Oral PHA-022121 for the acute treatment and prophylaxis Of angioedema attacks in Patients with Acquired C1-Inhibitor Deficiency

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20805

Source
Nationaal Trial Register

Brief title
POP-AID

Health condition

Acquired C1-inhibitor deficiency

Sponsors and support

Primary sponsor: Amsterdam UMC location AMC
Source(s) of monetary or material Support: None

Intervention

Outcome measures

Primary outcome

The main study parameter for part 1 is the change of the 3-symptom composite visual

analogue scale (VAS-3) score from pre-treatment to 4 h post-treatment. The main study parameter for part 2 is the number of investigator-confirmed angioedema attacksrecorded during the treatment period expressed as the normalized number of attacks per month of exposure.

Secondary outcome

• Part 1: mean symptom complex severity score (MSCS) score
• Part 1: treatment outcome score (TOS)
• Part 1: treatment satisfaction questionnaire for medication (TSQM) score
• Part 1: number of attacks requiring rescue medication
• Part 1: time to rescue medication use, if applicable
• Part 2: number of investigator-confirmed moderate or severe angioedema attacks during the treatment period
• Part 2: number of investigator-confirmed angioedema attacks requiring acute treatment during the treatment period
• Part 2: number and proportion of days with angioedema symptoms during the treatment period
• Part 2: time to first investigator-confirmed attack (i.e. duration that a patient is attack-free) in the treatment period
• Part 2: angioedema quality of life (AE-QoL) questionnaire
• Part 2: treatment satisfaction questionnaire for medication (TSQM) score
• Part 2: angioedema control test (AECT)
• Part 2: angioedema activity score (AAS)

Study description

Background summary

Background
Effective prophylactic and on demand treatment options for angioedema due to acquired C1-inhibitor deficiency (AAE-C1-INH) areneeded, as licensed treatments are currently lacking for this condition.

Objectives
Primary objectives: to evaluate the efficacy of three different single doses of PHA-022121 versus placebo in achieving angioedemasymptom relief during acute attacks and the efficacy of prophylactic treatment with PHA-022121 versus placebo in preventingbreakthrough angioedema attacks in patients with AAE-C1-INH. Secondary objectives: to further explore the clinical efficacy ofPHA-022121 versus placebo with regard to onset of symptom relief, time to complete symptom relief, to evaluate the frequency andtiming of rescue medication use, and to evaluate the safety of PHA-022121 versus placebo.

Study design

Double-blind, placebo-controlled, randomized cross-over intervention study

Population
Male or female patients with AAE-C1-INH (>35 years old, ≥3 angioedema attacks in the last 4 months or ≥2 attacks in the last 2 months).

Intervention
In part 1, patients will treat four consecutive angioedema attacks with three single doses of PHA-022121 (10, 20, and 30 mg) andone single dose of placebo, in a randomized and blinded order. In part 2, patients will be randomly allocated to one of two treatmentarms: a 20 mg dose of PHA-022121 or placebo twice daily for a total duration of eight weeks, followed by a cross-over to the other treatment arm.

Study objective

We hypothesize that PHA-022121 will be more effective in both the treatment and prophylaxis of acute angioedema attacks in patients with acquired C1-inhibitor deficiency when compared to placebo.

Study design

The expected study duration per patient amounts to approximately 34 weeks consisting of the screening period of up to 1 week, on demand treatment (part 1) of up to 16 weeks and prophylactic treatment (part 2) of about 16 weeks, followed by 1 week safety follow-up.

Intervention

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Contacts

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Eligibility criteria

Inclusion criteria

• Provision of signed and dated informed consent form
• Male or female, aged > 35 at enrollment
• Diagnosis of AAE-C1-INH based upon all of the following:
1. Documented clinical history consistent with AAE-C1-INH (subcutaneous or mucosal, nonpruritic swelling withoutaccompanying urticarial and C1-INH activity < 0.63mE/L)
2. At least one of the following:
+ Age at reported onset of first angioedema symptoms ≥ 40 years AND family history negative for angioedema
+ C1q below lower limit of normal (88 kU/L) AND absence of SERPING1 mutation
+ Serological confirmation of antibodies against C1-INH
• Documented history of at least three angioedema attacks in the last 4 months, or at least two angioedemaattacks in the last 2 months.
• Reliable access and experience to use icatibant to effectively manage acute angioedema attacks
• Female patients of childbearing potential must agree to be abstinent or to use highly effective forms ofcontraception methods from enrollment through the end of the study. This includes progestin-only oralcontraceptive associated with inhibition of ovulation (oral, injectable, or implantable), intrauterine device (IUD, alltypes) or intrauterine hormone releasing systems (IUS). A female of childbearing potential whose male partner hashad a vasectomy must agree to use one additional form of medically acceptable contraception.
• Male patients, including males who are surgically sterile (post vasectomy), who have a female partner ofchildbearing potential must agree to be sexually abstinent or use a medically acceptable form of barriercontraception for 2 weeks after each administration of study drug. In addition, they must agree to not donatesperm during study participation.

Exclusion criteria

Patients who meet any of the following criteria will be excluded from the study:
• Pregnancy or breast-feeding
• Clinically significant abnormal ECG, most notably a QTcF > 470 ms (for females) or > 450 ms (for males)
• Any clinically significant history of angina, myocardial infarction, syncope, stroke, left ventricular hypertrophy orcardiomyopathy, or any other cardiovascular abnormality within the previous year
• Any other systemic disease (e.g., gastrointestinal, renal, respiratory, neurological) or significant disease ordisorder that would interfere with the patient’s safety or ability to

participate in the study
• Active infection with human immunodeficiency virus (HIV) or hepatitis B virus (HBV) or hepatitis C virus (HCV)
• History of abnormal hepatic function (AST > 2×ULN, ALT > 2×ULN, or total bilirubin > 1.5×ULN)
• History of abnormal renal function (eGFR CKD-EPI < 60 mL/min/1.73 m2)
• History of alcohol or drug abuse within the previous year, or current evidence of substance dependence or abuse(self-reported alcoholic intake > 3 drinks/day)
• History of documented severe hypersensitivity to any medicinal product
• Participation in any other investigational drug study currently, within the last 30 days or within 5 half-lives of studydrug at enrollment (whichever was longer)
• Regular use of corticosteroids, antihistamines, narcotics, and other pain relief medications for acute angioedemaattack treatment
• Use of concomitant medication that are moderate or potent inhibitors/inducers of CYP3A4 or are metabolized byCYP3A4 and have a narrow therapeutic range, such as clarithromycin, erythromycin, diltiazem, itraconazole,ketoconazole, ritonavir, verapamil, goldenseal and grapefruit as well as phenobarbital, phenytoin, rifampicin, St.John's Wort, and glucocorticoids (not for topical use or inhalation)

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2021
Enrollment:	3
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N/A

Ethics review

Not applicable
Application type: Not applicable

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
NTR-new	NL9397
Other	METC AMC : METC 2021_103

Study results

Summary results
N/A