NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the long-term effects of QGE031 (ligelizumab) in people with chronic spontaneous urticaria (CSU) who completed a previous clinical trial with QGE031

Protocol number: CQGE031C2302E1

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 chronic spontaneous urticaria.

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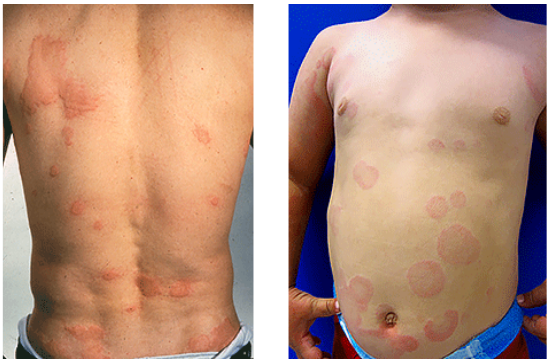
If the participants have any questions about the trial results, please talk to the doctor or staff at the trial site.

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 spontaneous urticaria (CSU)**.

Urticaria, commonly known as hives, results in a rash or bumps on the skin (known as 'hives', 'wheals', or 'weals'). It may be accompanied by an itch ('pruritis'). It is often caused by an allergic reaction to food, insect stings, or drugs. In some cases, CSU may develop suddenly without an obvious cause. This is called Spontaneous Urticaria.



Source: American Academy of Dermatology Association

Usually, it goes away quickly but for some people, the itch and hives come back again, with no known cause. When this occurs several times a week over 6 weeks or more, it is called **chronic spontaneous urticaria or CSU.**

What causes CSU?

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

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. CSU is a type of allergic disease in which the immune system becomes active even when there is no infection. The levels of a type of antibody called immunoglobulin E (IgE) are often increased in CSU. The standard or first-line treatment for CSU is antihistamines. These drugs block the release of histamines, which are responsible for allergies in our body.

QGE031, or Ligelizumab, attaches itself to IgE making IgE inactive. This way, **QGE031** blocks the effect of IgE. Ligelizumab is also referred to using its Novartis code **QGE031**.

In this trial, researchers wanted to learn about the long-term effects of **QGE031** in adults and adolescents with CSU who had previously completed the clinical trials CQGE031C2302 and CQGE031C2303. Novartis also wanted to give all patients who had previously completed trials CQGE031C2302, CQGE031C2303, CQGE031C2202 or CQGE031C1301 the opportunity to continue taking **QGE031**.

How long was this trial?

Each participant was planned to be in this trial for 9 months to 4 years. But the trial started in April 2020 and ended early in September 2022 after only 2 years and 5 months.

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

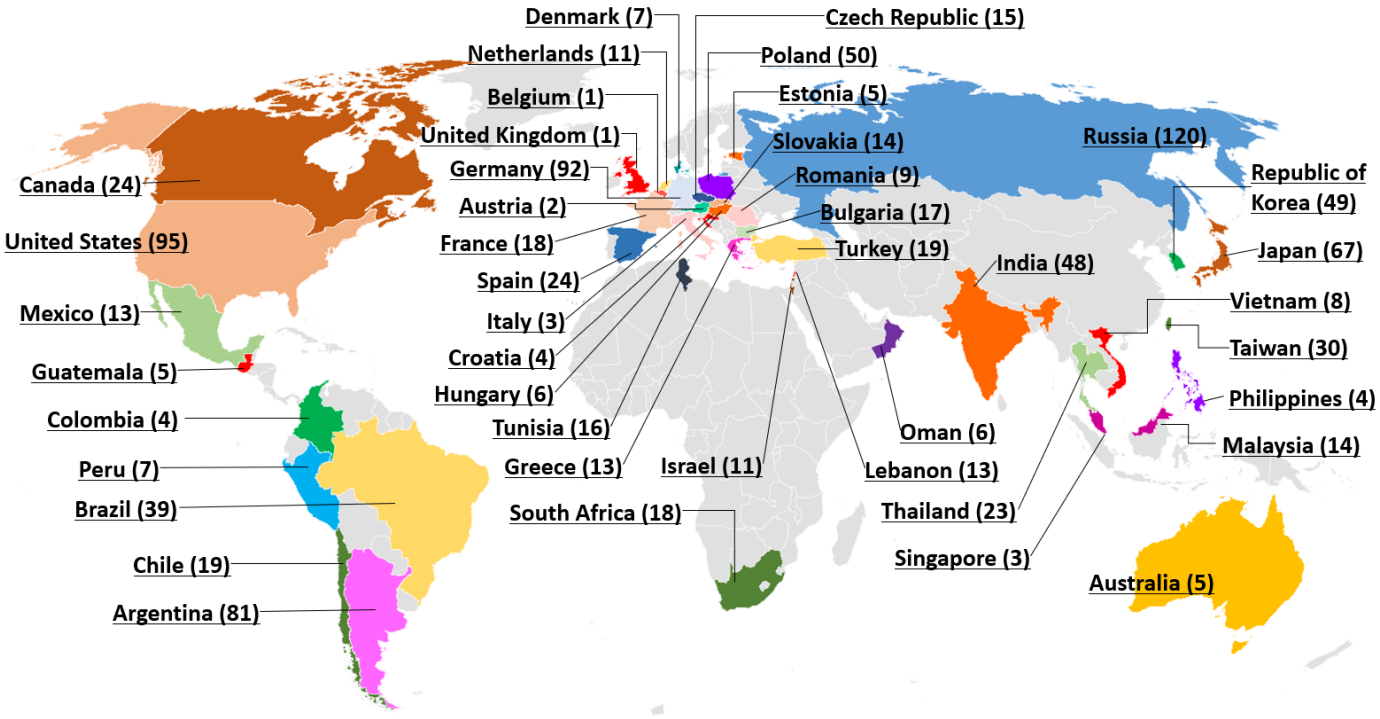
Who was in this trial?

The participants could take part in this trial if they:

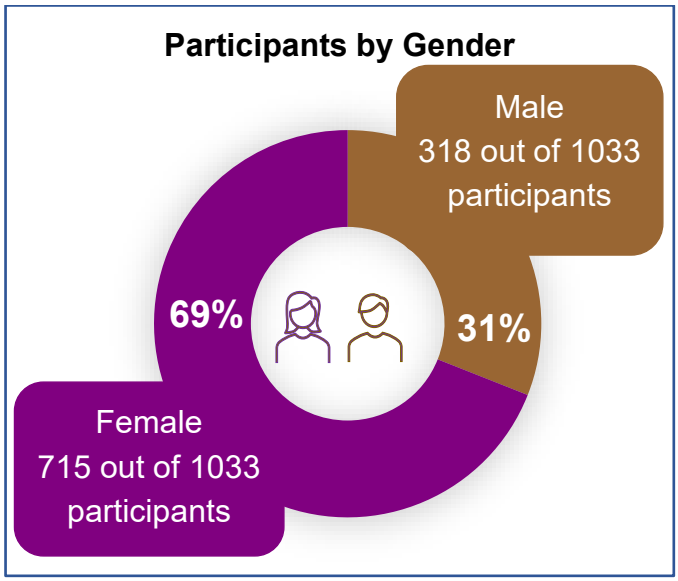
- were at least 12 years of age,
- were willing and able to follow the trial procedures, and
- had previously completed trials CQGE031C2302, CQGE031C2303, CQGE031C2202 or CQGE031C1301.

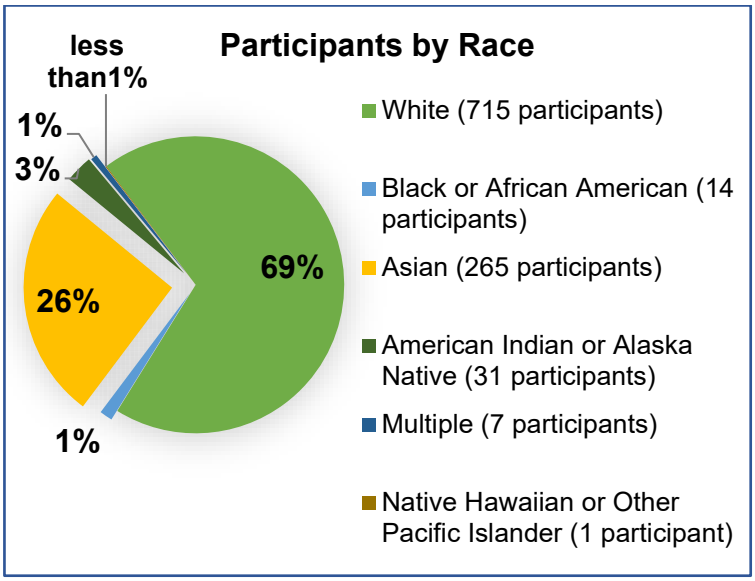
A total of 1033 participants from 44 countries received treatment.

Participants per country



Participants' ages ranged from 13 to 81 years. The average age of the participants was 43 years. Most of the participants were female (69%) and white (69%).





What treatment did the participants receive?

QGE031 is the trial drug used for the treatment of CSU. It is not an approved drug for treatment of CSU.

It was given at a dose of 72 milligrams (mg) or 120 mg injection under the skin every 4 weeks.

Along with the treatment above, participants could continue their CSU medicines. They could take rescue medications after 12 weeks of treatment if needed. Rescue medications are the medicines given to relieve symptoms immediately in case participants do not receive relief from their CSU symptoms during trial treatment.

Among those participants who received **QGE031**, during the first 12 weeks of the trial, the participants and trial team did not know which dose of **QGE031** treatment the participants received. For the rest of the trial, they received the same dose of **QGE031** 120 mg.

What happened during this trial?

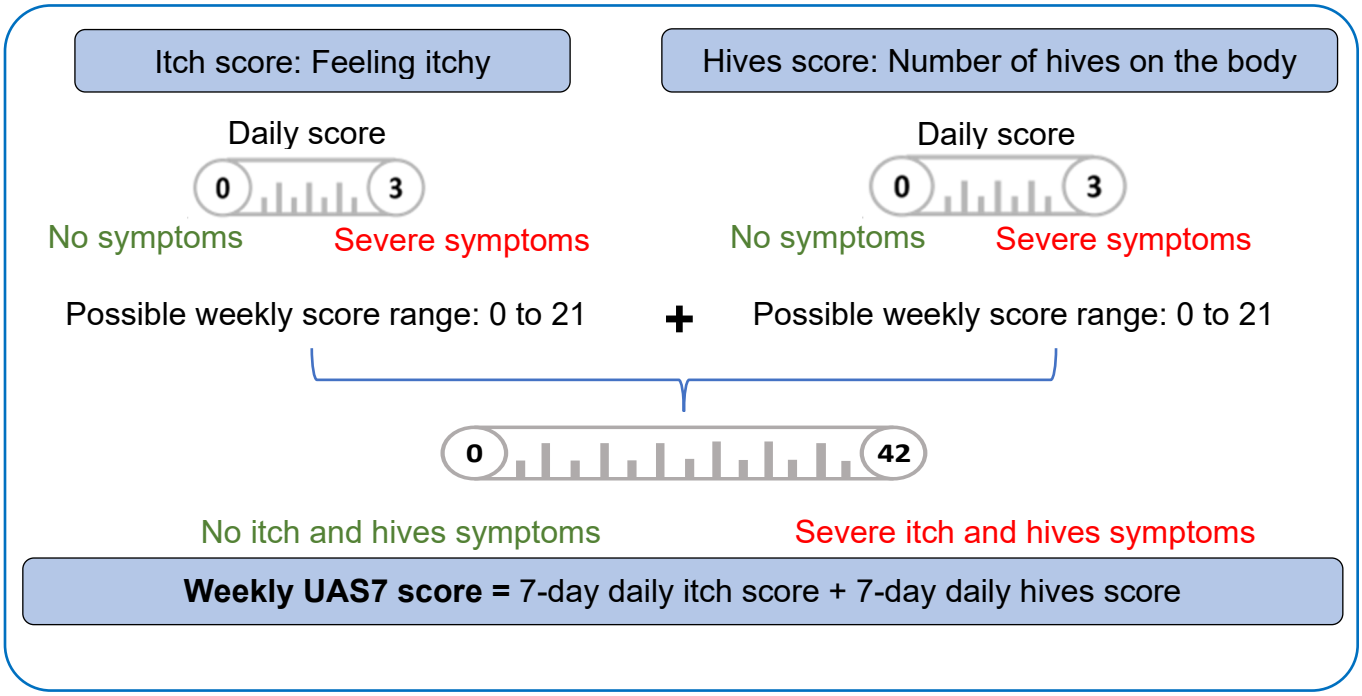
The treatment was given based on how severe the CSU symptoms were, which were measured as follows:

Participants recorded their CSU symptoms of itch and hives twice a day in e-Diaries using a scale called Urticaria Activity Score, or UAS.

Researchers monitored participants' weekly scores as shown in the figure below.

The weekly scores and their meanings are listed below.

Weekly UAS7 Score	Severity of CSU Symptoms
0	Completely controlled
1 to 6	Well-controlled
7 to 15	Mild disease
16 to 27	Moderate disease
28 to 42	Severe disease



Before treatment

Researchers included participants who had completed a previous **QGE031** trial. The trial doctors checked if participants could take part in this trial.

Up to 4 weeks

During treatment

1. Participants with **well-controlled or mild CSU** were observed during trial visits and not given treatment, for up to 36 weeks.
2. Participants with **moderate to severe CSU**, or those with **well-controlled or mild CSU** whose CSU got **worse** while being observed, were given **QGE031** as an injection under the skin every 4 weeks, for 52 weeks.

First 12 weeks
Liquid-in-vial injection every 4 weeks

Participants from trials CQGE031C2302 and CQGE031C2303

- were given the same dose of **QGE031** (72 mg or 120 mg) in this trial as they got in the previous trials.
- participants and the trial team did not know what dose of **QGE031** treatment was given.

Participants from trials CQGE031C2301 and CQGE031C2202

- were all given **QGE031** 120 mg.

After 12 weeks
Injection by prefilled syringe every 4 weeks

Participants switched to **QGE031** 120 mg for rest of the trial and were offered the opportunity to take the treatment by themselves.

Both participants and trial team knew what dose of treatment was given.

Up to 192 weeks

3. Participants whose CSU was **mild, moderate or severe**, but not **well-controlled**, were given **QGE031** 120 mg for another 52 weeks.
4. Participants whose CSU was **well-controlled** or **completely controlled** after the first 52 weeks of treatment, stopped taking **QGE031** treatment. They were observed for up to 52 weeks during trial visits. If their CSU got worse, they could start taking **QGE031** 120 mg. Participants were assessed by a phone call from the study site every 4 weeks.
5. Participants whose CSU stayed **well-controlled** or completely controlled left the trial at the end of the 52 weeks.

After treatment

Participants who completed both treatment periods entered a 52-week follow-up period. Those who did not, entered a 12-week follow-up period.

Participants' health was monitored during this follow-up period.

12 or 52 weeks

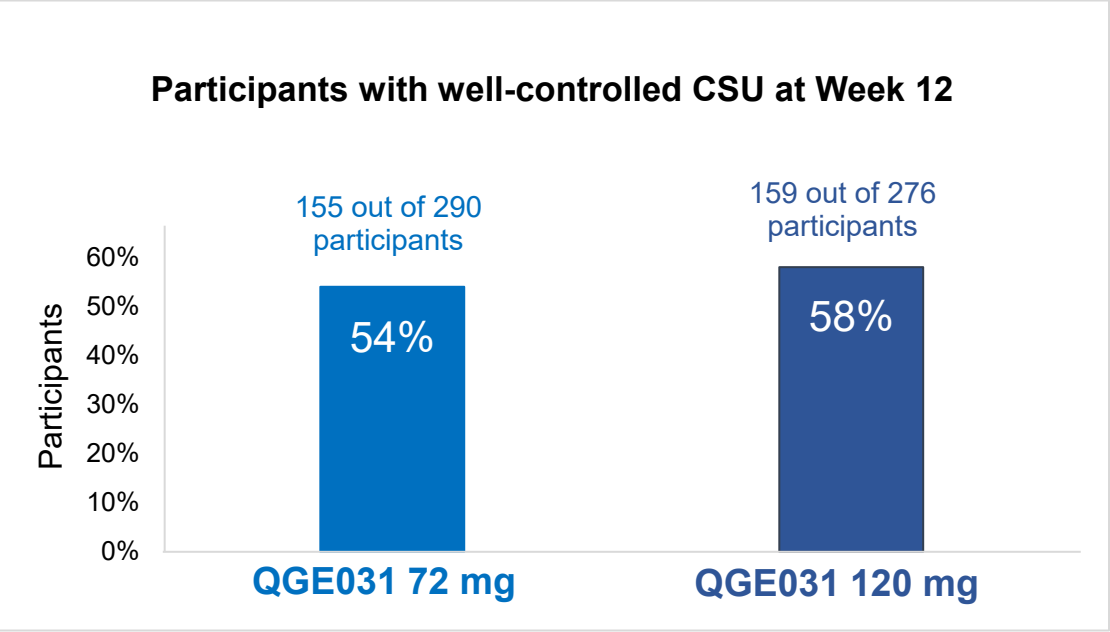
What was the main result of this trial?

How many participants who previously took part in clinical trials CQGE031C2302 or CQGE031C2303 had well-controlled* CSU at Week 12 after re-treatment with the same dose of QGE031?

*Researchers used the UAS7 scoring system to measure participants' CSU symptoms of itch and hives. A weekly UAS7 score of 1 to 6 meant participants had well-controlled CSU. A score of 0 meant participants had completely controlled CSU.

Re-treatment in this trial is when **QGE031** is given again when participant's CSU worsened after it was stopped due to well-controlled symptoms.

54% (155 out of 290) of participants on **QGE031** 72 mg and 58% (159 out of 276) of participants on **QGE031** 120 mg had well-controlled or completely controlled CSU at Week 12 after re-treatment.



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?

The adverse events that happened in the following groups during the trial are listed in the table below.

Number of Participants (%) With Adverse Events

	***QGE031 72 mg to QGE031 120 mg** (Out of 288 participants)	***QGE031 120 mg to QGE031 120 mg** (Out of 745 participants)	**Total** (Out of 1033 participants)
At least 1 other adverse event	65 (23%)	224 (33%)	289 (28%)
At least 1 serious adverse event	8 (3%)	44 (6%)	52 (5%)
Stopped drug due to adverse event	1 (<1%)	14 (2%)	15 (1%)
Deaths	0	3 (<1%)	3 (<1%)

* *Participants received QGE031 72 mg or QGE031 120 mg by liquid-in-vial injection for the first 12 weeks of treatment and then QGE031 120 mg by pre-filled syringe.*

Some participants stopped trial drug due to adverse events. All adverse events that led to trial drug treatment discontinuation were single events.

What were the most common serious adverse events?

The most common serious adverse events that happened in at least 2 participants in any group are shown below.

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

	*QGE031 72 mg to QGE031 120 mg (Out of 288 participants)	*QGE031 120 mg to QGE031 120 mg (Out of 745 participants)	Total (Out of 1033 participants)
Covid-19	1 (<1%)	11 (1%)	12 (1%)
Infection in the colon (Diverticulitis)	0	2 (<1%)	2 (<1%)
Kidney stones (Nephrolithiasis)	0	2 (<1%)	2 (<1%)

* *Participants received QGE031 72 mg or QGE031 120 mg by liquid-in-vial injection for the first 12 weeks of treatment and then QGE031 120 mg by pre-filled syringe.*

What were the most common other adverse events?

The most common other adverse events that happened in at least 4% (4 out of 100) participants are presented below.

Number of Participants (%) With Most Common Other Adverse Events

	*QGE031 72 mg to QGE031 120 mg (Out of 288 participants)	*QGE031 120 mg to QGE031 120 mg (Out of 745 participants)	Total (Out of 1033 participants)
Covid-19	38 (13%)	117 (16%)	155 (15%)
Headache	17 (6%)	64 (9%)	81 (8%)
Common cold (Nasopharyngitis)	12 (4%)	56 (8%)	68 (7%)
Fever (Pyrexia)	7 (2%)	39 (5%)	46 (4%)

* *Participants received QGE031 72 mg or QGE031 120 mg as a liquid-in-vial injection for the first 12 weeks of treatment and then QGE031 120 mg by pre-filled syringe.*

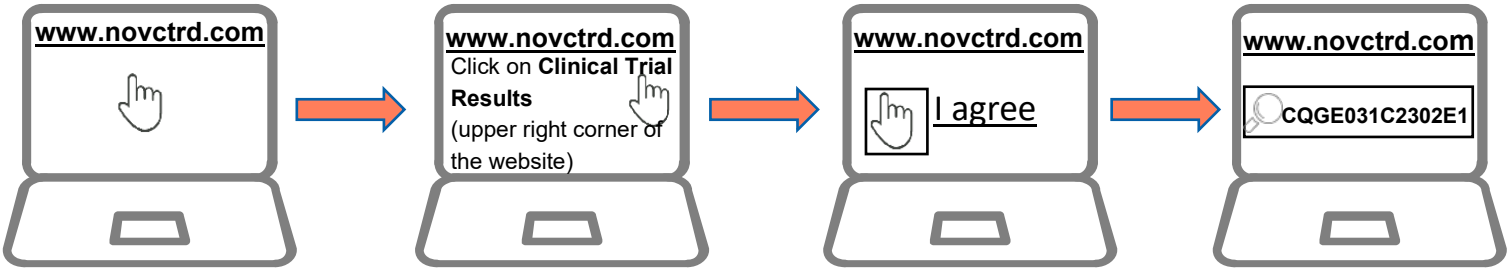
How has the trial helped?

The trial showed that **QGE031** 72 mg and 120 mg were effective in treating patients with **chronic spontaneous urticaria (CSU)** when given as a re-treatment. The trial also allowed participants to continue receiving **QGE031**. However, the sponsor ended this trial early because researchers learned from previous clinical trials, the effect of **QGE031** was not better than available biological treatment. **QGE031**'s safety was the same as seen in the previous **QGE031** trials. The sponsor has no plans to seek approval from the government to use **QGE031** for the treatment of 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 NCT04210843 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search Use the EudraCT identifier 2019-001792-37 in the search field.

Full clinical trial title: A multi-center, double-blinded and open-label extension study to evaluate the efficacy and safety of ligelizumab as retreatment, self-administered therapy and monotherapy in Chronic Spontaneous Urticaria patients who completed studies CQGE031C2302, CQGE031C2303, CQGE031C2202 or CQGE031C1301

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.

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