A Phase 1/2 Multi-Center Study Evaluating the Safety and Efficacy of KTE C19 in Subjects with Refractory Aggressive Non-Hodgkin Lymphoma (NHL) (ZUMA-1)

Published: 18-05-2016
Last updated: 20-04-2024

The primary objective of Phase 1 study is to evaluate the safety of axicabtagene ciloleucel regimens.The primary objective of Phase 2 pivotal study is to evaluate the efficacy of axicabtagene ciloleucel, as measured by objective response rate (ORR)...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lymphomas non-Hodgkin's unspecified histology
Study type	Interventional

Summary

ID

NL-OMON54771

Source
ToetsingOnline

Brief title
ZUMA-1

Condition

- Lymphomas non-Hodgkin's unspecified histology
- Lymphomas non-Hodgkin's unspecified histology

Synonym
Non-Hodgkin Lymphoma (NHL); lymph node cancer

Research involving
Human

Sponsors and support

Primary sponsor: Kite Pharma Inc
Source(s) of monetary or material Support: Kite Pharma Inc.

Intervention

Keyword: Axicabtagene ciloleucel, Efficacy, Non-Hodgkin Lymphoma (NHL), Safety

Outcome measures

Primary outcome

Phase 1 Study:

- Incidence of adverse events defined as dose-limiting toxicities (DLT)

Phase 2 Pivotal Study:

Objective response rate (complete response [CR] + partial response [PR]) per the revised International Working Group (IWG) Response Criteria for Malignant Lymphoma (Cheson et al, 2007) as determined by study investigators. All subjects who do not meet the criteria for an objective response by the analysis cutoff date will be considered non-responders.

Phase 2 Safety Management Study:

Incidence and severity of CRS and neurologic toxicities.

Secondary outcome

Phase 1 Study:

• Objective response rate (CR + PR) per the revised IWG Response Criteria for Malignant Lymphoma

• Duration of Response (DOR)

• Overall Survival (OS)

• Progression Free Survival (PFS)

• Incidence of adverse events and clinical significant changes in safety lab values

• Levels of anti-CD19 CAR T cells in blood

• Levels of cytokines in serum

• Incidence of anti-axicabtagene ciloleucel antibodies

Phase 2 Pivotal Study:

• Objective response rate per Independent Radiology Review Committee (IRRC)

• DOR

• PFS

• OS

• Incidence of adverse events and clinical significant changes in safety lab values

• Levels of anti-CD19 CAR T cells in blood

• Levels of cytokines in serum

• Incidence of anti-axicabtagene ciloleucel antibodies

Phase 2 Safety Management Study:

• Objective response rate (complete response [CR] + partial response [PR]) per the revised International Working Group (IWG) Response Criteria for Malignant Lymphoma (Cheson 2007) as determined by study investigators.

• DOR

• PFS

• OS

• Incidence of adverse events and clinically significant changes in safety lab values

• Levels of anti-CD19 CAR T cells in blood

• Levels of cytokines in blood

• Incidence of anti-axicabtagene ciloleucel antibodies

• Changes over time in the EQ-5D scale score and visual analogue scale (VAS) score (Phase 2 SMS only)

Study description

Background summary

Non-Hodgkin lymphoma (NHL) is a heterogeneous group of cancers originating in B lymphocytes, T lymphocytes or natural killer cells. There were an estimated 356,000 new cases of NHL and 192,000 deaths from NHL worldwide in 2008 (Ferlay et al 2010). NHL is the 8th most commonly diagnosed cancer in men and the 11th in women. The disease accounts for ~5.1% of all cancer cases and 2.7% of all cancer deaths (Bofetta 2011). Large B-cell lymphomas represent the most common sub-group of NHL (Rodriguez-Abreu 2007).

Diffuse large B cell lymphoma (DLBCL) is the most common subtype of NHL, accounting for approximately 30% of NHL cases.The past two decades, progress has been made in understanding the biological heterogeneity of DLBCL and in improving survival with combinations of CHOP and immunotherapy. The addition of ritixumab into combination therapies for DLBCL have greatly improved patient outcomes. However, patients with chemotherapy-refractory DLBCL following treatment under the current standards of care still have a particularly dire prognosis, with no curative treatment options (Flowers 2010).

As most advanced cancers eventually become refractory to conventional therapies, new treatment modalities are needed. Immunotherapy, which is based on the enhancement of an immune response against the tumour, is a promising approach to treating many cancer types. T cells play an important role in destroying diseased cells throughout the body. Studies with immune checkpoint

inhibitors and tumour infiltrating lymphocytes have demonstrated the potential of T cells to treat cancer. T cells need to possess the appropriate specificity for a tumour, be present in sufficient numbers, and overcome any local immunosuppressive factors to be effective. Engineered T cells are a promising approach for cancer therapy (Kershaw et al 2013).

Engineered Autologous Cell Therapy (eACT*) is a process by which a patient*s own T cells are collected and subsequently genetically altered to recognize and target antigens expressed on the cell surface of specific malignancies (Kochenderfer et al 2013). The ability to genetically engineer human T cells and use them to mediate cancer regression in patients has been demonstrated in a number of studies and has opened possibilities for the treatment of patients with a wide variety of cancer types including B cell malignancies expressing the CD19 antigen. CD19 is a 95 kDa transmembrane protein expressed only in the B cell lineage. It is expressed in all normal B cells starting at the pre-B cell stage until the final differentiation stage and is not expressed in pluripotent hematopoietic stem cells or most plasma cells. The pattern of CD19 expression is maintained in B cell malignancies including all subtypes of B cell NHL, chronic lymphocytic leukemia (CLL) and non T cell acute lymphoblastic leukemia (ALL) (Blanc et al 2011) with the exception of multiple myeloma. Although there have recent advances in novel therapies for these B cell malignancies (Wang et al 2013; Byrd et al 2013; and Furman et al 2014); most patients eventually develop resistance to approved therapies. Chimeric antigen receptor+ T cell therapy may circumvent mechanisms of resistance and potentially address the unmet medical need for these patients.

An anti-CD19 CAR was generated at the Surgery Branch of the National Cancer Institute (NCI). This CAR contained the mouse anti-human single chain variable fragment (scFv) derived from the antibody FMC63, the CD3-zeta T cell activation domain, and a CD28 co-stimulatory domain. In preclinical models, the anti-CD19 CAR recognized and killed CD19+ target cells in vitro and in vivo. A phase 1 study of this anti-CD19 CAR has been conducted at the NCI using anti-CD19 CAR+ T cells generated by retroviral transduction and manufactured at the NCI. Conditioning chemotherapy followed by infusion of anti-CD19 CAR+ T cells has demonstrated durable responses in the majority of patients with relapsed and refractory CLL, indolent NHL, diffuse large B cell lymphoma (DLBCL), and primary mediastinal B cell lymphoma (PMBCL) with the predominant toxicity of cytokine release syndrome (CRS). Axicabtagene ciloleucel utilizes the anti-CD19 CAR from the NCI and is produced through a streamlined, closed manufacturing process. Axicabtagene ciloleucel will be evaluated in patients with relapsed or refractory B cell malignancies.

For the ZUMA-1 (KTE-C19-101) study, subjects with the following refractory aggressive Non-Hodgkin Lymphoma sub-types are to be treated indications are to be studied within the phase 1/2 multi-center study evaluating the safety and efficacy of axicabtagene ciloleucel in subjects with refractory aggressive non-Hodgkin lymphoma: DLBCL, PMBCL, transformed follicular lymphoma (TFL) and

high grade B-cell
lymphoma (HGBCL). Please refer to section 2 of the clinical trial protocol for a description of the three sub-types.

Study objective

The primary objective of Phase 1 study is to evaluate the safety of axicabtagene ciloleucel regimens.

The primary objective of Phase 2 pivotal study is to evaluate the efficacy of axicabtagene ciloleucel, as measured by objective response rate (ORR) in subjects with diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), and transformed follicular lymphoma (TFL). Secondary objectives will include assessing the safety and tolerability of axicabtagene ciloleucel and additional efficacy endpoints.

The primary objective of the Phase 2 safety management study is to assess the impact of a prophylactic regimen or earlier interventions, debulking therapy, or prophylactic steroid use on the rate and severity of cytokine release syndrome (CRS) and neurologic toxicities.

The key secondary objectives include assessment of efficacy, levels of anti-CD19 chimeric antigen receptor (CAR) T cells, cytokines in blood/serum, and the change in European Quality of Life-5 Dimensions (EQ-5D) scores from baseline to Month 6.

Study design

Study KTE-C19-101 is a Phase 1/2 multicenter, open-label studyevaluating the safety and efficacy of axicabtagene ciloleucel in subjects
with relapsed or refractory aggressive non-Hodgkin lymphoma (NHL).

The trial will be separated into 3 distinct phases designated as the

Phase 1 study, Phase 2 pivotal study (Cohort 1 and Cohort 2), and Phase 2 safety management study (Cohort 3, Cohort 4, Cohort 5 and
Cohort 6).

> Phase 1 Study
During Phase 1 study, approximately 6 to 24 subjects with DLBCL, PMBCL, or TFL will be enrolled to evaluate the safety of axicabtagene
ciloleucel regimens. A safety review team (SRT), internal to the study sponsor, will review the safety data and make recommendations on
further study conduct of Phase 1 and progression to Phase 2 pivotal study as depicted in Figure 3 and outlined in Section 9.10.

> Phase 2 Pivotal Study In the Phase 2 pivotal study, approximately 92 subjects will enroll into 2 separate cohorts designated as Cohort 1 and Cohort 2:
- Cohort 1 will enroll approximately 72 adult subjects with refractory DLBCL.
- Cohort 2 will enroll approximately 20 adult subjects with refractory PMBCL and TFL. TFL is defined as subjects who received prior therapy for follicular lymphoma.

> Phase 2 Safety Management Study
In the Phase 2 safety management study (SMS), approximately 170 subjects will enroll into 4 separate cohorts designated as Cohort 3,
Cohort 4, Cohort 5 and Cohort 6.
- Cohort 3 will enroll approximately 40 adult subjects with relapsed or refractory transplant ineligible DLBCL, PMBCL, or TFL.
- Cohort 4 will enroll and dose approximately 40 adult subjects with relapsed or refractory DLBCL, PMBCL, TFL or HGBCL after 2 or more lines of systemic therapy.
- Cohort 5 will enroll and dose approximately 50 adult subjects with relapsed or refractory DLBCL, PMBCL, TFL or HGBCL after 2 or more lines of systemic therapy.
- Cohort 6 will enroll and dose approximately 40 adult subjects with relapsed or refractory DLBCL, PMBCL, TFL or HGBCL after 2 or more lines of systemic therapy.

Independent of the phase of the study each subject will follow the same study treatment schedule and procedural requirements. Each subject will proceed through the following study periods:
- Screening
- Enrollment/Leukapheresis period
- Bridging therapy (if applicable; safety management study only) or debulking therapy (if applicable, safety management study, Cohort 5
only)
- Conditioning chemotherapy period
- Investigational product (IP) treatment period
- Post-treatment assessment period
- Long-term follow-up period
for details.

At the end of KTE-C19-101, subjects who received an infusion of axicabtagene ciloleucel will complete the remainder of the 15-year follow-up assessments in a separate long-term Follow-up (LTFU) study, KT-US-982-5968.

Intervention

Investigational Product:
• Axicabtagene ciloleucel treatment consists of a single infusion of CAR transduced autologous T cells administered intravenously at a target dose of 2 x 10^6 anti-CD19 CAR T cells/kg. For subjects weighing greater than 100 kg, a

maximum flat dose of 2 x 10^8 anti-CD19 CAR T cells will be administered. Under circumstances where subjects initially respond and subsequently relapse, subjects may be eligible for a second course of conditioning chemotherapy and axicabtagene ciloleucel.

Bridging Therapy (Phase 2 Safety Management Study)
• At the discretion of the investigator, bridging therapy may be considered for subjects particularly with high disease burden at screening or baseline assessment (eg, bulky disease or rapidly progressing disease).

Debulking Therapy
• Subjects enrolled into the Phase 2 Safety Management Study, Cohort 5 should receive debulking therapy to reduce lymphoma burden. Debulking therapy options are outlined in Table 3 of the protocol.

Conditioning Chemotherapy
• Axicabtagene ciloleucel is administered after a conditioning chemotherapy regimen consisting of fludarabine 30 mg/m2/day and cyclophosphamide 500 mg/m2/day, administered x 3 days.
For subjects enrolled into the Phase 2 Safety Management Study, Cohort 5: Subjects who have not recovered their white blood cell (WBC) count by the time conditioning chemotherapy is scheduled to start, may skip the conditioning chemotherapy if the WBC is <= 1000/µL at this time. This option must be discussed with the Kite medical monitor.

Additional axicabtagene ciloleucel regimens may be explored in Phase 1 per Section 9.6 of the study protocol.

Study burden and risks

For a study treatment, the patient needs to be hospitalized for at least 7 days. Before infusion of axicabtagene ciloleucel the patient will receive 3 days of chemotherapy. The patient may experience side effects after treatment.

Contacts

Public
Kite Pharma Inc

Broadway 2400
Santa Monica CA 90404
US
Scientific
Kite Pharma Inc

Broadway 2400
Santa Monica CA 90404
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

101. Histologically confirmed aggressive B cell NHL, including the following types defined by WHO 2008 (Campo 2011):
- DLBCL not otherwise specified;
- T cell/histiocyte rich large B cell lymphoma;
- DLBCL associated with chronic inflammation;
- Epstein-Barr virus (EBV)+ DLBCL of the elderly; OR
- primary mediastinal (thymic) large B cell lymphoma
- transformation of follicular lymphoma to DLBCL will also be included
102. Chemotherapy-refractory disease, defined as one or more of the following:
- No response to first-line therapy (primary refractory disease); subjects who are intolerant to first-line therapy chemotherapy are excluded
- PD as best response to first-line therapy
- SD as best response after at least 4 cycles of first-line therapy (e.g., 4 cycles of R-CHOP) with SD duration no longer than 6 months from last dose of therapy OR
- No response to second or greater lines of therapy
- PD as best response to most recent therapy regimen
- SD as best response after at least 2 cycles of last line of therapy with SD duration no longer than 6 months from last dose of therapy OR
- Refractory post-ASCT
- Disease progression or relapsed <=12 months of ASCT (must have biopsy proven recurrence in relapsed subjects)
- If salvage therapy is given post-ASCT, the subject must have had no response to or relapsed after the last line of therapy
103. Subjects must have received adequate prior therapy including at a

minimum:
- anti-CD20 monoclonal antibody unless investigator determines that tumor is CD20 negative, and
- an anthracycline containing chemotherapy regimen;
- for subjects with transformed FL must have received prior chemotherapy for follicular lymphoma and subsequently have chemorefractory disease after transformation to DLBCL
104. At least 1 measurable lesion according to the revised IWG Response Criteria for Malignant Lymphoma) (Cheson 2007). Lesions that have been previously irradiated will be considered measurable only if progression has been documented following completion of radiation therapy
105. MRI of the brain showing no evidence of CNS lymphoma
106. At least 2 weeks or 5 half- lives, whichever is shorter, must have elapsed since any prior systemic therapy at the time the subject is planned for leukapheresis, except for systemic inhibitory/stimulatory immune checkpoint therapy. At least 3 half-lives must have elapsed from any prior systemic inhibitory/stimulatory immune checkpoint molecule therapy at the time the subject is planned for leukapheresis (e.g. ipilimumab, nivolumab, pembrolizumab, atezolizumab, OX40 agonists, 4-1BB agonists etc)
107. Toxicities due to prior therapy must be stable and recovered to <= Grade 1 (except for clinically non-significant toxicities such as alopecia)
108. Age 18 or older
109. Eastern cooperative oncology group (ECOG) performance status of 0 or 1
110. ANC >=1000/uL
111. Platelet count >=75,000/uL
112. Absolute lymphocyte count >=100/uL
113. Adequate renal, hepatic, pulmonary and cardiac function defined as:
- Creatinine clearance (as estimated by Cockcroft Gault) >= 60 mL/min
- Serum ALT/AST <=2.5 ULN
- Total bilirubin <=1.5 mg/dl, except in subjects with Gilbert*s syndrome.
- Cardiac ejection fraction >= 50% ,no evidence of pericardial effusion as determined by an ECHO, and no clinically significant ECG findings
- No clinically significant pleural effusion
- Baseline oxygen saturation >92% on room air
114. Females of childbearing potential must have a negative serum or urine pregnancy test (females who have undergone surgical sterilization or who have been postmenopausal for at least 2 years are not considered to be of childbearing potential)Additional criteria specific for Phase 2 safety management study (cohorts 3, 4 and 5):
115. Relapsed or refractory large B-cell lymphoma including DLBCL, PMBCL, TFL, and HGBCL after two systemic lines of therapy**

Exclusion criteria

201. History of malignancy other than nonmelanoma skin cancer or carcinoma in

situ (e.g. cervix, bladder, breast) or follicular lymphoma unless disease free for at least 3 years
202. History of Richter*s transformation of CLL
203. Autologous stem cell transplant with therapeutic intent within 6 weeks of planned axicabtagene ciloleucel infusion
204. History of allogeneic stem cell transplantation
205. Prior CD19 targeted therapy with the exception of subjects who received axicabtagene ciloleucel in this study and are eligible for re-treatment
206. Prior chimeric antigen receptor therapy or other genetically modified T cell therapy
207. History of severe, immediate hypersensitivity reaction attributed to aminoglycosides
208. Presence or suspicion of fungal, bacterial, viral, or other infection that is uncontrolled or requiring IV antimicrobials for management.
209. History of HIV infection or acute or chronic active hepatitis B or C infection. Subjects with history of hepatitis infection must have cleared their infection as determined by standard serological and genetic testing per current Infectious Diseases Society of America (IDSA) guidelines or applicable country guidelines.
210. Presence of any indwelling line or drain (e.g., percutaneous nephrostomy tube, indwelling Foley catheter, biliary drain, or pleural/peritoneal/pericardial catheter). Dedicated central venous access catheters such as a Port-a-Cath or Hickman catheter are permitted
211. Subjects with detectable cerebrospinal fluid malignant cells, or brain metastases, or with a history of CNS lymphoma or primary CNS lymphoma, cerebrospinal fluid malignant cells or brain metastases
212. History or presence of CNS disorder such as seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, or any autoimmune disease with CNS involvement
213. Subjects with cardiac atrial or cardiac ventricular lymphoma involvement
214. History of myocardial infarction, cardiac angioplasty or stenting, unstable angina, or other clinically significant cardiac disease within 12 months of enrollment
215. Expected or possible requirement for urgent therapy within 6 weeks due to ongoing or impending oncologic emergency (eg, tumor mass effect, tumor lysis syndrome)
216. Primary immunodeficiency
217. History of symptomatic deep vein thrombosis or pulmonary embolism requiring systemic anticoagulation within 6 months of enrollment
218. Any medical condition likely to interfere with assessment of safety or efficacy of study treatment
219. History of severe immediate hypersensitivity reaction to any of the agents used in this study
220. Live vaccine <= 6 weeks prior to planned start of conditioning regimen
221. Women of child-bearing potential who are pregnant or breastfeeding because of the potentially dangerous effects of the preparative chemotherapy on the fetus or infant. Females who have undergone surgical sterilization or who have

been postmenopausal for at least 2 years are not considered to be of childbearing potential
222. Subjects of both genders who are not willing to practice birth control from the time of consent through 6 months after the completion of conditioning therapy
223. In the investigators judgment, the subject is unlikely to complete all protocol-required study visits or procedures, including follow-up visits, or comply with the study requirements for participation
224. History of autoimmune disease (e.g. Crohn's, rheumatoid arthritis, systemic lupus) resulting in end organ injury or requiring systemic immunosuppression/systemic disease modifying agents within the last 2 years

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-05-2017
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO

Date:	18-05-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	15-12-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-01-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-03-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-04-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-07-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-07-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-08-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-08-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-02-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-02-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-06-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-08-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-09-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-10-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-12-2018

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-01-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-02-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-04-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-04-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-06-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-01-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-01-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	14-05-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-06-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-07-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-08-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-10-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-11-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-04-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-06-2021
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-07-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-03-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-05-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-09-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-11-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-02-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-05-2023
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
EudraCT	EUCTR2015-005007-86-NL
ClinicalTrials.gov	NCT02348216
CCMO	NL56662.000.16