CART19 to Treat B-Cell Leukemia or Lymphoma That Are Resistant or Refractory to Chemotherapy

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators.

⚠ Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT01029366

Recruitment Status : Completed
First Posted : December 10, 2009
Results First Posted : February 28, 2017
Last Update Posted : June 26, 2019

Sponsor:
University of Pennsylvania

Information provided by (Responsible Party):
University of Pennsylvania

Study Description

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Brief Summary:

This is a Pilot/Phase I, single arm, single center, open label study to determine the safety, efficacy and cellular kinetics of CART19 (CTL019) in chemotherapy resistant or refractory CD19+ leukemia and lymphoma subjects.

1) a Screening Phase, followed by 2) an Intervention/Treatment Phase consisting of apheresis, lymphodepleting chemotherapy (determined by the Investigator and based on subject's disease burden and histology, as well as on the prior chemotherapy history received), infusions of CTL019, tumor collection by bone marrow aspiration or lymph node biopsy (optional, depending on availability), and 3) a Follow-up Phase.

The suitability of subjects' T cells for CTL019 manufacturing was determined at study entry.

Subjects with adequate T cells were leukapheresed to obtain large numbers of peripheral blood mononuclear cells for CTL019 manufacturing. The T cells were purified from the peripheral blood mononuclear cells, transduced with TCR-ζ/4-1BB lentiviral vector, expanded in vitro and then frozen for future administration. The number of subjects who had inadequate T cell collections, expansion or manufacturing compared to the number of subjects who had T cells successfully manufactured is a primary measure of feasibility of this study.

Unless contraindicated and medically not advisable based on previous chemotherapy, subjects were given conditioning chemotherapy prior to CTL019 infusion. The chemotherapy was completed 1 to 4 days before the planned infusion of the first dose of CTL019.

Up to 20 evaluable subjects with CD19+ leukemia or lymphoma were planned to be dosed with CTL019. A single dose of CTL019 (consisting of approximately 5x10^9 total cells, with a minimal acceptable dose for infusion of 1.5x10^7 CTL019 cells) was to be given to subjects as fractions (10%, 30% and 60% of the total dose) on Day 0, 1 and 2. A second 100% dose of CTL019 was initially permitted to be given on Day 11 to 14 to subjects, providing they had adequate tolerance to the first dose and sufficient CTL019 was manufactured.

Condition or disease	Intervention/treatment	Phase
Hematopoietic/Lymphoid Cancer Adult Acute Lymphoblastic Leukemia in Remission B-cell Adult Acute Lymphoblastic Leukemia B-cell Chronic Lymphocytic Leukemia Prolymphocytic Leukemia Recurrent Adult Diffuse Large Cell Lymphoma Recurrent Grade 1 Follicular Lymphoma Recurrent Grade 2 Follicular Lymphoma Recurrent Grade 3 Follicular Lymphoma Recurrent Mantle Cell Lymphoma Refractory Chronic Lymphocytic Leukemia Stage III Adult Diffuse Large Cell Lymphoma Stage III Chronic Lymphocytic Leukemia Stage III Grade 1 Follicular Lymphoma Stage III Grade 2 Follicular Lymphoma	Biological: CART-19	Phase 1

Stage III Mantle Cell Lymphoma Stage IV Adult Diffuse Large Cell Lymphoma Stage IV Chronic Lymphocytic Leukemia Stage IV Grade 1 Follicular Lymphoma Stage IV Grade 2 Follicular Lymphoma Stage IV Grade 3 Follicular Lymphoma Stage IV Mantle Cell Lymphoma		

Detailed Description:

Primary objectives:

1. To evaluate the safety and feasibility of a single target dose of 5 times 10e9 total cells, acceptable range of 1.5 times 10e7 to 5 times 10e9 total cells comprised of autologous CART-19 cells that express the TCR zeta and 4-1 BB costimulatory domain.

Secondary objectives:

1. Proof of mechanism: determine if 2nd generation CAR expressing 4-1BB costimulation domains have improved persistence in patients.
2. Proof of concept: determine the effects of CART-19 on CD19 expression in vivo.
3. Proof of bioactivity: Evaluate changes in systemic soluble immune factors in patients
4. Proof of bioactivity: Evaluate impact of CART19 treatment on tumor burden
5. Explore whether CART-19 cells retain anti-tumor activity in vivo.
6. Determine if host immunity develops against CART-19.
7. Characterize the relative subsets of CART-19 T cells (Tcm, Tem, and Treg).
8. Describe survival and response rates

Study Design

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Study Type :	Interventional (Clinical Trial)
Actual Enrollment :	26 participants
Allocation:	Non-Randomized
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Pilot Study of Redirected Autologous T-cells Engineered to Contain Anti-CD19 Attached to TCR and 4-1BB Signaling Domains in Patient With Chemotherapy Resistant or Refractory CD19+ Leukemia and Lymphoma
Actual Study Start Date :	March 17, 2010

Actual Study Completion Date : May 2016

Resource links provided by the National Library of Medicine

MedlinePlus related topics: Leukemia Lymphoma

Drug Information available for: Tisagenlecleucel-T

Genetic and Rare Diseases Information Center resources: Lymphosarcoma Acute Lymphoblastic Leukemia Lymphoblastic Lymphoma Diffuse Large B-Cell Lymphoma Chronic Lymphocytic Leukemia Mantle Cell Lymphoma Follicular Lymphoma B-cell Lymphoma

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: CART-19 CLL CART-19 (autologous T cells transduced with CD19 TCR-ζ/4-1BB vector) administered as an IV infusion days 0, 1, 2 and 11 in the absence of disease progression or unacceptable toxicity.Minimum/maximum total dose: 1.5x10^7 / 5x10^9 administered to patients with chronic Lymphocytic Leukemia (CLL) and Acute Lymphoblastic Leukemia (ALL).	Biological: CART-19 Autologous T cells purified from the peripheral blood mononuclear cells of subjects, transduced with TCR-ζ/4-1BB lentiviral vector, expanded in vitro and then frozen for future administration.
Experimental: CART-19 ALL CART-19 (autologous T cells transduced with CD19 TCR-ζ/4-1BB vector) administered as an IV infusion days 0, 1, 2 and 11 in the absence of disease progression or unacceptable toxicity.Minimum/maximum total dose: 1.5x10^7 / 5x10^9 administered to patients with chronic Lymphocytic Leukemia (CLL) and Acute Lymphoblastic Leukemia (ALL).	Biological: CART-19 Autologous T cells purified from the peripheral blood mononuclear cells of subjects, transduced with TCR-ζ/4-1BB lentiviral vector, expanded in vitro and then frozen for future administration.

Primary Outcome Measures :

1. Number of Participants With Adverse Events [Time Frame: 5 years]

Secondary Outcome Measures :

1. Overall Response Summary [Time Frame: 5 years]

   Efficacy assessments for ALL were performed based on bone marrow and blood morphologic criteria and physical examination findings. The definitions for response are primarily based on the standardized response criteria defined by National Comprehensive Cancer Network (NCCN) Guidelines (NCCN, 2013 v.1).

   Efficacy assessments for CLL were based on lymphadenopathy, hepatomegaly, splenomegaly, bone marrow and blood morphologic and laboratory assessments. The response criteria are consistent with NCCN Guidelines Version 2.2012 CLL/SLL, which is based on the 2008 International Workshop Group on CLL (IWCLL) revisions of the original guidelines for evaluating disease response released in 1996 by the National Cancer Institute Working Group (NCI/WG).

Eligibility Criteria

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Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion

- Male and female subjects with CD19+ B cell malignancies in patients with no available curative treatment options (such as autologous or allogeneic SCT) who have limited prognosis (several months to < 2 year survival) with currently available therapies will be enrolled

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