PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

Title

Low-Dose TBI and Fludarabine Followed by Nonmyeloablative Unrelated Donor Peripheral Blood Stem Cell Transplantation Using Enhanced Postgrafting Immunosuppression for Patients With Hematologic Malignancies and Renal Cell Carcinoma - A Multi-center Trial

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

This phase I/II trial studies whether a new kind of blood stem cell (bone marrow) transplant, that may be less toxic, is able to treat underlying blood cancer. Stem cells are "seed cells" necessary to make blood cells. Researchers want to see if using less radiation and less chemotherapy with new immune suppressing drugs will enable a stem cell transplant to work. Researchers are hoping to see a mixture of recipient and donor stem cells after transplant. This mixture of donor and recipient stem cells is called "mixed-chimerism". Researchers hope to see these donor cells eliminate tumor cells. This is called a "graft-versus-leukemia" response.

Brief Summary in Scientific Language

PRIMARY OBJECTIVES:

I. To determine whether stable unrelated peripheral blood stem cell (PBSC) grafts can be safely established using nonmyeloablative pretransplant conditioning with intensified post-grafting immunosuppression and with every (q) 8 hours (hr) and possibly q 6 hr mycophenolate mofetil (MMF) dosing in patients with hematologic malignancies and renal cell carcinoma.

II. To determine if the incidence and severity of acute grades II-IV graft-versus-host disease (GVHD) can be reduced in patients with sustained engraftment with the use of q 8 hr MMF dosing.

SECONDARY OBJECTIVES:

I. To determine if engraftment can be maintained in patients with low chimerism and high risk of rejection with the use of a single dose of fludarabine (fludarabine phosphate) followed by donor lymphocyte infusion (DLI) on continued MMF/cyclosporine (CSP).

II. To compare survival and disease free survival to those achieved under protocol 1463.

OUTLINE:

REDUCED-INTENSITY CONDITIONING: Patients receive fludarabine phosphate intravenously (IV) on days -4, -3, and -2 and undergo total-body irradiation (TBI) on day 0.

TRANSPLANT: Patients undergo allogeneic peripheral blood stem cell transplant (PBSCT) on day 0.

IMMUNOSUPPRESSION: Patients receive cyclosporine orally (PO) twice daily (BID) on days -3 to 100 with taper to day 177 and mycophenolate mofetil PO every 8 hours on days 0-40 with taper to day 96.

After completion of study treatment, patients are followed up at 6 months, 1 year, 1.5 years, 2 years, and then annually thereafter.

Organizational Data

- DRKS-ID: **DRKS00006513**
- Date of Registration in DRKS: **2015/03/16**
- Date of Registration in Partner Registry or other Primary Registry: **2001/12/07**
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

Secondary IDs

- Primary Registry-ID: **NCT00027820 (ClinicalTrials.gov)**
- Sponsor-ID: **1641.00 (Fred Hutchinson Cancer Research Center)**
- Other Secondary-ID: **NCI-2012-00591**
- Other Secondary-ID: **P01CA018029**
- Other Secondary-ID: **P01CA018029**
- Other Secondary-ID: **1641.00**
- Other Secondary-ID: **P30CA015704**
- Other Secondary-ID: **P01CA018029**
- Other Secondary-ID: **P01CA018029**

Health condition or Problem studied

- Free text: **Adult Acute Myeloid Leukemia in Remission**
- Free text: **Childhood Acute Lymphoblastic Leukemia in Remission**
- Free text: **Childhood Acute Myeloid Leukemia in Remission**
- Free text: **Childhood Myelodysplastic Syndrome**
- Free text: **Childhood Renal Cell Carcinoma**
- Free text: **Chronic Myelomonocytic Leukemia**
- Free text: **Clear Cell Renal Cell Carcinoma**
- Free text: **de Novo Myelodysplastic Syndrome**
- Free text: **Metastatic Renal Cell Cancer**
- Free text: **Previously Treated Myelodysplastic Syndrome**
- Free text: **Progression of Multiple Myeloma or Plasma Cell Leukemia**
- Free text: **Recurrent Adult Acute Lymphoblastic Leukemia**
- Free text: **Recurrent Adult Acute Myeloid Leukemia**
- Free text: **Recurrent Adult Hodgkin Lymphoma**
- Free text: **Recurrent Adult Lymphoblastic Lymphoma**
- Free text: **Recurrent Adult Non-Hodgkin Lymphoma**
- Free text: **Recurrent Childhood Acute Lymphoblastic Leukemia**
- Free text: **Recurrent Childhood Acute Myeloid Leukemia**
- Free text: **Recurrent Childhood Lymphoblastic Lymphoma**
- Free text: **Recurrent Childhood Non-Hodgkin Lymphoma**
- Free text: **Refractory Anemia**
- Free text: **Refractory Anemia With Ringed Sideroblasts**
-

Free text: **Refractory Childhood Hodgkin Lymphoma**

- Free text: **Refractory Chronic Lymphocytic Leukemia**
- Free text: **Renal Medullary Carcinoma**
- Free text: **Type 1 Papillary Renal Cell Carcinoma**
- Free text: **Type 2 Papillary Renal Cell Carcinoma**
- Free text: **Untreated Adult Acute Lymphoblastic Leukemia**
- Free text: **Untreated Adult Acute Myeloid Leukemia**
- Free text: **Untreated Childhood Acute Lymphoblastic Leukemia**
- ICD10: **C81-C96 - Malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic and related tissue**
- ICD10: **C64 - Malignant neoplasm of kidney, except renal pelvis**

Interventions/Observational Groups

- Arm 1: **Drug: Fludarabine Phosphate**
- Arm 2: **Radiation: Total-Body Irradiation**
- Arm 3: **Procedure: Peripheral Blood Stem Cell Transplantation**
- Arm 4: **Procedure: Nonmyeloablative Allogeneic Hematopoietic Stem Cell Transplantation**
- Arm 5: **Drug: Cyclosporine**
- Arm 6: **Drug: Mycophenolate Mofetil**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Treatment**
- Assignment: **Single (group)**
- Phase: **I-II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- Risk of true graft rejection in patients with and without preceding chemotherapy;

time frame: Up to 5 years; The goal is to reduce the risk in patients without preceding chemotherapy to < 20% and with preceding chemotherapy to < 10%.
- Risk of grades II-IV acute GVHD in those patients with sustained engraftment; time frame: Up to 5 years; The goal is to reduce the incidence of grades II-IV acute GVHD from 50% to less than 35% in patients with sustained engraftment by increasing the dosing of MMF to every 8 hours. The impact of the enhanced post-grafting immunosuppression on objective measures of GVHD will be described. These include doses and duration of immunosuppression (in particular corticosteroids) and number of GVHD treatment regimens used within the first year. These parameters will be compared to the results of protocol 1463.

Secondary Outcome

- Incidence of reversing impending graft rejection (less than 40% donor cluster of differentiation [CD]3+ T cell chimerism); time frame: Up to 5 years; The secondary objective of reversing pending graft rejection with fludarabine phosphate and DLI will be evaluated in the context of overall engraftment. The number of patients given DLI in this context is expected to be small. The response to DLI will be followed and reported in a descriptive manner. The effect of this intervention on adverse outcomes will be followed.
- Overall survival; time frame: Up to 5 years
- Progression-free survival; time frame: Up to 5 years

Countries of recruitment

- US **United States**
- DE **Germany**
- IT **Italy**

Locations of Recruitment

- **Universitaet Leipzig, Leipzig**

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2001/08/31**
- Target Sample Size: **150**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**

Gender: **Both, male and female**

- Minimum Age: **no minimum age**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

- Ages > 50 years with hematologic malignancies treatable by unrelated hematopoietic stem cell transplantation (HSCT)

- Ages =< 50 years of age with hematologic diseases treatable by allogeneic HSCT who through pre-existing medical conditions or prior therapy are considered to be at high risk for regimen related toxicity associated with a conventional transplant (> 40% risk of transplant related mortality [TRM]) or those patients who refuse a conventional HSCT; transplants must be approved for these inclusion criteria by both the participating institution's patient review committee such as the Patient Care Conference (PCC at the Fred Hutchinson Cancer Research Center [FHCRC]) and by the principal investigator at the collaborating center; patients =< 50 years of age who have received previous autologous transplantation do not require patient review committee approval; all children < 12 years must be discussed with the FHCRC principal investigator (PI) prior to registration

- Patients with metastatic renal cell carcinoma with the histologic subtypes of clear cell, papillary and medullary may be accepted regardless of age

- The following diseases will be permitted although other diagnoses can be considered if approved by PCC or the participating institution's patient review committees and the principal investigator:

- Intermediate or high grade non-Hodgkin lymphoma (NHL) - not eligible for autologous HSCT or after failed autologous HSCT

- Low grade NHL - with < 6 month duration of complete remission (CR) between courses of conventional therapy

- Chronic lymphocytic leukemia (CLL) - must have failed two lines of conventional therapy and be refractory to fludarabine

- Hodgkin's disease (HD) - must have received and failed frontline therapy

- Multiple myeloma (MM) - must have received prior chemotherapy; consolidation of chemotherapy by autografting prior to nonmyeloablative HSCT is permitted

- Acute myeloid leukemia (AML) - must have < 5% marrow blasts at the time of transplant

- Acute lymphoblastic leukemia - must have < 5% blasts at the time of transplant

- Chronic myelogenous leukemia (CML) - patients will be accepted in chronic phase or accelerated phase; patients who have received prior autografts after high dose therapy or have undergone intensive chemotherapy with PBSC autologous or conventional HSCT for advanced CML may be enrolled provided they are in CR or chronic phase (CP) and have < 5% marrow blasts at time of transplant

- Myelodysplastic syndromes (MDS)/myeloproliferative disorder (MPD) - only patients with MDS/refractory anemia (RA) or MDS/refractory anemia with ringed sideroblasts (RARS) will be eligible for this protocol; additionally patients with myeloproliferative syndromes (MPS) will be eligible; those patients with MDS or MPS with > 5% marrow blasts (including those with transformation to AML) must receive cytotoxic chemotherapy and achieve < 5% marrow blasts at time of transplant

- Renal cell carcinoma - must have evidence of disease not amenable to surgical cure or history of or active metastatic disease by radiological and histologic criteria

- DONOR: FHCRC matching allowed will be grade 1.0 to 2.1; unrelated donors who are prospectively:

- Matched for human leukocyte antigen (HLA)-A, B, C, DRB1 and DQB1 by high resolution typing

- Only a single allele disparity will be allowed for HLA-A, B, or C as defined by

high resolution typing

- DONOR: A positive anti-donor cytotoxic crossmatch is an absolute donor exclusion

- DONOR: Patient and donor pairs homozygous at a mismatched allele are considered a two-allele mismatch, i.e., the patient is A*0101 and the donor is A*0201, and this type of mismatch is not allowed

- DONOR: PBSC only will be permitted as a hematopoietic stem cell (HSC) source on this protocol

Exclusion criteria

- Patients with rapidly progressive intermediate or high grade NHL

- Renal cell carcinoma patients:

- With expected survival of less than 6 months

- Disease resulting in severely limited performance status (< 70%)

- Any vertebral instability

- History of brain metastases

- Central nervous system (CNS) involvement with disease refractory to intrathecal chemotherapy

- Fertile men or women unwilling to use contraceptive techniques during and for 12 months following treatment

- Females who are pregnant

- Patients with non-hematological tumors except renal cell carcinoma

- Fungal infections with radiological progression after receipt of amphotericin B or active triazole for greater than 1 month

- Cardiac ejection fraction < 35%; ejection fraction is required if there is a history of anthracycline exposure or history of cardiac disease

- Diffusion capacity of the lung for carbon monoxide (DLCO) < 40% and/or receiving supplementary continuous oxygen

- The FHCRC PI of the study must approve of enrollment of all patients with pulmonary nodules

- Patients with clinical or laboratory evidence of liver disease would be evaluated for the cause of liver disease, its clinical severity in terms of liver function, and the degree of portal hypertension; patients will be excluded if they are found to have fulminant liver failure, cirrhosis of the liver with evidence of portal hypertension, alcoholic hepatitis, esophageal varices, a history of bleeding esophageal varices, hepatic encephalopathy, uncorrectable hepatic synthetic dysfunction evinced by prolongation of the prothrombin time, ascites related to portal hypertension, bacterial or fungal liver abscess, biliary obstruction, chronic viral hepatitis with total serum bilirubin > 3 mg/dL, and symptomatic biliary disease

- Karnofsky scores < 60 (except renal cell carcinoma [RCC])

- Patients with > grade II hypertension by common toxicity criteria (CTC)

- Human immunodeficiency virus (HIV) positive patients

- The addition of cytotoxic agents for "cytoreduction" with the exception of hydroxyurea and imatinib mesylate will not be allowed within two weeks of the initiation of conditioning

- DONOR: Marrow donors

- DONOR: Donors who are HIV-positive and/or, medical conditions that would result in increased risk for filgrastim (G-CSF) mobilization and harvest of PBSC

Addresses

■ **Primary Sponsor**

Fred Hutchinson Cancer Research Center

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

■ **Contact for Scientific Queries**

Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium
Brenda Sandmaier

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Brenda Sandmaier

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- **Collaborator, Other Address**

National Heart, Lung, and Blood Institute (NHLBI)

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

- **Collaborator, Other Address**

National Cancer Institute (NCI)

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

Sources of Monetary or Material Support

- **[---]***

Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***

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Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

Status

- Recruitment Status: **Recruiting complete, follow-up continuing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.
- Translation on version: 2
- Last processed date by ClinicalTrials.gov: 2015/06/25
Please note:
There are additional attributes available concerning this trial. To open an extended view please click here.