A multi-center, randomized, double-blind, active and placebo-controlled study to investigate the efficacy and safety of ligelizumab (QGE031) in the treatment of Chronic Spontaneous Urticaria (CSU) in adolescents and adults inadequately controlled with H1-antihistamines

Published: 18-09-2018
Last updated: 11-04-2024

The purpose of this study is to establish efficacy and safety of ligelizumab in adolescent and adult subjects with CSU who remain symptomatic despite standard of care treatment by demonstrating better efficacy over omalizumab.

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

Summary

ID

NL-OMON52375

Source
ToetsingOnline

Brief title
CQGE031C2303

Condition

- Angioedema and urticaria

Synonym
Chronic sponataneous Urticaria, Rash

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor van dit onderzoek)

Intervention

Keyword: Biological, CSU, Ligelizumab, Omalizumab

Outcome measures

Primary outcome

The primary objective of the study is to demonstrate that ligelizumab (72 mg q4w and/or 120 mg q4w) is superior to placebo and superior to omalizumab 300 mg q4w in change from baseline in UAS7 at Week 12

Secondary outcome

Objective 1: To demonstrate that a greater proportion of subjects achieve UAS7 = 0 at Week 12 who are treated with ligelizumab 72 mg q4w and/or 120 mg q4w compared to placebotreated subjects and compared with omalizumab 300 mg q4w treated subjects.

Objective 2: To demonstrate the superiority of ligelizumab 72 mg q4w and/or 120 mg q4w treated subjects with respect to a reduction from baseline in the weekly itch severity score at Week 12 compared to placebo-treated subjects and omalizumab 300 mg q4w treated subjects.

Study description

Background summary

QGE031 is a so-called monoclonal antibody, a drug that has been developed especially in the laboratory to inhibit the production of immunoglobulin E or IgE. IgE plays a role in allergic reactions. QGE031 resembles the drug Xolair (omalizumab), which is registered in the Netherlands for the treatment of asthma. Preclinical research showed QGE031 a more effective inhibitor than omalizumab which resulted in less allergic skin reactions. Through this study, the efficacy and safety of 52 weeks of treatment administered subcutaneously QGE031 (every 4 weeks) in patients with CSU is assessed.

Study objective

The purpose of this study is to establish efficacy and safety of ligelizumab in adolescent and adult subjects with CSU who remain symptomatic despite standard of care treatment by demonstrating better efficacy over omalizumab.

Study design

This is a Phase III multi-center, randomized, double-blind, active- and placebo-controlled, parallel-group study. There is a screening period of up to 28 days, a 52 week double-blind treatment period, and a 12 week post-treatment follow-up period.

Intervention

* Ligelizumab 120 mg sc q4w
* Ligelizumab 72 mg sc q4w
* Omalizumab 300 mg sc q4w
* Placebo 0 mg sc q4w

Study burden and risks

Burden:
- 26 s.c. injections every 4 weeks
- Physical examination 19x
- With length and weight: 4x
- Blood test: 19x decrease 5-30 ml each time
- Optional PK / PD blood test: 6x (max 10ml each time)
- Urine research: 4x
- For female subjects pregnancy test: 17x
- Examination test 1x of 3 stool samples
- Keeping daily diary twice a day, during the entire study

- ECG: 3x

Risks:
Adverse Events QGE031 and risks/burden studyprocedures
Known Adverse events QGE031:
- Most common reported: Hives, approx. 2 hrs post injection. Disappeared quickly after treatment of this allergic reaction.
- Allergic reactions (e.g., rash, swelling of throat and/or tongue) and some which on rare occasion may be severe (e.g., very low blood pressure and difficulty with breathing). The risk for a severe allergic reaction caused by the study drug is not known yet, however there have been no occurrences so far and the risk is considered low.
- Risks at s.c. injection site: Pain, swelling, redness and bruising.

Possible side effects of omalizumab
• Very common side effects (in 1 in 10 people or more) are side effects at the site of the injection: redness, pain, itching, swelling, bruise, bleeding and / or hives. Headache.
• Typical side effects (in 1 in 10 to 100 people) are hives and inflammation of the nose and throat, sinus and upper respiratory tract.
• Rare side effects (in 1 in 1,000 to 10,000 people) are signs of a severe allergic reaction and angioedema

Increased susceptibility to parasitic infections.

Risks/burden studyprocedures:
- Venapuncture (blood collection): Fainting, pain and/or bruising. Rarely, there may be a small blood clot or infection at the site of the needle puncture.

Contacts

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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

Signed informed consent must be obtained prior to participation in the study. The subject's, parent's or legal guardian's signed written informed consent and child's assent, if appropriate, must be obtained before any assessment is performed., * Male and female subjects >= 12 years of age at the time of screening.
* CSU diagnosis for >= 6 months (defined as onset of CSU with supporting documentation).
* Diagnosis of CSU refractory to H1-AH at locally label approved doses at the time of randomization, as defined by all of the following:
* The presence of itch and hives for >= 6 consecutive weeks at any time prior to Visit 1 (Day - 28 to Day -14) despite current use of non-sedating H1-antihistamine
* UAS7 score (range 0-42) >= 16 and HSS7 (range 0-21) >= 8 during the 7 days prior to randomization (Visit 110, Day 1)
* Subjects must be on H1-antihistamine at only locally label approved doses for treatment of CSU starting at Visit 1 (Day -28 to Day -14)
* Willing and able to complete a daily symptom eDiary for the duration of the study and adhere to the study visit schedules.
* Other protocol-defined inclusion criteria may apply

Exclusion criteria

History of hypersensitivity to any of the study drugs or their excipients or to drugs of similar chemical classes (i.e. to murine, chimeric or human antibodies).

* Subjects having a clearly defined cause of their chronic urticaria, other than CSU. This includes, but is not limited to, the following: symptomatic dermographism (urticaria factitia), cold-, heat-, solar-, pressure-, delayed pressure-, aquagenic-, cholinergicor contact-urticaria.
* Diseases, other than chronic urticaria, with urticarial or angioedema symptoms such as urticarial vasculitis, erythema multiforme, cutaneous mastocytosis (urticaria pigmentosa) and hereditary or acquired angioedema (eg, due to C1 inhibitor deficiency).
* Subjects with evidence of helminthic parasitic infection as evidenced by stools being positive for a pathogenic organism according to local guidelines. All subjects will be screened at Visit 1. If stool testing is positive for pathogenic organism, the subject will not be randomized and will not be allowed to rescreen.
* Any other skin disease associated with chronic itching that might influence in the investigators opinion the study evaluations and results (e.g. atopic dermatitis, bullous pemphigoid, dermatitis herpetiformis, senile pruritus, etc.).
* Prior exposure to ligelizumab, omalizumab and other IgE therapies.
* Any H2 antihistamine, LTRA (montelukast or zafirlukast) or H1-AH used as background medication at greater than local label approved doses after Visit 1.
* Other protocol-defined exclusion criteria may apply

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-04-2019
Enrollment:	32

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ligelizumab
Generic name:	Ligelizumab
Product type:	Medicine
Brand name:	Xolair
Generic name:	Omalizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	18-09-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-12-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-06-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-06-2019
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-11-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-03-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-03-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-04-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	11-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-04-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-03-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2018-000840-24-NL
ClinicalTrials.gov	NCT03580356
CCMO	NL66602.078.18