Can HDL Infusions Significantly Quicken Atherosclerosis Regression? A phase II, Multi-center, double-blind, ascending dose, placebo-controlled, dose-finding trial of CER-001 or placebo in subjects with acute coronary syndrome.

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To assess the impact of six IV infusions of 3, 6, or 12 mg/kg of CER-001 or placebo, given at weekly intervals, on atherosclerotic plaque volume, as measured by coronary IVUS.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON38390

Source
ToetsingOnline

Brief title
CHI SQUARE

Condition

- Coronary artery disorders

Synonym
Acute Coronary Syndrome, Heart Attack

Research involving
Human

Sponsors and support

Primary sponsor: Cerenis Therapeutics SA
Source(s) of monetary or material Support: Industry

Intervention

Keyword: ACS, HDL, IVUS

Outcome measures

Primary outcome

The primary endpoint for this study is the nominal change in total plaque volume (TPV) in a 30 mm segment of the target coronary artery assessed by 3-dimensional (3D) IVUS.

Secondary outcome

Secondary atherosclerosis efficacy parameters will include the percent change in plaque volume and the change in percent atheroma volume in the target 30 mm segment. The percent change in plaque volume will be calculated as the nominal change divided by the baseline value, multiplied by 100. Percent atheroma (obstructive) volume will be computed by dividing plaque volume by elastic external membrane (EEM) volume and then multiplying by 100. Secondary atherosclerosis efficacy parameters will also include the change in total vessel volume in the target 30 mm segment; as well as changes in plaque, lumen and total vessel volumes from baseline to follow-up in anatomically comparable 5 mm segments centered on the site with the smallest plaque burden at baseline, and the largest plaque burden at baseline on 3D IVUS.

Study description

Background summary

Cardiovascular disease remains the most pressing healthcare issue for developed countries and is becoming so for developing countries. There are a number of chronic therapies available for long-term management of risk. Short term therapies for subjects with an acute event, such as an episode of acute coronary syndrome (ACS), are focused on reperfusion and removing thrombus but most subsequent events are caused by ahterosclerotic plaque rupture at a different sit. There are no approved therapies that can rapidly reduce the burden of unstable, inflamed plaque in the overall coronary vascular bed. HDL has multiple actions that could lead to atherosclerotic plaque stabilization, such as rapid removal of large quantities of cholesterol from the vasculature, improvement in endothelial function, protection against oxidative damage and reduction in inflammation. This study will asses the effects of CER-001, an ApoA-I- based HDL mimetic, on indices of atherosclerotic plaque progression and regression as assessed by intravascular ultrasound (IVUS) measurements in patients with ACS.

Study objective

To assess the impact of six IV infusions of 3, 6, or 12 mg/kg of CER-001 or placebo, given at weekly intervals, on atherosclerotic plaque volume, as measured by coronary IVUS.

Study design

Subjects presenting with symptoms of ACS will be eligible to be screened for this
study. At the time of baseline catheterization, subjects need to have an adequate IVUS
evaluation of one *target* artery for IVUS which is not influenced by prior or present PCI, and
the proximal 4 cm of the target artery should have a diameter stenosis between 0 and 50% by
visual angiographic assessment, a reference diameter *2.5 mm and be free of filling defects
suggestive of thrombus. Once the baseline IVUS has been evaluated by the IVUS Core
Laboratory for overall quality, the presence of a suitable target vessel and the absence of
technical factors which can preclude accurate reading of the IVUS images, the subject will be
randomized to receive an intravenous, given over one hour, of placebo or one of

three
doses of CER-001 (3, 6, or 12 mg/kg). Randomized subjects will return at weekly intervals (i.e.,
every 7 to 11 days) for five additional infusions. End-of-treatment labs will be drawn one week
(5 to 9 days) after the last infusion. A follow-up IVUS will be conducted approximately 3 weeks
(14 to 35 days) after the last infusion. A follow-up visit will occur approximately 6 months (+/- 2 weeks) after the last infusion to collect samples for Anti-ApoA1 antibody testing and lipid profile and to monitor for MACE endpoints. The total study duration from randomization to follow up IVUS for a completed study subject can therefore range from approximately 7 to 8 months.

Intervention

Primary study parameters/outcome of the study
The primary endpoint for this study is the nominal change in total plaque volume (TPV) in a 30 mm segment of the target coronary artery assessed by 3-dimensional (3D) IVUS.

Study burden and risks

Subjects enrolled in this study will have a second coronary catheterization performed
approximately 8-10 weeks following their initial catheterization and will therefore be exposed to the risks associated with the second catheterization procedure. Cardiac catheterization is a common medical procedure that rarely causes serious problems, however, complications can include:
* Bleeding, infection, and pain where the catheter was inserted.
* Damage to blood vessels. Rarely, the catheter may scrape or poke a hole in a blood
vessel as it's threaded to the heart.
* An allergic reaction to the dye used.
Other, less common complications of the procedure include:
* Arrhythmias (irregular heartbeats). These often go away on their own, but may need
treatment if they persist.
* Damage to the kidneys caused by the dye used.
* Blood clots that can trigger stroke, heart attack, or other serious problems.
* Low blood pressure.
* A buildup of blood or fluid in the sac that surrounds the heart. This fluid can prevent the
heart from beating properly.
Subjects will receive six infusions of CER-001 (3, 6, or 12 mg/kg) or placebo during the study. In single-dose studies of CER-001 up to 45 mg/kg adverse

events were rare, mild in nature, and self-limiting. No adverse effects on the liver, kidney or red blood cells were observed in humans, however these effects have been seen in animals treated with higher doses (50 mg/kg and above dosed every second day for 4 weeks) in toxicology studies. Liver toxicity has been observed with the use of other HDL mimetics in humans. Minor adverse events such as headache, nausea, vomiting, abdominal pain or injection site reactions would also be reasonable o expect. Subjects in this trial will be allowed to be treated with all required medication to treat new or existing medical conditions, including their qualifying ACS event, and to maintain health and well-being. Subjects treated with placebo (25% chance) will receive no additional therapeutic benefit, however those treated with active drug (75% chance) are expected to derive therapeutic benefit from the removal of cholesterol from peripheral tissues including the vascular bed. The estimated treatment effect ranges from a reduction in total plaque volume of 4 mm3 (3 mg/kg) to 7 mm3 (12 mg/kg) beyond that seen in placebo-treated subjects under post-ACS standard-of-care treatment.

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

male or female up to and including 80 years of age, acute chest pain and diagnosis of ST segment elevation or non-ST elevation myocadial infarction or unstable angina, clincally indicated coranary angiography, evidence of coronary artery disease, and an appropriate target coronary artery.

Exclusion criteria

Subjects weighing more than 160 kg, uncontrolled diabetes, triglycerides greater than 500 mg/dl, baseline ivus of unacceptable quality, subjects for whom CABG is planned, hemodynamically or clinically unstable, and ejcection fraction less than 35%.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-09-2011
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Not Yet Available
Generic name:	Recombinant Human Apolipoprotein A-1/Phospholipids Complex

Ethics review

Approved WMO Date:	28-04-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-05-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-08-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-10-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-10-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-04-2012
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-08-2012
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	EUCTR2010-023611-34-NL
ClinicalTrials.gov	NCT01201837
CCMO	NL35626.018.11