A Phase II, single arm, multicenter open label trial to determine the efficacy and safety of tisagenlecleucel (CTL019) in adult patients with refractory or relapsed follicular lymphoma

Published: 31-08-2018
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This study has been transitioned to CTIS with ID 2023-508127-13-00 check the CTIS register for the current data. This single arm, multi-center, phase II study will determine the efficacy and safety of tisagenlecleucel in adult patients with FL who...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Lymphomas non-Hodgkin's B-cell
Study type	Interventional

Summary

ID

NL-OMON55846

Source
ToetsingOnline

Brief title
ELARA - CCTL019E2202

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
blood cancer, Follicular Lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V.

Intervention

Keyword: CAR-T, Follicular Lymphoma, Genetherapy, T-Cell Therapy

Outcome measures

Primary outcome

Evaluate the efficacy of tisagenlecleucel therapy as measured by complete response rate determined by Independent Review Committee in the full analysis set based on Lugano 2014 classification response criteria.

Secondary outcome

- Evaluate the efficacy of tisagenlecleucel as measured by additional efficacy measures, including Overall Response Rate (ORR), Duration of Response (DOR), Progression Free Survival (PFS) and Overall Survival (OS).
- Evaluate safety of tisagenlecleucel
- Characterize the in vivo cellular kinetics (levels, expansion, persistence) of tisagenlecleucel transduced cells into target tissues (blood, bone marrow, and other tissues if available) and CD3+ tisagenlecleucel cells in peripheral blood
- Characterize the incidence and prevalence of tisagenlecleucel immunogenicity (humoral and cellular)
- Characterize the impact of pre-existing and treatment induced immunogenicity on cellular kinetics, efficacy and safety
- Describe the effect of tisagenlecleucel therapy on patient reported outcomes

Study description

Background summary

Non-Hodgkin lymphomas (NHLs) comprise a heterogeneous group of lymphoid malignancies, including immature lymphoid neoplasms, mature B-cell neoplasms, mature T-cell and NK-cell neoplasms, and post-transplant lymphoproliferative disorders. Mature B-cell lymphomas are further classified into indolent lymphomas, e.g. follicular lymphoma (FL), and aggressive lymphomas, e.g. diffuse large B-cell lymphoma (DLBCL).
FL is the second most common histologic NHL subtype in the Western hemisphere. The estimated number of new cases in the US was 13,960 in 2016 (Teras et al 2016). Most patients are diagnosed during the sixth decade of their life but approximately 25% of patients are 40 years of age or younger. The translocation t(14;18)(q32;q21) is the genetic hallmark of follicular lymphoma, which results in the constitutive overexpression of B-cell lymphoma 2 protein (Bcl-2). FL cells also express surface immunoglobulins, B-cell lymphoma 6 protein (Bcl-6), and B-cell associated antigens such as CD10, CD19, CD20, and CD22. FL is classified histologically into three grades based on the number of centroblasts.

Study objective

This study has been transitioned to CTIS with ID 2023-508127-13-00 check the CTIS register for the current data.

This single arm, multi-center, phase II study will determine the efficacy and safety of tisagenlecleucel in adult patients with FL who failed at least 2 prior systemic therapies, including an anti-CD20 antibody (e.g. rituximab) and an alkylating agent.

Study design

Single arm, multi-center, phase II study that investigates the efficacy and safety of tisagenecleucel in patients with follicular lymphoma patients who are refractory or relapsed after multiple therapies. Patients are screened and the leukapheresis takes place during screening. The cells obtained in leukapheresis are genetically modified into the tisagenecleucel therapy. After screening, patients are treated with lymphodepleting chemotherapy (Fludarabine in combination with Cyclophosphamide or Bendamustine). Tisagenlecleucel is then administered. The study continues until the last infused patient has been followed for 24 months or previously stopped the study.

Intervention

Leukapheresis, lymphodepleting chemotherapy and tisagenlecleucel infusion.

Study burden and risks

Risks: side effects may occur after the tisagenlecleucel infusion, the leukapheresis procedure, lymphodepleting chemotherapy, and after study procedures such as bone marrow puncture, PET-CT scan, MUGA, blood collection, tumor biopsy, and lumbar puncture.

Burden: Leukapheresis procedure, lymphodepleting chemotherapy,tisagenlecleucel infusion, possible hospitalization D1 - D21 (depending on medical condition), 9 controls in the first 28 days after infusion, and at least 10 visits thereafter (depending on when the last one patient has reached the 24-month follow-up).

Physical examination: 6x in the first 28 days, then with each subsequent visit.
Blood tests: an average of 50ml, a maximum of 75ml per visit.
Leukapheresis: 1 time
Lymphodepleting chemotherapy: 1 time (2 to 6 days prior to infusion tisagenlecleucel)
CT / MRI: month 9, month 12, and every six months thereafter.
MUGA / Echo: screening
ECG: screening and day 1 (infusion)
PET-CT: screening, 4 weeks to 8 days prior to infusion, month 3 and month 6
CT / MRI: Month 9, month 12, month 18 and month 24 and every half year thereafter.
Bone marrow biopsy: screening, month 3 and if a complete response is achieved and the disease was in bone marrow when screened
Lumbar puncture: if clinically indicated
Tumor biopsy: screening and after month 3 if clinically indicated
Questionnaires: screening, and every study visit after month 3.
Optional use of body material (blood and tissues) and anonymous data for future research.

Contacts

Public
Novartis

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Written informed consent prior to any screening procedures
- >=18 years of age at the time of ICF signature
- Follicular Lymphoma (Grade 1, 2, 3A) confirmed histologically by central pathology review before tisagenlecleucel infusion.
- FL meeting one of the following criteria:
o Refractory to a second line or later line of systemic therapy (including anti-CD20 antibodies and alkylating agents) or relapsed within 6 months after completion of a second line or later line of systemic therapy
o Relapsed during anti-CD20 antibody maintenance (following at least two lines of therapies as above) or within 6 months after maintenance completion
o Relapsed after autologous Hematopoietic Stam Cell Transplant
- Radiographically measurable disease at screening

Exclusion criteria

- Evidence of histologic transformation
- Follicular Lymphoma Grade 3B
- Prior anti-CD19 therapy
- Prior gene therapy
- Prior adoptive T cell therapy
- Prior allogeneic hematopoietic stem cell transplant
- Active CNS involvement by malignancy

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-09-2019
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	RoActemra
Generic name:	tocilizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	31-08-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-10-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	28-11-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-07-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-07-2019
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-10-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-12-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-01-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-03-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-03-2020
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-04-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-06-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-06-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-06-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-07-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-08-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-09-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	19-02-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-04-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-06-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-07-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-07-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-12-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-02-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-05-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	23-06-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-07-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-07-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-04-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-05-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
EU-CTR	CTIS2023-508127-13-00
EudraCT	EUCTR2017-004385-94-NL
ClinicalTrials.gov	NCT03568461
CCMO	NL66135.000.18