A multicenter study of apheresis collection of peripheral blood mononuclear cells (PBMC) in patients with CD19 expressing malignancies who could be eligible for a CTL019 clinical research trial

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Haematological disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON43204

Source
ToetsingOnline

Brief title
CCTL019B2206

Condition

- Haematological disorders NEC

Synonym
CTL019 cells, leukapheresis

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: NOVARTIS

Intervention

Keyword: apheresis, CTL019

Outcome measures

Primary outcome

The primary objective of this study is the collection of PBMCs for potential utilization in a CTL019 research protocol via standardized procedures for apheresis, cryopreservation (if required), and storage (if required).

Secondary outcome

* Characterize the immunophenotype and the yield of total nucleated cells in the collected apheresed product

* Assess the association between the total nucleated cells obtained from each apheresis unit and baseline peripheral white blood cell counts, CD3 cell counts, as well as total blood volume processed

* Describe the AE profile of patients during the apheresis procedures until the end of Day 2 following apheresis

Study description

Background summary

Apheresis is a well-established clinical procedure by which blood being removed from a patient is continuously separated into component parts. The process of apheresis allows selected components of the blood to be collected while the

remainder is returned to the patient. Peripheral blood mononuclear cells (PBMC), which contain lymphocytes and monocytes, as well as circulating hematopoietic stem cells, have been collected through leukapheresis and have been used as a source of cells for both autologous and allogeneic hematopoietic stem cell transplants (HSCT).

In this protocol, patients with CD19 expressing malignancies who are potentially eligible for a CTL019 treatment protocol, will have unstimulated (non-mobilized) PBMCs collected through apheresis. Patients who subsequently meet both clinical eligibility criteria for a CTL019 treatment protocol and have an adequate unstimulated PBMC apheresis product that potentially could be used for CTL019 manufacturing may then be enrolled into the appropriate treatment protocol.

Study objective

The rationale for this protocol is to use standardized procedures to obtain PBMCs from adult patients with a diagnosis of a CD19 expressing malignancy for which a CTL019 treatment protocol is currently enrolling or under IRB/EC review, and to identify characteristics that are associated with a successful T cell collection.

Study design

This is a multi-center, phase II study to collect non-mobilized PBMCs for potential utilization in a CTL019 treatment trial via standardized procedures for apheresis.

Study burden and risks

patients will undergo apheresis and side effects is minimal.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Signed written informed consent, or signed parental permission form and assent form (as applicable), must be obtained prior to any study procedures
2. Males and females * 18 years of age at the time of initial diagnosis and weighing * 40 kg who are eligible to undergo a PBMC collection by apheresis for potential future CTL019 manufacturing for use in a CTL019 trial
3. CD19 expressing malignancy for which a CTL019 treatment protocol is currently enrolling or under IRB/EC review
4. Hemoglobin level * 9.0 g/dL at screening. Transfusion support can be provided within 24 hours of starting the apheresis procedure to meet this criterion
5. Platelet count * 50,000/microliter at screening. Transfusion support can be provided within 24 hours of starting the apheresis procedure to meet this criterion
6. Prothrombin Time (PT)/ Partial Thromboplastin Time (PTT) * 1.5 x ULN at screening. Transfusion support can be provided within 24 hours of starting the apheresis procedure to meet this criterion
7. Peripheral blood absolute lymphocyte count (ALC) * 500/microliter at screening or if ALC <500/uL, then the absolute CD3 lymphocyte count must be *150/uL at screening
8. For patients who have undergone allogeneic transplant, must be * 3 months from allogeneic SCT at the time of apheresis

Exclusion criteria

1. Pregnant or nursing (lactating) women, where pregnancy is defined as the state of a female

after conception and until the termination of gestation, confirmed by a positive hCG laboratory test at screening
3. Human Immunodeficiency Virus (HIV) infection at screening
5. Presence of grade 2 to 4 acute or extensive chronic graft-versus-host disease (GVHD) at screening
6. Any patient that in the opinion of the investigator is not medically stable to undergo the apheresis procedure or will not comply with the visit schedules or procedures
7. Treatment with any prior gene therapy product
8. Patient has participated in a research study using an investigational agent within the last 30 days prior to screening
9. Patient should not have received long-acting growth
factors or drugs used for cell mobilization (e.g. Neulastsa/pegflilgrastim) within 14 days of the eukapheresis procedure. Use of short-acting growth factors of drugs
used for cell mobilization (e.g. G-CSF/Neupogen/filgrastim, plerixafor) must be * 5 days leukapheresis procedure
11. The following treatments/medications are excluded:
**Chemotherapy:
**-Cytotoxic chemotherapy drugs must not be given within 2 weeks of apheresis
- Intrathecal chemotherapy (IT): Recommend holding IT prior to leukapheresis collection. If clinically indicated, IT Ara-C may be given and leukapheresis collection started any time following IT Ara-C. Leukapheresis collection may be started * 7 days after IT methotrexate (MTX)
**- Pegylated-asparaginase must be stopped >4 weeks prior to apheresis
**Low dose daily or weekly maintenance chemotherapy should be stopped * 2 weeks prior to apheresis
- Clofarabine may be associated with prolonged lymphopenia. This should be taken into consideration when evaluation the optimal timing for leukapheresis collection. An interval of * 8 weeks from the patient*s last clofarabine treatment is recommended
-Short-acting drugs(e.g tyrosine kinase inhibitors, ibrutinib and hydroxyurea) must not be given within a 72 hour window of the leukapheresis procedure
**Steroids: Therapeutic doses of steroids must be stopped > 72 hours prior to apheresis. However, the following physiological replacement doses of steroids are allowed: * 12 mg/m2/day hydrocortisone or equivalent
**Immunomodulatory drugs (e.g. IFN-gamma, anti-TNF-alpha): should be stopped * 2 weeks prior to apheresis
**Allogeneic cellular therapy:
- Must be * 3 months from allogeneic stem cell transplant at the time of leukapheresis.
- Must not have presence of grade 2 to 4 acute graft-versus-host disease (GVHD) or extensive chronic GVHD.
- Any donor lymphocyte infusions (DLI) must be completed > 4 weeks prior to apheresis
**GVHD therapies: Any drug used to prevent or treat GVHD must be stopped > 2 weeks prior to apheresis (e.g. calcineurin inhibitors, methotrexate or other chemotherapy drugs, mycophenolate, rapamycin, thalidomide, or immunosuppressive

antibodies such as anti-TNF-*, anti-IL6 or anti-IL6R). Topical steroids for localized treatment of GVHD are allowed
- Anti T-cell Directed Therapy: Administration of any T cell lytic or toxic agent (e.g. alemtuzumab) is strongly discouraged since residual lytic levels may destroy T-cells in the leukapheresis collection and/or prevent their in vitro CTL019 manufacturing.
- Anti-CD19 directed therapy Has had treatment with any prior anti-CD19/anti-CD3 therapy, or any other anti-CD19 therapy unless a specific Novartis CTL019 treatment protocol would allow for prior anti-CD19 directed therapy
12. Hepatitis B (see Appendix 1 for interpretation of Hepatitis B results) or active hepatitis C (HCV RNA positive)
13. Patients with an acute infection (bacterial, viral or fungal) or a positive blood culture should not undergo leukapheresis collection. A full course of anti-infective therapy must be administered before leukapheresis collection can occur to avoid contamination of the product.*

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-07-2016
Enrollment:	5
Type:	Actual

Ethics review

Approved WMO

Date:	03-06-2016

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-10-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL56763.018.16