A Double-blind, Randomized, Placebo-controlled Phase 2 Study to Evaluate Efficacy, Safety, and Tolerability of Olpasiran (AMG 890) (a GalNAc-conjugated Small Interfering RNA [siRNA]) in Subjects with Elevated Lipoprotein(a)

Published: 26-06-2020
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Primary Objective: • To evaluate the effect of Olpasiran administered subcutaneous (SC) once every 12 weeks (Q12W) compared with placebo, on percent change from baseline in lipoprotein(a) (Lp[a]) after 36 weeks of treatment. Secondary Objectives: •...

Ethical review	Approved WMO
Status	Completed
Health condition type	Lipid metabolism disorders
Study type	Interventional

Summary

ID

NL-OMON52533

Source
ToetsingOnline

Brief title
20180109 - OCEAN[a]-DOSE

Condition

- Lipid metabolism disorders

Synonym
atherosclerotic cardiovascular disease, heart and blood vessel disease

Research involving
Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Amgen

Intervention

Keyword: Atherosclerotic, Cardiovascular, Lipoprotein(a), Phase 2

Outcome measures

Primary outcome

• Percent change in Lp(a) from baseline at week 36

Secondary outcome

• Percentage change from baseline in:

- Lp(a) at week 48

- LDL-C at week 36 and week 48

- ApoB at week 36 and week 48

• PK parameters for olpasiran including, but not limited to, maximum observed

concentration (Cmax), and the area under the concentration time curve (AUC)

Study description

Background summary

ASCVD is a condition that may restrict the amount of blood and oxygen reaching your heart and other vital organs in your body due to a narrowing of your arteries. There are many factors that contribute to ASCVD, but some remain unknown. Known risk factors include smoking, high blood pressure, high cholesterol, diabetes and more. Current treatments that focus on these risk factors do not always work.

Lipoprotein(a) or Lp(a) is produced in the liver and found in the blood. Some people have high Lp(a) in their blood, and this has been found to increase the risk of developing ASCVD.
Olpasiran has been designed to lower Lp(a) in the blood by inhibiting its production in the liver. Based on this, the investigational study drug is being investigated in those with high Lp(a) and atherosclerotic cardiovascular disease to see how effective it is.

There are currently no approved drug treatments to reduce the risk of cardiovascular disease from specifically targeting high Lp(a).

For more information about the background of the study, please see protocol section 2.2.

Study objective

Primary Objective:
• To evaluate the effect of Olpasiran administered subcutaneous (SC) once every 12 weeks (Q12W) compared with placebo, on percent change from baseline in lipoprotein(a) (Lp[a]) after 36 weeks of treatment.

Secondary Objectives:
• To evaluate the effect of Olpasiran administered SC Q12W compared with placebo, on percent change from baseline in:
- Lp(a) after 48 weeks of treatment
- Low-density lipoprotein cholesterol (LDL C) after 36 and 48 weeks of treatment
- Apolipoprotein(B) (ApoB) after 36 and 48 weeks of treatment
• To characterize the pharmacokinetic (PK) properties of Olpasiran

Safety:
• To evaluate the safety and tolerability of olpasiran administered SC compared with placebo in subjects with elevated Lp(a)

Study design

This is a phase 2, double-blind, randomized, placebo-controlled, multicenter, dose finding study to evaluate efficacy, safety, and tolerability of Olpasiran on Lp(a) compared to placebo in subjects with atherosclerotic cardiovascular disease and with elevated Lp(a).
Subjects will be randomized in a 1:1:1:1:1 ratio to 1 of the following 5 treatment groups (some olpasiran arms will include placebo to maintain blind):
• Group 1: 10 mg Q12W
• Group 2: 75 mg Q12W
• Group 3: 225 mg Q12W
• Group 4: 225 mg Q24W
• Group 5: Placebo Q12W

The randomization will be stratified by screening Lp(a) > 200 vs. > 200 nmol/L and by region (Japan vs. Non-Japan).
The study treatment period is 48 weeks with doses at day 1, week 12, week 24, and week 36. After week 48 there is an extended safety follow-up without further dosing with investigational product for a minimum of 24 weeks.
Subjects will remain on standard of care (including stable lipid lowering therapy) per their local guidelines during the treatment period and extended safety follow-up period.

The overall study design is described by a study schema in protocol Section 1.2. The endpoints are defined in protocol Section 3.

Intervention

Subcutaneous administration of IP.

Study burden and risks

Please see E9 of the ABR form.

Contacts

Public
Amgen

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Breda 4817 ZK
NL
Scientific
Amgen

Minervum 7061
Breda 4817 ZK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

-Subject has provided informed consent prior to initiation of any study specific activities/procedures.
-Age 18 to 80 years
-Fasting Lp(a) > 150 nmol/L during screening by central laboratory (approximately corresponds to > 60 mg/dL: note that molarity determines eligibility)
-Atherosclerotic cardiovascular disease based on 1 of the following:
• History of coronary revascularization with percutaneous coronary intervention (PCI) or coronary
artery bypass grafting (CABG)
• Diagnosis of coronary artery disease with or without prior myocardial infarction
• Diagnosis of atherosclerotic cerebrovascular disease
• Diagnosis of peripheral arterial disease
-For subjects receiving lipid-altering therapy (not required to participate in this study), lipid-altering therapy, including statin dose, must remain stable per local guidelines for >= 4 weeks prior to and during screening

Exclusion criteria

Disease Related
-Severe renal dysfunction, defined as an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m2 during screening
-History or clinical evidence of active liver disease or hepatic dysfunction, defined as aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 3 x upper limit of normal (ULN), or total bilirubin (TBL) > 2 x ULN during screening
-Inherited or other bleeding disorders
-Recent major cardiovascular event (myocardial infarction, unstable angina, PCI, CABG, or stroke) within 6 months prior to day 1
-Planned cardiac surgery, PCI or carotid stenting, or planned major non-cardiac surgery during the study period

Other Medical Conditions
-Malignancy (except non-melanoma skin cancers, cervical in-situ carcinoma, breast ductal carcinoma in situ, or stage 1 prostate carcinoma) within the last

5 years prior to day 1
-Moderate to severe heart failure (New York Heart Association (NYHA) Functional Classification III or IV at day 1) or last known left ventricular ejection fraction < 30%
-Uncontrolled cardiac arrhythmia defined as recurrent and highly symptomatic ventricular tachycardia, atrial fibrillation with rapid ventricular response, or supraventricular tachycardia that are not controlled by medications, in the past 3 months prior to day 1
-Uncontrolled hypertension at day 1, defined as an average systolic blood pressure of >= 160 mmHg or an average diastolic blood pressure of >= 100 mmHg at rest
-Fasting triglycerides >= 400 mg/dL (4.5 mmol/L) during screening
-Type 1 diabetes or poorly controlled (HbA1c >= 8.5%) type 2 diabetes mellitus as determined by central laboratory at screening

Refer to page 31 of the protocol for more information.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	23-11-2020
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	26-06-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-09-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-11-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-12-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-05-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-05-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-07-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	20-07-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-08-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-09-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-12-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-01-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-07-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-09-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2019-003688-23-NL
ClinicalTrials.gov	NCT-nummernognietbekend.Hetnummervolgt.
CCMO	NL72368.000.20

Study results

Date completed: 08-11-2022

Results posted: 23-05-2023

First publication
01-05-2023