An Open-Label Study to Evaluate the Long-Term Safety and Efficacy of Lanadelumab for Prevention Against Acute Attacks of Non-histaminergic Angioedema with Normal C1-Inhibitor (C1-INH)

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Primary: To evaluate the long-term safety of repeated subcutaneous(SC) administrations of lanadelumab in adolescents and adults with nonhistaminergicangioedema with normal C1-INH

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Angioedema and urticaria
Study type	Interventional

Summary

ID

NL-OMON50984

Source
ToetsingOnline

Brief title
TAK-743-3001

Condition

- Angioedema and urticaria

Synonym
angioedema, severe swelling

Research involving

Human

Sponsors and support

Primary sponsor: Takeda
Source(s) of monetary or material Support: pharmaceutical industry

Intervention

Keyword: Angioedema, C1-INH deficiency, Lanadelumab, Prevention

Outcome measures

Primary outcome

Safety measures, including:

- Adverse events (AEs), including serious adverse events (SAEs) and adverse events of special interest (AESI)

- Clinical laboratory testing (hematology, clinical chemistry, coagulation, and urinalysis)

- Vitals signs including blood pressure, heart rate (HR), body temperature

- Weight and height (height for subjects <18 years old)

- 12-lead ECGs

Secondary outcome

- Number of investigator-confirmed angioedema attacks during the treatment period

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

- Number of high-morbidity angioedema attacks during the treatment period; a high-morbidity angioedema attack is defined as any attack that

has at least one of the following characteristics: severe, results in hospitalization (except hospitalization for observation <24 hours), hemodynamically significant (systolic blood pressure <90 mmHg, requires intravenous (IV) hydration, or associated with syncope or nearsyncope) or laryngeal.

- Analysis of pharmacokinetics (PK) effects through measurement of plasma concentrations of lanadelumab.

- Evaluation of the pharmacodynamic (PD) effects of lanadelumab through cHMWK and fluorogenic plasma kallikrein (pKal) assay with FXIIa activation.

- Presence of anti-drug antibodies (ADAs), including evaluation of neutralizing antibodies (if any confirmed positive anti-drug antibodies are detected)

- Health-related quality of life assessments will be assessed using the AE-QoL questionnaire.

- Lanadelumab Injection Report

Safety measures, including:

- AEs, including SAEs and AESIs

- Clinical laboratory testing (hematology, clinical chemistry, coagulation, and urinalysis)

- Vitals signs including blood pressure (BP), HR, body temperature

- Weight and height (height for subjects <18 years old)

- 12-lead ECGs

Efficacy measures, including:

- Number of investigator-confirmed angioedema attacks during the treatment period

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

- Number of high-morbidity angioedema attacks during the treatment period; a high-morbidity angioedema attack is defined as any attack that has at least one of the following characteristics: severe, results in hospitalization (except hospitalization for observation <24 hours), hemodynamically significant (systolic blood pressure <90 mmHg, requires IV hydration, or associated with syncope or near-syncope) or laryngeal.

Study description

Background summary

Unlike HAE Types I and II, there are no approved treatments for the other forms of non-histaminergic angioedema which are unresponsive to conventional antihistamine / glucocorticoid treatment. Lanadelumab is expected to fulfil an unmet medical need for patients with non-histaminergic angioedema with normal C1-INH and AAE due to C1-INH deficiency by providing a long-term safe, effective and convenient intervention to prevent angioedema attacks. Based on the mechanism of action and past case studies with icatibant and ecallantide, there is a strong scientific rationale to expand the use of lanadelumab.

The targeted indications for lanadelumab (TAK-743/SHP643) currently under study are:
• prophylaxis to prevent attacks of non-histaminergic angioedema with normal C1-INH in patients 12 years and older
• prophylaxis to prevent attacks of AAE due to C1-INH deficiency in patients 30 years and older.

Study objective

Primary: To evaluate the long-term safety of repeated subcutaneous (SC) administrations of lanadelumab in adolescents and adults with nonhistaminergic
angioedema with normal C1-INH

Study design

An Open-Label Study to Evaluate the Long-Term Safety and Efficacy of Lanadelumab for
Prevention Against Acute Attacks of Non-histaminergic Angioedema with Normal C1-Inhibitor (C1-INH)

Intervention

Subjects may receive lanadelumab 300 mg every 2 weeks (q2wks) or may consider lanadelumab 300 mg q4wks if they have been well-controlled (eg, attack-free) for 26 consecutive weeks across Study SHP643-303 and Study TAK-743-3001. The dose frequency change to q4wks will be based on the investigator*s discretion and consultation with the sponsor*s medical monitor.

Study burden and risks

Subjects will need to complete up to 14 study visits over the course of the study. Subjects will also receive 1 telephone call from the study team. Subjects participation in the study will last for 196 days. The subjects will need to visit the site every 2 - 4 weeks and will, next to the intervention described above, be subjected to: measurement of vital signs, physical exam, ECGs, Urine sample collection, blood tests, completing an injection report, daily angioedema attack diary and study questionnaires

The most common side effects (reported in more than 10% of subjects) were:
- Injection site pain (53.6%),
- Viral upper respiratory tract infection (43.2%),
- Headache (27.7%),
- Upper respiratory tract infection (25.9%),
- Injection site redness (18.2%),
- Injection site bruising (13.6%),
- Joint pain (13.2%),
- Back pain (12.7%),
- Nausea (11.4%),
- Urinary tract infection (11.4%),
- Diarrhea (10.9%),
- Sinusitis (10.9%),
- Abdominal pain (10.5%),
- Fatigue (10.0%),
- Influenza (10.0%),

- Pain in the extremities (10.0%)..

Based on the mechanism of action and past case studies with icatibant (FIRAZYR®) and ecallantide (KALBITOR®), there is a strong scientific rationale and high unmet medical need to expand the use of lanadelumab as a prophylactic therapy for patients with likely bradykinin-mediated angioedema other than Type I/II HAE.

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Males and females, 12 years of age and older diagnosed with nonhistaminergic

normal C1-INH angioedema at the time of enrollment into the antecedent Study SHP643-303.
2. Subjects must have completed the treatment period (through Day 182) of Study SHP643-303 without reporting a clinically significant treatment-emergent adverse event (TEAE) that would preclude subsequent exposure to lanadelumab.
3. Agree to adhere to the protocol-defined schedule of treatments, assessments, and procedures.
4. Males, or non-pregnant, non-lactating females who are of childbearing potential and who agree to be abstinent or agree to comply with the applicable contraceptive requirements of this protocol for the duration of the study;
or females of non-childbearing potential, defined as surgically sterile (status post hysterectomy, bilateral oophorectomy, or bilateral tubal ligation) or post-menopausal for at least 12 months.
5. The subject (or the subject's parent/legal guardian, if applicable) has provided written informed consent approved by the institutional review board/research ethics board/ethics committee (IRB/REB/EC) at any time prior to study start. If the subject is a minor (ie, <18 years of age), have a parent/legal guardian who is informed of the nature of the study provide written informed consent (ie, permission) for the minor to participate in the study before any study-specific procedures are performed. Assent will be obtained from minor subjects.

Exclusion criteria

1. Discontinued from Study SHP643-303 after enrollment but before Visit 26 for any reason.
2. Presence of important safety concerns identified in Study SHP643-303 that would preclude participation in this study.
3. Dosing with an investigational product (IP, not including IP defined in antecedent Study SHP643-303) or exposure to an investigational device within 4 weeks prior to Day 0.
4. Subject has a known hypersensitivity to the investigational product or its components.
5. Have any condition (surgical or medical) that, in the opinion of the investigator or sponsor, may compromise their safety or compliance, preclude the successful conduct of the study, or interfere with interpretation of the results (eg, significant pre-existing illness or other major comorbidities that the investigator considers may confound the interpretation of study results).

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-03-2022
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Takhzyro
Generic name:	lanadelumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	10-06-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-10-2021
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	EUCTR2019-004823-20-NL
Other	IND 116647
CCMO	NL75740.056.21