A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety, Tolerability, and Effect on Microvascular Obstruction of Temanogrel in Subjects Undergoing Percutaneous Coronary Intervention

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

Summary

ID

NL-OMON51876

Source
ToetsingOnline

Brief title
APD791202

Condition

- Coronary artery disorders

Synonym
Atherosclerosis, Percutaneous Coronary Intervention

Research involving

Human

Sponsors and support

Primary sponsor: Arena Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Arena Pharmaceuticals;Inc.

Intervention

Keyword: Coronary Artery Disease, Microvascular Obstruction, Percutaneous Coronary Intervention

Outcome measures

Primary outcome

Primary endpoint:

• Change in IMR from Baseline to Post PCI

Secondary outcome

Secondary endpoints:

• Change from Baseline to Post PCI with the study drug versus placebo for the

following assessments:

- Coronary physiology indices (coronary flow reserve [CFR], fractional

flow reserve [FFR])

- Angiographic measures (corrected thrombolysis in myocardial infarction

frame count [cTFC], TFG, thrombolysis in myocardial infarction

myocardial perfusion grade [TMPG])

- Myocardial injury markers (creatine kinase [CK], creatine kinase

myocardial band [CK MB], cTn)

• The incidence of procedural myocardial injury

• Observed Maximum Plasma Concentration (Cmax) of study drug and its

Metabolites;

• Safety and tolerability of the study drug

Study description

Background summary

During a percutaneous coronary intervention procedure, a short wire-mesh tube, called a stent, is inserted into the narrowed or blocked coronary artery (a big blood vessel that supplies the blood to the heart). This opens the artery and allows blood to flow more freely. However, in some people, blood flow within the heart does not return to healthy levels even after this procedure. It is thought this may be due to a condition called microvascular obstruction (MVO).

Microvascular obstruction is associated with poor recovery from this type of procedure. Several treatment options for MVO have been explored but none have been proven to help in preventing or treating MVO after a PCI. Therefore, there is a need to develop and find new therapies to prevent or treat MVO in people undergoing PCI treatment for CAD.

Study objective

The objection of the study is to assess the safety, tolerability, and effect on microvascular obstruction of study drug in subjects undergoing Percutaneous Coronary Intervention.

NL specific sub-study:
The aim of this substudy is to investigate changes in Rμ and MRR from Baseline (prior to percutaneous coronary intervention [PCI] and administration of study treatment) to Pre-PCI (following study treatment administration ie, post-drug but pre-PCI) and Post-PCI (following PCI). These assessments will be performed immediately following measurements of IMR at sites participating in this substudy using the same Coroventis software utilized in the parent APD791-202 study. It is anticipated this may provide assessment of the coronary microcirculation that is complementary to, but distinct from, IMR. Specifically, these measures may provide insight into the effect of temanogrel on microcirculation at resting conditions, which may not be apparent during adenosine-induced hyperemia utilized when performing IMR assessments, as well as providing an absolute assessment of microvascular resistance.

Study design

This is a Phase 2, multicenter, randomized, double blind, placebo controlled

study to be conducted in 2 stages (Stage A and Stage B). Each stage includes a Screening Period of up to 14 days, a single dose of randomized study treatment (temanogrel or placebo) on Day 1, and a Follow Up phone call 7 days (± 2 days) after administration of study treatment for a total study duration of 6 to 24 days.

Intervention

The study drug is an IV formulation containing active pharmaceutical ingredient provided as 25 mg/mL strength. Subjects will receive a single IV dose of study treatment on Day 1 of the study.

The study drug dose to be administered to Cohort 1 of Stage A will be 20 mg. The dose administered in Cohort 2 is planned to be 40 mg. Selected doses from Stage A are planned to be investigated in Stage B of the study

Study burden and risks

As of the date of this protocol, the safety, tolerability, PK, and PD of the study drug have been assessed in 5 Phase 1 studies. Single and repeated doses of oral study drug were evaluated in 4 studies, and single IV doses of the study drug were evaluated in a separate study. In completed clinical studies, doses of study drug planned to be used in this study were well-tolerated and there were no associated safety concerns

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

- Stable angina patients suitable for elective PCI or patients suitable for PCI for diagnosis of NSTEMI/UA. NSTEMI/UA patients are to be consistently hemodynamically stable until the time of PCI and have a thrombolysis in myocardial infarction (TIMI) Flow Grade () 2 or 3 on the diagnostic angiography.

- Target lesions for PCI must appear suitable for stenting as confirmed on the diagnostic angiography. Acceptable lesions cannot be in the left main artery or in a vein or arterial graft, or be a chronic total occlusion or in-stent restenosis. Two or more sequential lesions may be treated in the same artery, as long as they are treated in the same session and at least one of the lesions meets inclusion criteria:

• For elective PCI patients and non-urgent NSTEMI/UA patients (PCI >12 hours after diagnosis), the lesion must be located in a >= 2.75 mm diameter coronary artery; the lesion must also be >= 18 mm long and require the use of one or more stents that in total must be >= 20 mm long.
• For NSTEMI patients treated with PCI urgently (within 12 hours after diagnosis), the coronary artery diameter of the culprit lesion must be >= 2.75 mm.

- Both men and women participants agree to use a highly effective method of birth control throughout the entire study period, from informed consent through the adverse
event reporting period, if the possibility of conception exists

Exclusion criteria

- Planned or anticipated use of rotational atherectomy/ablation or shockwave therapies during the PCI procedure;

- Any history of stroke, seizure, intracranial bleeding, or intracranial

aneurysm;

- Transient ischemic attack within the 6 months prior to Screening;

- History of major trauma, major surgery, and/or clinically significant head injury or hemorrhage within the last 6 months of Screening;

- Any ST-elevation myocardial infarction (STEMI) within 10 days of Screening or STEMI within the target vessel territory within the last 6 months of Screening (eg, a patient with a NSTEMI because of a lesion in a diagonal may not be included if there is a history of anterior STEMI due to left anterior descending artery lesion that occurred within the last 6 months);

- Known history of heart failure with reduced ejection fraction (HFrEF) defined as left
ventricular ejection fraction <= 40% prior to current hospital admission.

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):	02-08-2021
Enrollment:	27
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Temanogrel
Generic name:	3-Methoxy-N-[3-(2-methylpyrazol-3-yl)-4-(2-morpholin-4-ylethoxy)phenyl]benzamide hydrochloride

Ethics review

Approved WMO Date:	24-12-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-05-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-06-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-06-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-09-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	11-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-02-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-07-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-07-2022
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
EudraCT	EUCTR2020-000238-16-NL
CCMO	NL75791.100.20

Study results

Date completed: 23-08-2022

Results posted: 12-04-2023

Summary results
Trial ended prematurely

First publication
19-01-2023