Evaluation of the Safety and Efficacy of Short-term A 002 Treatment in Subjects with Acute Coronary Syndromes

Published: 09-07-2010
Last updated: 30-04-2024

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Ethical review	Approved WMO
Status	Pending
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON34504

Source
ToetsingOnline

Brief title
VISTA-16

Condition

- Cardiac disorders, signs and symptoms NEC

Synonym
Heart Attack, Heart Disease

Research involving
Human

Sponsors and support

Primary sponsor: Anthera Pharmaceuticals, Inc
Source(s) of monetary or material Support: pharmaceutisch bedrijf

Intervention

Keyword: A-002, Acute Coronary Syndromes (ACS), atorvastatin, Phase 3

Outcome measures

Primary outcome

The primary objective of the study is to determine whether 16 weeks of treatment with A-002 plus atorvastatin and standard of care is superior to placebo plus atorvastatin and standard of care for reducing the hazard of the first occurrence of the combined endpoint of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or documented unstable angina with objective evidence of ischemia requiring hospitalization.

Secondary outcome

A secondary objective of the study is to determine whether A-002 plus atorvastatin and standard of care is superior to placebo plus atorvastatin and standard of care for reducing the occurrence of the hazard of the combined endpoint of all-cause mortality, non-fatal myocardial infarction, non-fatal stroke or documented unstable angina with objective evidence of ischemia requiring hospitalization or multiple occurrences of the nonfatal components of the composite primary endpoint

Study description

Background summary

Recently the safety and efficacy of A-002 has been established in 2 studies of subjects with stable coronary artery disease (CAD) in which significant decreases in secretory phospholipase A2 (sPLA2), low-density lipoprotein-cholesterol(LDL-C), as well as C-reactive protein (CRP) were documented
(Rosenson 2009). The potential clinical importance of reducing inflammation has also been reported in the setting of primary prevention (Ridker 2008) as well as the acute setting (PROVE-IT [Cannon 2004] and Kinlay 2003). These data along with the literature documenting the association between elevated levels of sPLA2 and cardiovascular risk in subjects with acute coronary syndrome (ACS)(Kugiyama 2000; Mallat 2005), support the investigation of the safety and efficacy of A-002 in a study of subjects presenting with an ACS.

Intervention with a specific sPLA2 inhibitor could salvage non-lethally jeopardized cells following an ischemic episode and thus could result in a reduction in the area of infarcted damage.

Study objective

The objective of this study is to evaluate the safety and efficacy of A-002 when added to atorvastatin plus standard-of-care in subjects with an ACS. Specifically this study will examine the effect of treatment on morbidity and mortality as defined by the respective primary and secondary efficacy composite variables: cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or documented unstable angina with objective evidence of ischemia requiring urgent hospitalization; and all-cause mortality, non-fatal myocardial infarction, non-fatal stroke, or documented unstable angina with objective evidence of ischemia requiring hospitalization.

Study design

This is a double-blind randomized parallel group placebo controlled study in subjects presenting with an ACS. Subjects will be randomized to receive either A-002 500 mg QD or placebo tablets in addition to atorvastatin plus standard-ofcare. Randomization must occur within *96 hours of hospital admission for the index ACS event, or if already hospitalized, within *96 hours of index event diagnosis.
Follow-up visits or blood draws will occur at 6, 12, 24, 48, 72, 96 hours (for the first 1500 patients) postrandomization and Weeks 1, 2, 4, 8, and 16. All lipid lowering therapies other than atorvastatin must be withdrawn prior to randomization.

All enrolled subjects will be followed until they have completed 16 weeks of treatment. The survival status of all subjects who have not died or withdrawn consent will be ascertained 6 months after they finish treatment.

Intervention

Following confirmation of eligibility, subjects will be randomized to A-002 500 mg QD or placebo plus atorvastatin. The dose of atorvastatin to be used will be at the discretion of the treating clinician but must be *20 mg daily. There will be an opportunity to adjust the atorvastatin dose at Week 8 if LDL-C levels remain above 100 mg/dL, but otherwise it must remain stable throughout the 16-week duration of the study. All other lipid lowering therapies (e.g., ezitimibe, fibrates, niacin, sequestrants) must be withdrawn prior to randomization and are not permitted during the treatment period of the study (16 weeks).

Study burden and risks

Patient should start the use of Atorvastatin (which might mean a switch of statin) and start the use of the study medication at the same time.
The patient should be able to visit the clinic and have blood withdrawn during each visit.

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

1. Men and women *40 years of age
2. Written informed consent from the subject
3. All subjects must have the presence of at least one of the following risk factors:
i. Diabetes Mellitus or
ii. Presence of any 3 of the following characteristics of metabolic syndrome
- Waist circumference >102 cm in males, >88 cm in females
- Serum triglycerides *150 mg/dL (*1.7 mmol/L)
- HDL-C <40 mg/dL (<1 mmol/L) in males, <50 mg/dL (<1.3 mmol/L) in females
- Blood pressure *130/85 mmHg
- Plasma glucose *110 mg/dL (*6.1 mmol/L) or
- history of cerebrovascular disease (stroke or TIA) o
- HDL <42 mg/dL or
- eGFR <60 mL/min or
- angiographic evidence of CAD (>50%)
- history of peripheral vascular disease or
- previous CABG or
- previous documented myocardial infarction or
- previous coronary revascularization
4. Subjects must be randomized within *96 hours of hospital admission for the index event, or if already hospitalized, within *96 hours of index event diagnosis
5. Percutenous revascularization, if required or planned, must occur prior to randomization

Exclusion criteria

1. Subjects enrolled in another experimental (interventional) protocol within the past 30 days prior to Screening.
2. Subjects treated for cancer within the previous 5 years except for skin basal cell carcinoma or carcinoma in situ of the cervix, with measures other than a minor, complete surgical excision or radiation therapy, (e.g., chemotherapy).
3. The presence of any severe liver disease with cirrhosis, active hepatitis, active chronic

hepatitis, alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >3 x ULN, biliary obstruction with
hyperbilirubinemia (total bilirubin >2 x ULN)
4. Active cholecystitis, gall bladder symptoms, or any hepato-biliary abnormalities
5. The presence of severe renal impairment (creatinine clearance [CrCl] <30 mL/min or creatinine >3 x ULN), nephrotic syndrome, or subjects undergoing dialysis
6. Uncontrolled diabetes mellitus (known hemoglobin A1c [HbA1c] >11% within the last 1 month prior to Screening)
7. Females who are nursing, pregnant, or intend to become pregnant during the time of the study, or females of child-bearing potential who have a positive pregnancy test during screening evaluation. Women of childbearing potential must also use a reliable method of birth control during the study and for 1 month following completion of therapy. A reliable method for this study is defined as one of the following: oral or injectable contraceptives, intrauterine device (IUD), contraceptive implants, tubal ligation, hysterectomy, a double barrier method (diaphragm with spermicidal foam or jelly, or a condom).
8. Subjects who have a history of alcohol or drug abuse within 1 year of study entry
9. Subjects living too far from participating center or unable to return for followup visits
10. Subjects who have a history of statin intolerance or a significant myopathy or rhabdomyolysis with any lipid-altering drugs
11. Subjects currently treated with the maximum labeled dose of a statin and not at LDL-C target for their level of risk as defined by NCEP ATP

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2010
Enrollment:	576
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Lipitor
Generic name:	Atorvastatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Nog niet beschikbaar
Generic name:	Varespladib Methyl

Ethics review

Approved WMO Date:	09-07-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-11-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-11-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-01-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-01-2011
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-10-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-03-2012
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	EUCTR2009-016812-18-NL
CCMO	NL32613.018.10