NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of LOU064 in people with chronic spontaneous urticaria

Thank you!

Thank you to the participants who took part in the clinical trial for the trial drug **LOU064**, also called remibrutinib. Every participant helped the researchers learn more about **LOU064** for people with chronic spontaneous urticaria.

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.

Trial information

Trial number: CLOU064A2302

Novartis drug studied: **LOU064**, also called remibrutinib

Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

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

What was the main purpose of this trial?

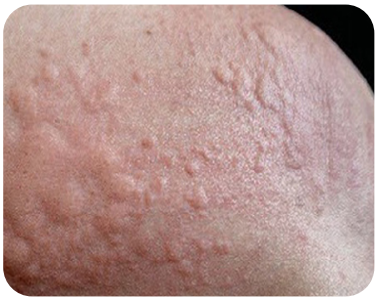
The purpose of this trial was to learn about the effects of **LOU064** for people with chronic spontaneous urticaria. Everyone in this trial had chronic spontaneous urticaria that was not well controlled with H1-antihistamines. **H1-antihistamines**, such as cetirizine, are the usual treatment for chronic spontaneous urticaria, but do not work for every person. In this trial, researchers compared the effects of **LOU064** to a **placebo**.

Chronic spontaneous urticaria (CSU) is a type of allergic disease in which the immune system becomes active even when there is no trigger (cause). When active, a protein called Bruton's Tyrosine Kinase (BTK) sends signals to release proteins that can cause inflammation in the body. This causes the symptoms of CSU.

LOU064, also called remibrutinib, is a trial drug designed to bind to the protein BTK on certain cells in the immune system and lower the activity of these cells. By lowering the activity of these cells, researchers think **LOU064** could lessen symptoms of CSU.

A **placebo** looks like the trial drug but does not have any drug in it. Using a **placebo** helps researchers better understand the effect of a trial drug.

Hives from CSU



Source:
Oregon Medical Research Center
oregonmedicalresearch.com

Trial drug
LOU064 also called remibrutinib

Pronounced as
rem-ee-bru-tih-nib

The trial's purpose was to answer these main questions:

- Did LOU064 lower the severity of participants' itch and hives?
- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

How long was this trial?

The trial began in December 2021 and ended in January 2024. Each participant was in the trial for about 14 months.

This trial had 2 parts:

- **Part 1** (6 months): Participants took **LOU064** or **placebo**
- **Part 2** (7 months): Participants who stayed in the trial after completing Part 1 took **LOU064**

Who was in this trial?

455 participants with CSU joined this trial – 158 men and 297 women. Participants' ages ranged from 18 to 81 years. Their average age was 42 years.

The number of participants by race is shown below.

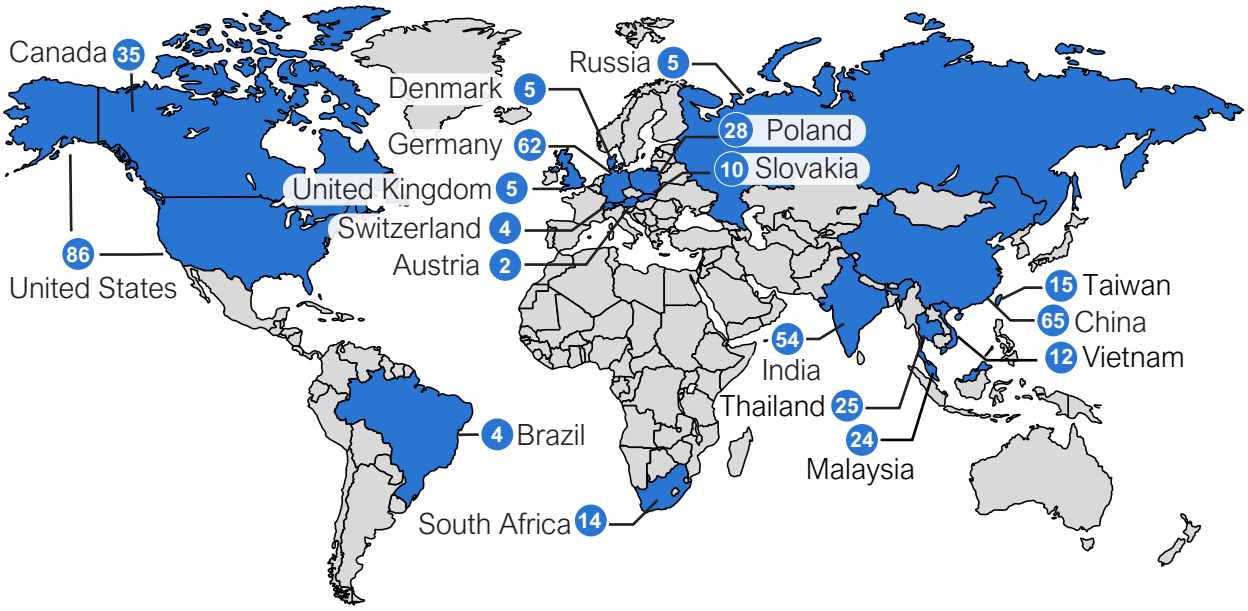
Race

202 Asian	10 Black or African American
238 White	4 More than one race
1 Not reported	

The participants could take part in this trial if they:

- Had CSU for at least 6 months before joining the trial
- Continued to have CSU while taking H1-antihistamines before joining the trial
- Did not have certain other skin conditions that might look or feel like CSU

455 participants from 18 countries joined the trial. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

The treatments in this trial were:

LOU064, also called remibrutinib, 25 milligrams, which was taken by mouth as a tablet twice a day.

Placebo, which was taken by mouth as a tablet twice a day. A **placebo** looks like the trial drug but does not have any drug in it. Using a **placebo** helps researchers better understand the effect of a trial drug.

Along with the trial treatment, all participants received antihistamines as background medicine. If a participant's CSU symptoms got worse during trial treatment, they could take more antihistamines to lessen symptoms.

During **Part 1**, researchers used a computer program to randomly assign participants to their treatments. Twice as many participants were assigned to **LOU064** than **placebo**. The participants, researchers, and trial staff did not know what treatment the participants were receiving. Some trials are done this way because knowing what treatment the participants receive can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.

During **Part 2**, the participants, researchers, and trial staff knew what treatment each participant took. All participants took **LOU064**.

What happened during this trial?

Before treatment

Up to 1 month

The trial staff checked to make sure the participants could be in this trial.

During treatment

About 1 year

Of the 455 participants who joined the trial, 450 received treatment.

In **Part 1**, participants took one of these treatments for 6 months:

LOU064 – 297 participants

Placebo – 153 participants

In **Part 2**, 426 participants from Part 1 who stayed in the trial took **LOU064** for 7 months.

After treatment

1 month

Trial staff checked participants for any medical problems for up to 1 month after participants' last dose of trial treatment.

At the end of this trial, some participants who completed the trial were invited to join another trial called CLOU064A2303B to learn more about the effects of **LOU064**.

Trial staff checked the participants' general health throughout the trial.

What were the main results of this trial?

Did LOU064 lower the severity of participants' itch and hives?

At Week 12 of treatment, participants who took **LOU064** had less severe itch and hives, on average, than those who took **placebo**.

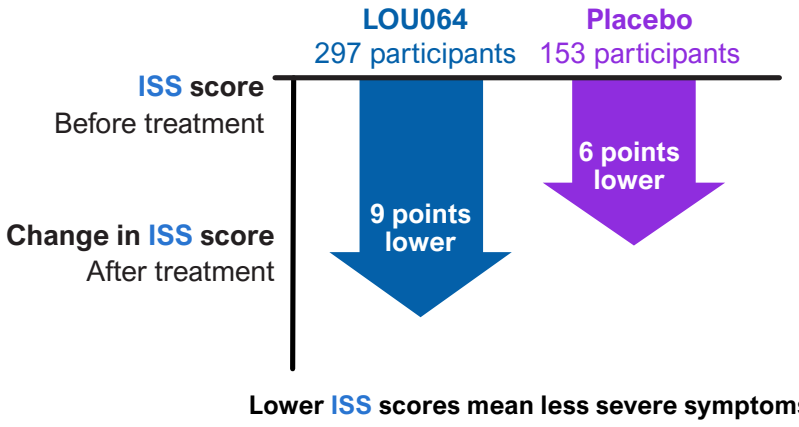
To learn this, researchers looked at participants' answers to questions about their itchiness and number of hives. Participants answered these questions before and during trial treatment. Researchers measured how much each participant's total weekly score changed from before they started trial treatment to Week 12 of trial treatment. **Lower scores mean less severe symptoms**.

Researchers measured each participant's weekly:

- **Itch Severity Score (ISS)**, which ranges from 0 to 21, with 21 being the most severe itchiness.
- **Hive Severity Score (HSS)**, which ranges from 0 to 21, with 21 being the largest number of hives.
- **Urticaria Activity Score (UAS)**, which is the total of the **ISS** and **HSS** scores. It ranges from 0 to 42, with 42 being the most severe itchiness and largest number of hives.

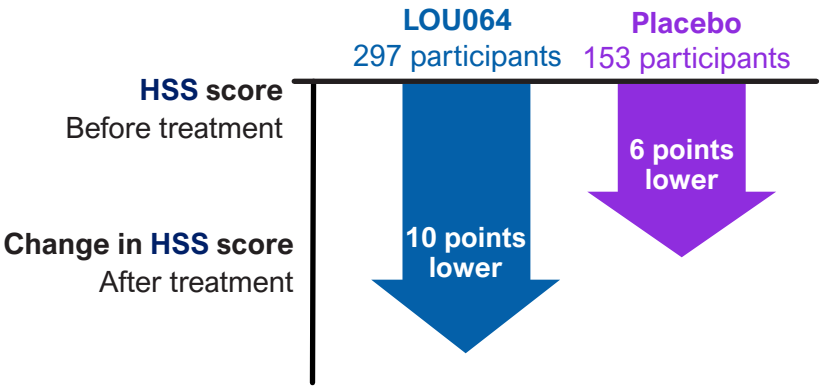
Change in itch severity score (ISS)

The graph below shows the change in participants' average weekly **ISS** score from before treatment to Week 12. The average weekly **ISS** score went down 9 points for participants taking **LOU064** and 6 points for participants taking **placebo**.



Change in hive severity score (HSS)

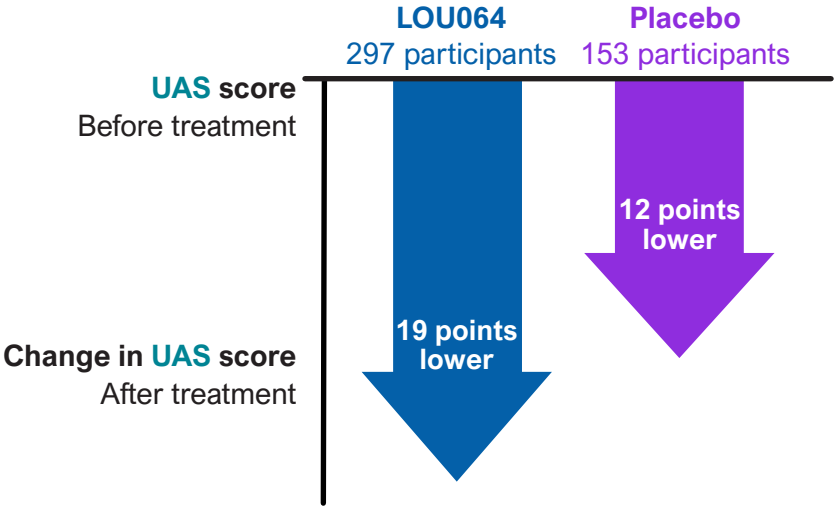
The graph below shows the change in participants' average weekly **HSS** score from before treatment to Week 12. The average weekly **HSS** score went down 10 points for participants taking **LOU064** and 6 points for participants taking **placebo**.



Lower HSS scores mean less severe symptoms

Change in urticaria activity score (UAS)

The graph below shows the change in participants' average weekly **UAS** score from before treatment to Week 12. The average weekly **UAS** score (the total of the **ISS** and **HSS** scores) went down 19 points for participants taking **LOU064** and 12 points for participants taking **placebo**.



Lower UAS scores mean less severe symptoms

What were the other results of this trial?

Did participants who took LOU064 have changes in their itch and hives?

Compared to those who took **placebo**, participants who took **LOU064** were at least twice as likely to have:

- Fewer hives and milder itchiness (weekly **UAS** of 6 or less) at Week 2 or 12 of treatment
- No impact from CSU on their skin-related quality of life at Week 12 of treatment

How many weeks did participants have less severe itch and hives symptoms between the start of treatment and Week 12?

On average, participants had fewer hives and milder itchiness for:

- 5 weeks for participants who took **LOU064**
- 1 week for participants who took **placebo**

On average, participants had no swelling under their skin (angioedema) for:

- 9 weeks for participants who took **LOU064**
- 7 weeks for participants who took **placebo**

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of treatment until 1 month after the last treatment.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

While taking **LOU064**:

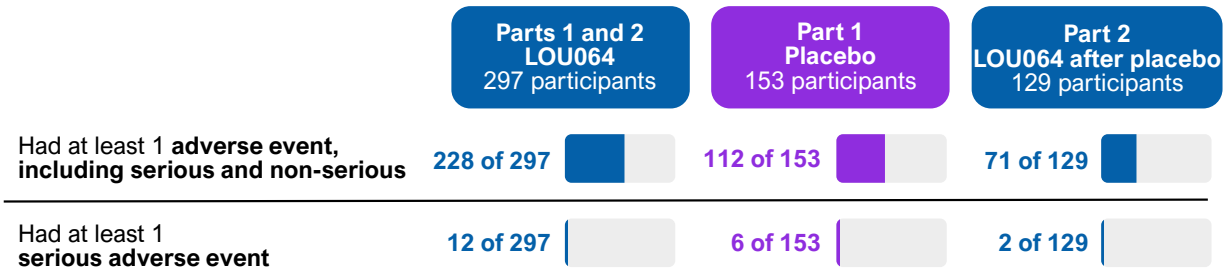
- 299 of 426 participants (70%) had adverse events, including adverse events that were considered serious and non-serious
- 14 participants had adverse events that were considered serious
- 13 participants left the trial due to an adverse event

While taking **placebo**:

- 112 of 153 participants (73%) had adverse events, including adverse events that were considered serious and non-serious
- 6 participants had adverse events that were considered serious
- 8 participants left the trial due to an adverse event

No participants died. The researchers concluded there were no new safety concerns for **LOU064** in this trial.

How many participants had adverse events?



What serious adverse events did the participants have?

14 participants had serious adverse events while taking **LOU064**, and 6 participants while taking **placebo**. No participants died.

The table below shows the most common types of serious adverse events that happened in **4 or more** participants, which were viral or bacterial infections. Additional serious adverse events happened in fewer participants.

	Parts 1 and 2 LOU064 297 participants	Part 1 Placebo 153 participants	Part 2 LOU064 after placebo 129 participants
A lung infection Pneumonia	0 of 297 0%	1 of 153 1%	0 of 129 0%
Infection in the appendix Appendicitis	0 of 297 0%	1 of 153 1%	0 of 129 0%
Infection in the stomach or digestive tract Gastrointestinal infection	1 of 297 Less than 1%	0 of 153 0%	0 of 129 0%
A pus-filled lump Wound abscess	1 of 297 Less than 1%	0 of 153 0%	0 of 129 0%

What other non-serious adverse events did the participants have?

The table below shows the most common types of other non-serious adverse events that happened in **5% or more** participants. Additional adverse events happened in fewer participants.

	Parts 1 and 2 LOU064 297 participants	Part 1 Placebo 153 participants	Part 2 LOU064 after placebo 129 participants
COVID-19	62 of 297 21%	21 of 153 14%	13 of 129 10%
The common cold Nasopharyngitis	33 of 297 11%	9 of 153 6%	3 of 129 2%
Headache	22 of 297 7%	8 of 153 5%	1 of 129 1%
Infection in the ear, nose, throat, or airways Upper respiratory tract infection	22 of 297 7%	4 of 153 3%	8 of 129 6%
An infection thought to be COVID-19 Suspected COVID-19	16 of 297 5%	5 of 153 3%	4 of 129 3%

What was learned from this trial?

Researchers learned about the effects of **LOU064** in people with chronic spontaneous urticaria (CSU) that was not well controlled with H1-antihistamines.

The researchers concluded that:

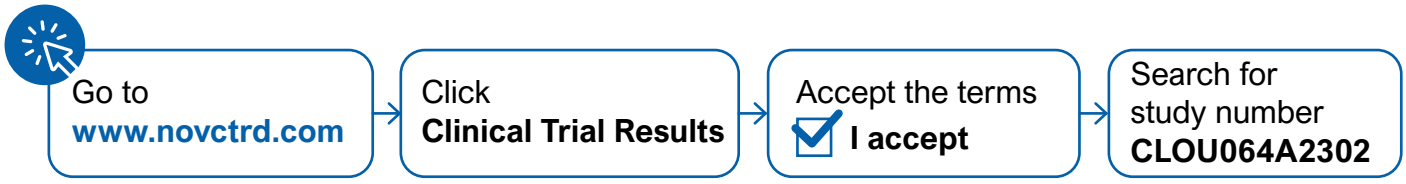
- Compared to participants who took **placebo**, the participants who took **LOU064**:
  - Had less severe itch and hives at Week 12 of treatment
  - Had fewer hives and mild itchiness at Weeks 2 and 12 of treatment
  - Had no impact from CSU on their skin-related quality of life at Week 12
  - Had 4 more weeks of less severe itch and hives symptoms between the start of treatment and Week 12
  - Had 2 more weeks of no swelling under their skin between the start of treatment and Week 12
- There were no new safety concerns for **LOU064** in this trial

When this summary was written, an extension trial CLOU064A2303B was ongoing.

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**

Follow these steps to find the scientific summary:



For more information about this trial, go to any of these websites:

- **clinicaltrials.gov** – search using the number **NCT05032157**
- **clinicaltrialsregister.eu** – search using the number **2021-000424-35**

Other trials of **LOU064** may appear on the public websites above. When there, search for **LOU064** or remibrutinib.

Full clinical trial title: A multicenter, randomized, double-blind, placebo-controlled Phase 3 study of remibrutinib (LOU064) to investigate the efficacy, safety and tolerability for 52 weeks in adult chronic spontaneous urticaria (CSU) patients inadequately controlled by H1-antihistamines

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

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