Modifying Orphan Disease Evaluation (MODE) Study: A multicenter, open-label study of the effects of CER-001 on plaque volume in subjects with Homozygous Familial Hypercholesterolemia

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

Summary

ID

NL-OMON39438

Source
ToetsingOnline

Brief title
MODE

Condition

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

Synonym
Homozygous Familial Hypercholesterolemia; elevated cholesterol

Research involving
Human

Sponsors and support

Primary sponsor: Cerenis Therapeutics, S.A.
Source(s) of monetary or material Support: Cerenis Therapeutics uit Frankrijk

Intervention

Keyword: CER-001, Familial, Homozygous, Hypercholesterolemia

Outcome measures

Primary outcome

percent change from baseline to follow-up in carotid mean vessel wall area as

measured by 3TMRI

Secondary outcome

*Assessment of six month efficacy data for determination of continuation of

extension phase

* Percent change in carotid vessel wall volume

* Absolute change in carotid vessel wall volume

* Percent change in the mean of the carotid normalized wall index

* Percent change in maximum vessel wall thickness

* Percent change in mean vessel wall thickness

* Percent change in thoracic aorta vessel wall volume as measured by 3TMRI

* Percent change in thoracic aorta mean vessel wall area

* Absolute change in thoracic aorta vessel wall volume

* Percent change in carotid lipid core volume

* Absolute change in carotid lipid core volume

* Percentage change in carotid calcified vessel wall volume

* Absolute change in carotid calcified vessel wall volume

* Percent change in carotid intra-plaque hemorrhage volume

* Absolute change in carotid intra-plaque hemorrhage volume

Assessment of six month efficacy data for determination of continuation of

extension

phase

Secondary efficacy measurements for the extension phase will include:

* Percent change from baseline to twelve months in carotid mean vessel wall

area as

measured by 3TMRI

* Percent change from six months to twelve months in carotid mean vessel wall

area as

measured by 3TMRI

* Overall percent change from baseline to twelve months carotid mean vessel

wall area

as measured by 3TMRI

* Continued safety monitoring throughout the study duration

Study description

Background summary

Familial hypercholesterolemia (FH) is an autosomal dominant disorder of low-density lipoprotein (LDL) receptors. Absence or gross malfunctioning of

the LDL receptors impair the normal processing of circulating LDL, leading to severe elevations in total cholesterol and LDL-cholesterol. LDL receptor function can range from absent to about 25% of normal activity. The heterozygous form of the disease (HeFH) affects approximately 1 in 500 persons worldwide. The homozygous form (HoFH) is much less common, affecting approximately 1 in 1 million persons worldwide.
Without intervention patients die during their adolescence.

Study objective

The purpose of the study is to assess the effects of CER-001, given by intravenous infusion with regards to plaque burden of the carotid arteries and the descending thoracic aorta using 3T magnetic resonance imaging (3TMRI).

The objective of the extension phase is to assess the additional benefit as well as the safety of continued use of CER-001 for a one year period (24 infusions).

Study design

The study consists of a screeningperiod including two 3TMRI's. This period can take up to 30 days.

-The following treatment period is 48 weeks consisting of 24 infusion visits (biweekly)
-There will be a follow-up visit with a 3TMRI, 1 to 3 weeks after the 12th dose is administered. and a 3TMRI 1 to 3 weeks after the last dose is administered.
- Finally there will be a follow-up visit 5-6 weeks after the last dose is administered.

The study will be performed at about 10 sites worldwide.
It concerns an open label, non comparing, study in which all patients receive 8 mg/kg CER001 as a treatment.

Intervention

The intervention for all participants will be 24 times, intravenous administerded dosage of 8 mg/kg CER001, with intervals of two weeks.

Study burden and risks

So far, 32 healthy volunteers and more than 50 patients with acute coronary syndromes have been given similar or higher doses of CER-001 without any clinically significant side effects related to the drug. Minor adverse events such as headache, nausea, vomiting and abdominal pain would be reasonable to

expect.

As of June 18, 2012, in the ongoing multiple-dose study (434 subjects have received at least 1 dose of study drug), twelve subjects have withdrawn from the trial due to side effects that happened either during or soon after infusion of study drug. Serious and Non-Serious side effects have involved local injection site reactions and infusion reactions. The side effects experienced included one or more of the following: wheezing, eye itching, eye swelling, facial swelling, rash, feeling cold, decrease in body temperature, cold sweats, cold shivers, chest pressure, chest pain, jaw pain, decreased blood pressure, increased blood pressure, fatigue, dizziness, headache, nausea, vomiting, stomach pains, and diarrhea. These cases were fixed either by themselves or with the help of the study doctor.

During the study the subjects will undergo the following procedures:
- Conversation about their medical history (once)
- Physical Examination (twice)
- Vital signs measurement (heartrate, bloodpressure) (24 times)
- Blood sample drawn (25 times approx. 28 ml)
- pregnancy test (6times)
- 3TMRI (4 times)
- ECG (twice)
- Administration of investigational product (24 times)

The total duration of the study for 1 subject will be approximately 516 days.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1.Male or female subject 12 years or older
2.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) or abstinence.
3. Subject diagnosis of Homozygous FH defined as:
* Genetic testing on record classifying the subject as Homozygous FH
-or -
* Genetic testing on record classifying the subject as Compound Heterozygous FH with accompanying phenotypical criteria of:
* a history of LDL-C *220 mg/dL (5.69 mmol/L) while receiving maximally tolerated lipid-lowering therapy with <15% response
-and-
* LDL-C above the 90th percentile in *2 first-degree relatives
-and-
* the presence of tendinous xanthomas and/or manifestations of premature coronary heart disease or corneal arcus.

Exclusion criteria

1. Subjects weighing more than 100 kg at Screening
2.Subjects with significant health problems in the recent past including blood disorders, cancer, or digestive problems but not cardiovascular disease as manifested in inclusion criteria #3 above.
3.Females who are pregnant, breastfeeding, or plan to become pregnant during the study.

4.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
5.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.
6.Subject has participated in any investigational drug study within 30 days prior to randomization, or expects to participate in any other investigational drug study during his/her planned participation in this study. The last dose of any investigational product must have been taken at least 30 days prior to the first dose of CER-001.
7.Subject has previously participated in this study or another study involving CER-001.

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):	15-04-2012
Enrollment:	16
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	11-11-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-02-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-03-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-06-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-10-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2013

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-05-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-08-2013
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	EUCTR2011-003998-28-NL
CCMO	NL38345.018.11