NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects and safety of ligelizumab (QGE031) in participants with chronic spontaneous urticaria (CSU)

Protocol number: CQGE031C2202

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. Novartis would like to thank all the adolescents and their parents/guardians for taking part in this trial for the drug ligelizumab, also known as QGE031. You helped researchers learn about the effects and safety of ligelizumab in people with chronic spontaneous urticaria, also known as CSU.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings. 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. Websites listed at the end of the summary may have more information about this trial. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

Why was the research needed?

Urticaria, commonly known as itch and hives, are swollen, itchy, pale red bumps on the skin. These bumps are often caused by an allergic reaction to food, insect stings or drugs. 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 (CSU). CSU can develop suddenly without an obvious cause. Normally, the immune system makes and uses antibodies (blood protein) 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 it is not active anymore. This way ligelizumab blocks the effect of IgE.

In this trial, researchers wanted to learn about the effects and safety of ligelizumab in adolescents from 12 to less than 18 years of age, including those adolescents who turn 18 during the study, with CSU.

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

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Did the participants show improvements in the signs and symptoms of their itch and hives after 24 weeks of treatment as compared to the start of the trial?

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

- How many participants' itch and hives completely disappeared after treatment?
- Did participant's quality of life improve after treatment?

Trial drugs

The drugs given in this trial were:

Ligelizumab (QGE031) is being tested for the treatment of CSU at a dose of 24 milligrams (mg) and 120 mg injection under the skin. Ligelizumab is not yet available to the public, so it can only be used in a research trial such as this one.

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.

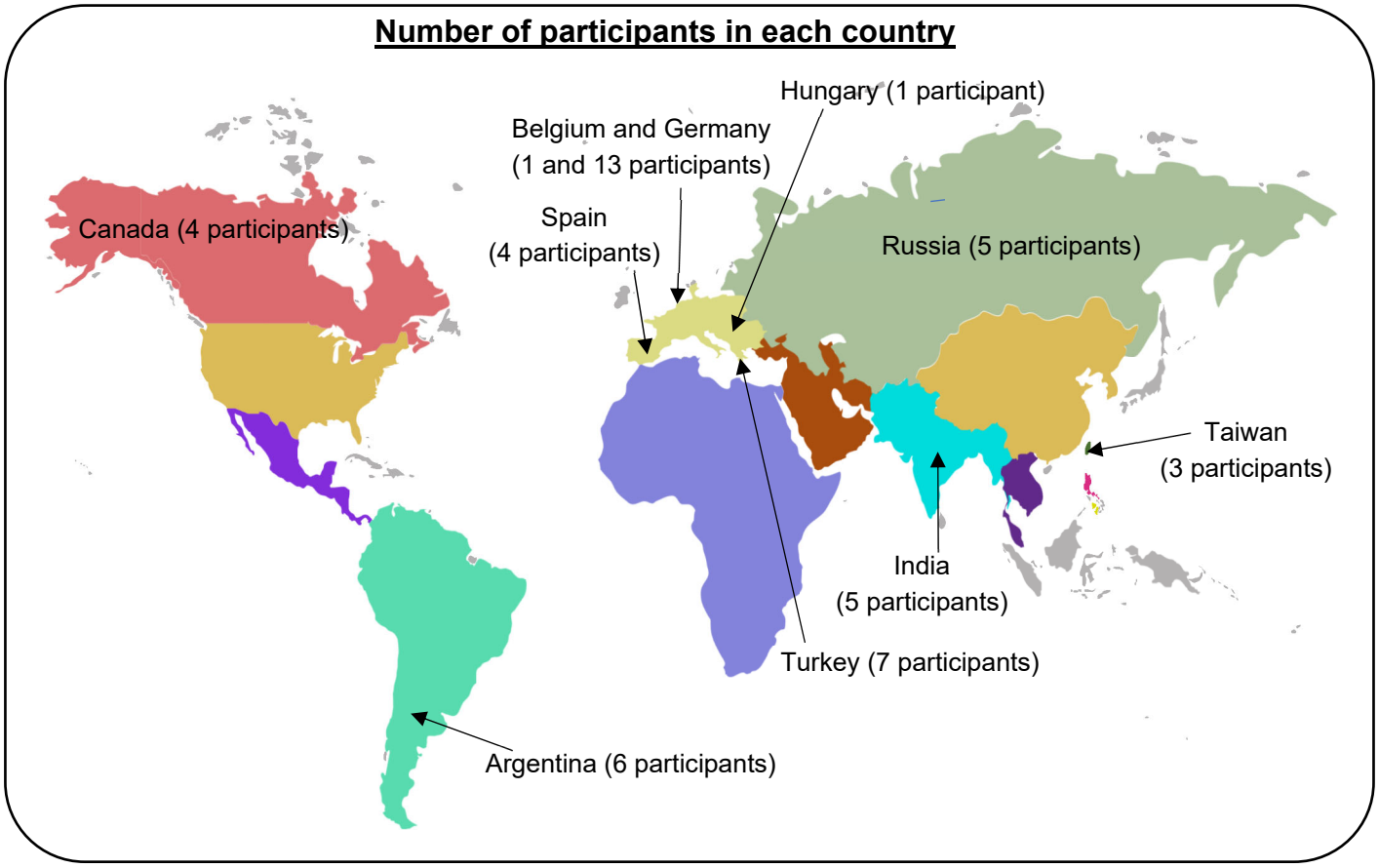
Throughout the trial, the participants continued to take their regular CSU medicine called antihistamines. Participants were also given extra doses of antihistamines to manage episodes of CSU, if needed. This medicine is known as “rescue” medicine.

Who was in this trial?

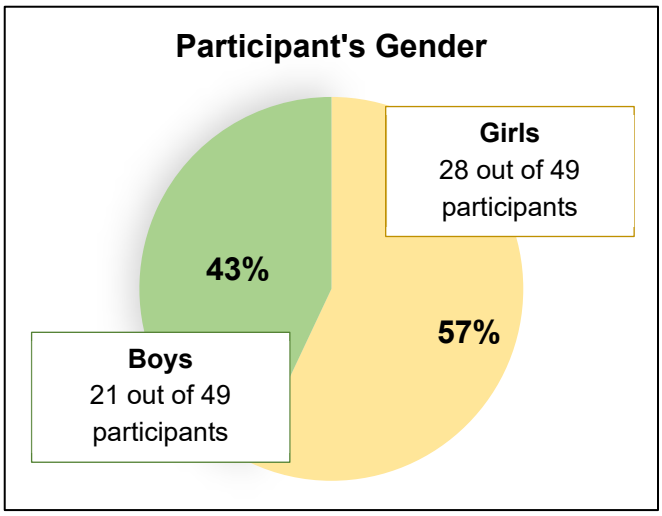
The participants could take part in this trial if they:

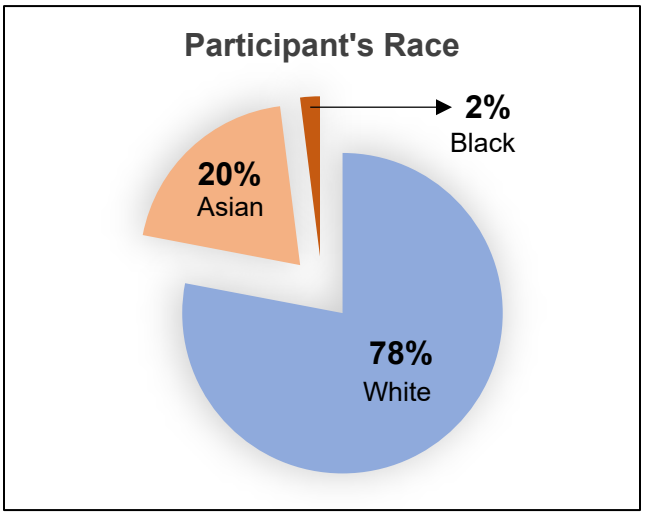
- were between 12 to 18 years of age,
- had CSU longer than 6 months,
- had CSU which could not be managed with available treatment options,
- did not have any other skin disease.

A total of 49 participants from 20 sites across 10 countries participated in this trial.



The average age of participants was 15 years. Participants' age ranged from 12 to 17 years. Majority of the participants were girls, 28 out of 49 (57%).





How was this trial done?

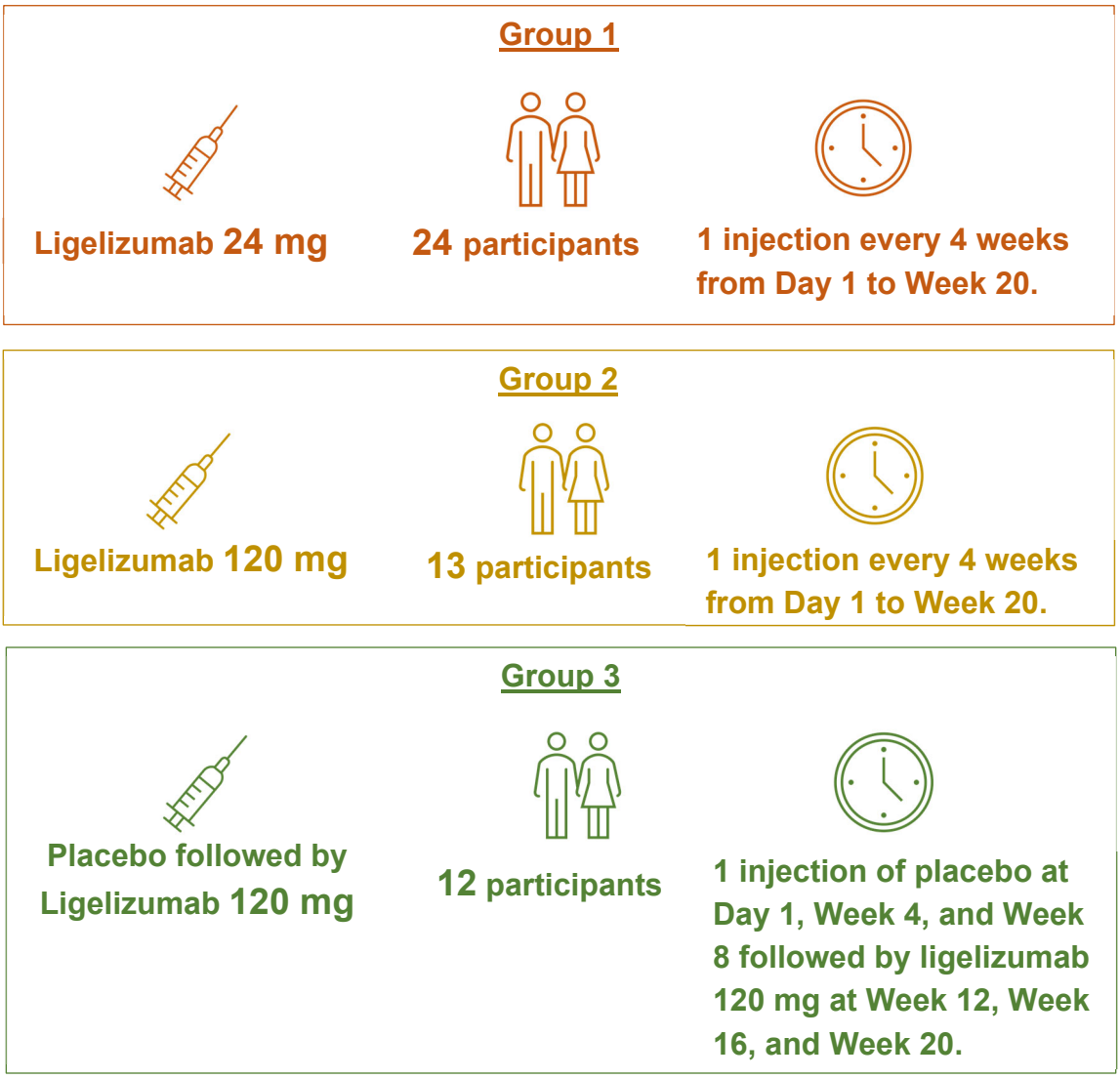
Before Treatment

At the start of the trial, the trial doctors checked if participants could take part in the trial.

During Treatment

None of the participants, trial doctors, or trial staff knew what treatment participants were receiving.

Eligible participants were randomly assigned to the following 3 groups:



After Treatment

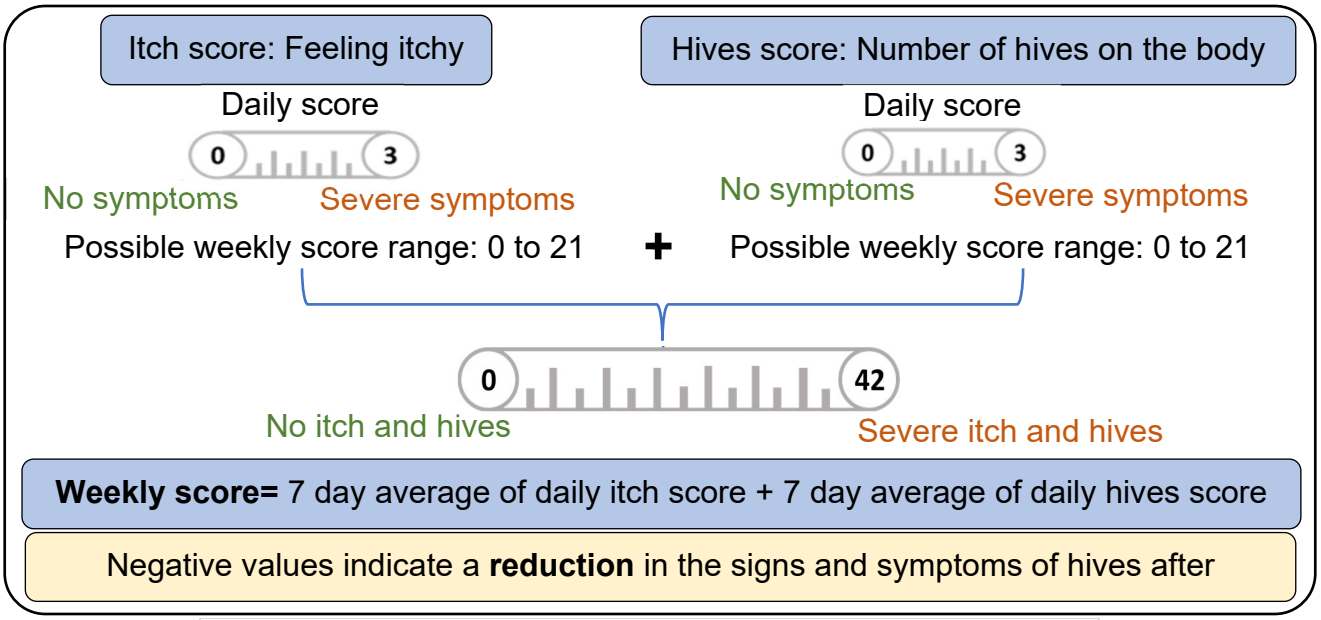
No trial drugs were given to the participants during this period. The after treatment period lasted for 16 weeks. However, participants continued to take their regular CSU medicines. During this period it was monitored if participants CSU came back.

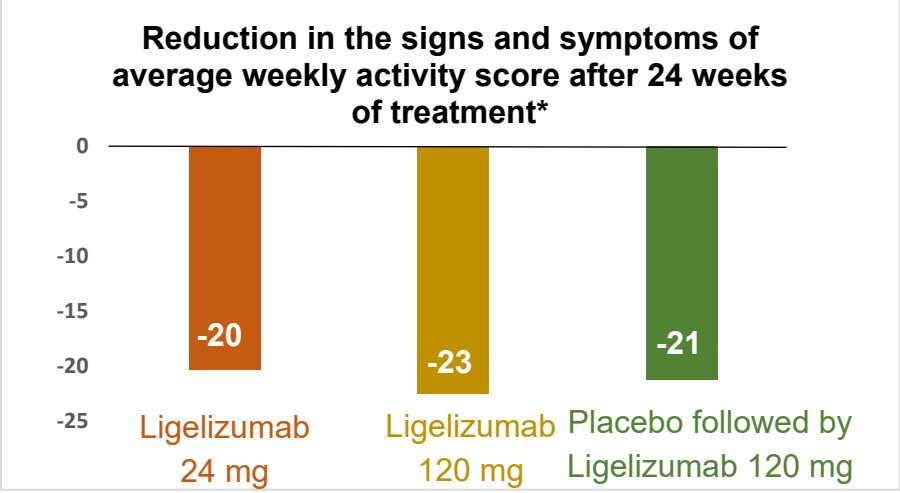
Researchers closely monitored the overall health of the participants throughout the trial. Researchers completed this trial as planned.

What were the key results of this trial?

Did the participants show improvements in the signs and symptoms of their hives after 24 weeks of treatment as compared to the start of the trial?

At the start of the trial, researchers gave participants a handheld e-Diary which contained questions about itch and hives. Participants recorded their itch and hives scores twice a day in their e-Diaries on a scale of 0 (none) to 3 (severe). Researchers monitored their weekly activity score as shown in the figure below.



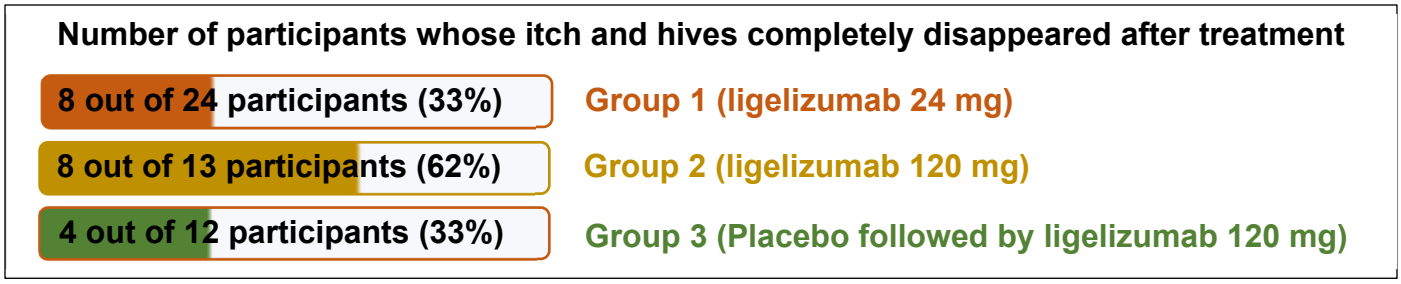


*Negative values indicate a reduction in the signs and symptoms of itch and hives

Improvement in the signs and symptoms of CSU was observed in all the 3 groups.

What were the other results of this trial?

How many participants' itch and hives completely disappeared after treatment?



Participants who switched from placebo to ligelizumab 120 mg after Week 12, also showed similar results as **Group 2 (ligelizumab 120 mg)**. Researchers noted that the participants' itch and hives slowly came back after the trial treatment was stopped during the 'After Treatment' period.

Did the participants' quality of life improve after treatment?

Participants were asked to fill a questionnaire called the Children's Dermatology Life Quality Index (CDLQI) to know the impact of skin disease on quality of life (QoL) in adolescents.

Researchers noted that the quality of life improved in all 3 groups at Week 24.

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

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 summary may have more information about all the adverse events that happened in this trial.

How many participants had adverse events?

38 out of 49 (78%) participants had 1 or more adverse events. During the trial, 2 out of 49 (4%) participants stopped the drug early because of adverse events. Serious adverse events happened in 2 out of 49 (4%) participants in the trial.

Number of Participants (%) With Adverse Events

	Group 1 Ligelizumab 24 mg (24 participants)	Group 2 Ligelizumab 120 mg (13 participants)	Group 3 Placebo followed by ligelizumab 120 mg (12 participants)
At least 1 adverse event	18 (75%)	11 (85%)	9 (75%)
At least 1 serious adverse event	1 (4%)	0	1 (8%)
Stopped drug due to adverse event	1 (4%)	0	1 (8%)

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 10% (10 out of 100) of participants in any group are presented below.

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

Groups (Total number of participants)	Group 1 Ligelizumab 24 mg (24 participants)	Group 2 Ligelizumab 120 mg (13 participants)	Group 3 Placebo followed by ligelizumab 120 mg (12 participants)
Common cold (Upper respiratory tract infection)	3 (13%)	2 (15%)	0
Diarrhea (Diarrhoea)	2 (8%)	0	2 (17%)
Feeling sick to the stomach (Nausea)	1 (4%)	3 (23%)	1 (8%)
Fever (Pyrexia)	2 (8%)	2 (15%)	0
Flu (Influenza)	2 (8%)	1 (8%)	2 (17%)

Groups (Total number of participants)	Group 1 Ligelizumab 24 mg (24 participants)	Group 2 Ligelizumab 120 mg (13 participants)	Group 3 Placebo followed by ligelizumab 120 mg (12 participants)
Headache (Headache)	5 (21%)	1 (8%)	4 (33%)
Infection in the urinary system (Urinary tract infection)	1 (4%)	2 (15%)	1 (8%)
Nose and throat infection (Nasopharyngitis)	7 (29%)	4 (31%)	4 (33%)
Stomach pain (Abdominal pain)	3 (13%)	0	1 (8%)
Stuffy nose (Rhinitis)	0	2 (15%)	0
Vomiting (Vomiting)	1 (4%)	3 (23%)	0
Worsening of CSU (Chronic spontaneous urticaria)	5 (21%)	0	0

What were the serious adverse events?

Overall, 2 out of 49 participants (4%) had serious adverse event. One participant in **Group 1 (Ligelizumab 24 mg)** tried to commit suicide (suicide attempt) but continued with trial treatment and completed the trial. Another participant in **Group 3 (Placebo followed by ligelizumab 120 mg)** had 2 leaky heart valves (pulmonary valve incompetence and tricuspid valve incompetence) prior to entering the trial. These conditions worsened and required hospitalization and surgery.

How many participants stopped trial drug due to adverse events?

During the trial, 2 out of 49 (4%) participants stopped ligelizumab early due to adverse events. One participant in **Group 1 (Ligelizumab 24 mg)** had worsening of CSU and another participant in **Group 3 (Placebo followed by ligelizumab 120 mg)** had worsening of 2 leaky heart valves (pulmonary valve incompetence and tricuspid valve incompetence).

How was this trial useful?

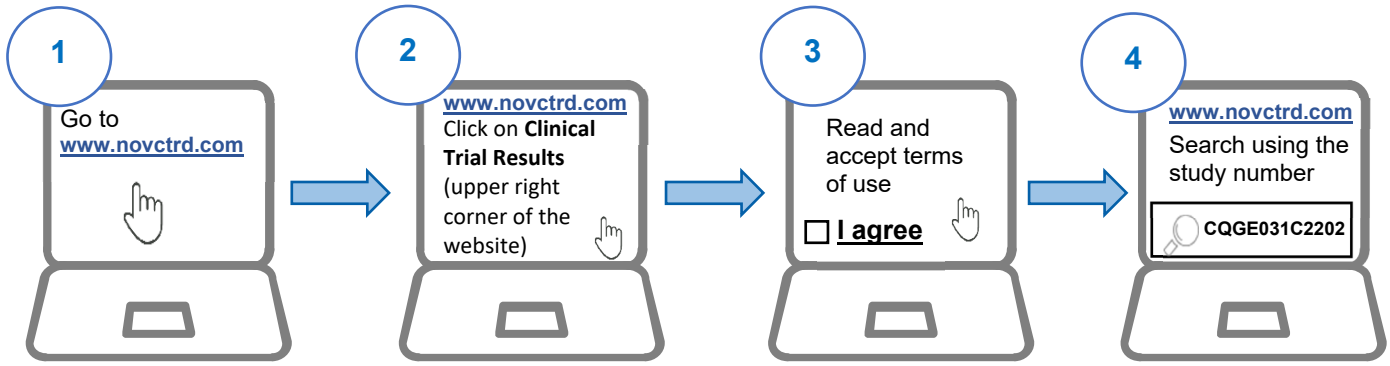
Researchers learned that ligelizumab worked in adolescents between the age of 12 and 18 years with CSU without any safety concerns. In addition, this trial helped researchers to select a suitable dose of ligelizumab for adolescents between the age of 12 and 18 years with CSU.

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).

Please follow the below steps:



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

- www.clinicaltrials.gov Use the NCT identifier NCT03437278 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search/search Use the EudraCT identifier 2017-004207-52 in the search field.
- **Full clinical trial title:** A multicenter, randomized, double-blind, placebo controlled phase 2b dose-finding study to investigate the efficacy and safety of ligelizumab (QGE031) in adolescent patients with Chronic Spontaneous Urticaria (CSU)

Trial Dates: The trial started in August 2018 and ended in February 2021.

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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