CER-001 Infusions in Subjects with Familial HDL-c Deficiency

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Evaluate the effects of CER-001 - adminstered as iv infusion - on plaque size/burden in arteries, plaque inflammation in the artery wall and the rate of cholesterol transport in the body

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON39134

Source
ToetsingOnline

Brief title
CER-001-CLIN-007

Condition

- Metabolic and nutritional disorders congenital
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
genetic low HDLc states, low HDL cholesterol

Research involving
Human

Sponsors and support

Primary sponsor: Cerenis Therapeutics, SA
Source(s) of monetary or material Support: Cerenis Therapeutics;Frankrijk

Intervention

Keyword: CER-001, cholesterol, HDL

Outcome measures

Primary outcome

* Single dose pharmacokinetics of ApoA-I following the first and final doses

* Peak free cholesterol levels (as a surrogate marker for ApoA-I Cmax values)

* Changes in pharmacodynamic parameters over time

Secondary outcome

* Change in cholesterol flux (TICE and TCE) from baseline to Week 26

* Incidence and severity of AEs from routine monitoring

* Incidence of abnormalities and changes from baseline in clinical laboratory

parameters from testing of blood and urine, including antibody development

Study description

Background summary

Patients with genetically determined low HDLc have a strongly increased cardiovascular risk.
To date, no efficient options are available to increase HDLc and thereby increase the reverse cholesterol transport.
CER-001 has in early studies shown to effectively increase cholesterol mobilization.

Study objective

Evaluate the effects of CER-001 - adminstered as iv infusion - on plaque size/burden in arteries, plaque inflammation in the artery wall and the rate of cholesterol transport in the body

Study design

Prior to the CER-001 infusions, patients will be evaluated for atherosclerotic

plaques (MRI), vessel wall inflammation (PET-CT) and reverse cholesterol transport rates (cholesterol flux studies).
After a period of CER-001 infusions we will evaluate whether and to what extent the vessel wall plaques (MRI), vessel wall inflammation (PET-CT) and reverse cholesterol transport have been improved following CER-001 infusion.
This will be evaluated in an open, non-comaparative investigation in which the patients will receive infusions of CER-001 (8mg/kg) up to 20 times during a 6-months time phrame.

Intervention

20 times an infusion of CER-001 (8mg/kg), at an interval of 3 days (first four weeks) followed by weekly administration.

Study burden and risks

To date, no significant side effect following CER-001 infusions have been observed in the 150 patients who have received these infusions.

During the project, patients will be subjected to the following research:
a. 2x MRI (no radiation)
b. 2x PET-CT: 4.6 mSv ; in total 2x in 4 weeks (resulting in a radiation exposure well below the legally alowed exposure)
c. cholesterol flux: burden because of the infusions, and frequent collection of faeces samples, urinary samples and blood withdrawals. No serious side effects to be expected.
d. 1x 24 u urine (cortisol)
e. 1x synacthen test

The total duration of the research project for a patient will last 6-7 months.
Total volume of blood draws in this period approx. 470 ml.

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

Eligible subjects must meet the following criteria before they are enrolled into the study:;1. Subject must read and sign the informed consent, as approved by the EC/IRB prior to performance of any screening procedures.
2. Male or female subjects age 18 or above.
3. Females of childbearing potential that agree and commit to use an acceptable form of birth control for the entire study. Acceptable forms of birth control for this study are defined as a barrier method plus hormonal therapy (implants, injections, oral contraceptives and IUDs), double barrier method or abstinence.
4. Subject diagnosis of genetically confirmed homozygous familial ApoA-I deficiency.
5. Subject is on stable dosages of lipid lowering therapies for at least 6 weeks prior to baseline procedures.
6. Subject must be willing to participate in the study and comply with all protocol requirements.

Exclusion criteria

Subjects meeting the following criteria are not eligible for the study:;1. Females who are pregnant, breastfeeding, or plan to become pregnant during the study and males wishing to beget a child during the study..
2. Subject has known major hematologic, renal [serum creatinine > 2.0 mg/dL (180 *mol/L)], hepatic (liver enzymes greater than twice the upper limits of normal for the performing laboratory), metabolic, gastrointestinal or endocrine dysfunction in the judgment of the Investigator.
3. Subject is likely to be unreliable as a study participant based on the Investigator's (or

designee*s) knowledge of the subject (e.g., alcohol or other drug abuse, inability or unwillingness to adhere to the protocol, or psychosis)
4. Subject has a contraindication to MRI scanning such as imbedded metal (e.g., schrapnel), implanted metal objects (e.g., pacemaker), claustrophobia, allergy to gadolinium chelate contrast or severe renal insufficiency (e.g., GFR < 30 mL/min/1.73m2) that would preclude the use of contrast-enhanced 3TMRI.
5. Subject has received an investigational agent within 30 days prior to baseline procedures.

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):	20-02-2012
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CER-001
Generic name:	CER-001

Ethics review

Approved WMO

Date:	27-12-2011
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-12-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-12-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-10-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-03-2014
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
EudraCT	EUCTR2011-006188-23-NL
CCMO	NL39219.018.11