# Oral ONCE Daily prophylaxis with PHA-022121 in Patients with Acquired C1-Inhibitor Deficiency

Published: 17-02-2023
Last updated: 04-06-2024

Primary objectives: To evaluate the efficacy of long-term prophylactic treatment with deucrictibant (PHA-022121) in preventing breakthrough angioedema attacks in patients with AAE-C1-INH. Secondary objectives: To evaluate the safety of long-term...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Immune disorders NEC |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON51499

**Source**
ToetsingOnline

**Brief title**
ONCE-AID

### Condition

- Immune disorders NEC

**Synonym**
Acquired C1-inhibitor deficiency

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Pharvaris

## Intervention

**Keyword:** Acquired C1-inhibitor deficiency, Bradykinin, Deucrictibant, PHA-022121

## Outcome measures

### Primary outcome

Normalized number of investigator-confirmed angioedema attacks per 28 days of exposure compared to baseline (deucrictibant (PHA-022121) naive participants) or compared to baseline of the POP-AID study (previous POP-AID participants)

### Secondary outcome

Efficacy:

• Number of investigator-confirmed moderate or severe angioedema attacks during the treatment period

• Number of investigator-confirmed angioedema attacks requiring acute treatment during the treatment period

• Duration in days of the longest attack free interval

• Change from baseline (deucrictibant (PHA-022121) naïve patients) or change from baseline of POP-AID (previous POP-AID participants) in Angioedema Control Test (AECT) score

• Change from baseline (deucrictibant (PHA-022121) naïve patients) or change from baseline POP-AID (previous POP-AID participants) in Angioedema Quality of Life (AE-QoL) score after completion of the treatment period

• AE-QoL-score at 1, 3, 6, 9, 12, 15, 18 and 20 months

• Treatment satisfaction questionnaire for Medication (TSQM) score at 1, 3, 6, 9, 12, 15, 18 and 20 months

Safety:

Occurrence of treatment-emergent adverse events (TEAEs), treatment-related

adverse events (AEs), and treatment-emergent serious adverse events (TESAEs),

including clinically significant changes in clinical laboratory tests, vital

signs or ECG reported as AE until the end of the study.

# Study description

### Background summary

Effective prophylactic treatment options for angioedema due to acquired C1-inhibitor deficiency (AAE-C1-INH) are needed, as licensed treatments are currently lacking for this condition. Deucrictibant (PHA-022121) is studied in a healthy population and in patients with hereditary angioedema. This compound is furthermore studied the POP-AID study, an investigator-initiated, randomized, placebo-controlled study in a small group of AAE-C1-INH patients. In the ONCE-AID we will study the effectivity and safety of long-term prophylactic use of deucrictibant (PHA-022121) in an extended release tablet in patients with AAE-C1-INH.

### Study objective

Primary objectives: To evaluate the efficacy of long-term prophylactic treatment with deucrictibant (PHA-022121) in preventing breakthrough angioedema attacks in patients with AAE-C1-INH.
Secondary objectives: To evaluate the safety of long-term prophylactic treatment with deucrictibant (PHA-022121) in patients with AAE-C1-INH.

### Study design

Open-label, single-arm study where subjects are participating for one year

### Intervention

Patients will receive 40 mg of deucrictibant (PHA-022121) in an extended-release (XR) tablet once daily for a maximum of 20 months.

### Study burden and risks

Patients will visit the study site on six occasions, at each visit blood and urine samples will be collected, physical examinations and ECG*s will be performed and patients will be asked to complete three questionnaires (Treatment Satisfaction Questionnaire for Medication, Angioedema Quality of Life questionnaire and Angioedema Edema Control Test). The maximum amount of blood that will be drawn per study visit is 20 ml. Patients are requested to complete a daily angioedema attack diary for the entire study duration of maximum 20 months. Patients will be contacted by phone or e-mail once every two weeks during the duration of the study. Available preclinical and human data indicate that deucrictibant (PHA-022121) is a potent and highly selective B2 receptor antagonist with excellent oral bioavailability that is well tolerated, with the potential to have a beneficial effect in prevention of AAE-C1-INH attacks. All patients have on demand medication (icatibant) available, which they can use for breakthrough attacks. All patients have previously responded well to icatibant.

## 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

- Provision of signed and dated informed consent form - Male or female, aged >= 35 at enrolment - Diagnosis of AAE-C1-INH based upon all of the following: 1. Documented clinical history consistent with AAE-C1-INH (subcutaneous or mucosal, nonpruritic swellings without accompanying urticaria 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 four months, or at least two angioedema attacks in the last two months. For patients that previously participated in POP-AID part 2, a historical attack-rate of at least three attacks in four months or two attacks in two months previous to the start of POP-AID part 2 is required • Reliable access to and experience with using icatibant to effectively manage acute angioedema attacks • Female patients of childbearing potential must agree to be abstinent or to use highly effective forms of contraception methods from enrolment through the end of the study. This includes progestin-only oral contraceptive associated with inhibition of ovulation (oral, injectable, or implantable), intrauterine device (IUD, all types) or intrauterine hormone releasing systems (IUS). A female of childbearing potential whose male partner has had 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 of childbearing potential must agree to be sexually abstinent or use a medically acceptable form of barrier contraception for two weeks after each administration of study drug. In addition, they must agree to not donate sperm during study participation.

## Exclusion criteria

• 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 or cardiomyopathy, or any other cardiovascular abnormality within the previous year • Any other systemic disease (e.g., gastrointestinal, renal, respiratory, neurological) or significant disease or disorder 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 > three drinks/day) • History of documented severe hypersensitivity to any medicinal product • Participation in any investigational drug study within five half-lives of study drug at enrolment • Regular use of corticosteroids, antihistamines, narcotics, and other pain relief medications for acute angioedema attack treatment • Use of concomitant medication that are moderate or potent inhibitors/inducers of CYP3A4 or are metabolized by CYP3A4 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

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| Study phase: | 2 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Prevention |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 15-05-2023 |
| Enrollment: | 5 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Registration: | No |
| Product type: | Medicine |
| Brand name: | Deucrictibant (PHA-022121) |
| Generic name: | Deucrictibant (PHA-022121) |

# Ethics review

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| Approved WMO Date: | 17-02-2023 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 28-02-2023 |
| Application type: | First submission |
| Review commission: | MEC Academisch Medisch Centrum (Amsterdam)<br><br>Kamer G4-214<br><br>Postbus 22660<br><br>1100 DD Amsterdam<br><br>020 566 7389<br><br>mecamc@amsterdamumc.nl |
| Approved WMO Date: | 21-03-2024 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 22-04-2024 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# 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 | EUCTR2022-003168-25-NL |
| CCMO | NL82655.018.22 |