A phase I/II, multicenter study evaluating the feasibility, safety, and efficacy of point-of-care manufactured 19CP02 in subjects with relapsed/refractory B-cell non-Hodgkin lymphoma

Published: 21-06-2021
Last updated: 14-09-2024

This study has been transitioned to CTIS with ID 2022-502661-23-00 check the CTIS register for the current data. The primary objective of the study is to evaluate the feasibility, safety, and efficacy of point-of-care manufactured 19CP02 in subjects...

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

Summary

ID

NL-OMON51902

Source
ToetsingOnline

Brief title
Atalanta-1

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
cancer of the lymphatic system, Lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: CellPoint B.V.
Source(s) of monetary or material Support: Opdrachtgever CellPoint B.V.

Intervention

Keyword: CAR T-cell therapy, CD19 CAR T cells, Non-Hodgkin Lymphoma, Point-of-care manufacturing

Outcome measures

Primary outcome

Primary endpoints of the study:

Phase I: Incidence of (S)AEs, including dose-limiting toxicities (DLTs) until

D28

Phase II: ORR until 2 years post 19CP02 dose per Lugano classification

Secondary outcome

Secondary endpoints of the study:

Type, frequency and severity of AEs

Objective response rate (ORR) until 2 years post 19CP02 dose per Lugano

classification, Duration of response (DOR), Metabolic complete response rate

(mCR), Event-free survival (EFS), Progression-free survival (PFS), Overall

survival (OS), Minimal Residual Disease (MRD)

Levels of anti-CD19 CAR T cells in blood, bone marrow, CSF, and other

tissues, if available

Levels of chemokines and cytokines in serum over time

Number of successfully manufactured 19CP02 products within the predefined

release specifications

Study description

Background summary

Non-Hodgkin lymphoma (NHL) comprises of a heterogenous group of lymphoid malignancies, originating primarily from B lymphocytes, and to a lesser extent from T lymphocytes and NK cells. In 2020, the reported incidence and mortality in Europe were approximately 120.000 and 50.000 respectively. NHL are largely comprised of mature B-cell neoplasms, which can be divided into two main subgroups; indolent and aggressive lymphoma subtypes. Follicular lymphoma (FL) and marginal zone lymphoma are prevalent forms of the indolent subtype, while diffuse large B-cell lymphoma (DLBCL) and most forms of mantle cell lymphoma (MCL) are of aggressive nature.
In recent years, several new therapies to treat NHL have been approved. These treatments have significantly increased the overall survival rates for patients. Despite this progress however, a large group of patients will relapse eventually. Especially patients with primary treatment failure have a poor prognosis.
Anti-CD19 CAR T cell therapy has proven to be a breakthrough in the treatment of hematological malignancies with impressive response rates after a single treatment. However, current implementation of these novel treatments in clinical practice worldwide faces several challenges, such as the long vein-to-vein time (from apheresis to treatment) ranged from 23 to 54 days resulting in drop-out rates up to 33%. Also, the majority of patients requires bridging therapy. In addition, the manufacturing comes with high costs and logistics are very complicated.
By providing CAR T-cell manufacturing at the point-of-care, in a facility in or in the near proximity of the clinical center, it is the aim to shorten the vein-to-vein time to 1 week and administer a fresh product to the patient. A fast manufacturing process is expected to improve overall clinical outcomes by lowering drop-out rates and reducing the need for bridging therapy. If the expected safety and efficacy can be proven, the point-of-care model has the potential to address the current unmet medical need for r/r NHL patients.

Study objective

This study has been transitioned to CTIS with ID 2022-502661-23-00 check the CTIS register for the current data.

The primary objective of the study is to evaluate the feasibility, safety, and efficacy of point-of-care manufactured 19CP02 in subjects with relapsed/refractory B-cell non-Hodgkin lymphoma.
In the phase I part of the study the main objective is to evaluate the safety of 19CP02 and determine the recommended Phase 2 dose (RP2D).
In the phase II part of the study the main objective is to evaluate the

efficacy of 19CP02 in the different NHL subtypes.

Secondary objectives of the study:
Evaluate safety of 19CP02
Evaluate efficacy of 19CP02
Evaluate 19CP02 pharmacokinetics and pharmacodynamics
Evaluate feasibility of 19CP02 manufacturing

Study design

This is a phase I/II, multicenter, non-randomized, open label study.
In the phase I part of the study approximately 15 subjects with r/r NHL will be included via a dose escalation strategy based on the Bayesian Optimal INterval (BOIN) design. Based on the different dose levels and pre-specified dose-limiting toxicities (DLT), the recommended phase II dose (RP2D) can be determined.
In the phase II part of the study up to 30 additional subjects per disease cohort (based on NHL subtype) may be enrolled. The sponsor may decide to open one or multiple cohorts for enrollment, based on outcomes from the Phase I part of the study.

Intervention

Leukapheresis of mononuclear cells
Lymphodepletion chemotherapy regimen for 3 days consisting of Cyclophosphamide IV 300 mg/m2/day and Fludarabine IV 30 mg/m2/day
Infusion of 19CP02 consisting of a single fixed dose of autologous anti-CD19 CAR-positive T cells at the designated dose level

Study burden and risks

The study consists of a screening period, leukapheresis, 3 days of chemotherapy, treatment at the clinic (with at least 7 days of hospitalization), a stay in 1-hour proximity of the clinic until day 28, intensive monitoring during the first six months, and from month 6 onwards a 3-monthly visit until month 24 or progressive disease. Long term follow-up until a maximum of 15 years after treatment will be continued under a different protocol. During each visit, multiple assessments will be conducted. Especially during hospitalization, the subjects will be monitored for AEs intensively. The subject can consider this as a burden.
Risks for subjects through study participation are mainly comprised of (serious) adverse events as CRS, TLS, neurotoxicity, B-cell aplasia, hypogammaglobulinemia and (serious) infections.
These potential (severe) side effects are explained in the patient information sheet and it is of critical importance the investigator reviews these with the potential subject prior to informed consent is given. The burden of additional

assessments and radiation exposure are approximately the same compared to when the patient would receive different lymphoma treatment per institutional guidelines.

Contacts

Public
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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 informed consent form
2. Age >= 18 years
3. Histologically confirmed diagnosis of one of the following non-Hodgkin lymphoma subtypes: DLBCL, FL grade 1, 2 or 3A, MZL, or MCL
4. Relapsed or refractory disease
5. Measurable disease according to the Lugano classification
6. ECOG performance status of 0 or 1 (ECOG 2 is allowed when serum albumin >=

3.4 g/dL)
7. Adequate bone marrow, renal, hepatic and pulmonary function

Exclusion criteria

1. Primary CNS B-cell lymphoma, Burkitt lymphoma, or Richter*s transformation
2. Selected prior treatments as defined in the protocol
3. History of another primary malignancy that requires intervention beyond surveillance or that has not been in remission for at least 3 years (exceptions per protocol)
4. Active CNS involvement (with neurological changes) by disease under study
5. Infection with HIV, hepatitis B or hepatitis C virus

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-03-2022
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Genetic modified organism
Product type:	Medicine
Brand name:	19CP02
Generic name:	CAR-positive viable T cells

Ethics review

Approved WMO Date:	21-06-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-10-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-08-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-11-2022
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	CTIS2022-502661-23-00
EudraCT	EUCTR2021-003272-13-NL
CCMO	NL77808.000.21