Obicetrapib and Cardiovascular Outcomes: A Placebo-Controlled, Double-Blind, Randomized Phase 3 Study to Evaluate the Effect of 10 mg Obicetrapib in Participants With Atherosclerotic Cardiovascular Disease (ASCVD) Who are Not Adequately Controlled Despite Maximally Tolerated Lipid-Modifying Therapies

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This study has been transitioned to CTIS with ID 2023-507795-51-00 check the CTIS register for the current data. The primary objective of this study is to evaluate the effect of obicetrapib on the risk of major adverse CV events (MACE), including CV...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Interventional

Summary

ID

NL-OMON53473

Source
ToetsingOnline

Brief title
PREVAIL

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
atherosclerosis, Atherosclerotic Cardiovascular Disease

Research involving
Human

Sponsors and support

Primary sponsor: NewAmsterdam Pharma BV
Source(s) of monetary or material Support: NewAmsterdam Pharma BV

Intervention

Keyword: ASCVD, Atherosclerosis, cholesterol, LDL

Outcome measures

Primary outcome

The primary efficacy endpoint is the time from Randomization to the first

confirmed occurrence of any component of the composite endpoint, including the

following:

• CV death;

• Non-fatal MI;

• Non-fatal stroke; or

• Non-elective coronary revascularization.

SAFETY

• AEs and events of special interest (ESIs);

• Vital signs (including blood pressure);

• Electrocardiograms; and

• Clinical laboratory assessment

Secondary outcome

The secondary efficacy endpoints, in hierarchical order, include the following:

• The time from Randomization until the first confirmed occurrence of a composite of CV death, non-fatal MI, or non-fatal stroke;

• The time from Randomization until the first confirmed occurrence of a composite of all-cause mortality, non-fatal MI, non-fatal stroke, or non-elective coronary revascularization;

• A total event analysis, defined as the number of CV death events, and first and subsequent/recurrent events of non-fatal MIs, non-fatal strokes, and non-elective coronary revascularization from Randomization until the EOS Visit;

• The time from Randomization until the first confirmed occurrence of non-fatal MI;

• The time from Randomization until the first confirmed occurrence of non-elective coronary revascularization;

• The time from Randomization until the first confirmed occurrence of CV death;

• The time from Randomization until the first confirmed occurrence non-fatal stroke;

• The time from Randomization until the confirmed occurrence of allcause mortality;

• The time from Randomization until the first confirmed occurrence of NODM;

• Percent change in LDL-C from Baseline to Day 365 and to the EOT Visit;

• Percent change in non-HDL-C from Baseline to Day 365 and to the EOT Visit;

• Percent change in ApoB from Baseline to Day 365; and

• Percent change in HbA1c in participants with diabetes mellitus and HbA1c

>=7% at Baseline, from Baseline to Day 365 and to the EOT Visit.

The exploratory efficacy endpoints include the time from Randomization until

the first confirmed occurrence of the following:

• Hospitalization for unstable angina and/or chest pain;

• Hospitalization for HF; and

• TIA

Study description

Background summary

Despite advances in treatment, cardiovascular (CV) disease (CVD) is the leading cause of death globally, resulting in over 17 million deaths annually. Elevated low-density lipoprotein (LDL) cholesterol (LDL-C) is a major modifiable risk factor for the development of CVD. Lowering LDL-C has been shown to reduce the risk of death or myocardial infarction (MI), and the clinical risk reduction is linearly proportional to the absolute LDL-C reduction. Approximately 100 million people worldwide are treated with lipid-lowering therapies, predominantly statins, to reduce LDL-C and the associated risk of CV events. Patients with documented atherosclerotic CVD (ASCVD) are at very high risk for CV events and require intensive pharmacologic intervention. For a variety of reasons, many with ASCVD are unable to attain aggressive LDL-C treatment goals despite the addition of lipid-lowering agents to maximally tolerated statin therapy.

Patients with ASCVD who require additional lipid-lowering therapy despite treatment with maximally tolerated lipid-lowering therapy, including maximally tolerated doses of statins, have an unmet medical need. The study medicine may offer a useful option for these patients. The study medicine has been well tolerated to date and its Phase 2 data demonstrate significant LDL-C lowering

thus prompting further evaluation in Phase 3 clinical studies.

Study objective

This study has been transitioned to CTIS with ID 2023-507795-51-00 check the CTIS register for the current data.

The primary objective of this study is to evaluate the effect of obicetrapib on the risk of major adverse CV events (MACE), including CV death, non-fatal MI, non-fatal stroke, or non-elective coronary revascularization.

Study design

This is a multi-site, placebo-controlled, double-blind, randomized Phase 3 study.

Intervention

Approximately 9000 eligible participants will be randomized in a 1:1 ratio to the following treatment groups:
- Study Medicine group: One 10 mg study medicine tablet QD; or
- Placebo group: One placebo tablet QD.

Study burden and risks

The primary pharmacology in in vitro, ex vivo, and in vivo studies have demonstrated that obicetrapib has the ability to inhibit CETP, decrease LDL-C levels, increase HDL-C levels, and importantly, reduce the number of atherogenic ApoB-containing particles in a way that is useful in the treatment of dyslipidemia.

The safety pharmacology studies have demonstrated that obicetrapib has no adverse effect on critical physiological systems (eg, central nervous system, respiratory system, gastric emptying, urinary tract, and steroidal hormonal production [including aldosterone levels]) at doses up to 300 mg/kg in rats.

In clinical studies in patients, obicetrapib was also well tolerated after daily dosing of 10 mg for 12 weeks, both alone and in combination with 2 different statins. There were no dose-related AEs identified and no clinically significant changes in vital signs, ECGs, or hematology or biochemistry parameters in any clinical studies.

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. Male or female and >=18 years of age at Screening (Visit 1);

2. Have a history of ASCVD, defined by at least 1 of the following conditions:
- Coronary artery disease
- Cerebrovascular disease
- Peripheral arterial disease

3. Are on maximally tolerated lipid-modifying therapy as an adjunct to a lipid lowering diet and other lifestyle modifications, defined as follows:
- A statin at a maximally tolerated stable dose;
- Ezetimibe for at least 8 weeks with or without a maximally tolerated statin prior to Screening (Visit 1);

- Bempedoic acid for at least 8 weeks in combination with a maximally tolerated statin prior to Screening (Visit 1);
- A PCSK9-targeted therapy alone or in combination with other lipidmodifying therapy for at least 4 stable doses prior to Screening (Visit 1);
- At least 70% of the participants enrolled into this study must be taking HISs. Documentation in the eCRF of the reason why a participant is unable to take HISs is required. HISs include the following:
o Atorvastatin 40 and 80 mg; and
o Rosuvastatin 20 and 40 mg

4. Have a fasting serum LDL-C at Screening (Visit 1) as follows:
- Have a fasting serum LDL-C >=70 mg/dL to <100 mg/dL with at least 1 of the following risk enhancers:
- Recent MI (>3 and <12 months prior to Randomization);
- Type 2 diabetes mellitus;
- Fasting triglycerides (TG) >150 mg/dL (>1.7 mmol/L); and/or
- Fasting high density lipoprotein cholesterol <40 mg/dL (<1.0 mmol/L). OR
- Have a fasting serum LDL-C >=100 mg/dL.

5. Have fasting TG <400 mg/dL (<4.52 mmol/L) at Screening (Visit 1); and

6. Have an estimated glomerular filtration rate (eGFR) >=30 mL/min/1.73 m2 calculated using the Chronic Kidney Disease Epidemiology Collaboration equation at Screening (Visit 1).

Other protocol-defined criteria apply.

Exclusion criteria

1. Have current or any previous history of New York Heart Associationclass III or IV HF or left ventricular ejection fraction <30%;

2. Have been hospitalized for HF within 5 years prior to Screening (Visit 1);

3. Have had any of the following clinical events within 3 months prior to Screening (Visit 1):
- Non-fatal MI;
- Non-fatal stroke;
- Non-elective coronary revascularization; and/or
- Hospitalization for unstable angina and/or chest pain;

4. Have uncontrolled severe hypertension, defined as either systolic blood pressure >=160 mmHg or diastolic blood pressure >=100 mmHg

prior to Randomization, taken as the average of triplicate measurements. One triplicate retest will be allowed during the same visit, at which point if the retest result is no longer exclusionary, the participant may be randomized;

5. Have a formal diagnosis of homozygous familial hypercholesterolemia;

6. Have active liver disease, defined as any known current infectious, neoplastic, or metabolic pathology of the liver; unexplained elevations in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >3× upper limit of normal (ULN); or total bilirubin >2 × ULN at Screening (Visit 1);

7. Have an HbA1c >=10.0% or a fasting glucose >=270 mg/dL at Screening (Visit 1);

8. Have a thyroid-stimulating hormone >1.5 × ULN at Screening (Visit 1);

9. Have a creatine kinase >3 ×ULN at Screening (Visit 1);

10. Are taking gemfibrozil or have taken gemfibrozil within 30 days of Screening (Visit 1).

Other protocol-defined criteria apply.

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:	Recruiting
Start date (anticipated):	28-06-2022
Enrollment:	500

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	TA-8995
Generic name:	Obicetrapib

Ethics review

Approved WMO Date:	22-02-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-05-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-07-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-07-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-10-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-11-2022
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-03-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-04-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EU-CTR	CTIS2023-507795-51-00
EudraCT	EUCTR2021-005092-39-NL
ClinicalTrials.gov	NCT05202509
CCMO	NL79675.100.22