NOVARTIS

# Clinical Trial Results Summary

# A clinical trial to learn about the effects and safety of ligelizumab (QGE031) in people with Chronic Spontaneous Urticaria (CSU)

**Protocol number:** CQGE031C2302

## 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.

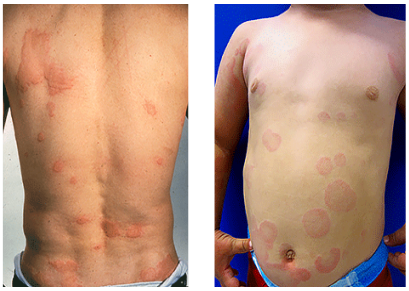
Thanks to the participants for taking part in this trial for the drug ligelizumab, also known as QGE031. They helped researchers learn more about how ligelizumab works in people with CSU.

**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).



*Source: American Academy of Dermatology Association*

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'). These bumps are often red and swollen and may merge together to cover a larger area. They 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 CSU.

CSU can develop suddenly without an obvious cause. 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 are antihistamines. These drugs block the release of histamines, which are responsible for allergies in our body.

Ligelizumab (**QGE031**) attaches itself to IgE so that it is not active anymore. This way, **QGE031** blocks the effect of IgE. Ligelizumab is also called **QGE031** because it is not yet approved for use.

**Omalizumab** (also known as Xolair®) stops IgE from working in a similar way to **QGE031**. **Omalizumab** is approved for use and is available for the treatment of severe allergic asthma, a lung disease associated with tightening of the air passages, and CSU. **Omalizumab** is the current recommended treatment for CSU when it cannot be controlled properly with antihistamines.

However, **omalizumab** is not effective at treating CSU in some patients. Therefore, there is still a need for alternative treatment options for those people with CSU that cannot be controlled with standard treatment or **omalizumab**.

| ***Drug*** | ***Pronounced as*** |
|---|---|
| *Ligelizumab* | li-gu-LIZ-oo-mab |
| *Omalizumab* | oh-ma-LIZ-oo-mab |

In this trial, researchers wanted to learn about the effects and safety of **QGE031** in **adults** and **adolescents** with moderate to severe CSU which could not be controlled with standard treatment

(antihistamines). Researchers also wanted to find out how effective **QGE031** is for treating CSU compared to **placebo** or **omalizumab.**

# How long was this trial?

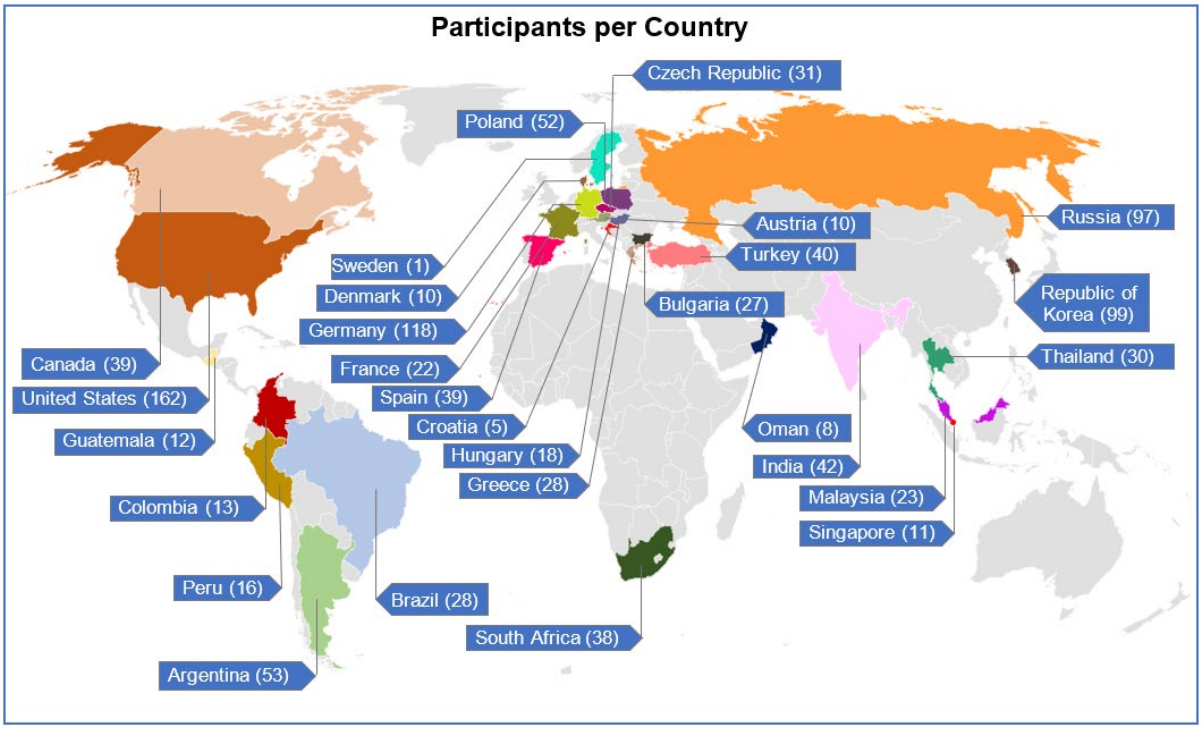
This trial started in October 2018 and ended in June 2022. The entire duration, from enrolling the first participant to the last participant completing the trial was around 3 years and 8 months. An individual participant was in this trial for an average of 1 year and 3 months.

# Who was in this trial?

The participants could take part in this trial if they:

- were at least 12 years of age,
- had CSU diagnosed at least for 6 months before the start of the trial,
- had CSU continuously for 6 weeks or more,
- had CSU which could not be controlled with standard treatment, and
- did not have any other skin disease.

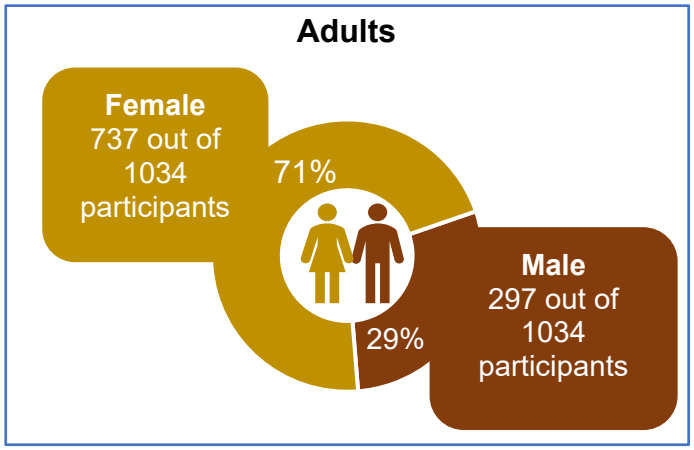
A total of 1072 participants from 28 countries were randomly assigned to treatment groups using a computer system. This process is called randomization. It means that each participant could be assigned to any group, and it helps to make sure the groups are distributed fairly.

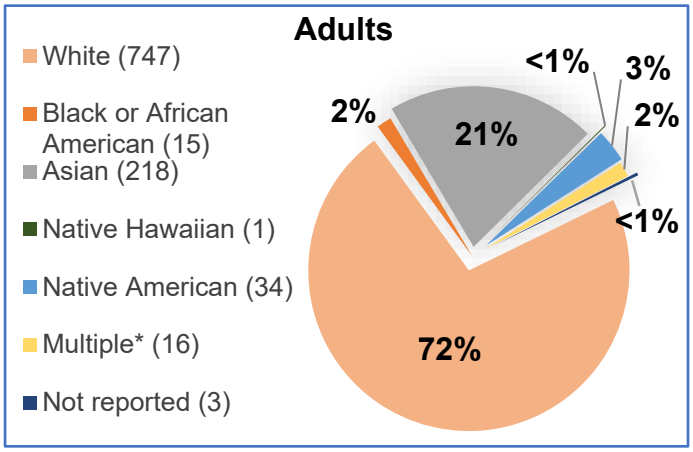


## ADULTS

1034 participants from 18 to 80 years of age participated in this trial. The average age of **adult** participants was 43 years. The majority of the **adult** participants were female (71%) and white (72%).

**Adult participants by gender and race**



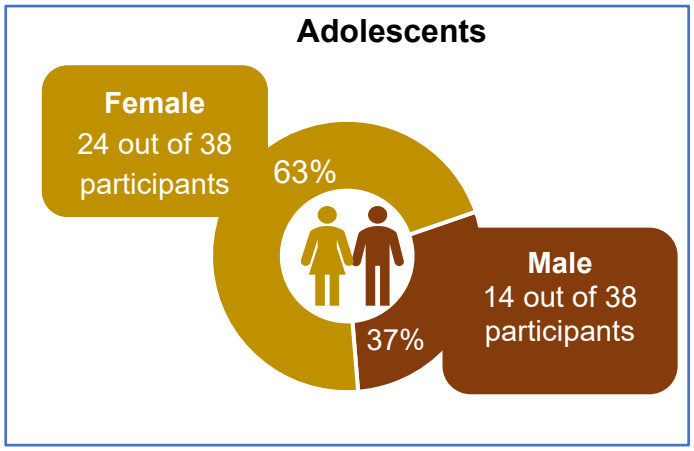



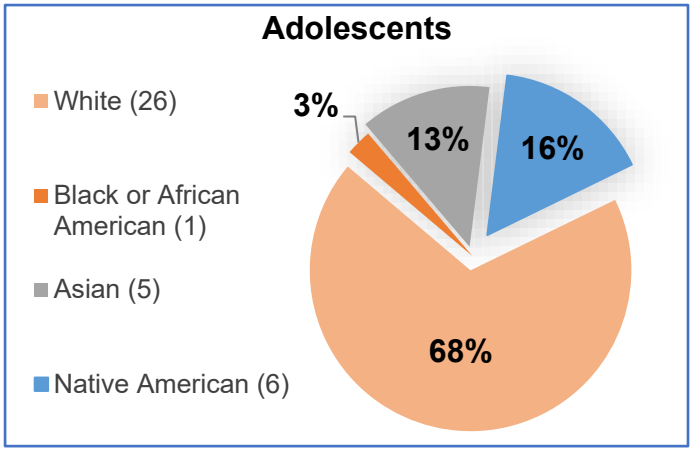

*Multiple is when a participant chooses more than one race.

## ADOLESCENTS

38 participants from 12 to 17 years of age participated in this trial. The average age of **adolescent** participants was 15 years. The majority of the **adolescent** participants were female (63%) and white (68%).

**Adolescent participants by gender and race**



# What treatments did the participants take?

Participants received either **QGE031** with **placebo**, or **omalizumab** alone

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

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

**Omalizumab** is an active **comparator** approved for the treatment of CSU. A comparator drug is an already approved and licensed drug available in the market for a disease condition. As there are many similar drugs for a disease condition, one of them will be chosen to be used as a comparator drug for a clinical trial.

It was given at a dose of 300 mg 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.

Participants also took anti-allergic drugs and steroid as rescue medications to relieve their CSU symptoms.

In this trial, 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. Doing a trial this way helps to make sure that the results are looked at with fairness towards all treatments.

Researchers randomly assigned participants to treatment groups using a computer system.

# What happened during this trial?

### Before treatment

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

Up to 4 weeks before treatment

### During treatment

Participants were randomly assigned to any of the following 4 groups.

- **Group 1**: **QGE031** 72 mg (307 **adults** and 10 **adolescents**)
- **Group 2**: **QGE031** 120 mg (312 **adults** and 12 **adolescents**)
- **Group 3**: **Omalizumab** 300 mg (309 **adults** and 13 **adolescents**)
- **Group 4**: **Placebo** for 24 weeks followed by **QGE031** 120 mg for 24 weeks (106 **adults** and 3 **adolescents**)

Participants were 3 times more likely to receive either dose of **QGE031** or **omalizumab** 300 mg than **placebo**.

Participants received their treatment as 2 injections at the start of the trial, and then 2 injections every 4 weeks until Week 48 (last dose).

Up to 52 weeks

### After treatment

No trial drug was given; however, participants were allowed to take medications to relieve their CSU symptoms.

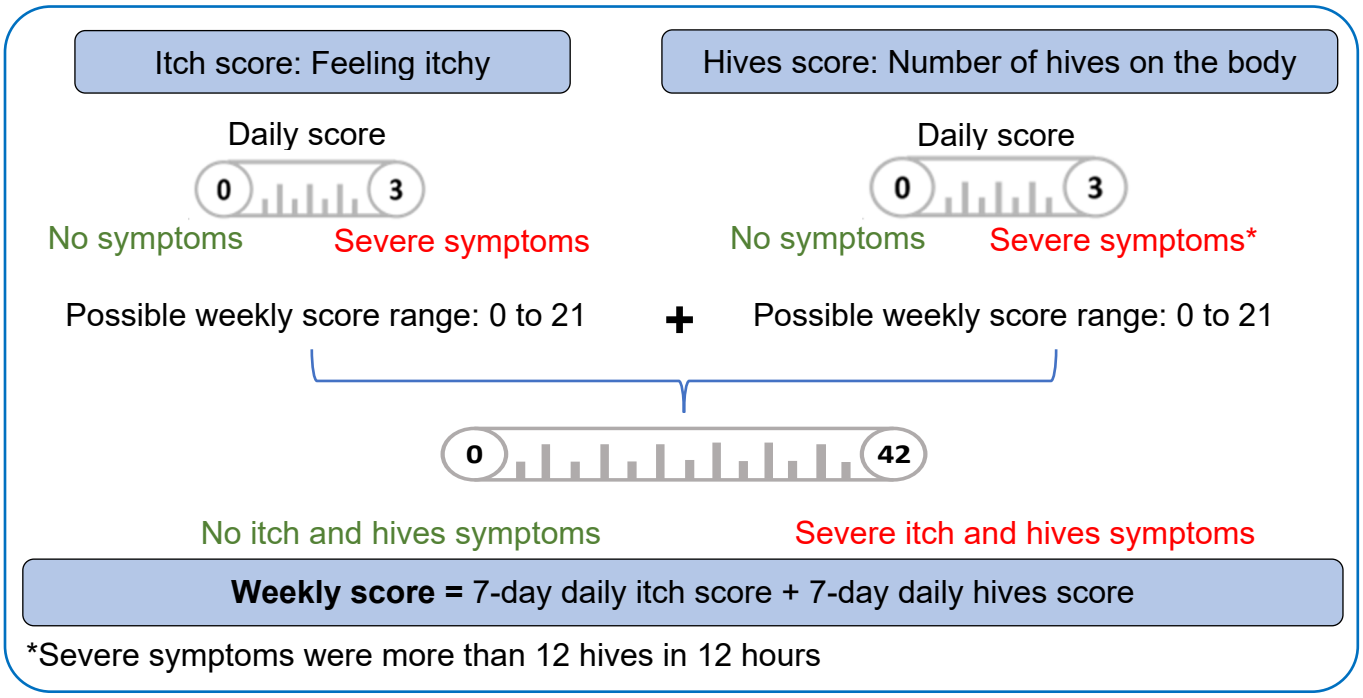
Researchers monitored the health of participants throughout the trial.

Up to 12 weeks after treatment

# What were the main results of this trial?

## Did the participants show improvements in the signs and symptoms of their hives and itch after 12 weeks of treatment compared to the start of the trial?

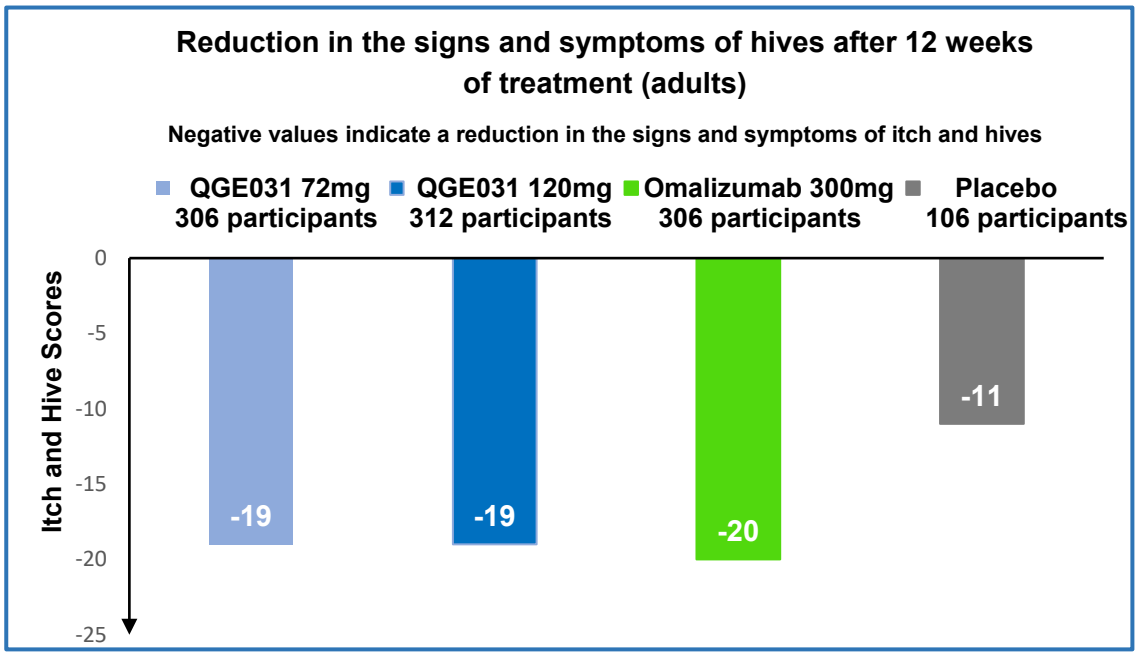
At the start of the trial, researchers gave participants an electronic diary that contained questions about hives. Participants recorded their hives and itch scores twice a day in their e-Diaries on a scale of 0 (none) to 3 (severe). Researchers monitored their weekly activity score as shown in the figure below. The range of the score was 0 (no score) to 6 (highest score) each day. For a week, the maximum total score could be 42.



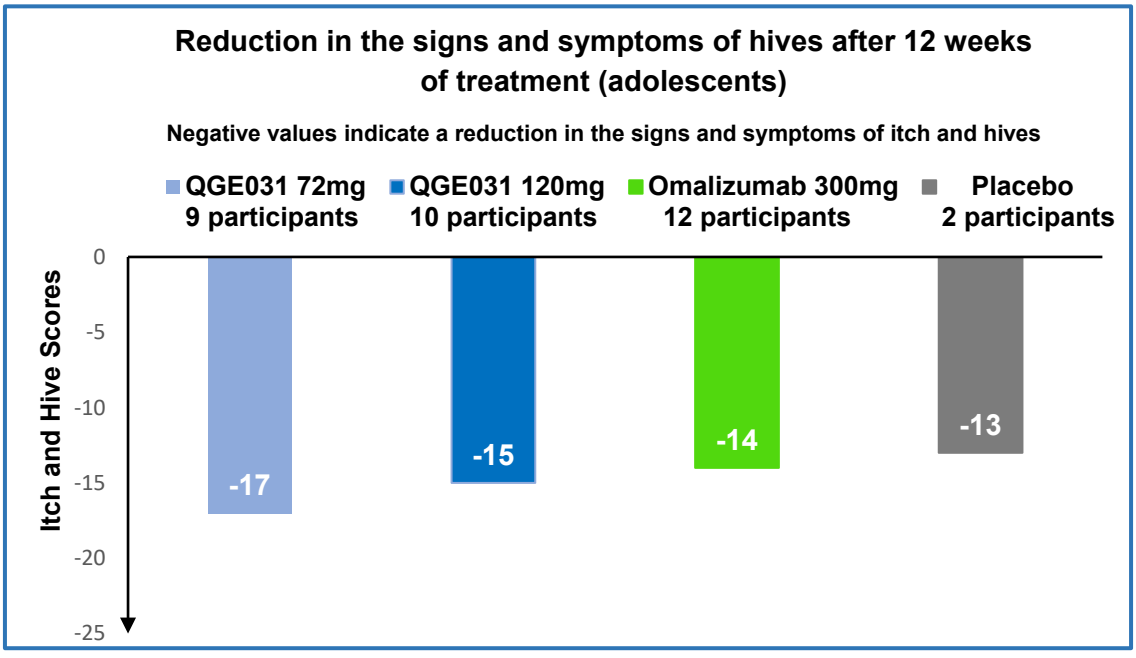

The average change in weekly score at the start of the trial and after 12 weeks of treatment was calculated for each treatment group using the above scale.

1 **adult** participant in the ligelizumab 72 mg group and 3 **adult** participants in the **omalizumab** group were not included in the results as these participants were mistakenly enrolled in the trial and did not receive treatment. Also, data from 5 of the adolescent participants were not included in the main results. However, they were included in the safety results.

**ADULTS**: Participants showed a reduction in the signs and symptoms of CSU in all 4 groups after 12 weeks of treatment. The average reduction in signs and symptoms was greater for participants who took **QGE031** or **omalizumab** compared with those who took **placebo**.




**ADOLESCENTS**: Participants showed a reduction in the signs and symptoms of CSU in all 4 groups after 12 weeks of treatment. However, there were not enough **adolescents** in the trial for the results to be meaningful. So, the results are to be interpreted with caution.



# What were the other results of this trial?

## How many participants' itch and hives symptoms completely disappeared by Week 12?

Overall, about one third of participants who took **QGE031** had their itch and hive symptoms go away by Week 12.

**ADULTS**: Itch and hives symptoms completely disappeared by Week 12 in

- 33% (102 out of 306) participants in the **QGE031** 72 mg group,
- 33% (104 out of 312) in the **QGE031** 120 mg group,
- 38% (116 out of 306) in the **omalizumab** group and
- 8% (8 out of 106) in the **placebo** group.

**ADOLESCENTS**: Itch and hives symptoms completely disappeared by Week 12 in

- 33% (3 out of 9) participants in the **QGE031** 72 mg group,
- 30% (3 out of 10) in the **QGE031** 120 mg group,
- none (0 out of 12) in the **omalizumab** group and
- 50% (1 out of 2) in the **placebo** group.

## How many participants reported their CSU symptoms as having no impact on their quality of life by Week 12?

Participants rated the impact their CSU symptoms had on their quality of life over 7 days by completing a questionnaire called the Dermatology Life Quality Index (DLQI). An overall score from 0 to 30 was calculated for each participant. The higher the score, the worse the quality of life due to their symptoms. A score of 0 to 1 indicated no impact on participants' quality of life.

Nearly half of the participants who took **QGE031** reported no impact on their quality of life.

**ADULTS**: No impact on their quality of life by Week 12 in

- 43% (133 out of 306) participants in the **QGE031** 72 mg group,
- 48% (150 out of 312) in the **QGE031** 120 mg group,
- 48% (147 out of 306) in the **omalizumab** group and
- 21% (22 out of 106) in the **placebo** group.

**ADOLESCENTS**: No impact on their quality of life by Week 12 in

- 33% (3 out of 9) participants in the **QGE031** 72 mg group,
- 55% (6 out of 11) in the **QGE031** 120 mg group,
- 17% (2 out of 12) in the **omalizumab** group and
- 33% (1 out of 3) in the **placebo** group.

# 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, disease, or physical accident 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.***

**Adolescent** and **adult** participants had similar numbers and types of adverse events during the trial. However, the low number of **adolescent** participants in this trial meant it was difficult to interpret the results. Therefore, the most common serious adverse events and non-serious adverse events presented below are from both the **adult** and **adolescent** participants.

## How many participants had adverse events?

**ADULTS:**

**Number of Adult Participants (%) With Adverse Events**

| | Group 1 | Group 2 | Group 3 | Group 4* | |
|---|---|---|---|---|---|
| | QGE031 72 mg (306 participants) | QGE031 120 mg (312 participants) | Omalizumab 300 mg (306 participants) | Placebo (106 participants) | Moved to QGE031 120 mg (99 participants) |
| At least 1 adverse event | 230 (75%) | 234 | 248 (81%) | 56 (53%) | 56 (57%) |
| At least 1 serious adverse event | 22 (7%) | 31 (10%) | 23 (8%) | 3 (3%) | 4 (4%) |
| Stopped drug due to adverse event | 8 (3%) | 16 (5%) | 8 (3%) | 1 (<1%) | 0 |

** Participants in Group 4 received placebo for 24 weeks and then moved to QGE031 120 mg for 24 weeks.*

**ADOLESCENTS:**

**Number of Adolescent Participants (%) With Adverse Events**

| | Group 1 | Group 2 | Group 3 | Group 4* | |
|---|---|---|---|---|---|
| | QGE031 72 mg (10 participants) | QGE031 120 mg (12 participants) | Omalizumab 300 mg (13 participants) | Placebo (3 participants) | Moved to QGE031 120 mg (3 participants) |
| At least 1 adverse event | 7 (70%) | 10 (83%) | 10 (77%) | Not reported | 2 (67%) |
| At least 1 serious adverse event | 0 | 1 (8%) | 0 | 0 | 0 |
| Stopped drug due to adverse event | 0 | 1 (8%) | 0 | Not reported | 0 |

** Participants in Group 4 received **placebo** for 24 weeks and then moved to **QGE031** 120 mg for 24 weeks.*

No deaths were reported in any group in the study.

Some **adult** participants stopped trial drug due to adverse events. The most common adverse events that led to trial drug discontinuation during the study were life-threatening allergic reaction (anaphylactic reaction) and worsening of hives (exacerbation of urticaria). 1 **adolescent** participant stopped trial drug due to increase in blood creatinine.

## What were the most common serious adverse events?

The most common serious adverse events that happened in at least 3 participants in any group are shown below:

**Number of Participants (%) With Adverse Events**

| | Group 1 | Group 2 | Group 3 | Group 4* | |
|---|---|---|---|---|---|
| | QGE031 72 mg (316 participants) | QGE031 120 mg (324 participants) | Omalizumab 300 mg (319 participants) | Placebo (109 participants) | Moved to QGE031 120 mg (102 participants) |
| **Back injury** (Intervertebral disc protrusion) | 3 (1%) | 0 | 0 | 0 | 0 |
| **COVID-19** | 0 | 3 (1%) | 1 (<1%) | 0 | 0 |

** Participants in Group 4 received **placebo** for 24 weeks and then moved to **QGE031** 120 mg for 24 weeks.*

## What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 5% (5 out of 100) of participants in any group are presented below.

**Number of Participants (%) With Adverse Events**

| | Group 1 | Group 2 | Group 3 | Group 4 | |
|---|---|---|---|---|---|
| | QGE031 72 mg (316 participants) | QGE031 120 mg (324 participants) | Omalizumab 300 mg (319 participants) | Placebo (109 participants) | Moved to QGE031 120 mg (participants) |
| **Back pain** | 12 (4%) | 9 (3%) | 16 (5%) | 1 (1%) | 0 |
| **Common cold** (Upper respiratory tract infection) | 20 (6%) | 24 (7%) | 28 (9%) | 4 (4%) | 1 (1%) |
| **Diarrhea** | 10 (3%) | 9 (3%) | 18 (6%) | 4 (4%) | 3 (3%) |
| **Headache** | 40 (13%) | 30 (9%) | 39 (12%) | 6 (6%) | 4 (4%) |
| **Hives** (Urticaria) | 17 (5%) | 15 (5%) | 10 (3%) | 2 (2%) | 3 (3%) |
| **Injection site reaction** | 15 (5%) | 15 (5%) | 7 (2%) | 0 | 6 (6%) |
| **Joint pain** (Arthralgia) | 9 (3%) | 19 (6%) | 16 (5%) | 1 (1%) | 5 (5%) |
| **Nose and throat infection** (Nasopharyngitis) | 35 (11%) | 32 (10%) | 38 (12%) | 10 (9%) | 8 (8%) |
| **Throat pain** (Oropharyngeal pain) | 9 (3%) | 7 (2%) | 18 (6%) | 2 (2%) | 1 (1%) |

** Participants in Group 4 received **placebo** for 24 weeks and then moved to **QGE031** 120 mg for 24 weeks.*

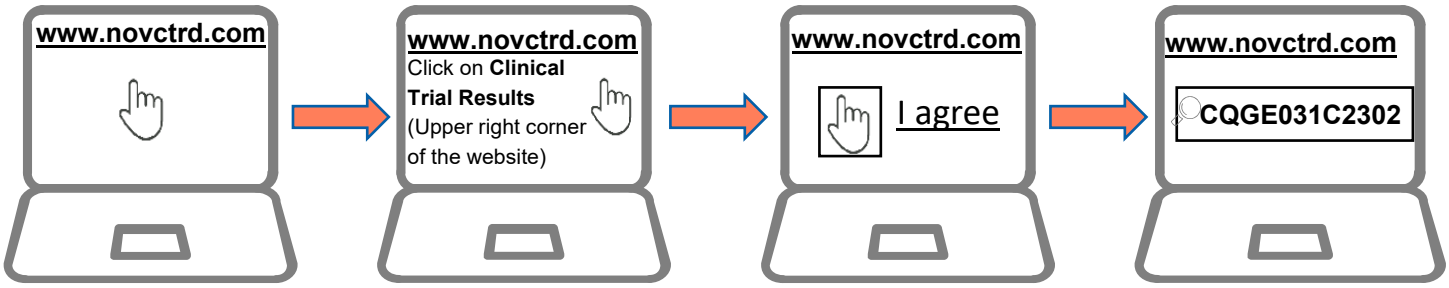
# How was this trial useful?

The trial helped researchers to learn about the effects and safety of **QGE031** in both **adults** and **adolescents** with moderate to severe CSU which could not be controlled with antihistamines. Results from this trial showed that **QGE031** had a better effect than **placebo** but did not show a better effect than **omalizumab**. The researchers did not find any new significant safety events for **QGE031** in this trial. The data from this trial may be used to decide if **QGE031** could be used for the treatment of other diseases.

# 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 NCT03580369 in the search field.
- **https://www.clinicaltrialsregister.eu/ctr-search/search** Use the EudraCT identifier 2018-000839-28 in the search field.

**Full clinical trial title:** A multi-center, randomized, double-blind, active and placebo-controlled study to investigate the efficacy and safety of ligelizumab (QGE031) in the treatment of Chronic Spontaneous Urticaria (CSU) 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