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

Gepubliceerd: 09-04-2021 Laatst bijgewerkt: 13-12-2022

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.

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20805

Bron
Nationaal Trial Register

Verkorte titel
POP-AID

Aandoening

Acquired C1-inhibitor deficiency

Ondersteuning

Primaire sponsor: Amsterdam UMC location AMC
Overige ondersteuning: None

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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)

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-06-2021
Aantal proefpersonen:	3
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Toelichting
N/A

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9397
Ander register	METC AMC : METC 2021_103

Resultaten

Samenvatting resultaten
N/A