NOVARTIS

Clinical Trial Results Summary

A trial to learn about the long-term safety of LOU064 in people with chronic spontaneous urticaria (CSU) who previously participated in trial CLOU064A2201

Protocol number: CLOU064A2201E1

Thank You!

Thank you to the participants who took part in this extension trial. Every participant helped the researchers learn more about the long-term safety of the drug **LOU064**, also called remibrutinib.

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. We hope this helps the participants understand their important role in medical research.

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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.

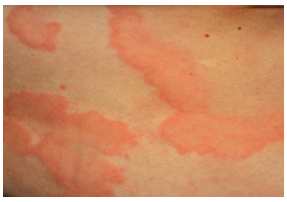
This summary shows the results of a single clinical trial. Other clinical trials may have different findings.

Why was the research needed?

Researchers were looking for a better way to treat **chronic spontaneous urticaria (CSU)**.

Drug	*Pronounced as*
Remibrutinib	Remi-BROO-ti-nib

Urticaria results in a rash or bumps on the skin, known as 'hives', 'wheals' or 'weals', and might also be itchy. They could be caused by an allergic reaction to food, insect stings or drugs, but many times the cause is unknown. 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.**



Source: https://dermnetnz.org/

One of the functions of the body's immune system is to fight against foreign agents, such as bacteria and viruses, but sometimes the immune system could be activated by unknown causes. **CSU** is a type of allergic disease in which the immune system becomes active even when there is no infection. When active, it produces a protein called Bruton's Tyrosine Kinase (BTK). BTK then sends signals to release proteins that can cause inflammation in the body. This causes the symptoms of **CSU.**

LOU064 attaches itself to BTK so that it is not active anymore. This way, it blocks the effect of BTK and stops the signals that cause inflammation. **LOU064** is currently not approved for the treatment of **CSU**.

Antihistamines are one of the current treatments available for treatment of **CSU**. These are medicines that are used to treat allergic reactions. They are not effective in treating **CSU** in some people. So, there is still a need for new treatment options for these people.

In this extension trial, researchers wanted to learn about the long-term safety of **LOU064** in people with **CSU** who previously participated in the CLOU064A2201 trial.

How long was this trial?

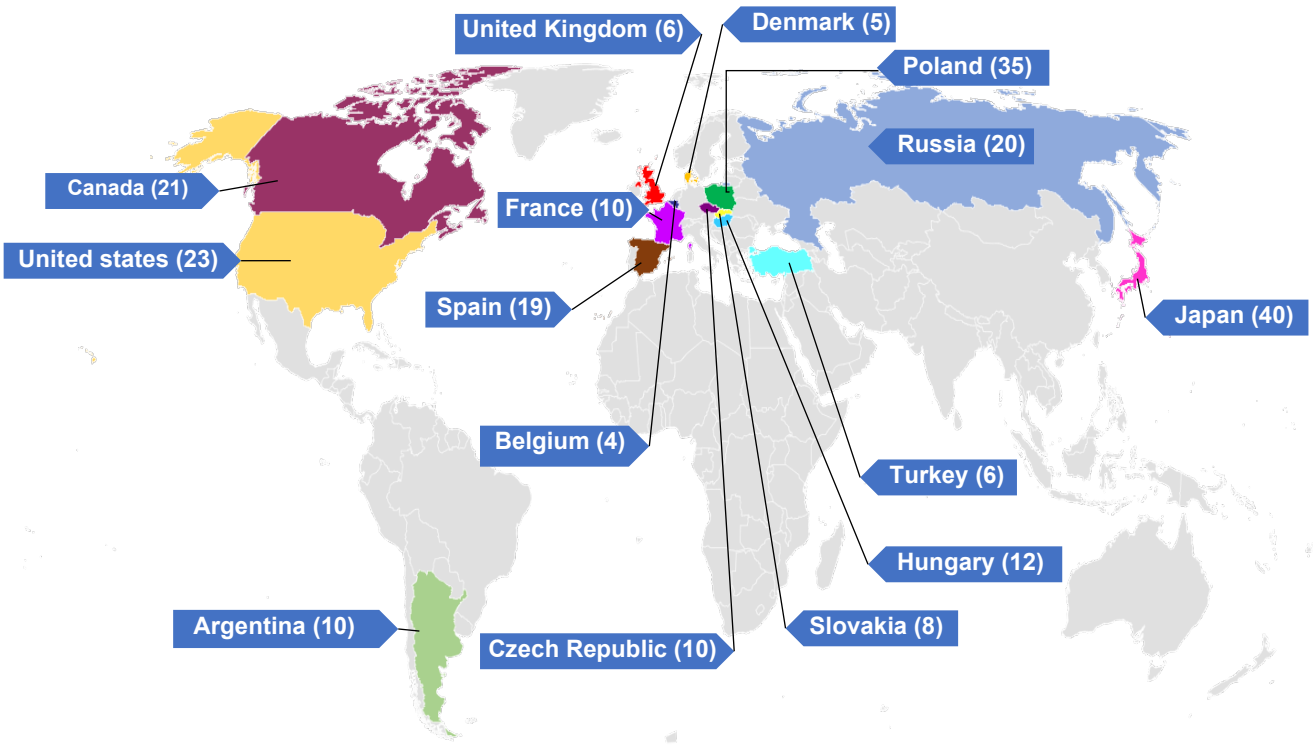
This trial started in October 2019 and ended in September 2022. The entire duration, from enrolling the first participant to the last participant completing the trial was around 2 years and 10 months. An individual participant was in this trial for an average of 1 year and 4 months. The participant may or may not have been part of an additional 3-month observation period.

Who was in this trial?

The participants could take part in this trial if they had completed the previous trial CLOU064A2201 until Week 12 or Week 16.

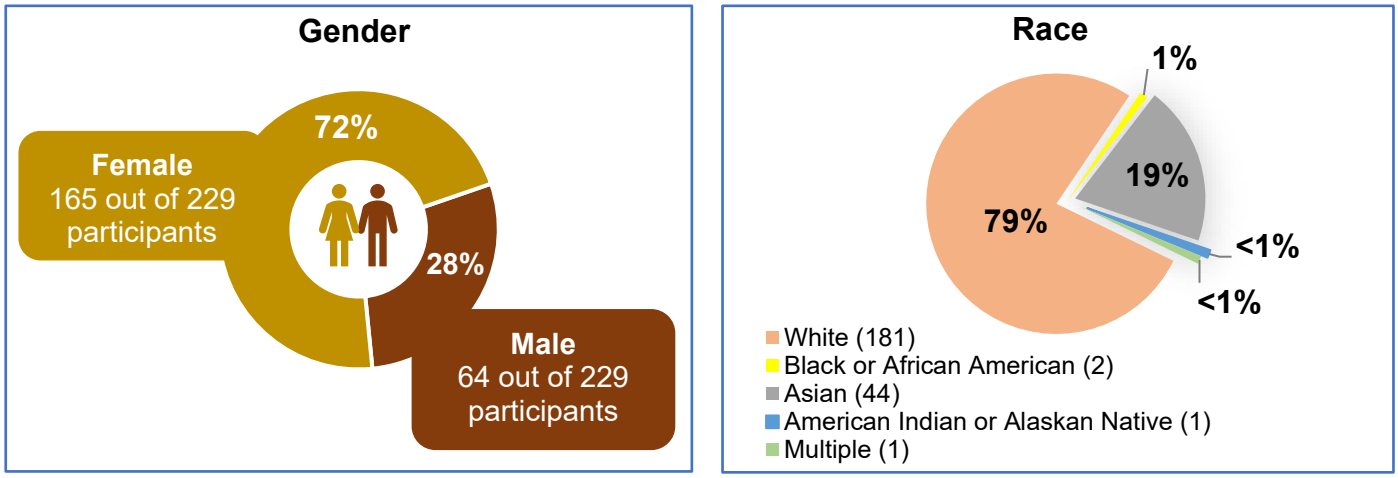
A total of 229 participants from 15 countries participated in this trial. Out of those, 68 entered the treatment-free observation period to check if they will need treatment or not. Of these 68, 33 received treatment. In total, only 194 participants received treatment. The other 35 out of 68 participants with controlled or mild CSU symptoms remained treatment-free and completed the trial without any treatment.

Participants per country



The 229 participants were from 18 to 77 years of age. The average age of the participants was 45 years. Most of the participants were female (72%) and White (79%).

Participants by gender and race



What treatment did the participants take?

The treatment in this trial was:

LOU064, two capsules of 50 milligrams (mg) each, two times a day, once in the morning and once in the evening. So, a participant took a total of 4 capsules daily.

Participants could take rescue medications if needed. Rescue medications are the medicines given to relieve symptoms immediately in case participants do not feel relief from their **CSU** symptoms during the trial treatment. Use of these medicines is decided on a daily basis. The rescue medicines used in this trial were anti-allergic drugs called antihistamines.

The participants and clinical trial team knew what treatment each participant took.

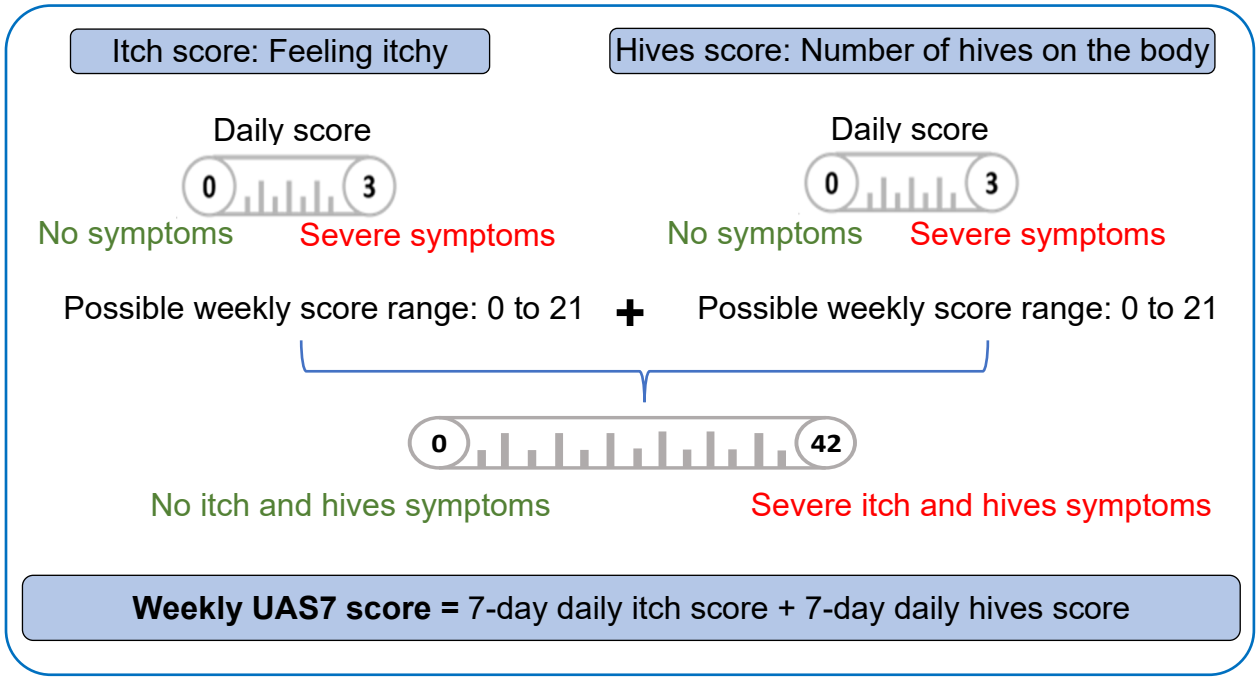
What happened during this trial?

The participants received their treatment based on the severity of their **CSU** symptoms. This was measured using scores from questionnaires which were completed by participants electronically using an e-Diary.

Participants recorded their **CSU** symptoms of itch and hives twice a day in the e-Diaries on a scale of 0 (none) to 3 (severe) using a scoring system called the Urticaria Activity Score (UAS). UAS7 is

participants' weekly UAS. The scores ranged from 0 to 6 each day. For one week, the maximum total UAS7 could be 42. The weekly scores and their meanings are listed below.

Weekly UAS (UAS7)	How severe were 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

The trial doctors checked if 229 participants from the previous trial CLOU064A2201 were willing to join this extension trial.

Participants coming from the previous trial CLOU064A2201, with UAS7 scores of

- 16 or more, entered the treatment period of this trial.
- less than 16, entered the observation period, without the trial drug.

During the 12 weeks observation period, if participants' UAS7 scores

- increased to 16 or more, even once, the participants entered the treatment period.
- remained less than 16, the participants completed the trial without any treatment.

Of the 229 participants who were enrolled, 68 participants entered the treatment-free observation period to check if they will need the treatment or not.

Of these 68 participants, 33 moved to the treatment period of this trial. The other 35 participants remained treatment-free and completed the trial without any treatment.

Up to 12 weeks

During treatment

A total of 194 participants received the treatment.

- They received two capsules of **LOU064**, 50 mg each, two times a day.
- After 4 weeks of receiving the trial treatment, some participants also took background medicines. Background medicines in this trial were antihistamines. Background medicines are different from rescue medicines and the trial medicine.

Up to 52 weeks

After treatment

- After the participants completed or stopped their treatment early, they were observed for 4 weeks.
- Participants whose UAS7 scores remained 6 or less at the end of the treatment were observed up to a maximum of 16 weeks.

Up to 16 weeks

What was the main result of this trial?

What medical problems did the participants have during the trial?

To answer this question, the researchers monitored the medical problems that happened 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 to the participants who took **LOU064** treatment or were part of the treatment-free group during the trial are listed in the table below.

Number of Participants (%) With Adverse Events

	LOU064 (Out of **194** participants)	**Treatment-free group** (Out of **68** participants)
At least 1 adverse event	139 (72%)	11 (16%)
At least 1 serious adverse event	6 (3%)	1 (1%)
Stopped drug due to adverse event	11 (6%)	— Participants received no trial drug

During this trial, no deaths were reported.

How many participants stopped trial drug due to adverse events?

During this trial, 11 out of 194 participants (6%) discontinued the trial treatment due to adverse events. The most common adverse event leading to discontinuation of trial drug was diarrhea. It was reported in 2 out of 194 participants (1%).

What were the most common serious adverse events?

During this trial, 6 out of 194 participants (3%) who took **LOU064** reported serious adverse events. 2 out of 194 participants (1%) reported **chest infection due to COVID virus** (COVID-19 pneumonia). The others reported a single event each of **blood in stools** (melaena), **inflammation of the appendix** (appendicitis), **chest pain**, **leg fracture** (tibia fracture) and **fluid filled sac in the ovary** (ovarian cyst).

In the treatment-free group, 1 out of 68 participants (1%) reported serious adverse event. The adverse event was **spread of superficial skin cancer at an unknown stage** (superficial spreading melanoma stage unspecified).

What were the most common other adverse events?

The most common other adverse events that happened in at least 5% (5 out of 100) participants who took **LOU064** treatment are presented below. In the treatment-free group, no other adverse events were reported.

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

	LOU064 (Out of 194 participants)
Worsening of CSU (Chronic spontaneous urticaria)	22 (11%)
COVID-19	16 (8%)
Headache	13 (7%)
A condition that makes your skin red and itchy (Eczema)	10 (5%)

What were the other results of this trial?

What changes were reported in participants' CSU symptoms after 4 weeks of treatment?

To answer this question, the researchers used the UAS7 scoring system to measure participants' **CSU** symptoms and response to treatment. After 4 weeks of treatment, the average UAS7 score of participants had gone down by 18 points from the start of the trial. It was observed that, in general, the CSU symptoms changed from severe to mild in the participants.

How many participants reported UAS7 score of 6 or less after 4 weeks of treatment?

In this trial, 99 out of 194 participants (51%) reported a UAS7 score of 6 or less (well-controlled or completely controlled disease) after 4 weeks of treatment.

How many participants had their CSU symptoms completely controlled after 4 weeks of treatment?

In this trial, 53 out of 194 participants (27%) had their **CSU** symptoms completely controlled with a UAS7 score of zero after 4 weeks of treatment.

How was this trial useful?

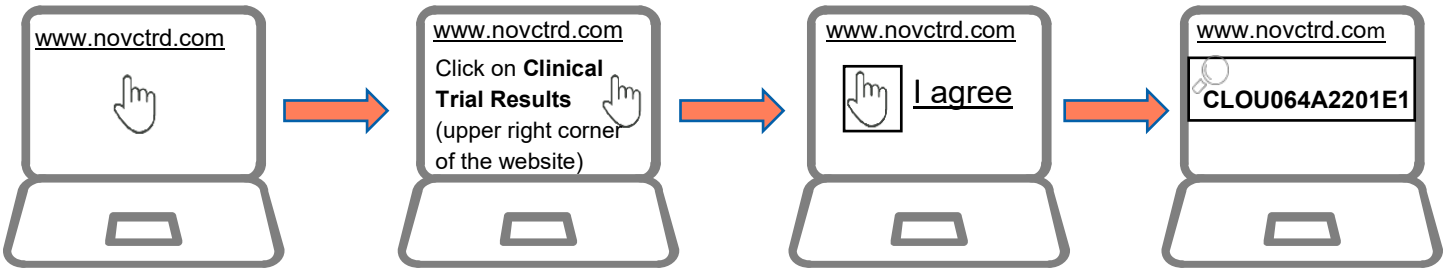
The extension trial helped researchers to learn about the long-term safety of **LOU064** in participants with moderate to severe **CSU**. Safety results from this trial were similar to the earlier results of the CLOU064A2201 trial.

At the time of this report, future trials for **CSU** with **LOU064** are planned.

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 NCT04109313 in the search field.
- **https://www.clinicaltrialsregister.eu/ctr-search** Use the EudraCT identifier 2019-001074-29 in the search field.

Full clinical trial title: An open-label, multicenter, extension study to evaluate the long-term safety and tolerability of LOU064 in eligible subjects with CSU who have participated in CLOU064A2201

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.

NOVARTIS

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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