HDL Acute Lipid Optimization Open Label Study

Published: 24-03-2016
Last updated: 19-04-2024

1. Assess the effectiveness of serial infusions of autologous selectively delipidated HDL/preβ enriched plasma following use of HDL Therapeutics PDS-2* System on lipid core burden in the study lipid core containing plaque segment(s) as...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON42644

Source
ToetsingOnline

Brief title
HALO-OLS

Condition

- Coronary artery disorders

Synonym
atherosclerosis; hardening of the arteries

Research involving
Human

Sponsors and support

Primary sponsor: HDL Therapeutics, Inc.
Source(s) of monetary or material Support: the sponsor HDL Therapeutics

Intervention

Keyword: Acute coronary syndrome, Cholesterol, PDS-2

Outcome measures

Primary outcome

1. Lipid core burden in the study lipid core containing plaque segment(s) as assessed by the InfraReDx TVC Imaging System at 2 weeks (± 1 week) following the final (7th) infusion visit paired with the baseline value.

2. Cumulative adverse events, serious adverse events, and unanticipated adverse device events from the start of infusion visit 1 to 8 weeks post-infusion visit 1, with the evaluated adverse events to include but not be limited to, hypotension, n-Butanol solvent toxicity, hypoglycemia, hypocalcemia, and the major adverse cardiac events (MACE) of cardiac death, recurrent ACS (including nonfatal myocardial infarction), ischemic stroke and revascularization of the PCI vessel or the vessel containing the study segment(s).

Secondary outcome

n/a

Study description

Background summary

Coronary atherosclerosis is by far the most frequent cause of ischemic heart disease, and plaque disruption with superimposed thrombosis is the primary cause of the acute coronary syndromes like unstable angina, myocardial infarction, and sudden death. The typical advanced atherosclerotic plaque is characterized by a core of lipid with an overlying fibrous collagen-rich cap. Such lesions may transform into a complex type of lesion with either rupture or

erosion of the fibrous cap and resultant thrombus formation. The lipid composition of the plaque, in addition to its volume and the severity of stenosis, is now recognized as being an important determinant of the development of thrombus-mediated acute coronary events.

A near infrared spectroscopic (NIRS) catheter system has been developed that identifies lipid core containing plaques (LCP) of interest in the coronary arteries and provides a quantitative image summary metric of lipid core burden. Both LCP and LCB measures have been validated vs. histology with good accuracy and has received CE Mark for clinical use. The use of NIRS permits the identification and quantification of LCPs whose presence could not reliably be determined by coronary angiography or IVUS alone. The development of the NIRS system now permits the evaluation of new specific medical therapies to reduce lipid core burden in lipid core containing plaques and potentially decrease recurrent clinical cardiovascular events.

A study in African Green monkeys demonstrated that treating plasma with a novel selective delipidation procedure converts large to small HDL [HDL-selectively delipidated (HDL-sdl)]. Treatment with delipidated plasma significantly reduced diet-induced aortic atherosclerosis in monkeys, as measured by intravascular ultrasound. These findings link the infusion of delipidated HDL/preβ enriched plasma and conversion of small to large HDL, in vivo, to improvement in atherosclerosis.

The HDL Therapeutics PDS-2* System is intended to produce autologous selectively delipidated HDL/pre-β enriched plasma for infusion in subjects with acute coronary syndrome in order to reduce lipid core burden in lipid core containing plaques in their coronary arteries.

For more detailed information please see section 1.1 of the study protocol.

Study objective

1. Assess the effectiveness of serial infusions of autologous selectively delipidated HDL/preβ enriched plasma following use of HDL Therapeutics PDS-2* System on lipid core burden in the study lipid core containing plaque segment(s) as assessed by the InfraReDx® TVC Imaging System*

2. Provide a complete summary of the safety profile associated with the use of the HDL Therapeutics PDS-2* System

Study design

This study will evaluate if serial infusions of the selectively delipidated HDL/preβ enriched plasma added to standard of care will reduce the lipid core burden of the identified lipid core containing plaque segment(s) in this

subject population.

Up to 10 subjects in up to two centers in Europe will be enrolled in this study. Subjects will receive serial infusions of autologous selectively delipidated HDL/preβ-HDL enriched plasma following use of HDL Therapeutics PDS-2 system . All enrolled subjects will be scheduled for 7 serial infusion visits, 1 infusion per week, within an approximately 7 week infusion visit period, with the visits scheduled 1 week ± 3 days apart beginning <=10 days following the clinically indicated screening catheterization procedure. All enrolled subjects will return for a follow-up catheterization with the TVC Imaging System 2 weeks (±1 week) following their final infusion visit. The total study duration will be 2-3 months.

Intervention

Subjects will receive serial infusions of autologous selectively delipidated HDL/preβ-HDL enriched plasma following use of HDL Therapeutics PDS-2 system. All enrolled subjects will be scheduled for 7 serial infusion visits, 1 infusion per week, within an approximately 7 week infusion visit period, with the visits scheduled 1 week ± 3 days apart beginning <=10 days following the clinically indicated screening catheterization procedure.

Study burden and risks

For an overview of the expected risks and side-effects please see the subject information sheet.

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

Screening stage 1: Presentation with ACS
1. Individual is >= 18 years of age and <=85 years of age ;2. ACS diagnosis (defined for the study as unstable angina/Non-ST elevation MI) <=7 days prior to a scheduled, clinically indicated, coronary angiographic study ;ACS defined as having at least one of the following:
a. Unstable angina, defined as at least 1 of the following:
- Rest angina (occurring at rest and prolonged, usually >20 minutes);
- New onset angina (within the past 2 months, of at least Canadian Cardiovascular Society Class III severity);
- Increasing angina (previously diagnosed angina that has become distinctly more frequent, longer in duration, or increased by 1 or more Canadian Cardiovascular Society class to at least CCS III severity).
b. Cardiac biomarkers (Total CK, CK-MB or Troponin) over the upper limit of normal
c. Ischemic ECG changes ;3. Meet the criteria for serial plasmapheresis:
• Weight of >= 50 kg (110 lbs.)
• Hemoglobin >= 12.5 g/dL
• No other condition that would preclude the subject from successfully completing the series of plasmapheresis visits in the investigator*s opinion ;4. Provide written informed consent before any study-specific procedures are performed. The subject must give consent by signing and dating an EC approved consent form. A subject may be excluded for any reason that, in the Investigator*s judgment, interferes with the ability to provide informed consent. ;5. Subjects must be willing to commit to completing all clinic visits and all associated procedures ;Screening stage 2: Angiographic and Central Laboratory Criteria
At least one (1) study segment will be identified for each subject and all will remain constant throughout the study. The qualifying study lipid core containing plaque segment(s) will meet all of the following criteria:
• 30-80 mm in length
• >= 20% and <= 50% stenosis by visual estimate not planned for PCI or other coronary revascularization
• At least one (1) 10mm segment within the study segment with a LCBI >=250 accessible by

and as assessed by the TVC Imaging System
• Has not undergone previous Coronary Artery Bypass Grafting (CABG)
• Has not had a prior percutaneous coronary intervention (PCI) ;6. HDL >=32 mg/dL as assessed by the central laboratory ;7. ApoA-I level of >= 95 mg/dL as assessed by the central laboratory ;8. Fasting triglycerides <300 mg/dL as assessed by the central laboratory ;9. Core laboratory approval of the TVC Imaging System images and results from the clinically indicated screening catheterization as meeting core lab criteria ;Screening stage 3: First infusion visit
10. Reaffirm the following inclusion criteria continue to be met:
- Subject meets the criteria for serial plasmapheresis:
• Weight of >= 50 kg (110 lbs.)
• Hemoglobin >= 12.5 g/dL
• Collection of at least 800 ml (>= 800 ml) of plasma
• No other condition that would preclude the subject from successfully completing the series of plasmapheresis visits in the investigator*s opinion
- Subject must be willing to commit to completing all clinic visits and the procedures associated with them

Exclusion criteria

Subjects must meet none of the following exclusion criteria prior to enrollment into the trial: ;Screening stage 1: Presentation with ACS
1. ST elevation myocardial infarction (MI) <=72 hours prior to screening procedures, as evidenced by any of the following:
• ST elevations >2mm in at least 2 contiguous precordial leads OR
• ST elevation of >1mm in at least 2 limb leads OR
• >2mm ST segment depression in precordial leads V1-V2, V2-V3, or V1-V3 OR
• Left bundle branch block not previously known to be present ;2. Diabetes mellitus type 1 ;3. Pregnant or lactating women, women who had a pregnancy, regardless of outcome, <=6 months prior to screening, or women who are unwilling to practice effective birth control or refrain from breastfeeding. Note: A urine pregnancy test will be performed at screening and at each infusion visit on all premenopausal women. ;4. Active liver disease or hepatic dysfunction with liver enzymes [ALT and AST] >3 times upper limit of normal of the reference range during Screening Visits 1 and 2 ;5. Active cholesystitis, gall bladder symptoms, or potential hepato-biliary abnormalities defined as alkaline phosophatase >3 times above the upper limit of the normal reference range. Note: subjects who have had a cholecystectomy are not excluded for this study. ;6. Currently undergoing renal dialysis or presence of renal dysfunction defined as GFR <60 ml/min ;7. Planned invasive surgery that would require a general anesthetic or a potential hospital stay during the study period ;8. History of a bleeding diathesis, or evidence of active abnormal bleeding within 30 days before enrollment ;9. History of intracranial hemorrhage, intracranial or spinal cord surgery, or central nervous system tumor or aneurysm ;10. Current cancer (treated or untreated) at the time of screening date for this study ;11. Unstable or uncontrolled hypertension defined as two consecutive measurements (after at least 5 minutes of sitting) of blood pressure with systolic >180 mm Hg and/or diastolic >110 mmHg whether taking or not taking an acceptable

concurrent antihypertensive medication ;12. Severe valvular stenosis or regurgitation as defined by ACC/AHA criteria ;13. History of major surgery <= 2 weeks prior to clinically indicated screening catheterization ;14. History of stroke <= 3 months prior to clinically indicated screening catheterization ;15. Unstable hypotension defined as two consecutive measurements of systolic blood pressure < 90 mmHg (a minimum of 30 minutes apart) ;16. Cardiac insufficiency defined as NYHA functional Class III or Class IV, as assessed by the investigator ;17. History of illicit drug or alcohol abuse <=1 year prior to screening ;18. Life expectancy less than 1 year ;19. Active enrollment, or previous enrollment within the past 180 days, in another investigational study ;20. Other conditions or criteria that, in the investigator*s opinion, precludes the subject from participation ;Screening stage 2: Angiographic Criteria
21. Left main coronary artery stenosis >50% by visual angiographic estimation ;22. Decreased left ventricular function as evidenced by a left ventricular ejection fraction (LVEF) <40% (within the previous 180 days prior to ACS episode or during ACS hospitalization, evaluation by either echocardiogram or ventriculography) ;Screening stage 3: First infusion visit
Subject is considered by his/her attending physician or the investigator to have continued or new hemodynamic instability (per blood pressure or other criteria) following the ACS episode, or to have any other type of clinical instability, at the time of the first infusion visit.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Generic name:	Plasma Delipidation System 2 (PDS-2)
Registration:	No

Ethics review

Approved WMO Date:	24-03-2016
Application type:	First submission
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
CCMO	NL55096.018.15