The effects and safety of LOU064 for people with Sjögren's syndrome

Thank you!

Thank you to the participants who took part in the clinical trial for Sjögren's syndrome. Every participant helped the researchers learn more about **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.

Trial information

Trial number: CLOU064E12201
Drug studied: LOU064
Sponsor: Novartis

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects and safety of LOU064 for people with Sjögren's syndrome.

Sjögren's syndrome (SjS) is a long-lasting condition in which the immune system is overactive. When that happens, the immune system mistakenly attacks the body, including the glands that make fluid, like tears, saliva, and sweat. People with SjS have dryness of the mouth, eyes, and other areas. They also have pain and tiredness that severely affect their daily lives.

LOU064 is a trial drug designed to lower the activity of certain cells in the immune system. Researchers know that these immune cells play a role in SjS.

Placebo – looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

The main questions this trial was designed to answer:

- Did the participants have less severe SjS symptoms after taking LOU064?
- What medical problems did the participants have during this trial?
  Keeping track of the medical problems helped to learn about the safety of LOU064.

Main results: After 6 months, the participants who took LOU064 had less severe SjS symptoms than those who took placebo.

The researchers also concluded there were no new safety concerns for LOU064 in this trial.

How long was this trial?

This trial began in July 2019. It was planned to be a 2-part trial, but only Part 1 was done. For Part 1, it was planned for participants to be in the trial for about 8 months.

In April 2022, the sponsor reviewed data from Part 1 and decided to stop this trial early before starting Part 2. The sponsor decided there was enough data to understand how LOU064 works in people with SjS. The decision to stop was not related to safety.

Who was in this trial?

73 participants were in this trial – 2 men and 71 women. The participants were 22 to 75 years old. Their average age was 52.

Participants reported their race as:

- White – 50 participants
- Asian – 21 participants
- Black or African American – 1 participant
- Unknown – 1 participant

Every participant in this trial had moderate to severe SjS and:

- Was able to make some saliva on their own
- Did not have any other condition caused by an overactive immune system

This trial took place in Australia, Belgium, Bulgaria, China, Denmark, Germany, Hungary, Spain, Switzerland, Taiwan, the United Kingdom, and the United States.

Visit **novctrd.com** for more information about:

- Who could and could not be in this trial
- Which medicines they could or could not take
- Reasons why the participants did not complete the trial

Use trial number **CLOU064E12201** to find the scientific summary.

What trial treatments did the participants take?

Participants were randomly assigned to 1 of these treatment groups:

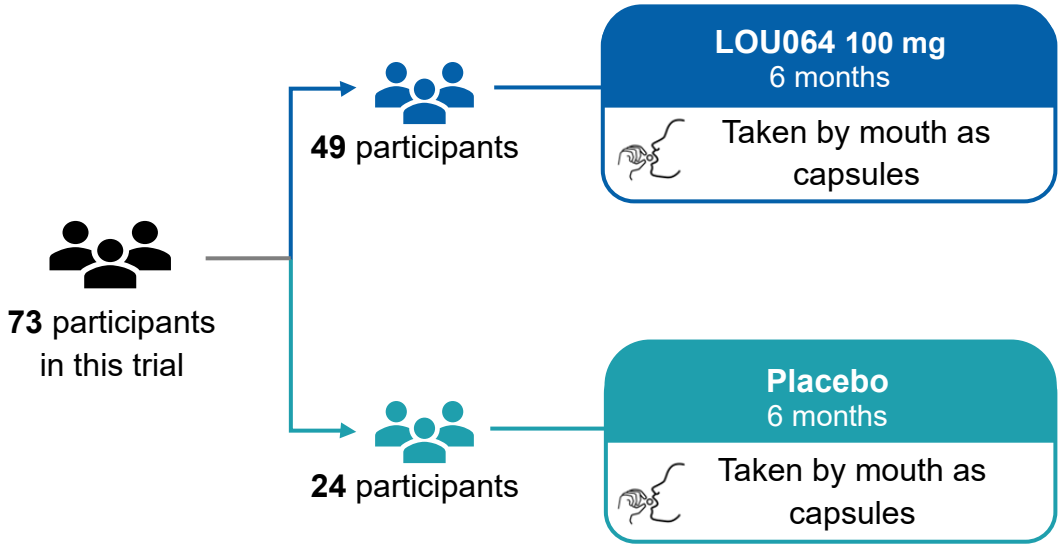
- **LOU064** – 100 milligrams (mg)
  - Participants were assigned to take LOU064 either 1 or 2 times a day
- **Placebo** – looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

Participants received their treatment as capsules. Participants also continued taking their standard treatment for SjS.

A computer program was used to randomly assign the treatments. This helped make sure the researchers compared the results as fairly as possible.

The participants and trial staff did not know what treatment each participant took during the trial. Some trials are done this way because knowing what treatment participants take can influence the results. Not knowing what treatment participants take helps make sure the results are looked at fairly.

The graphic below shows how many participants were assigned each treatment.



What were the main results of this trial?

This is a summary of the overall results of this trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results.

Always talk to a doctor before making any changes to your health care.

Did the participants have less severe SjS symptoms after taking LOU064?

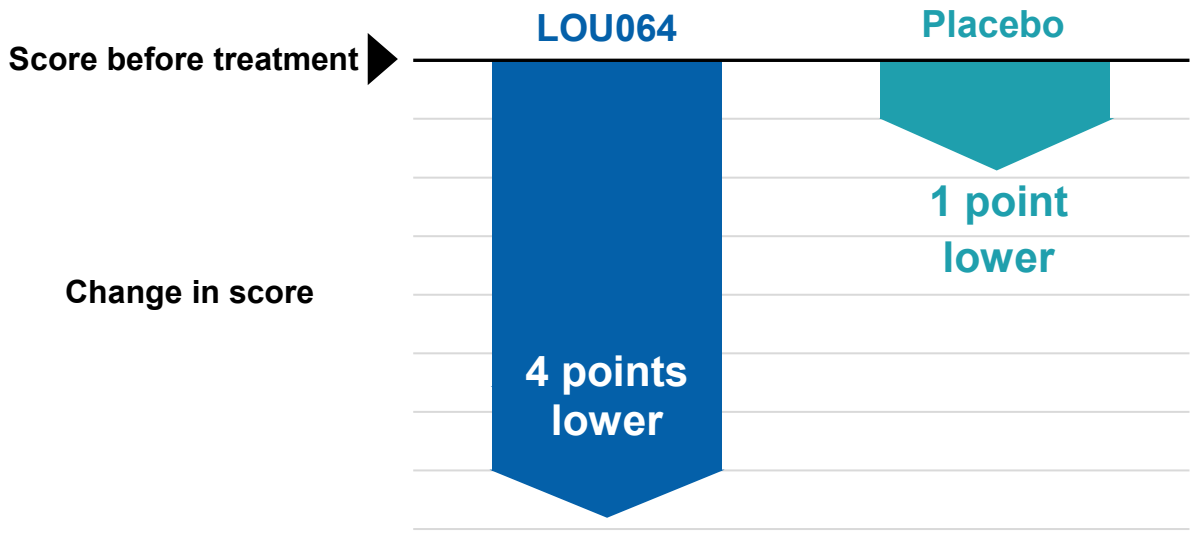
Yes, after 6 months, the participants who took LOU064 had less severe SjS symptoms than those who took placebo.

To find this out, the trial doctors measured how severe the participants' symptoms were before and after receiving LOU064 or placebo for 6 months. They did this by using the EULAR Sjögren's Syndrome Disease Activity Index, also called the ESSDAI. ESSDAI is a tool used by doctors to measure the effect of SjS on different parts of the body. The ESSDAI scores can range from 0 to 123. Lower scores mean SjS symptoms are less severe.

After 6 months, the ESSDAI score was lower for participants who took LOU064 compared to those who took placebo. This means SjS symptoms were less severe for participants who took LOU064.

Average change in ESSDAI score after treatment

The graph below shows the average change in the ESSDAI score after receiving either dose of LOU064 or placebo for 6 months. The researchers compared the ESSDAI scores from before treatment to after treatment.



A **lower** ESSDAI score means SjS symptoms are **less severe**

The researchers also looked at the participant's ESSDAI scores during the 6 months of treatment. Throughout treatment, ESSDAI scores were also lower for those who took LOU064 compared to those who took placebo.

What other results were learned?

Did LOU064 change the measures of the participants' health and quality of life?

Participants and their trial doctor used 2 other questionnaires to measure their severity of SjS symptoms and overall condition at different time points. They used the:

- Physician Global Assessment Scale, also called PhGA
- EULAR Sjögren's Syndrome Patient Reported Index, also called ESSPRI

Using the PhGA and ESSPRI, the researchers found that the participants' overall SjS symptom severity and condition were not meaningfully different between LOU064 and placebo groups.

The participants also answered questions about their quality of life, such as their ability to do their daily activities. Overall, the researchers concluded that LOU064 did not show a meaningful effect on quality of life compared to placebo.

What medical problems did the participants have during this trial?

Medical problems that happen during trials are called "adverse events".

Trial doctors keep track of **all** adverse events that happen in trials, 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.

An adverse event is:

- Any **unwanted 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.

The adverse events in this section include any that happened during treatment and up to 1 month after completing treatment.

Most of the participants (63 of 73 participants) had adverse events. In the LOU064 and placebo groups, a similar percentage of participants had adverse events. 3 participants had adverse events that were considered serious. The most common type of adverse event was headache. The researchers concluded there were no new safety concerns for LOU064 in this trial.

What serious adverse events did the participants have?

LOU064: 2 of the 49 participants or 4% had a serious adverse event.

Placebo: 1 of the 24 participants or 4% had a serious adverse event.

Participants who had:	LOU064 49 Participants	Placebo 24 Participants
Shingles Herpes zoster	2% 1 of 49	0% 0 of 24
Lung infection due to COVID-19 COVID-19 pneumonia	2% 1 of 49	0% 0 of 24
Lung infection Pneumonia	0% 0 of 49	4% 1 of 24

There were no deaths during the trial.

What other adverse events did the participants have?

LOU064: 43 of the 49 participants or 88% had an adverse event.

Placebo: 20 of the 24 participants or 83% had an adverse event.

The table below shows the adverse events that happened in **5 or more participants**. Additional adverse events happened to fewer participants.

Participants who had:	LOU064 49 Participants	Placebo 24 Participants
Headache Headache	8% 4 of 49	21% 5 of 24
Feeling sick Nausea	10% 5 of 49	8% 2 of 24
Nose and throat infection Nasopharyngitis	6% 3 of 49	13% 3 of 24
Tiredness Fatigue	6% 3 of 49	8% 2 of 24
Common cold Upper respiratory tract infection	6% 3 of 49	8% 2 of 24

What was learned from this trial?

This trial helped researchers learn about the effects and safety of LOU064 for people with SjS.

The researchers concluded that after finishing 6 months of treatment, the participants who took either dose of LOU064 had less severe SjS symptoms than those who took placebo. SjS symptoms were also less severe during the 6 months of treatment. The researchers found no new safety concerns for LOU064 in this trial.

Using other questionnaires, the researchers also learned that after 6 months of treatment, there was no meaningful difference in:

- overall SjS symptom severity and condition between the LOU064 and placebo groups
- quality of life of participants between the LOU064 and placebo groups

These are the results of a single trial. Other trials may have different results. This was one of many trials a drug goes through. This type of trial helps researchers learn about how well a trial drug works and if there are any new safety concerns in a small number of participants.

Where can I learn more about this and future trials?

For more information about this trial go to any of the following websites:

- **novctrd.com** – search using the study number **CLOU064E12201**
- **clinicaltrials.gov** – search using the number **NCT04035668**
- **clinicaltrialsregister.eu/ctr-search** – search using the number **2018-004387-54**

If more trials are planned, they will appear on the public websites above. When there, search for **LOU064**, **remibrutinib**, or **Sjögren's syndrome**.

Full trial title:
An adaptive Phase 2 randomized double-blind, placebo-controlled multi-center study to evaluate the safety and efficacy of multiple LOU064 doses in patients with moderate to severe Sjögren's Syndrome (LOUiSSe)

? If you participated in the trial and have **questions** about the results, please speak with the trial doctors or staff at your trial site.

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