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Laboratory-Treated Donor Cord Blood Cell Infusion Following Combination Chemotherapy in Treating Younger Patients With Relapsed or Refractory Acute Myeloid Leukemia

This study is currently recruiting participants.

Verified August 2013 by Fred Hutchinson Cancer Research Center

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

Collaborators:
National Cancer Institute (NCI)
Seattle Children's Research Institute Center for Clinical and Translational Research
Bayley Family Foundation

Information provided by:
Fred Hutchinson Cancer Research Center

ClinicalTrials.gov Identifier:
NCT01701323

First received: October 3, 2012
Last updated: August 13, 2013
Last verified: August 2013
History of Changes

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

Purpose

This pilot clinical trial studies infusion of laboratory-grown donor **cord blood** cells following combination chemotherapy in treating younger patients with relapsed or refractory **acute myeloid leukemia**. Chemotherapy drugs work in different ways to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. Chemotherapy also kills healthy infection-fighting cells, increasing the risk of infection. The infusion of laboratory-grown **cord blood** cells may be able to replace **blood**-forming cells that were destroyed by chemotherapy. This may decrease the risk of infection following chemotherapy, and allow for more chemotherapy to be given so that more cancer cells are killed.

Condition	Intervention
Acute Leukemias of Ambiguous Lineage 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) Recurrent Adult **Acute Myeloid Leukemia** Recurrent Childhood **Acute Myeloid Leukemia**	Biological: filgrastim Drug: fludarabine phosphate Drug: cytarabine Procedure: ex vivo-expanded **cord blood** progenitor cell infusion

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

Official Title: Pilot Study Evaluating the Use of Ex Vivo Expanded **Cord Blood** Progenitors as Supportive Care Following Induction Chemotherapy (FLAG) in Patients With Relapsed/Refractory AML

Resource links provided by NLM:

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

MedlinePlus related topics: Acute Myeloid Leukemia Cancer Leukemia

Drug Information available for: Cytarabine Fludarabine Fludarabine phosphate Filgrastim Lenograstim Granulocyte colony-stimulating factor

U.S. FDA Resources

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

Primary Outcome Measures:

- Occurrence of grade > 3 infusional toxicity with administration of ex vivo expanded **cord blood** therapy according to the National Cancer Institute (NCI) Common Toxicity Criteria for Adverse Events (CTCAE) version 4.0 [Time Frame: Up to 2 years] [Designated as safety issue: Yes]
- Occurrence of transfusion associated graft-versus-host disease (GVHD) [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Incidence of platelet refractoriness in the presence of alloimmunization as a direct result of ex vivo expanded **cord blood** product infusion [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Delayed marrow recovery [Time Frame: After day 42] [Designated as safety issue: No]
- Rates of treatment related mortality [Time Frame: Up to 2 years] [Designated as safety issue: No]

Secondary Outcome Measures:

- Time to neutrophil recovery (absolute neutrophil count [ANC] > 100/ul and 500/ul) [Time Frame: Up to 2 years] [Designated as safety issue: No]
- In vivo persistence of ex vivo expanded cellular therapy by peripheral **blood** cell sorted deoxyribonucleic acid (DNA) chimerisms of the cluster of differentiation **myeloid** and lymphoid cell lineages as well as whole marrow chimerisms [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Incidence of grade 3 or 4 infections per NCI CTCAE version 4 in the neutropenic period following FLAG administration [Time Frame: Up to 2 years] [Designated as safety issue: Yes]
- Incidence of grade > 3 chemotherapy-related toxicity in the first 30 days following FLAG therapy defined by NCI CTCAE version 4.0 [Time Frame: Up to 30 days] [Designated as safety issue: Yes]
- Rate of CR [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Rate of CRi [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Rate of CRp [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Overall survival [Time Frame: Up to 2 years] [Designated as safety issue: No]
- **Leukemia**-free survival [Time Frame: Up to 2 years] [Designated as safety issue: No]

Estimated Enrollment:	15
Study Start Date:	December 2012
Estimated Primary Completion Date:	May 2014 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Treatment (ex vivo expanded **cord blood** progenitors) Patients receive filgrastim SC or IV on days 1-7, fludarabine phosphate IV over 30 minutes on days 2-6, cytarabine IV over 4 hours on days 2-6, and ex vivo-expanded **cord blood** progenitor cells IV over 30 minutes on day 8.	Biological: filgrastim Given SC or IV Other Names: • G-CSF • Neupogen Drug: fludarabine phosphate Given IV Other Names: • 2-F-ara-AMP • Beneflur • Fludara Drug: cytarabine Given IV Other Names: • ARA-C • arabinofuranosylcytosine

	• arabinosylcytosine • Cytosar-U • cytosine arabinoside Procedure: ex vivo-expanded **cord blood** progenitor cell infusion Given IV

Detailed Description:
PRIMARY OBJECTIVES:

I. Assess the safety of infusing "off-the-shelf" non-human leukocyte antigen (HLA) matched expanded cord blood cells as supportive care following administration of FLAG (fludarabine phosphate, cytarabine, and filgrastim) reinduction chemotherapy in pediatric and young adult patients with relapsed/refractory acute myeloid leukemia (AML).

SECONDARY OBJECTIVES:

I. Assess the kinetics of autologous recovery when compared to historical cohorts.

II. Assess the ability of the product to provide transient myeloid engraftment/recovery.

III. Examine the in vivo persistence of the ex vivo expanded cord blood cells by determining the kinetics and durability of potential engraftment.

IV. Estimate the incidence of clinically significant infections (e.g. bacterial, viral, or fungal) observed in patients treated with FLAG reinduction chemotherapy followed by "off-the-shelf" non-HLA matched expanded cord blood cells.

V. Assess the percentage of patients that achieve complete remission (CR)/complete remission with incomplete blood count recovery (CRi)/complete remission with partial recovery of platelet count (CRp) with this therapy approach.

VI. Assess long term efficacy (overall survival [OS]/disease free survival [DFS]) of FLAG reinduction chemotherapy followed by "off-the-shelf" non HLA matched expanded cord blood cells in pediatric relapsed AML patients during long term follow up.

OUTLINE:

Patients receive filgrastim subcutaneously (SC) or intravenously (IV) on days 1-7, fludarabine phosphate IV over 30 minutes on days 2-6, cytarabine IV over 4 hours on days 2-6, and ex vivo-expanded cord blood progenitor cells IV over 30 minutes on day 8.

After completion of study treatment, patients are followed up every 6 months for 2 years.

Eligibility

Ages Eligible for Study:	6 Months to 30 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria
Inclusion Criteria:

- Patients must have a diagnosis of AML or acute leukemia of ambiguous lineage according to World Health Organization (WHO) classification with >= 5% of disease in bone marrow (BM), with or without extramedullary disease or biopsy-proven isolated myeloid sarcoma (myeloblastoma, chloroma, including leukemia cutis) in the absence of marrow involvement
- AML or acute leukemia of ambiguous lineage:
  - If relapse AML or acute leukemia of ambiguous lineage:
    - Must have a prior diagnosis of AML or acute leukemia of ambiguous lineage and be in 1st or greater relapse
    - Must not have received prior reinduction therapy for this relapse
  - If primary refractory AML or acute leukemia of ambiguous lineage:
    - Must have had a prior diagnosis of AML or acute leukemia of ambiguous lineage and
    - Must not have received more than 3 previous induction attempts
  - Patients meeting above criteria are eligible regardless of central nervous system (CNS) classification
- Recipients of prior allogeneic hematopoietic stem cell transplantation are eligible if they have quiescent graft versus host disease (GVHD) whether or not they are receiving immunosuppressive therapy
- Must have a Lansky or Karnofsky performance status of >= 50; use Karnofsky for patients > 16 years of age and Lansky for patients =< 16 years of age
- Patients must have recovered from the acute toxicity of all prior chemotherapy; patients may not have received cytotoxic chemotherapy within 2 weeks of first dose of G-CSF (filgrastim) therapy, with exception of hydroxyurea, which is allowed for up to 24 hours prior to first dose of G-CSF, and intrathecal chemotherapy, which is allowed prior to, or in the 1st 72 hours after start of G-CSF therapy
- The following amounts of time must have elapsed prior to entry on study:

- 2 weeks from local radiation therapy (XRT)
- 8 weeks from prior craniospinal or if > 50% of the pelvis has been irradiated
- 6 weeks must have elapsed if other bone marrow radiation has occurred

- Creatinine within normal range for age (per institutional defined lab value ranges)
- Direct bilirubin =< 1.5 upper limit of normal (ULN) age unless elevation thought to be due or hepatic infiltration by the hematologic malignancy
- Alanine aminotransferase (ALT) < 5 x ULN age
- Adequate cardiac function as defined as shortening fraction of > 27% OR ejection fraction of > 50%
- Patients must have a calculated QT (QTc) interval < 450 ms on baseline echocardiogram
- Patients must demonstrate a respiratory rate that is within normal limits for age, measured when afebrile and at rest (measured for a full minute) and pulse oximetry > 93% on room air
- Signed informed consent
- Patient must have a life expectancy of at least 2 months
- Females of childbearing potential must have a negative serum pregnancy test performed within 7 days prior to the start of treatment
- Females of childbearing potential and males should agree to use adequate contraception (barrier method of birth control) prior to study entry and for the duration of study participation

Exclusion Criteria:

- Recipients of prior allogeneic hematopoietic stem cell transplant (HSCT) with active acute or chronic GVHD
- Patients with history of Down's syndrome, Fanconi anemia or other known marrow failure condition
- Patients currently receiving other investigational drugs are not eligible
- Current concomitant chemotherapy, radiation therapy, or immunotherapy other than as specified in the protocol with the exception of intrathecal chemotherapy; this includes the tyrosine kinase inhibitor sorafenib which must not be initiated until patient demonstrates count recovery
- Patients with a systemic fungal, bacterial, viral, or other infection not controlled despite appropriate antibiotics or other treatment; uncontrolled systemic infections require infectious disease consultation for verification
- Patients who are platelet refractory prior to initiation of protocol therapy; platelet refractoriness is defined by platelet count < 50K when platelet count is obtained 1 hour post platelet transfusion
- Pregnant or lactating patients
- Any significant concurrent disease, illness, or psychiatric disorder that would compromise patient safety or compliance, interfere with consent, study participation, follow up, or interpretation of study results

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01701323

Locations

United States, Georgia

Emory University — **Not yet recruiting**
Atlanta, Georgia, United States, 30322
Contact: Muna Qayed 404-268-6806
Principal Investigator: Muna Qayed

United States, Washington

Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium — **Recruiting**
Seattle, Washington, United States, 98109
Contact: Ann E. Dahlberg 206-667-1959
Principal Investigator: Ann E. Dahlberg

Sponsors and Collaborators

Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium

National Cancer Institute (NCI)

Seattle Children's Research Institute Center for Clinical and Translational Research

Bayley Family Foundation

Investigators

Principal Investigator: Ann Dahlberg Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium

More Information

No publications provided

ClinicalTrials.gov Identifier:	NCT01701323 History of Changes
Other Study ID Numbers:	2584.00, NCI-2012-01724, 2584.00, P30CA015704
Study First Received:	October 3, 2012
Last Updated:	August 13, 2013
Health Authority:	United States: Food and Drug Administration

Additional relevant MeSH terms:

Leukemia
Leukemia, Myeloid, **Acute**
Leukemia, Myeloid
Congenital Abnormalities
Neoplasms by Histologic Type
Neoplasms
Cytarabine
Fludarabine monophosphate
Vidarabine
Fludarabine
Lenograstim
Antimetabolites, Antineoplastic
Antimetabolites
Molecular Mechanisms of Pharmacological Action
Pharmacologic Actions
Antineoplastic Agents
Therapeutic Uses
Antiviral Agents
Anti-Infective Agents
Immunosuppressive Agents
Immunologic Factors
Physiological Effects of Drugs
Adjuvants, Immunologic

ClinicalTrials.gov processed this record on September 22, 2013