A multi-center, randomized, double-blind, placebo controlled study of ligelizumab (QGE031) in the treatment of Chronic Inducible Urticaria (CINDU) in adolescents and adults inadequately controlled by H1-antihistamines

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The purpose of this study is to establish efficacy and safety of ligelizumab (QGE031) versus placebo in participants with chronic inducible urticaria who remain symptomatic despite treatment with H1 antihistamine.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Angioedema and urticaria
Study type	Interventional

Summary

ID

NL-OMON50883

Source
ToetsingOnline

Brief title
CQGE031E12301

Condition

- Angioedema and urticaria

Synonym
Chronic Inducible Urticaria, inducible rash

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: CINDU, hives, Ligelizumab

Outcome measures

Primary outcome

To demonstrate superiority of ligelizumab versus placebo with regards to the change from baseline in response to a standardized provocation test for each CINDU subtype.

Secondary outcome

To demonstrate superiority of ligelizumab versus placebo with regard to proportion of participants with a complete response after standardized provocation test

To demonstrate superiority of ligelizumab versus placebo in itch NRS following the provocation test.

To assess the safety of ligelizumab

Study description

Background summary

Patient with chronic urticaria suffer from itchy hives, with symptoms that are difficult to treat and last for more than 6 weeks. Urticaria can occur spontaneously (chronic spontaneous urticaria (CSU)), or be triggered by external stimuli (chronic inducible urticaria (abbreviated CINDU)).
The standard treatment for CINDU is an H1 antihistamine. Approximately half of

the patients do not benefit sufficiently from this treatment, not even in higher doses. There is therefore a need for better treatments.
QGE031 is a so-called monoclonal antibody, a drug that was specially developed in the laboratory to counteract the production of a body substance (immunoglobulin E or IgE). IgE plays a role in allergic reactions. QGE031 is similar to the medicine Xolair (omalizumab), which is registered in the Netherlands for the treatment of CSU. Laboratory tests showed that QGE031 was better at inhibiting the production of IgE and better at countering allergic skin reactions than omalizumab.

Study objective

The purpose of this study is to establish efficacy and safety of ligelizumab (QGE031) versus placebo in participants with chronic inducible urticaria who remain symptomatic despite treatment with H1 antihistamine.

Study design

This is a Phase III multi-center, randomized, double-blind, active and placebo-controlled, parallel study. There is a screening period of up to 28 days, a double-blind 12-week treatment period followed by a 12-week treatment period in which everyone receives QGE031. Finally, there is a 12-week follow-up period after treatment.

Intervention

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

Study burden and risks

Burden:
- 6 s.c. injections every 4 weeks
- Physical examination 1x
- Measurement of height and weight : 4x
- Blood test : 11x sampling 5-35 ml each time
- Urine examination : 4x
- Pregnancy test for female subjects: 12x
- Fecal analysis 2x of 3 fecal samples
- Keep a diary (daily), during the whole study
- ECG: 2x

There is a possibility that side effects may occur from the study medication or from the study tests. At this time, not all possible side effects of the study medication are known.

Possible side effects of ligelizumab
- Very common side effects (in about 1 person in 10) are reactions at the injection site: redness, pain, itching, swelling, bruising, heat, infiltrate (hard swelling) and/or oedema (fluid).
- Common side effects (in about 1 person in 100) are urticaria (hives) and generalized itching.
- Rare side effects (in about 1 person in 10,000) are angioedema and Anaphylactic reaction.

naphylaxis:
There is a possibility that your child/ward may experience a severe allergic reaction or anaphylaxis (which can be a life-threatening condition) after receiving study medication.
Your study doctor will monitor you closely for symptoms of an allergic reaction while you are receiving study treatment at the study site and, in particular, for a period of time after your injections. Your study doctor should talk to you about seeking urgent medical assistance if you have symptoms of an allergic reaction after leaving the study site.
Signs and symptoms of a severe allergic reaction are:
* Wheezing, shortness of breath, chest tightness or trouble breathing
* Low blood pressure, dizziness, fainting, rapid or weak heartbeat, anxiety, flushing, feeling warm or the feeling that something bad is about to happen (impending doom)
* Swelling of the throat or tongue, throat tightness, hoarse voice, or trouble swallowing
Parasitic Infections:
There is a possibility that you may experience diarrhea or other symptoms that could be from a parasitic infection. This could occur at any time between visits before end of study. If that happens, please inform your study doctor, since additional stool sampling to check for parasitic infections has to be collected as soon as possible.

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

1. Signed informed consent must be obtained before any assessment is performed.
2. Participant's parent's or legal guardian's signed informed consent and child's assent, if appropriate, must be obtained before any assessment is performed.
3. Male and female participants * 12 years of age at the time of screening.
4. Confirmed CINDU diagnosis (as per guidelines) for symptomatic dermographism, cold urticaria or cholinergic urticaria for * 4 months (defined as onset of CINDU with supporting documentation (e.g medical record, clinical history, photographs)).
5. Diagnosis of CINDU (symptomatic dermographism, cold urticaria or cholinergic urticaria) inadequately controlled with H1-AH at local label approved doses at the time of randomization.
6. Participants must be able to physically perform the protocol defined provocation test specific to the participant's CINDU.
7. Cholinergic urticaria participants must show sweating in performing the pulse-controlled ergometry test on day of randomization. Participants with anhidrosis must not be included.
8. Willing and able to complete a daily symptom eDiary as per protocol requirement and adhere to the study visit schedules.

Exclusion criteria

1. Use of other investigational drugs within 5 half-lives of enrollment, or within 30 days for small molecules prior to the screening visit or until the expected pharmacodynamic effect has returned to baseline for biologics, whichever is longer.
2. History of hypersensitivity to any of the study drugs or its components or to drugs of similar classes (i.e. to murine, chimeric or human antibodies) or to the provocation test or items used in provocation tests.
3. Participants who have any concomitant CSU at screening.
4. Participants who have a familial form (e.g familial cold autoinflammatory syndrome, familial cold urticaria) of the target CINDU that is being considered for the participant's inclusion in this study.
5. Participants having a more defined other form of inducible urticaria than the target CINDU that is being considered for the participant's inclusion in this study.
6. Diseases, other than chronic inducible 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).
7. Any other skin disease associated with chronic itching that might influence, in the investigator's opinion, the study evaluations and results (eg, atopic dermatitis, bullous pemphigoid, dermatitis herpetiformis, senile pruritus, etc.) or skin diseases associated with only wheals and no itch e.g asymptomatic dermographism.
8. Prior exposure to ligelizumab, omalizumab or other anti-IgE therapies.
9. Female participants, including adolescent females of 12 to less than 18 years of age, of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using effective methods of contraception during dosing of study treatment.

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:	Will not start
Enrollment:	12
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Ligelizumab
Generic name:	Ligelizumab

Ethics review

Approved WMO Date:	08-09-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-02-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-05-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2020-003018-11-NL
ClinicalTrials.gov	NCT05024058
CCMO	NL77053.100.21