A FIRST-IN-HUMAN, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, SINGLE ASCENDING DOSE AND MULTIPLE ASCENDING DOSE STUDY TO INVESTIGATE THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS (INCLUDING FOOD EFFECT) OF IMB1018972 IN HEALTHY SUBJECTS

Published: 28-01-2019
Last updated: 09-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON48517

Source
ToetsingOnline

Brief title
IMB1018972 SAD and MAD study

Condition

- Heart failures

Synonym
heart failure, ischemic cardiovascular disease

Research involving
Human

Sponsors and support

Primary sponsor: Imbria Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: First-in-human, Food-effect, IMB1018972, Pharmacokinetics

Outcome measures

Primary outcome

To assess the safety and tolerability of single and multiple ascending oral

doses of IMB1018972, single oral doses of trimetazidine, single oral doses of

MR formulations of IMB1018972, and multiple oral doses of the 200 mg 8-hour MR

formulation of IMB-1018972 in healthy subjects

Secondary outcome

To assess the pharmacokinetic (PK) profile of single and multiple ascending

oral doses of IMB1018972, single oral doses of trimetazidine, single oral

doses of MR formulations of IMB1018972, and multiple oral doses of the 200 mg

8-hour MR formulation of IMB-1018972 in healthy subjects

To assess the effect of food on the absorption and the PK profile of IMB

1018972 following a single oral dose of IMB1018972 in healthy subjects

To evaluate the effect of food on the safety and tolerability of IMB1018972

following a single oral dose of IMB1018972 in healthy subjects

To assess the absorption and PK profile of the 200 mg 8-hour MR formulation of

IMB-1018972 following multiple oral doses taken with food in healthy subjects

To evaluate the safety and tolerability of the 200 mg 8-hour MR formulation of

IMB-1018972 following multiple oral doses taken with food in healthy subjects

Study description

Background summary

IMB-1018972 is a new compound that may eventually be used for the treatment of patients with angina.

Under normal conditions, the heart muscle uses fatty acids to generate energy that is required to pump blood and this process requires oxygen. However, when heart muscle doesn't get as much blood as it needs, glucose metabolism produces more energy per oxygen molecule than fatty acid metabolism. IMB-1018972 shifts the production of energy in the heart muscle from fatty acids towards glucose.

Study objective

The purpose of this study is to investigate how safe the new compound IMB-1018972 is and how well it is tolerated when it is administered to healthy volunteers. It will also be investigated how quickly and to what extent IMB 1018972 is absorbed and eliminated from the body (this is called pharmacokinetics). In addition, the effect of food on the absorption of IMB-1018972 in the body will be investigated (Groups 3 and 4 of Part 1 only).

In Group 5 of the study instead of IMB-1018972, trimetazidine will be administered. Trimetazidine is a metabolite of IMB1018972, the compound which has been administered to volunteers in the other groups of this study. Although trimetazidine is an approved drug for angina and has been on the market in Europe since 1987, not many details on pharmacokinetics are known of trimetazidine. The Sponsor is interested in these details and therefore, trimetazidine will be administered in Group 5 to investigate the pharmacokinetics of trimetazidine.

In part 3 and 4 a modified-release tablet will be administered to the subjects.

Study design

The actual study will consist of 1 period (2 periods for Group 3) during which the subject will stay in the research center for 4/17/8 days (3/16/7 nights). The time between study compound administrations for Group 3 will be at least 1

week.

Day 1 is the first day of administration of the study compound. The subjects will leave the research center on Day 3/17/7 of the study.

IMB-1018972 or placebo will be given as oral capsules or tablets with 240 milliliters (mL) of water.

Intervention

IMB-1018972 or placebo will be given as oral capsules or tablets with 240 milliliters (mL) of water.

For Group 3 only: During the first 4 hours after administration of the study compound the subjects will not be allowed to lie down (except when indicated as such by one of the investigators), as this may influence the uptake of the study compound.

In Group 3, all volunteers will receive the study compound once without a breakfast and once with breakfast. In the second period the subjects will receive a high-fat breakfast with a standard composition, which must be started exactly on time and must be finished within 20 minutes. The entire breakfast must be consumed.

Study burden and risks

Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.

In total, we will take a maximum of 200 milliliters of blood from the subjects. This amount does not cause any problems in adults.

To make a heart tracing, electrodes (small, plastic patches) will be pasted at specific locations on your arms, chest and legs. To monitor your heart rate, electrodes (small, plastic patches) will be pasted at specific locations on the chest and abdomen. Prolonged use of these electrodes can cause skin irritation (rash and itching).

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. Gender: male or female.
2. Age:18 to 65 years, inclusive, at screening.
3. Body mass index : 18.0 to 32.0 kg/m2.
4. Status: healthy subjects.
5. At screening, females can be of childbearing potential (but not pregnant or lactating), or of nonchildbearing potential (either surgically sterilized or physiologically incapable of becoming pregnant, or at least 1 year postmenopausal [amenorrhea duration of 12 consecutive months]); nonpregnancy will be confirmed for all females by a serum pregnancy test conducted at screening and each admission.

Exclusion criteria

1. Previous participation in the current study.
2. Employee of PRA or the Sponsor.
3. History of relevant drug and/or food allergies.
4. Using tobacco products within 3 months prior to (the first) drug administration.

5. History of alcohol abuse or drug addiction (including soft drugs like cannabis products).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-02-2019
Enrollment:	128
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Vastarel MR
Generic name:	Trimetazidine
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	28-01-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	29-01-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-03-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-04-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-04-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-05-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-05-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-06-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-08-2019
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-08-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2018-004576-35-NL
CCMO	NL68672.056.19