A randomized, double-blind, placebo-controlled, single ascending dose study to examine the safety, tolerability and pharmacokinetics of orally administered PHA-022121 in healthy subjects.

Published: 29-04-2020
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Primary ObjectiveTo assess the tolerability and safety of single ascending oral doses of PHA-022121 administered after a standard meal and of a single 40 mg dose under fasted conditions in healthy adult subjects.To assess the PK characteristics of...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Congenital and hereditary disorders NEC
Study type	Interventional

Summary

ID

NL-OMON49665

Source
ToetsingOnline

Brief title
CS0348-200190 Pharvaris SAD

Condition

- Congenital and hereditary disorders NEC

Synonym
Hereditary Angioedema (HAE)

Research involving
Human

Sponsors and support

Primary sponsor: Pharvaris B.V.
Source(s) of monetary or material Support: Pharvaris B.V.

Intervention

Keyword: pharmacokinetics, SAD, safety, tolerability

Outcome measures

Primary outcome

Primary Endpoints:

Primary endpoint, safety:

All standard safety assessments including physical examination, vital signs,

adverse events, hematology, chemistry, urinalysis and ECG.

Primary endpoint, pharmacokinetics:

Plasma PK parameters tmax, Cmax, AUC0-12h, AUC0-24h, AUClast, AUCinf, t1/2,

CL/F and Vz/F of PHA-022121.

Secondary outcome

Plasma PK parameters tmax, Cmax, AUC0-12h, AUC0-24h, AUClast, AUCinf, and t1/2,

of the major metabolite M2-D.

QT, and the heart rate-corrected QT interval by Fridericia*s formula (QTcF)

Study description

Background summary

An oral treatment for HAE attacks is currently not available rendering the

management of this disease difficult: all of the currently approved drugs for HAE, except for androgens, can only be applied by i.v. or sc route, which is often associated with a delay of drug administration, discomforts, local side effects and with a reduction in the QoL for the patients. Therefore, there is a strong unmet medical need for an efficacious orally bioavailable drug for the treatment and/or prevention of acute HAE attacks.
Of all products available to patients or in development, only one other antagonizes the B2 receptor, namely icatibant. Extensive clinical experience has demonstrated the selectivity, safety, and rapid onset of action of this mechanism to resolve HAE attacks of all causes. PHA-022121 retains these characteristics through the shared mechanism, as demonstrated preclinically in the BK challenge model adapted from human clinical experience to monkey.

Study objective

Primary Objective
To assess the tolerability and safety of single ascending oral doses of PHA-022121 administered after a standard meal and of a single 40 mg dose under fasted conditions in healthy adult subjects.
To assess the PK characteristics of PHA-022121 after administration of single ascending oral doses.

Secondary Objectives
To assess the PK characteristics of the major active metabolite M2-D after administration of single ascending doses of PHA-022121.
To assess the concentration-QTc effect of PHA-022121 after single ascending doses.

Study design

This is a randomized, double-blind, placebo-controlled study for PHA 022121 and will be conducted in healthy subjects at a single study center.
This study is an extension of the SAD range of PHA-022121 as studied in trial PHA022121-C001 by four sequential cohorts. Within each cohort, 8 subjects will be randomized to PHA-022121 (N = 6) and to matching placebo (N = 2). Accordingly, up to 32 subjects will be enrolled in this study. Each cohort must comprise at least 3 female subjects.
After each cohort, safety and PK data will be available and submitted to the Safety Monitoring Committee (SMC) and Ethics Committee (EC), which will decide on predefined safety and PK decision criteria whether the next higher single dose can be administered.

Intervention

PHA-022121 will be made available as an oral self-micro emulsifying drug

delivery system (SMEDDS) solution containing 50 mg/mL PHA-022121.

Study burden and risks

Since the study is being executed in healthy volunteers, there are no anticipated benefits of the IMP. Please see the IB for further information.

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

Healthy male and female subjects of non-childbearing potential.
Between 18 and 65 years of age, inclusive.

Body mass index (BMI) between 18.0 and 30.0 kg/m2 (inclusive).
Healthy on the basis of physical examination, medical history, vital signs, clinical laboratory tests, and 12-lead ECG performed at screening. If any of the results are abnormal, the subject may be included only if the investigator judges that the abnormalities or deviations from normal are not clinically significant. This determination must be recorded in the subject's source documents and initialled by the investigator.
A resting heart/pulse rate (supine position for 5 minutes) between 40 and 100 beats per minute (bpm). If heart/pulse rate is out of range, up to 2 repeated assessments are permitted.
A resting blood pressure (supine position for 5 minutes) between 90 and 140 mmHg systolic, inclusive, and between 40 to 90 mmHg diastolic. If blood pressure requirements are out of range, up to 2 repeated assessments are permitted.

Exclusion criteria

Clinically relevant allergy (except for untreated, asymptomatic, seasonal allergies at time of dosing) or drug hypersensitivity.
Known hypersensitivity to the drug substance, or any inactive ingredient(s) of the investigational product (refer to investigator's brochure).
History of any medical condition or prior surgery of the GI-tract that could alter the absorption of orally administered drugs (does not apply to history of appendectomy).
History or current evidence of any form of angioedema.
History or current evidence of any form of bronchial asthma.

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:	Will not start
Enrollment:	32
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Nap.
Generic name:	Nap.

Ethics review

Approved WMO Date:	29-04-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-05-2020
Application type:	First submission
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	EUCTR2020-002013-18-NL
CCMO	NL73764.056.20