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Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of different strengths of QGE031, compared with omalizumab or placebo, in participants with chronic spontaneous urticaria

Protocol number: CQGE031C2201

Thank You!

Novartis, the sponsor of this clinical trial, would like to thank you for taking part in this trial for the drug QGE031, also known as ligelizumab. You helped researchers learn more about how QGE031 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.

Important note: This summary only shows the results of a single clinical trial. Other clinical trials may have different findings. Researchers and health authorities 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 was designed so that an individual participant could take part for close to 11 months. The trial started in July 2015 and ended in June 2017. The entire duration, from enrolling the first participant to the last participant completing the trial, was close to 2 years.

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

Why was the research needed?

Researchers were looking for a better way to treat chronic spontaneous urticaria, also known as CSU. People affected with CSU develop hives and itch that appear suddenly without an obvious cause. Hives are swollen, itchy, pale red bumps on the skin. For the hives to be classified as chronic, they need to last longer than 6 weeks and appear without any warning in an unpredictable way. CSU is a type of allergic disease in which the body's immune system becomes active and produces itchy hives, even when there is no known cause or trigger. A type of antibody called immunoglobulin E, also known as IgE, is thought to play a major part in the condition of CSU.

Trial drugs

The drugs given in this trial were:

- QGE031, also known as ligelizumab, blocks the effect of the IgE antibody. QGE031 is not yet available to the public, so it can only be used in a research trial such as this one. Three different strengths of QGE031 were studied in this trial.
- Omalizumab stops IgE from working in a similar way to QGE031. It is available to the public to treat CSU.
- Placebo, which looks like the trial drug, does not have any medicine in it. It helps researchers better understand the effect of a trial drug.

Throughout the trial, the participants were allowed to continue taking the CSU medicines that they were already taking. They were also given extra doses of anti-histamine medicine when needed to manage episodes of increased hives and itch. This medicine was known as “rescue” medicine.

Trial purpose

This trial was done to learn more about the effects and safety of QGE031. The main questions the researchers wanted to answer in this trial were:

- How many participants had complete relief from hives at week 12 (close to 3 months after the first dose)? The researchers collected this information for 3 different strengths of QGE031, one strength of omalizumab, and placebo.
- What medical problems did the participants have during this trial?

Who was in this trial?

The participants could take part in this trial if:

- they were between 18 and 75 years of age,
- they had CSU for longer than 6 months,
- their CSU was difficult to manage with the medicines they were already taking, and
- they did not have any major disease(s) that made them unsuitable for participation in the trial.

A total of 382 participants from 10 countries participated in this trial. The participants were enrolled in trial sites in Australia, Canada, Germany, Greece, Japan, Russia, Spain, Taiwan, the United Kingdom, and the United States of America.

The average age of participants was 43 years. Participants' age ranged from 18 to 74 years. The majority of participants were female (286 out of 382; which is 75% of the trial participants).

What kind of trial was this?

This trial is called a double-blind trial. This means that 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 patient is getting can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness towards all treatments.

What happened during this trial?

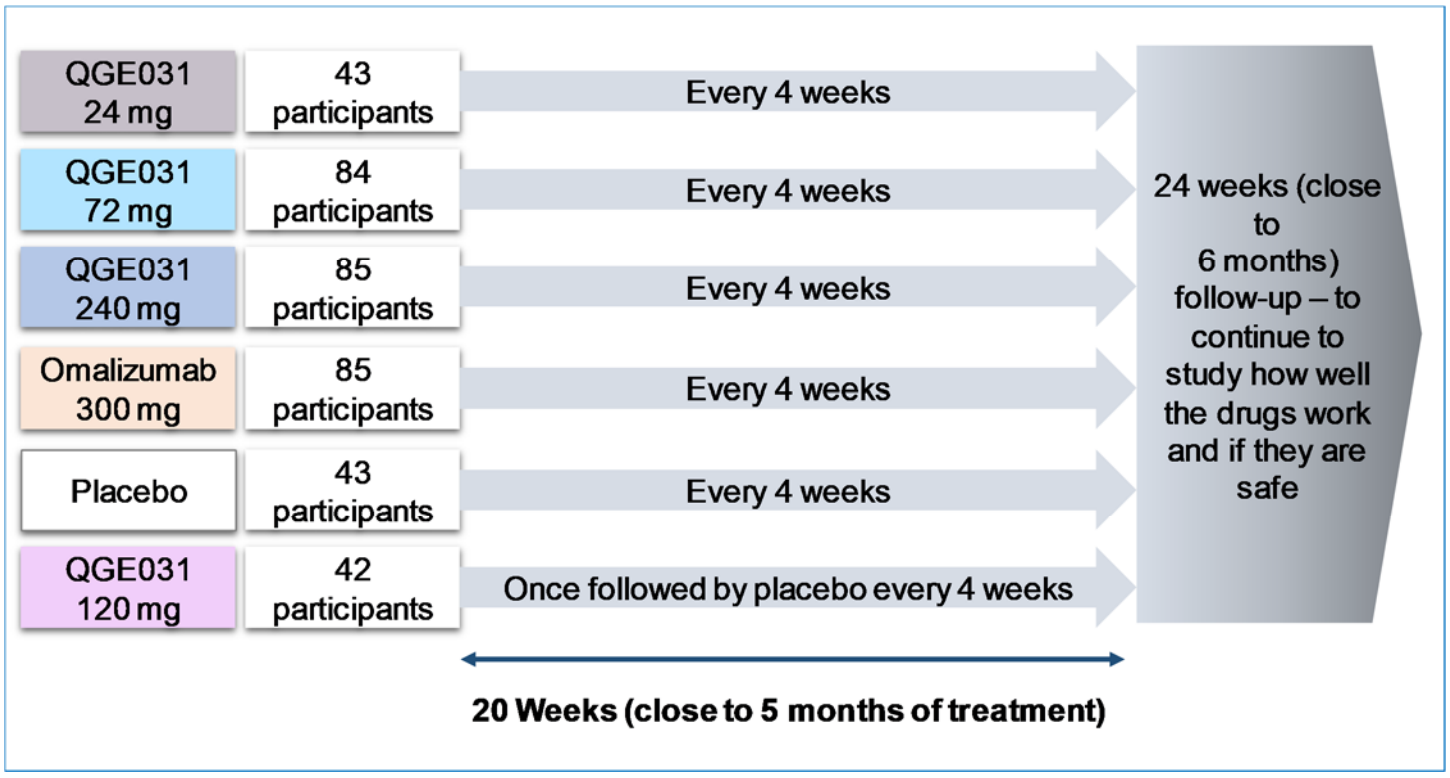
At the start of the trial, the researchers randomly assigned the participants to receive:

- 24 milligram (mg) of QGE031,
- 72 mg of QGE031,
- 240 mg of QGE031,
- 300 mg of omalizumab, or
- placebo,

which were given once every 4 weeks

or

- 120 mg of QGE031 given once and then placebo given once every 4 weeks. The researchers studied this particular treatment to see how long QGE031 was in the body and how long its effect lasted.



During the treatment period of 20 weeks (close to 5 months), participants received a total of 10 injections over 5 visits. At each visit, all participants were given 2 injections under the skin – in either the arm, the thigh, or the lower part of the stomach. Each visit was 4 weeks apart.

After completing the treatment, the participants visited the trial site 6 times. At each visit, the researchers observed the participants' general health and looked to see if their hives or itch reappeared. Each visit was scheduled 4 weeks apart. All participants (including those who received omalizumab or placebo) were given the option to enter another trial on QGE031 three months after completing the treatment. In this other trial, all participants received treatment with QGE031.

The researchers asked the participants to record their CSU symptoms twice a day in an electronic diary. They also tracked participants' health throughout the trial.

What were the key results of this trial?

This is a summary of the average results for all participants for different treatment groups. 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 complete relief from hives at week 12?

The researchers asked participants to record the number of hives they had twice a day.

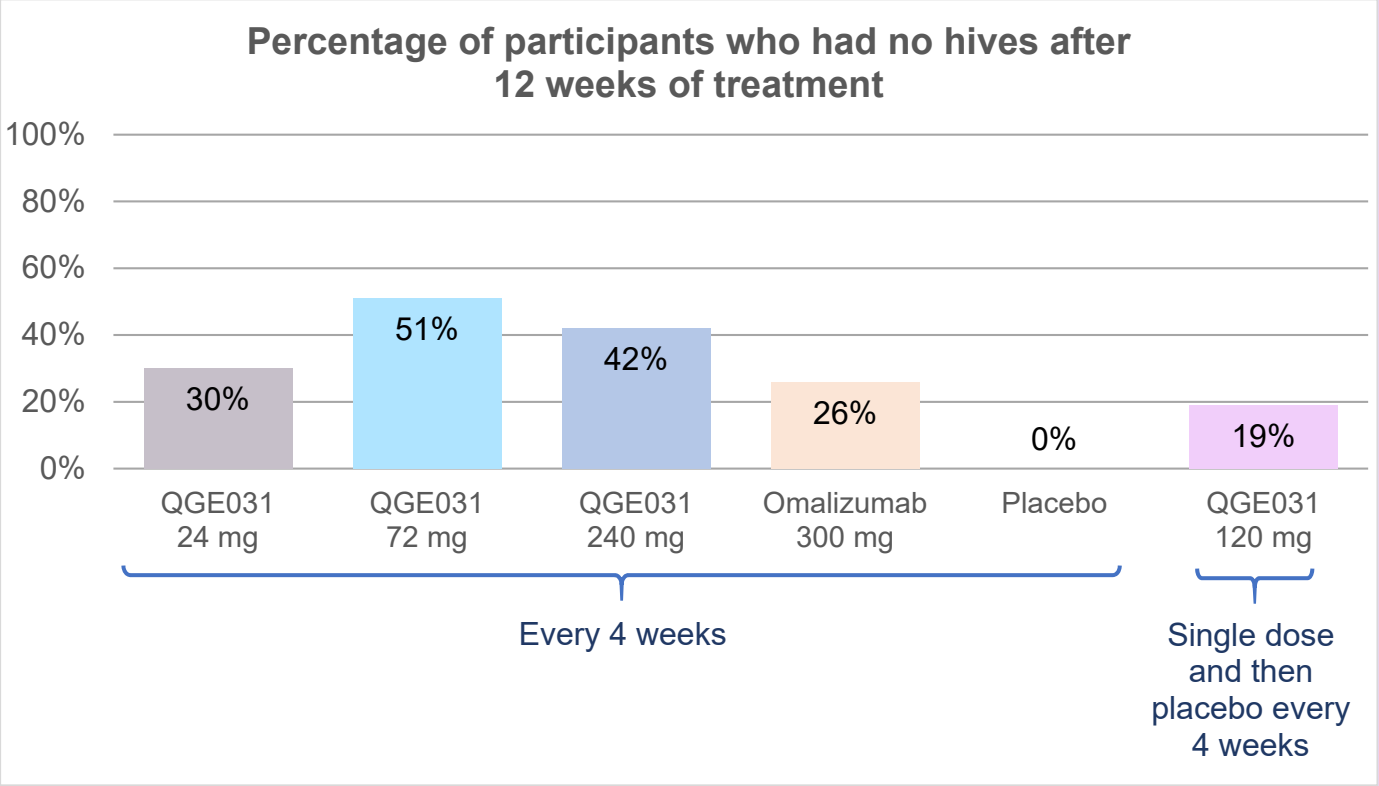
The researchers found that QGE031 helped to control hives in participants with CSU. Participants who were given QGE031 every 4 weeks were more likely to have no hives compared to:

- participants who were given omalizumab,
- participants who were given QGE031 only once in the trial, or
- participants who were given placebo.

The researchers found that the results for participants who were given 240 mg of QGE031 and 72 mg of QGE031 were similar.

Similarly, the researchers found that QGE031 helped in controlling itch.

The percentage of participants who had no hives at week 12 (close to 3 months after the first dose) in each treatment group is shown in the diagram below.



What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called “adverse events”. An adverse event is an unwanted sign or symptom 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.

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. So, 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 the adverse events that happened in this trial.

How many participants had adverse events?

Not all participants in this trial had adverse events. 295 out of 382 participants (77%) had 1 or more adverse events. During the trial, 8 out of 382 participants (2%) stopped the drug early because of adverse events. Serious adverse events happened in 18 out of 382 participants (5%) in the trial. No participant died during this trial.

Adverse Events in this Trial						
	QGE031			Omalizumab 300 mg	Placebo	QGE031 120 mg Single dose, then placebo every 4 weeks
	24 mg	**72 mg**	**240 mg**	Every 4 weeks		
Total number of participants	43	84	85	85	43	42
Any adverse event	36 (84%)	63 (75%)	63 (74%)	62 (73%)	34 (79%)	37 (88%)
Serious adverse event	3 (7%)	2 (2%)	2 (2%)	3 (4%)	4 (9%)	4 (10%)
Stopped drug early due to an adverse event	0 (0%)	1 (1%)	1 (1%)	2 (2%)	2 (5%)	2 (5%)

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%) in 1 or more groups are listed below:

Most Common Non-Serious Adverse Events in this Trial						
	QGE031			**Omalizumab 300 mg**	**Placebo**	**QGE031 120 mg single dose, then placebo every 4 weeks**
	24 mg	**72 mg**	**240 mg**	**Every 4 weeks**		
Total number of participants	43	84	85	85	43	42
Diarrhea	2 (5%)	4 (5%)	5 (6%)	6 (7%)	2 (5%)	2 (5%)

Most Common Non-Serious Adverse Events in this Trial						
	QGE031			Omalizumab 300 mg	Placebo	QGE031 120 mg single dose, then placebo every 4 weeks
	24 mg	72 mg	240 mg			
	Every 4 weeks					
Stomach infection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (7%)
Nausea	1 (2%)	1 (1%)	2 (2%)	5 (6%)	2 (5%)	1 (2%)
Redness at the injection site	0 (0%)	2 (2%)	5 (6%)	0 (0%)	0 (0%)	1 (2%)
Injection site reaction	0 (0%)	3 (4%)	6 (7%)	0 (0%)	1 (2%)	0 (0%)
Swelling in the throat	1 (2%)	1 (1%)	0 (0%)	5 (6%)	1 (2%)	0 (0%)
Flu	1 (2%)	4 (5%)	4 (5%)	5 (6%)	1 (2%)	1 (2%)
Infection of the nose and throat	7 (16%)	7 (8%)	10 (12%)	10 (12%)	6 (14%)	9 (21%)
Urinary tract infection (UTI)	0 (0%)	5 (6%)	4 (5%)	5 (6%)	0 (0%)	2 (5%)
Viral infection of the nose and throat	7 (16%)	13 (15%)	17 (20%)	17 (20%)	13 (30%)	10 (24%)
Decreased kidney function	1 (2%)	3 (4%)	3 (4%)	2 (2%)	4 (9%)	1 (2%)
Joint pain	1 (2%)	6 (7%)	1 (1%)	2 (2%)	1 (2%)	1 (2%)
Back pain	0 (0%)	1 (1%)	0 (0%)	1 (1%)	1 (2%)	3 (7%)

Most Common Non-Serious Adverse Events in this Trial						
	QGE031			Omalizumab 300 mg	Placebo	QGE031 120 mg single dose, then placebo every 4 weeks
	24 mg	72 mg	240 mg			
	Every 4 weeks					
Dizziness	2 (5%)	5 (6%)	2 (2%)	2 (2%)	4 (9%)	0 (0%)
Headache	7 (16%)	9 (11%)	7 (8%)	12 (14%)	7 (16%)	1 (2%)
Itchy, red patches on skin	1 (2%)	5 (6%)	4 (5%)	2 (2%)	1 (2%)	3 (7%)
Hives	1 (2%)	9 (11%)	3 (4%)	4 (5%)	5 (12%)	7 (17%)
High blood pressure	1 (2%)	5 (6%)	2 (2%)	2 (2%)	3 (7%)	3 (7%)

What were the most common serious adverse events?

The table below shows the most common serious adverse events that happened in at least 2% of participants in 1 or more groups. All serious adverse events were reported by no more than 1 participant per group and there was no particular pattern to the serious adverse events reported.

For a full list of the serious adverse events that occurred in this trial, please visit the websites listed at the end of this summary.

Most Common Serious Adverse Events in this Trial						
	QGE031			Omalizumab 300 mg	Placebo	QGE031 120 mg single dose, then placebo every 4 weeks
	24 mg	72 mg	240 mg			
	Every 4 weeks					
Total number of participants	43	84	85	85	43	42
Chest pain	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)
Swelling of the stomach	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)

Most Common Serious Adverse Events in this Trial						
	QGE031			Omalizumab 300 mg	Placebo	QGE031 120 mg single dose, then placebo every 4 weeks
	24 mg	72 mg	240 mg			
	Every 4 weeks					
Stomach pain	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)
Tear in the colon wall (large bowel)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Soft tissue bulging through the groin muscles	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)
Gallstones	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)
Liver cyst	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)
Liver infection	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0% (0)
Pneumonia (lung infection)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)
Swelling in the lower large bowel	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Bulging of spinal disc	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)
Degeneration of salivary and tear glands	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Non-cancerous lung tumor	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)
Breast cancer	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)
Non-cancerous	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)

Most Common Serious Adverse Events in this Trial						
	QGE031			Omalizumab 300 mg	Placebo	QGE031 120 mg single dose, then placebo every 4 weeks
	24 mg	72 mg	240 mg			
	Every 4 weeks					
tumor of the blood vessels in liver						
Thyroid cancer	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)
Deep swelling of the area beneath skin	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hives	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

How was this trial useful?

This trial helped researchers learn how well QGE031 works, if it is safe to use in people with CSU, and which dose of QGE031 is appropriate to test further. Results from this trial may be used in other clinical trials for people with CSU.

Please remember, this summary only shows the results of a single clinical trial. Other clinical trials may have different results. Researchers and health authorities 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.

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). Once on the site, click “Clinical trial results” at the bottom of the page. After agreeing to enter the Novartis website, type CQGE031C2201 into the keyword search box and click “Search”.

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

- www.clinicaltrials.gov. Use the NCT identifier NCT02477332 in the search field.
- www.clinicaltrialsregister.eu. Use the EudraCT identifier 2014-005559-16 in the search field.

Full clinical trial title: A multicenter, randomized, double-blind, placebo and active controlled phase 2b dose-finding study of QGE031 as add-on therapy to investigate the efficacy and safety in patients with chronic spontaneous urticaria (CSU)

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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