety issue: No]

  Groups will be compared using Gray's test and log-rank test.

Estimated Enrollment:	160
Study Start Date:	December 2012
Estimated Primary Completion Date:	October 2017 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Active Comparator: Arm I (standard of care) CONDITIONING REGIMEN: Patients receive fludarabine phosphate IV over 30 minutes on days -8 to -6 and cyclophosphamide IV on days -7 to -6. Patients also undergo TBI BID on days -4 to -1. TRANSPLANT: Patients undergo single-unit or double-unit unmanipulated UCB transplant on day 0. GVHD PROPHYLAXIS: Patients receive cyclosporine IV over 1 hour twice daily (adults) or three times a day (children) on days -3 to 100 with taper beginning on day 101. Patients also receive MMF IV three times a day on days 0-7 then may receive MMF orally three times a day. Patients remain on MMF three times a day for a minimum of 30 days, and then may begin a taper if there is no evidence of GVHD and are well-engrafted from one donor unit.	Procedure: umbilical **cord blood** transplantation Undergo single-unit unmanipulated umbilical **cord blood** transplant Other Names: • **cord blood** transplantation • transplantation, umbilical **cord blood**

	• UCB transplantation Procedure: double-unit umbilical **cord blood** transplantation Undergo double-unit unmanipulated umbilical **cord blood** transplant Drug: fludarabine phosphate Given IV Other Names: • 2-F-ara-AMP • Beneflur • Fludara Drug: cyclophosphamide Given IV Other Names: • CPM • CTX • Cytoxan • Endoxan • Endoxana Radiation: total-body irradiation Undergo TBI Other Name: TBI Drug: cyclosporine Given IV Other Names: • ciclosporin • cyclosporin • cyclosporin A • CYSP • Sandimmune Drug: mycophenolate mofetil Given IV or PO Other Names: • Cellcept • MMF
Experimental: Arm II (experimental) CONDITIONING REGIMEN: Patients receive fludarabine phosphate IV and cyclophosphamide IV, and undergo TBI as in Standard of Care Arm. TRANSPLANT: Patients undergo single-unit or double-unit unmanipulated UCB transplant on day 0. Patients also undergo infusion of ex vivo-expanded **cord blood** progenitor cell infusion at least 4 hours after completion of UCB transplant. GVHD PROPHYLAXIS: Patients receive cyclosporine IV and mycophenolate mofetil IV or PO as in Standard of Care Arm.	Procedure: ex vivo-expanded **cord blood** progenitor cell infusion Given IV Procedure: umbilical **cord blood** transplantation Undergo single-unit unmanipulated umbilical **cord blood** transplant Other Names: • **cord blood** transplantation • transplantation, umbilical **cord blood** • UCB transplantation

	Procedure: double-unit umbilical **cord blood** transplantation Undergo double-unit unmanipulated umbilical **cord blood** transplant Drug: fludarabine phosphate Given IV Other Names: • 2-F-ara-AMP • Beneflur • Fludara Drug: cyclophosphamide Given IV Other Names: • CPM • CTX • Cytoxan • Endoxan • Endoxana Radiation: total-body irradiation Undergo TBI Other Name: TBI Drug: cyclosporine Given IV Other Names: • ciclosporin • cyclosporin • cyclosporin A • CYSP • Sandimmune Drug: mycophenolate mofetil Given IV or PO Other Names: • Cellcept • MMF

Detailed Description:
PRIMARY OBJECTIVES:

I. Compare the time to neutrophil engraftment (absolute neutrophil count [ANC] >= 500) in patients receiving a standard of care myeloablative cord blood transplant (CBT) augmented with an off-the-shelf pre-expanded and cryopreserved cord blood product to those who do not receive the product.

SECONDARY OBJECTIVES:

I. Provide initial data on clinical and economic benefit, such as time to platelet engraftment, duration of initial hospitalization, day 200 transplant related mortality (TRM), death without engraftment, and incidence of severe infections in the first 100 days post transplant.

II. The kinetics of immune system recovery will also be evaluated in both arms.

OUTLINE: Patients are randomized to 1 of 2 treatment arms.

Standard of Care Arm:

CONDITIONING REGIMEN: Patients receive fludarabine phosphate intravenously (IV) over 30 minutes on days -8 to -6 and cyclophosphamide IV on days -7 to -6. Patients also undergo total-body irradiation (TBI) twice daily (BID) on days -4 to -1.

TRANSPLANT: Patients undergo single-unit or double-unit unmanipulated umbilical cord blood (UCB) transplant on day 0.

GRAFT-VERSUS-HOST DISEASE (GVHD) PROPHYLAXIS: Patients receive cyclosporine IV over 1 hour twice daily (adults) or three times a day (children) on days -3 to 100 with taper beginning on day 101. Patients also receive mycophenolate mofetil (MMF) IV three times a day on days 0-7 then may receive MMF orally (PO) three times a day. Patients remain on MMF three times a day for a minimum of 30 days, and then may begin taper if there is no evidence of graft-versus-host disease (GVHD) and are well-engrafted from one donor unit.

Experimental Arm:

CONDITIONING REGIMEN: Patients receive fludarabine phosphate IV and cyclophosphamide IV, and undergo TBI as in Standard of Care Arm.

TRANSPLANT: Patients undergo single-unit or double-unit unmanipulated UCB transplant on day 0. Patients also receive an infusion of ex vivo-expanded cord blood progenitors at least 4 hours after completion of UCB transplant.

GVHD PROPHYLAXIS: Patients receive cyclosporine IV and mycophenolate mofetil IV or PO as in Standard of Care Arm.

After completion of study treatment, patients are followed up periodically for 2 years.

Eligibility

Ages Eligible for Study:	6 Months to 45 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Acute myeloid leukemia:
  - High risk first complete remission (CR1) as evidenced by preceding myelodysplastic syndromes (MDS), high risk cytogenetics (for example, monosomy 5 or 7, or as defined by referring institution treatment protocol), >= 2 cycles to obtain complete remission (CR), erythroblastic or megakaryocytic leukemia; >= second complete remission (CR2)
  - All patients must be in CR as defined by hematologic recovery and < 5% blasts by morphology within the bone marrow and a cellularity of >= 15% for age
  - Patients in which adequate marrow/biopsy specimens cannot be obtained to determine remission status by morphologic assessment, but have fulfilled criteria of remission by flow cytometry, recovery of peripheral blood counts with no circulating blasts, and/or normal cytogenetics (if applicable) may still be eligible; reasonable attempts must be made to obtain an adequate specimen for morphologic assessment, including possible repeat procedures; these patients must be discussed with the principal investigator prior to enrollment
- Acute Lymphoblastic Leukemia
  - High risk CR1 [for example, but not limited to: t(9;22), t(1;19), t(4;11) or other mixed-lineage leukemia (MLL) rearrangements, hypodiploid]; greater than 1 cycle to obtain CR; CR2 or greater
  - All patients must be in CR as defined by hematologic recovery and < 5% blasts by morphology within the bone marrow and a cellularity of >= 15% for age
  - Patients in which adequate marrow/biopsy specimens cannot be obtained to determine remission status by morphologic assessment, but have fulfilled criteria of remission by flow cytometry, recovery of peripheral blood counts with no circulating blasts, and/or normal cytogenetics (if applicable) may still be eligible; reasonable attempts must be made to obtain an adequate specimen for morphologic assessment, including possible repeat procedures; these patients must be discussed with the principal investigator prior to enrollment
- Chronic myelogenous leukemia excluding refractory blast crisis; to be eligible in first chronic phase (CP1) patient must have failed or be intolerant to tyrosine kinase inhibitor therapy
- Myelodysplasia (MDS) International Prognostic Scoring System (IPSS) intermediate (Int)-2 or High risk (i.e., refractory anemia with excess blasts [RAEB], refractory anemia with excess blasts in transformation [RAEBt]) or refractory anemia with severe pancytopenia or high risk cytogenetics; blasts must be < 10% by a representative bone marrow aspirate morphology
- Karnofsky (>= 16 years old) >= 70 or Eastern Cooperative Oncology Group (ECOG) 0-1
- Lansky (< 16 years old) >= 60
- Adults: calculated creatinine clearance must be > 60 mL and serum creatinine =< 2 mg/dL
- Children (< 18 years old): calculated creatinine clearance must be > 60 mL/min
- Total serum bilirubin must be < 3mg/dL unless the elevation is thought to be due to Gilbert's disease or hemolysis
- Transaminases must be < 3 x the upper limit of normal
- Diffusing capacity of the lung for carbon monoxide (DLCO) corrected > 60% normal
- For pediatric patients unable to perform pulmonary function tests, oxygen (O2) saturation > 92% on room air
- May not be on supplemental oxygen
- Left ventricular ejection fraction > 45%
- OR shortening fraction > 26%
- Ability to understand and the willingness to sign a written informed consent document

Exclusion Criteria:

- Uncontrolled viral or bacterial infection at the time of study enrollment
- Active or recent (prior 6 month) invasive fungal infection without infectious disease (ID) consult and approval
- History of human immunodeficiency virus (HIV) infection
- Pregnant or breastfeeding
- Prior myeloablative transplant containing full dose TBI (greater than 8 Gy)
- Any prior myeloablative transplant within the last 6 months
- Extensive prior therapy including > 12 months alkylator therapy or > 6 months alkylator therapy with extensive radiation
- CNS leukemic involvement not clearing with intrathecal chemotherapy and/or cranial radiation prior to initiation of conditioning

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01690520

Locations

United States, California

City of Hope Medical Center — **Not yet recruiting**
Duarte, California, United States, 91010
Contact: Chatchada Karanes 626-359-8111
Principal Investigator: Chatchada Karanes

United States, Colorado

University of Colorado — **Recruiting**
Denver, Colorado, United States, 80217-3364
Contact: Jonathan A. Gutman 720-848-0644
Principal Investigator: Jonathan A. Gutman

United States, Massachusetts

Dana-Farber Harvard Cancer Center — **Not yet recruiting**
Boston, Massachusetts, United States, 02115
Contact: Christine N. Duncan 617-632-6255
Principal Investigator: Christine N. Duncan

United States, North Carolina

Duke University Medical Center — **Not yet recruiting**
Durham, North Carolina, United States, 27710
Contact: Joanne Kurtzberg 919-668-1100
Principal Investigator: Joanne Kurtzberg

United States, Tennessee

Monroe Carell Jr. Children's Hospital at Vanderbilt — **Active, not recruiting**
Nashville, Tennessee, United States, 37232

United States, Washington

Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium — **Recruiting**
Seattle, Washington, United States, 98109
Contact: Colleen Delaney 206-667-1385
Principal Investigator: Colleen Delaney

Sponsors and Collaborators

Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium

National Heart, Lung, and **Blood** Institute (NHLBI)

National Cancer Institute (NCI)

Investigators

Principal Investigator: Colleen Delaney Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium

More Information

No publications provided

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Health Authority:	United States: Food and Drug Administration

Additional relevant MeSH terms:

Myelodysplastic Syndromes
Preleukemia
Congenital Abnormalities
Anemia
Anemia, Refractory
Anemia, Refractory, with Excess of Blasts
Leukemia
Leukemia, Lymphocytic, Chronic, B-Cell
Leukemia, Lymphoid
Precursor Cell Lymphoblastic Leukemia-Lymphoma
Leukemia, Myeloid, Acute
Leukemia, Myeloid
Leukemia, Myeloid, Accelerated Phase
Leukemia, Myelogenous, Chronic, BCR-ABL Positive
Leukemia, Myeloid, Chronic-Phase
Anemia, Aplastic
Hematologic Diseases
Bone Marrow Diseases
Neoplasms by Histologic Type
Neoplasms
Leukemia, B-Cell
Lymphoproliferative Disorders
Lymphatic Diseases
Immunoproliferative Disorders
Immune System Diseases
Myeloproliferative Disorders
Precancerous Conditions
Cyclophosphamide
Cyclosporins
Cyclosporine

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