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Clinical Trial Results Summary

A clinical study to learn about the effects and safety of ligelizumab (QGE031) in adolescents and adults with Chronic Inducible Urticaria (CINDU) which could not be controlled with H1-antihistamines

Protocol number: CQGE031E12301

Thank You!

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public.

Thanks to the participants for taking part in this trial for the drug ligelizumab, also known as QGE031. They helped researchers learn more about how ligelizumab works in people with CINDU which could not be controlled with H1-antihistamines.

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If the participants have any questions about the trial results, please talk to the doctor or staff at the trial site.

This summary shows the results of a single clinical trial. Other clinical trials may have different findings.

Why was the research needed?

Researchers were looking for a better way to treat **chronic inducible urticaria (CINDU)**.

Urticaria is a raised, itchy rash that shows up on the skin. It is also called hives, wheals, welts, or nettle rash. These rashes may appear on one part of the body and spread across larger areas.

An itchy rash on the skin occurring for more than 6 weeks is called chronic urticaria. If this is caused by any particular physical or non-physical stimuli, such as heat, cold, or pressure, it is called CINDU. The most common CINDUs are itchy hives that appear in response to scratching or rubbing, cold, or a raised body temperature.

CINDU is a type of allergic disease in which the immune system becomes active even when there is no infection. Normally, the immune system makes and uses antibodies (types of proteins in the blood) to identify and fight foreign objects, such as bacteria and viruses. In CINDU, the antibody known as IgE is over-produced leading to a rise in histamines. Histamines are what causes itchy hives. Antihistamines are medicines that are used to treat CINDU which stop our body from making histamines.

Ligelizumab, also called **QGE031**, is a trial drug that has not yet been approved for the treatment of CINDU. **QGE031** attaches itself to IgE so it prevents the release of histamines in the blood.

Drug	***Pronounced as***
Ligelizumab	li-gu-LIZ-oo-mab

In this trial, researchers wanted to learn about the effects and safety of **QGE031** in adolescents and adults with CINDU which could not be controlled with antihistamines, the standard treatment for CINDU.

How long was this trial?

This trial started in November 2021 and ended in August 2022. The entire duration, from enrolling the first participant to the last participant completing the trial, was around 9 months. An individual participant was in this trial for an average of 8 months.

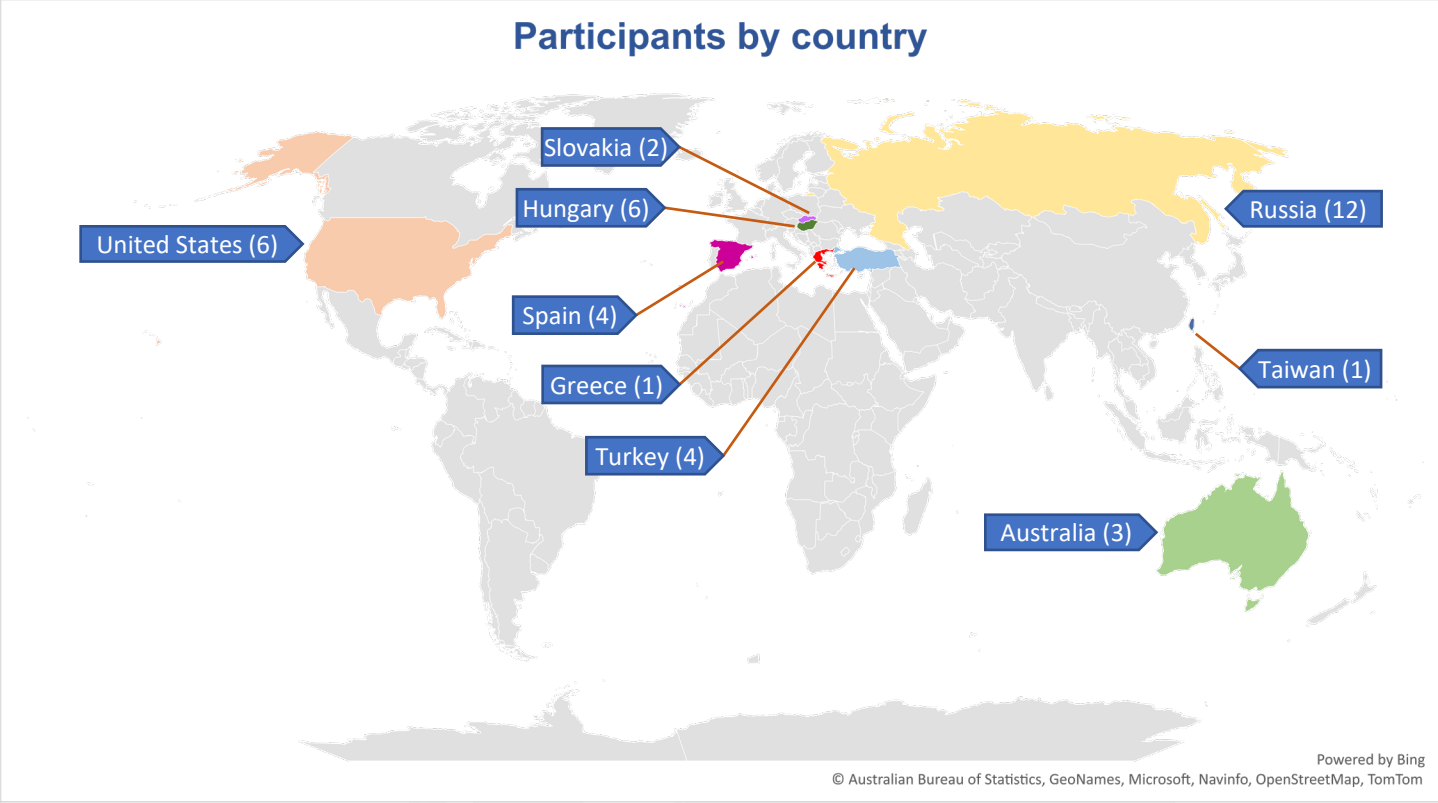
The sponsor ended this trial early because of a strategic company decision and not because of any safety concerns with **QGE031**. When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Who was in this trial?

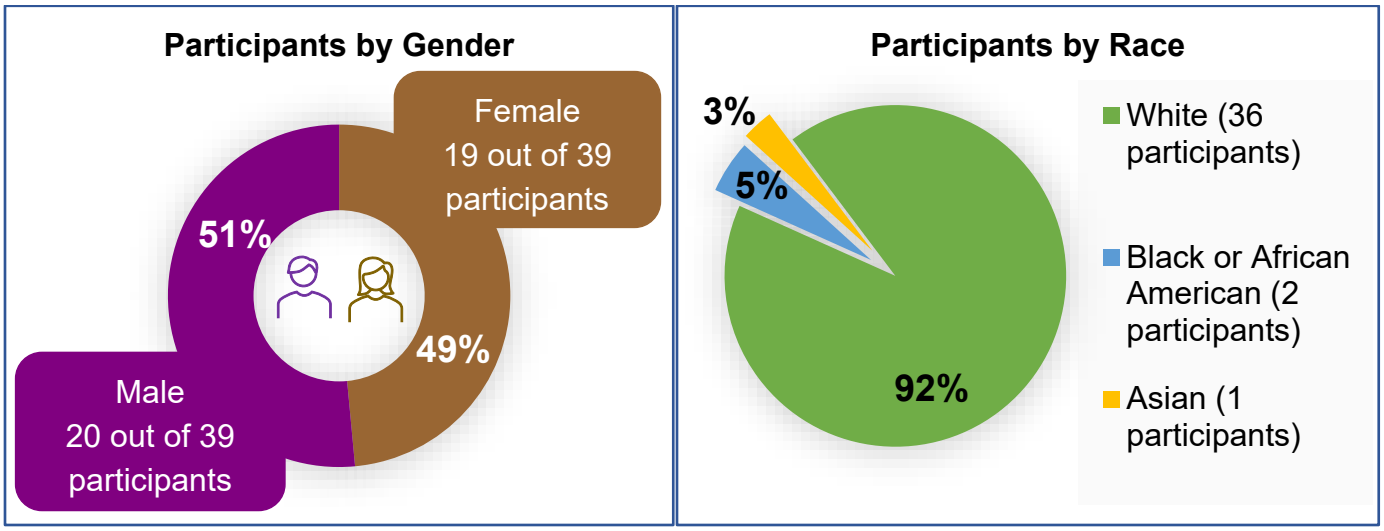
The participants could take part in this trial if they:

- were at least 12 years of age,
- had CINDU diagnosed at least 4 months before the start of the trial,
- had CINDU which could not be controlled with standard treatment (antihistamines).

A total of 39 participants from 9 countries were randomly assigned to treatment groups using a computer system. This process is called randomization. It means that each participant could be assigned to any treatment group, and it helped to make sure the groups were distributed fairly and neither the doctor nor the participant knew the treatment assigned to them.



Five participants in the study were adolescents aged 12 to 17 years, and 34 participants were adults aged 18 to 64 years. The average age of the adult participants was 27 years.



What treatments did the participants take?

	QGE031, the trial drug, is not approved for the treatment of CINDU. It was given at a dose of 72 milligrams (mg) or 120 mg as an injection under the skin every 4 weeks.
	Placebo which looked like the trial drug, but did not have any medicine in it. Using a **placebo** helps researchers better understand the effect of a trial drug by making sure that the changes were not happening by chance.

Along with **QGE031** or **placebo**, participants could continue to take antihistamines and could take rescue medications if needed.

What happened during this trial?

Before treatment

The trial doctors checked if participants could take part in this trial.

This was a trial where none of the participants, trial doctors, or trial staff knew what treatment participants were receiving. Some trials are done this way because knowing what treatment each participant is getting can affect the results of the trial.

Up to 4 weeks before treatment

During treatment

Participants were randomly assigned to the following 4 groups.

- **Group 1** (8 participants): **QGE031** 72 mg for 24 weeks
- **Group 2** (15 participants): **QGE031** 120 mg for 24 weeks
- **Group 3** (5 participants): **Placebo** for 12 weeks followed by **QGE031** 72 mg for 12 weeks
- **Group 4** (11 participants): **Placebo** for 12 weeks followed by **QGE031** 120 mg for 12 weeks

Participants received their treatment as an injection every 4 weeks up to and including Week 20 (the last dose).

Up to 24 weeks

After treatment

No trial drug was given; however, participants were allowed to take medications (antihistamines and rescue medication) to relieve their symptoms.

Researchers monitored the health of the participants throughout the trial.

Up to 12 weeks after treatment

What were the main results of this trial?

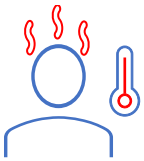
Did the participants' itch and hives improve after 12 weeks of treatment compared to placebo?

Most participants did not completed the trial because the sponsor decided to end this trial due to a strategic company decision. Therefore no conclusions can be made regarding the effect of QGE031 on CINDU.

The researchers divided the participants into 3 groups according to the cause of their CINDU.

No participants with CINDU caused by **scratching or rubbing** completed 12 weeks of treatment. Thus, improvement in participants' symptoms for this group could not be measured.

Two participants with CINDU caused by **cold** completed 12 weeks of treatment. After 12 weeks of treatment, the participants did not have itch and hives symptoms at the temperature that caused the symptoms at the start of the study. This means that the itch and hives symptoms improved for both participants.



One participant with CINDU caused by raised **body temperature** completed 12 weeks of treatment. After 12 weeks of treatment, the participant did not have itch and hives symptoms at the temperature that caused the symptoms at the start of the study. This means that the itch and hives symptoms improved for this participant.

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "adverse events".

A lot of research is needed to know whether a drug causes an adverse event. **During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug.** When new drugs are being studied, researchers keep track of all adverse events participants have.

This section is a summary of the adverse events that happened during this trial. The websites listed at the end of this summary may have more information about all the adverse events that happened in this trial.

An adverse event is any sign, symptom, or disease that participants have during a trial.

An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drug.

How many participants had adverse events?

During this trial some participants experienced at least one adverse event:

- 3 out of 8 participants (38%) on **QGE031** 72 mg,
- 6 out of 15 participants (40%) on **QGE031** 120 mg,
- 3 out of 5 participants (60%) who transitioned from **placebo** to **QGE031** 72 mg, and
- 1 out of 11 participants (9%) who transitioned from **placebo** to **QGE031** 120 mg.

No participant in this trial experienced any serious adverse event, stopped the trial drug due to an adverse event, or died.

What serious adverse events did the participants have?

No serious adverse event was observed.

What other adverse events did the participants have?

The most common non-serious adverse events that happened to the participants in any group are presented below. Some participants might have experienced more than one adverse event.

Number of Participants (%) With Most Common Non-Serious Adverse Events

Groups (Number of participants)	**QGE031 72 mg** (Out of 8 participants)	**QGE031 120 mg** (Out of 15 participants)	**Placebo to QGE031 72 mg** (Out of 5 participants)	**Placebo to QGE031 120 mg** (Out of 11 participants)
Stuffy Nose (Nasopharyngitis)	0	2 (13%)	0	0
Slower heart rate than normal (Bradycardia)	0	0	1 (20%)	0
Persistent ringing in ears (Tinnitus)	1 (13%)	0	0	0
Dizziness (Vertigo)	0	1 (7%)	0	0
Short supply of the hormone from the brain (Hypopituitarism)	0	1 (7%)	0	0
Stomach pain (Abdominal pain)	0	1 (7%)	0	0
Feeling sick to your stomach (Nausea)	1 (13%)	0	0	0
Breathing illness caused by a virus (COVID-19)	0	1 (7%)	0	0
Cold sores (Herpes simplex)	1 (13%)	0	0	0
Flu (Influenza)	0	1 (7%)	0	0
Pus formation next to one of the tonsils (Peritonsillar abscess)	0	0	1 (20%)	0
Breathing problem persisting beyond 4 weeks of start of COVID-19	0	1 (7%)	0	0

Groups (Number of participants)	**QGE031 72 mg** (Out of 8 participants)	**QGE031 120 mg** (Out of 15 participants)	**Placebo to QGE031 72 mg** (Out of 5 participants)	**Placebo to QGE031 120 mg** (Out of 11 participants)
(Post-acute COVID-19 syndrome)				
Chest infection (Respiratory tract infection)	1 (13%)	0	0	0
Common cold (Upper respiratory tract infection)	0	1 (7%)	0	0
Infection in the urinary system (Urinary tract infection)	0	1 (7%)	0	0
High glucose level in blood (Glucose tolerance impaired)	0	1 (7%)	0	0
High uric acid level in blood (Hyperuricaemia)	0	1 (7%)	0	0
Insufficient Vitamin D in body (Vitamin D deficiency)	0	1 (7%)	0	0
Joint pain (Arthralgia)	0	0	1 (20%)	0
Pain in the area where legs join front of your body (Groin pain)	1 (13%)	0	0	0
Muscle cramps (Muscle spasms)	1 (13%)	0	0	0
Muscle pain (Myalgia)	0	1 (7%)	0	0
Headache	0	0	1 (20%)	0

Groups (Number of participants)	QGE031 72 mg (Out of 8 participants)	QGE031 120 mg (Out of 15 participants)	Placebo to QGE031 72 mg (Out of 5 participants)	Placebo to QGE031 120 mg (Out of 11 participants)
Migraine headache (Migraine)	0	0	0	1 (9%)
Pain or tightness around forehead or back of the head (Tension headache)	0	1 (7%)	0	0
Cough	1 (13%)	0	0	0
Throat pain (Oropharyngeal pain)	0	1 (7%)	0	0

How was this trial useful?

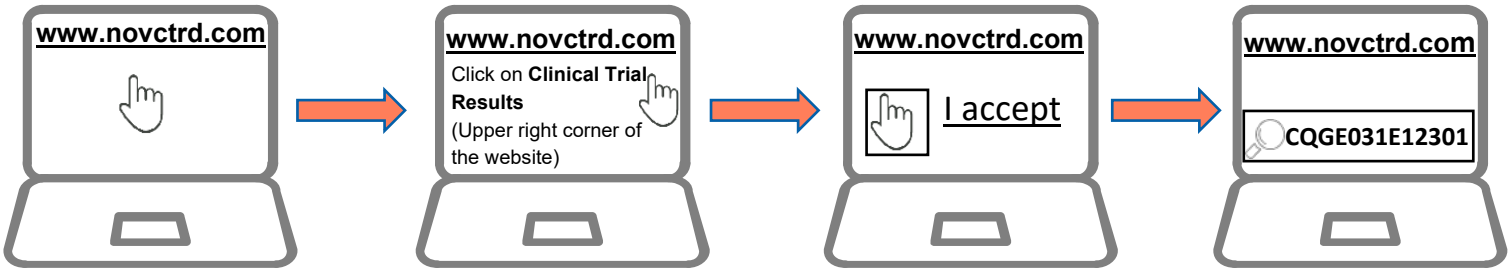
The trial helped researchers to learn about the effect and safety of **QGE031** in both adults and adolescents with CINDU which could not be controlled with antihistamines.

The study was stopped early due to a strategic company decision. At that time, only a small number of participants completed the 12 weeks of treatment. Hence, no meaningful conclusion related to effect or safety could be drawn. However, **QGE031** safety was similar to that of **QGE031** studies for chronic spontaneous urticaria (CSU).

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website, **www.novctrd.com**.

Please follow the steps below:



You can find more information about this trial on the following websites:

- www.clinicaltrials.gov Use the NCT identifier NCT05024058 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search Use the EudraCT identifier 2020-003018-11 in the search field.

Full clinical trial title: A multi-center, randomized, double-blind, placebo controlled study to investigate the efficacy and safety of ligelizumab (QGE031) in the treatment of Chronic Inducible Urticaria (CINDU) in adolescents and adults inadequately controlled with H1-antihistamines.

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of people around the world. You helped researchers answer important health questions and test new medical treatments.

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Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

1-888-669-6682 (US); +41-61-324-1111 (EU); www.novartisclinicaltrials.com