Clinical Trial Results Summary

An extension trial to learn more about the long-term safety and effects of ligelizumab (QGE031) in participants with itch and hives who completed the trial CQGE031C2201

Protocol number: CQGE031C2201E1

Thank You!

Novartis sponsored this trial and believes it is important to share the results of the trial with you and the public. Thank you for taking part in this trial for the drug QGE031, also known as ligelizumab. You helped researchers learn more about how ligelizumab works in people with chronic spontaneous urticaria, also known as CSU.

As a clinical trial participant, you belong to a large community of people around the world. Your invaluable contribution to medicine and healthcare is greatly appreciated.

This summary is for this extension trial only. It shows the results of this single trial. Other clinical trials may have different findings. This trial was used to look for and evaluate the long-term safety of participants with itch and hives who completed an earlier ligelizumab CQGE031C2201 trial and entered into this extension trial. Researchers and health authorities, such as the Food and Drug Administration (FDA) in the United States and the European Medicines Agency (EMA) in Europe, look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

How long was this trial?

This trial, CQGE031C2201E1, is an extension trial of the core trial CQGE031C2201. Participants who completed treatment in the core trial, and presented with itch and hives symptoms after at least 16 weeks from the last injection in the core trial had an opportunity to continue ligelizumab (QGE031) treatment in this extension trial.

This extension trial was designed so that an individual participant could take part for up to almost 2 years, which includes 1 year of treatment and almost 1 year of follow-up with no ligelizumab (QGE031) treatment. The trial started in May 2016 and ended in May 2019.

The researchers completed this trial as planned. When the trial ended, the researchers collected information on the trial treatment, ligelizumab (QGE031), and created a report of the trial results. This summary is based on that report.

Why was the research needed?

Urticaria consists of itchy hives. A person affected with hives develops swollen, itchy, pale red bumps on the skin. Chronic spontaneous urticaria (CSU) also known as chronic idiopathic urticaria (CIU), in this summary, refers to hives and itchiness that appear suddenly and without an obvious cause. For the hives to be classed as chronic, they need to last longer than 6 weeks, be uncontrolled, and unpredictable. Normally, the immune system makes and uses antibodies 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.

Ligelizumab (QGE031) attaches itself to IgE so that the immunoglobulin is not active anymore. This way ligelizumab blocks the effect of the IgE antibody. Ligelizumab was found to work in an earlier ligelizumab trial, CQGE031C2201, referred as the ‘core trial’ in this summary, when added to the participant’s regular itch and hives medicine. In this trial, researchers wanted to know more about the safety of ligelizumab when given to people with itch and hives for 1 year after at least a 16-week washout after the last injection in CQGE031C2201 study.

Trial drug

The drug given in this trial was:

Ligelizumab (QGE031) is an investigational drug, not yet available to the public, so it can only be used in a research trial such as this one. It was studied in this trial for the treatment of itch and hives at a dose of 240 mg (2 injections of 120 mg each) under the skin every 4 weeks.

Throughout the trial, the participants continued to take their regular itch and hives medicine called antihistamines.

Participants were also given extra doses of antihistamines to manage episodes of itch and hives, if needed. This medicine is known as “rescue” medicine.

Trial purpose

This trial was done to learn more about the safety of ligelizumab (QGE031) when used for a longer time in addition to the regular itch and hives medicine in participants with CSU.

The main question the researchers wanted to answer in this trial was:

- How many participants had adverse events during the trial?

Medical problems that happen in clinical trials are called “adverse events”. Adverse events are defined on Page 6 in this summary.

The other questions researchers wanted to answer in this trial were:

- How many participants had well-controlled disease at the end of the treatment period and the follow-up period?
- For the participants with well-controlled disease at the end of one year of treatment, how long did it take until their itch and hive symptoms reappeared?

What kind of trial was this?

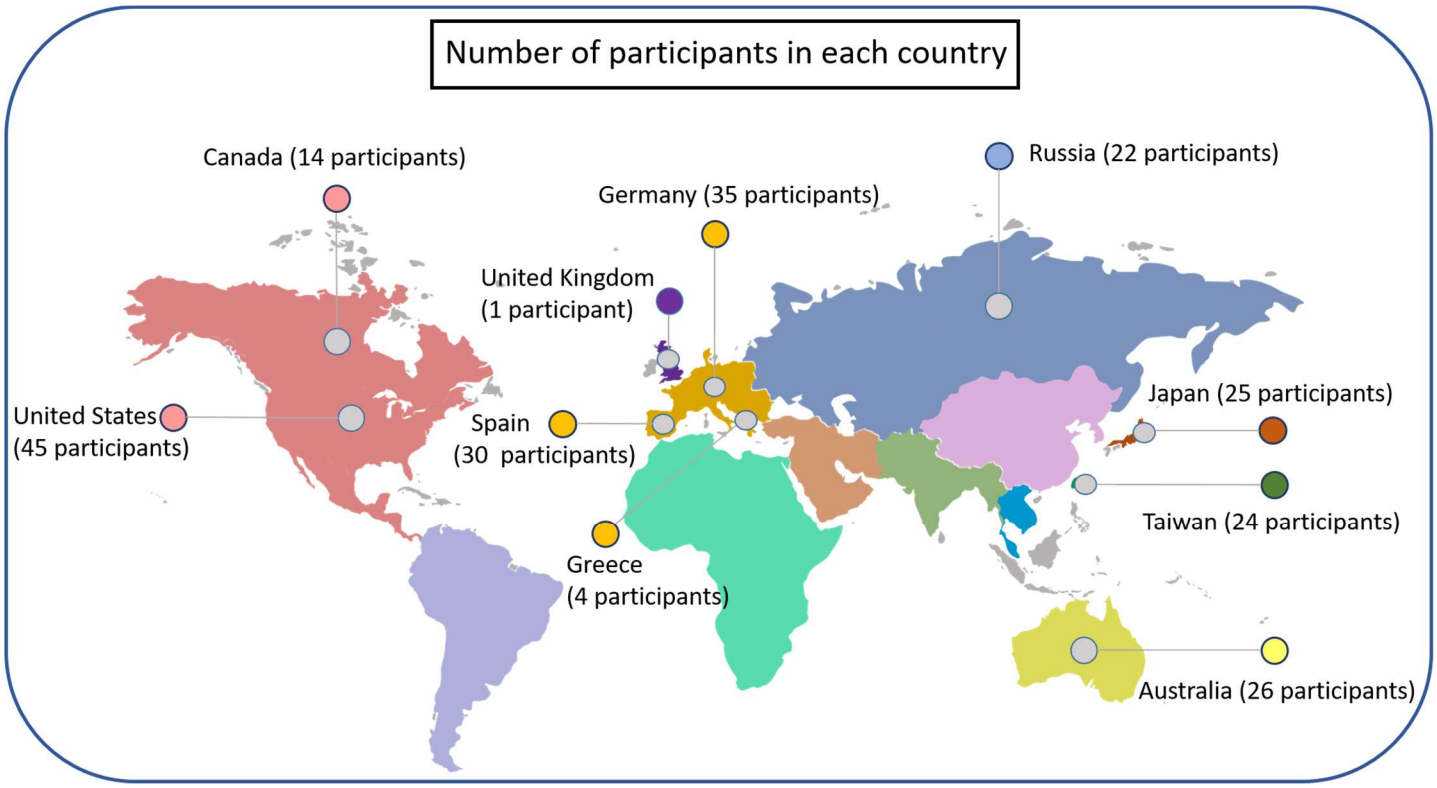
This trial is called an open-label trial. This means that the participants, trial doctors, and trial staff knew the participants were receiving ligelizumab (QGE031).

Who was in this trial?

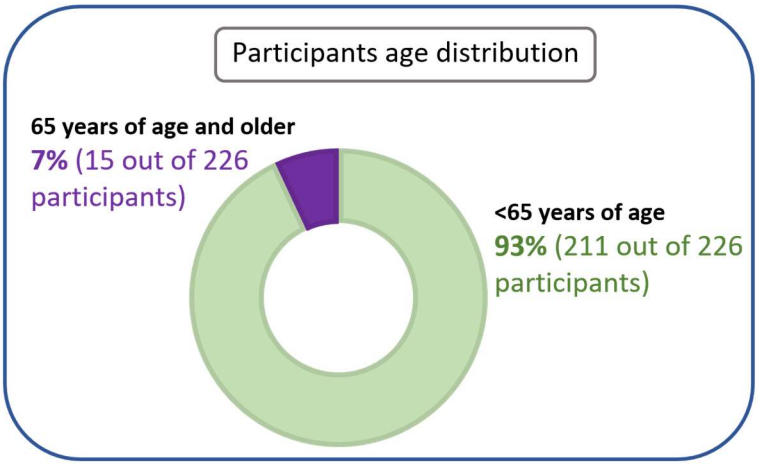
The participants could take part in this trial if:

- they were between 18 and 75 years of age,
- they completed the core trial treatment and presented with symptoms of itch and hives after 16 weeks from the last injection in the core trial.

A total of 226 participants from 10 countries, who had completed the earlier CQGE031C2201 core trial, participated in this trial.



The average age of participants was 45 years. Participants' age ranged from 19 to 74 years. About 75% of the trial participants, or 170 out of 226, were female.

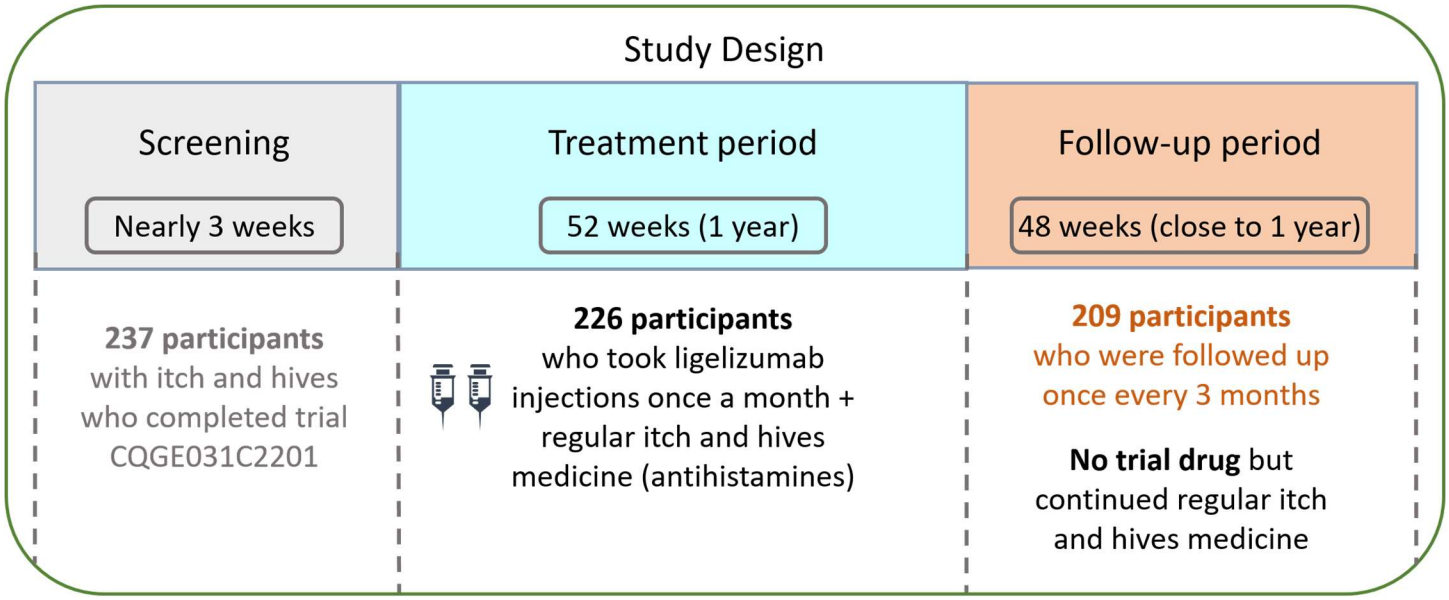


What happened during this trial?

The participants who completed the core trial with symptoms of itch and hives underwent tests (screening) to see if they could enter this trial. Eligible participants were enrolled in this trial over a period of 2 to 3 weeks after completing the core trial, CQGE031C2201. The participants continued to record their itch and hives symptoms throughout the trial in an electronic diary (e-diary) provided to them.

During the treatment period (1 year), the participants received a monthly dose of 240 mg ligelizumab. The participants were given 2 ligelizumab injections, of 120 mg each, under the skin - in either the arm, thigh or the lower part of the stomach. Participants could receive a maximum of 13 doses of ligelizumab injections in this trial. While the participants were being monitored during the treatment period, they were also recording their symptoms in e-diaries.

After completing 1 year of ligelizumab treatment, the participants entered into the follow-up period for close to 1 year where no trial drug was given but the participants continued with their regular itch and hives medicine. During the follow-up period, the participants had a follow-up visit once every 3 months. Throughout the trial, researchers checked for the itch and hives symptoms and the well-being of the participants.



What were the key results of this trial?

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

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 the trial. The websites listed at the end of this summary also report the information about the adverse events that happened in this trial.

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

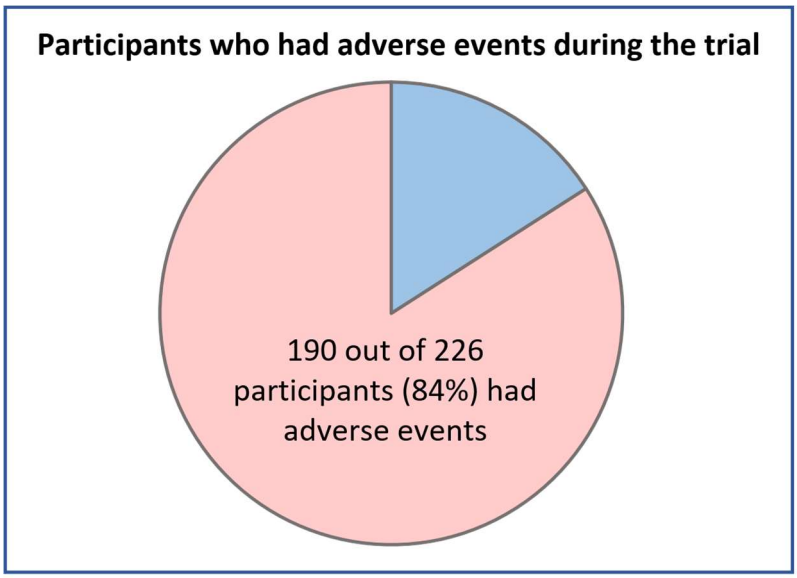
An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drug.

This is a summary of the average results of all the participants. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total group of participants. A detailed presentation of the results can be found on the websites listed at the end of this summary.

How many participants had adverse events during the trial?

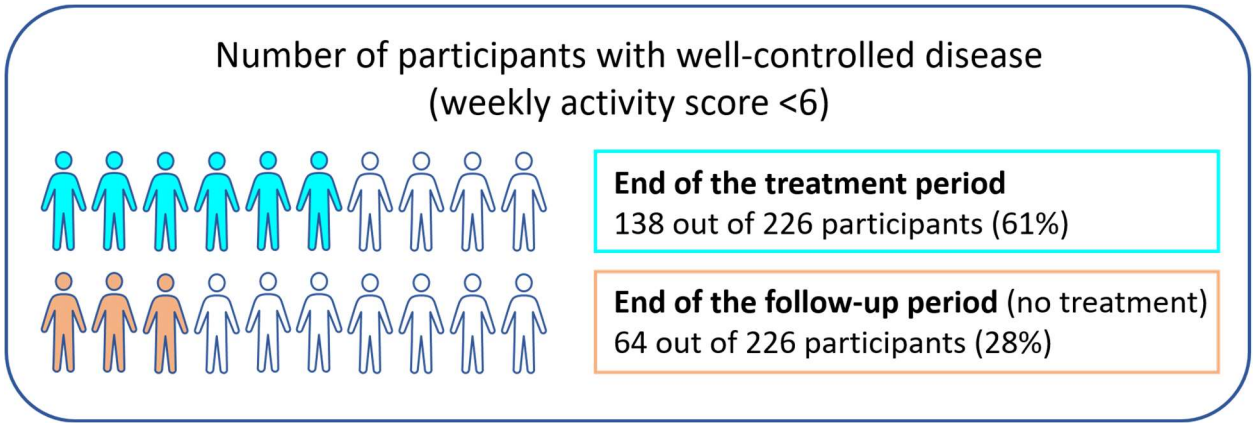
190 out of 226 (84%) participants had at least one adverse event that happened from the first injection up until 16 weeks after the last injection of trial drug.

The most common adverse events are presented in the “What adverse events did the participants have during the trial?” section on page 9 of this summary.



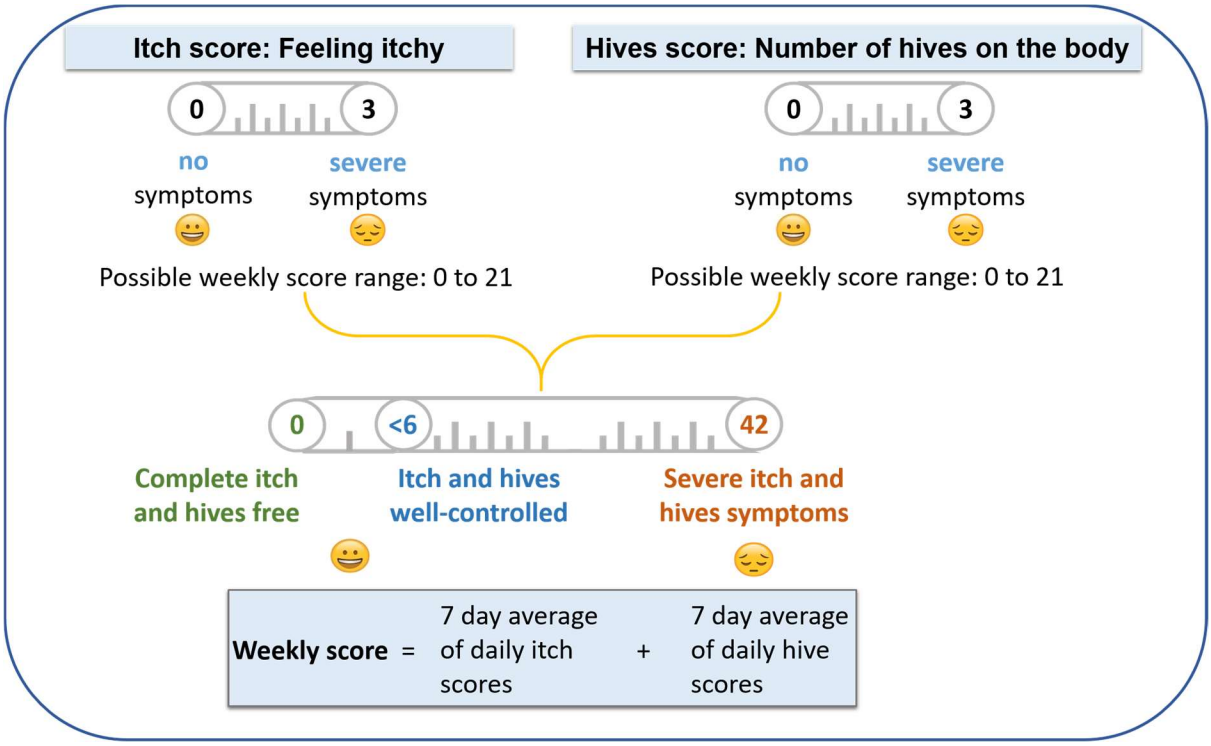
What were the other results of this trial?

How many participants had well-controlled disease at the end of the treatment period and the follow-up period?



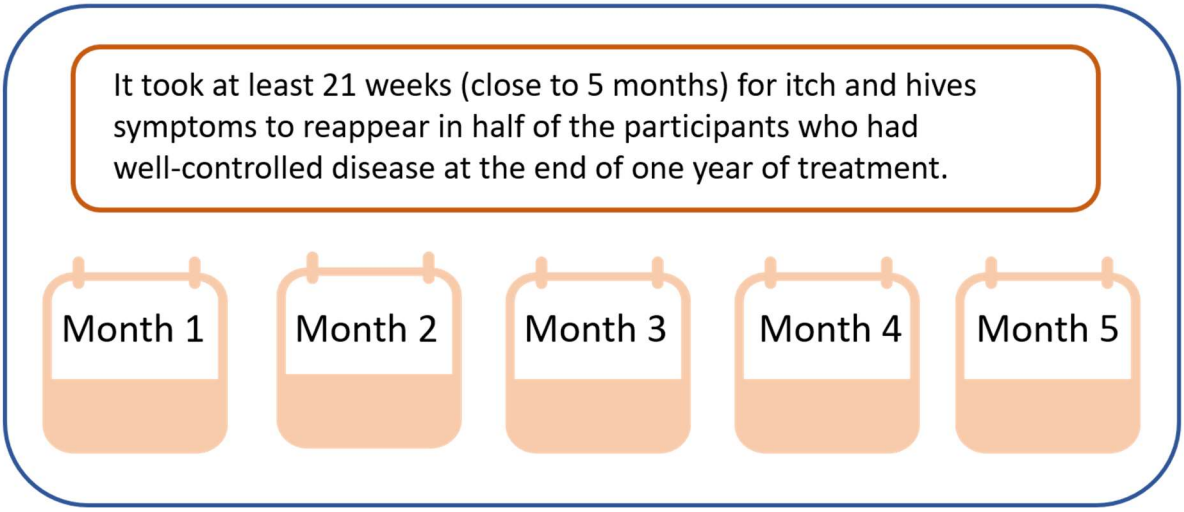
How were these results measured?

Researchers monitored their weekly activity score as shown in the next figure. An overall score of <6 meant that the participant's itch and hives was well-controlled.



For the participants with well-controlled disease at the end of one year of treatment, how long did it take until their itch and hive symptoms reappeared?

During the follow-up period in which participants did not receive ligelizumab (QGE031), the itch and hive symptoms of the participants gradually increased.



What adverse events did the participants have during the trial?

How many participants had adverse events?

Not all participants in this trial had adverse events. In this trial, adverse events were reported separately, according to the period of time in which they started. All adverse event information in this summary is presented as:

- Adverse events which started anytime from 1st dose till 16 weeks from the last injection,
- Adverse events which started after 16 weeks from the last injection.

Number of Participants (%) With Adverse Events

	AEs within 16 weeks from last injection	AEs after 16 weeks from last injection
	(Out of 226 participants)	(Out of 226 participants)
At least 1 adverse event	190 (84%)	103 (46%)
At least 1 serious adverse event	15 (7%)	6 (3%)
Stopped drug due to adverse events	6 (3%)	Not applicable

One participant (<1%) died due to cancer of pancreas (pancreatic neoplasm). This adverse event happened within 16 weeks from the last injection.

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 5 out of 100 participants (5%) are listed in the table below:

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

	AEs within 16 weeks from last injection (Out of 226 participants)	AEs after 16 weeks from last injection (Out of 226 participants)
Nose and throat infection (Nasopharyngitis)	57 (25%)	10 (4%)
Headache (Headache)	29 (13%)	2 (<1%)
Hives (Urticaria)	23 (10%)	18 (8%)
Common cold (Upper respiratory tract infection)	23 (10%)	3 (1%)
Back pain (Back pain)	16 (7%)	2 (<1%)
Runny, stuffy nose and facial pain (Sinusitis)	13 (6%)	2 (<1%)
Pain and swelling due to injection (Injection site erythema)	13 (6%)	0
Urinary tract infection (Urinary tract infection)	12 (5%)	3 (1%)
Increase of a blood protein called creatinine (Blood creatinine increased)	12 (5%)	1 (<1%)
Pains in the joints (Arthralgia)	12 (5%)	1 (<1%)

What were the serious adverse events?

The serious adverse events that happened in the trial are shown in the table below:

Number of Participants (%) With Serious Adverse Events

	AEs within 16 weeks from last injection (Out of 226 participants)	AEs after 16 weeks from last injection (Out of 226 participants)
A problem in the brain due to harmful chemicals	0	1 (<1%)

Number of Participants (%) With Serious Adverse Events

	AEs within 16 weeks from last injection (Out of 226 participants)	AEs after 16 weeks from last injection (Out of 226 participants)
(Toxic encephalopathy)		
A problem in the brain due to failure of other internal organs (Metabolic encephalopathy)	0	1 (<1%)
Abnormal fast heartbeat (Supraventricular tachycardia)	1 (<1%)	0
Allergic reaction (Hypersensitivity)	1 (<1%)	0
Appendicitis (Complicated appendicitis)	1 (<1%)	0
Cancer of the pancreas (Pancreatic neoplasm)	1 (<1%)	0
Cancer that started in lower part of the uterus (Cervix carcinoma stage 0)	1 (<1%)	0
Change in the mental status (Mental status changes)	0	1 (<1%)
Chest pain, not caused by heart attack (Non-cardiac chest pain)	1 (<1%)	0
Chest pain (Angina pectoris)	1 (<1%)	0
Cyst in the mouth (Mouth cyst)	1 (<1%)	0
Fainting (Syncope)	0	1 (<1%)
Feeling of dizziness and faintness (Presyncope)	1 (<1%)	0
Foot disorder (Foot deformity)	0	1 (<1%)
Headache (Headache)	1 (<1%)	0
Heart attack (Myocardial infarction)	0	1 (<1%)
High blood pressure (Hypertension)	1 (<1%)	0

Number of Participants (%) With Serious Adverse Events

	AEs within 16 weeks from last injection (Out of 226 participants)	AEs after 16 weeks from last injection (Out of 226 participants)
Hives (Urticaria)	1 (<1%)	0
Increased blood pressure (Blood pressure increased)	1 (<1%)	0
Injuries to the soft tissues that connect joints (Ligament rupture)	0	1 (<1%)
Infection in a specific part of the body (Localized infection)	1 (<1%)	0
Inflammation in the large intestine (Colitis)	0	1 (<1%)
Injury to the kidney (Acute kidney injury)	1 (<1%)	0
Kidney stones (Nephrolithiasis)	1 (<1%)	0
Loss of fluids in the body (Dehydration)	1 (<1%)	0
Low blood pressure (Hypotension)	1 (<1%)	0
Low levels of calcium in the blood (Hypocalcaemia)	1 (<1%)	0
Lung infection (Pneumonia)	0	1 (<1%)
Miscarriage (Abortion Spontaneous)	1 (<1%)	0
Sensation of spinning (Vertigo)	1 (<1%)	0
Skin cancer (Basal cell carcinoma)	0	1 (<1%)
Swelling in the gall bladder (Cholecystitis)	1 (<1%)	0
Swelling in the gall bladder that continues over time (Cholecystitis chronic)	1 (<1%)	0

Number of Participants (%) With Serious Adverse Events

	AEs within 16 weeks from last injection (Out of 226 participants)	AEs after 16 weeks from last injection (Out of 226 participants)
Swelling of the stomach lining (Gastritis)	1 (<1%)	0
Swollen veins in the lower part of rectum and anus (Haemorrhoids)	1 (<1%)	0
Tearing of the tissues that attach muscles to the bones (Tendon rupture)	1 (<1%)	0
Urinary tract infection (Urinary tract infection)	0	1 (<1%)
Viral infection (Viral infection)	0	1 (<1%)

How many participants stopped trial drug due to adverse events?

During the trial, 6 out of 226 (3%) participants stopped the trial drug early due to enlarged spleen (splenomegaly), cancer of the pancreas (pancreatic neoplasm), reaction at the injection site (injection site reaction), allergic reaction (hypersensitivity), CSU, and swelling of the tissue lining the sinuses which is a part of the nasal cavity (sinusitis).

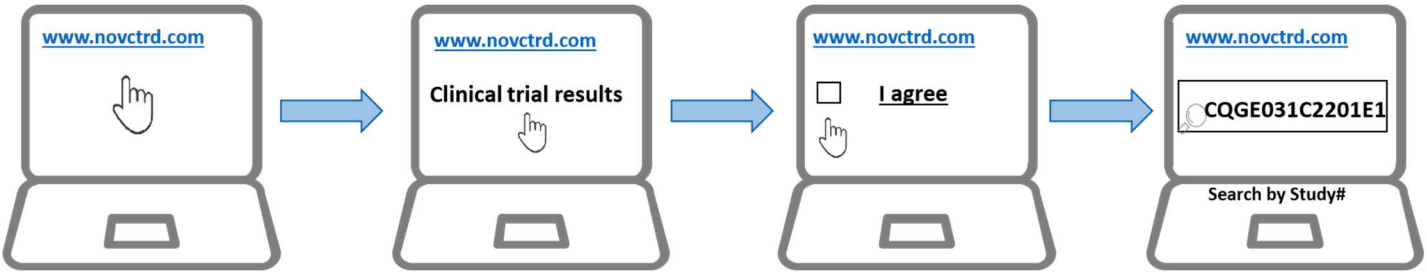
How was this trial useful?

This trial helped researchers learn about the long-term safety of ligelizumab (QGE031) when used along with regular itch and hives medicine in participants with CSU. Results from this and other ligelizumab (QGE031) trials will be used to seek approval for the treatment of CSU.

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

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).



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

- www.clinicaltrials.gov Use the NCT identifier NCT02649218 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search/search Use the EudraCT identifier 2015-003636-13 in the search field.

Full clinical trial title: An open label, multicenter, extension study to evaluate the long-term safety of QGE031 240 mg s.c. given every 4 weeks for 52 weeks in Chronic Spontaneous Urticaria patients who completed study CQGE031C2201

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of participants 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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