NOVARTIS

## Clinical Trial Results Summary

# A clinical trial to learn more about the effects and safety of ACZ885 and LNA043 in people with knee osteoarthritis with inflammation

## Thank you!

Thank you to the participants who took part in the clinical trial for knee osteoarthritis with inflammation. Every participant helped the researchers learn more about the trial drugs **ACZ885**, also called canakinumab, and **LNA043**.

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:** CLNA043A12203

**Novartis drugs studied:** **ACZ885**, also called canakinumab, and **LNA043**

**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 and safety of **ACZ885** and **LNA043** when taken alone or together in people with knee osteoarthritis with inflammation.

**Knee osteoarthritis** is a long-term condition in which the cartilage in the knee joint is damaged and wears away over time. When this happens, the bones in the knee joint rub together. This can cause inflammation in the knee, making it difficult and painful to move.

**Cartilage** is the bendable tissue that covers the ends of bones, so they don't rub together. It cushions the bones, like a shock absorber, and helps the knee move smoothly.

**What is inflammation?**
**Inflammation** is part of the body's response to damage or infection. Too much inflammation can be harmful.

The drug **ACZ885** is designed to lower inflammation. **ACZ885** is approved in the United States and other countries to treat conditions related to inflammation, including a type of arthritis in children.

The trial drug **LNA043** is a protein designed to help cartilage grow and heal.

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

- Did LNA043 change the amount of participants' knee cartilage?
- Did ACZ885 change participants' knee pain?
- 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 August 2021 and ended in June 2024. The participants started the trial on different dates.

In December 2023, the sponsor decided to stop adding participants and end the trial early. The decision to stop was not related to safety concerns with **ACZ885** or **LNA043**.

# Who was in this trial?

23 participants with knee osteoarthritis with inflammation received treatment in this trial – 7 men and 16 women. Participants' ages ranged from 52 to 79 years. Their average age was 62 years.

The number of participants by race is shown below.

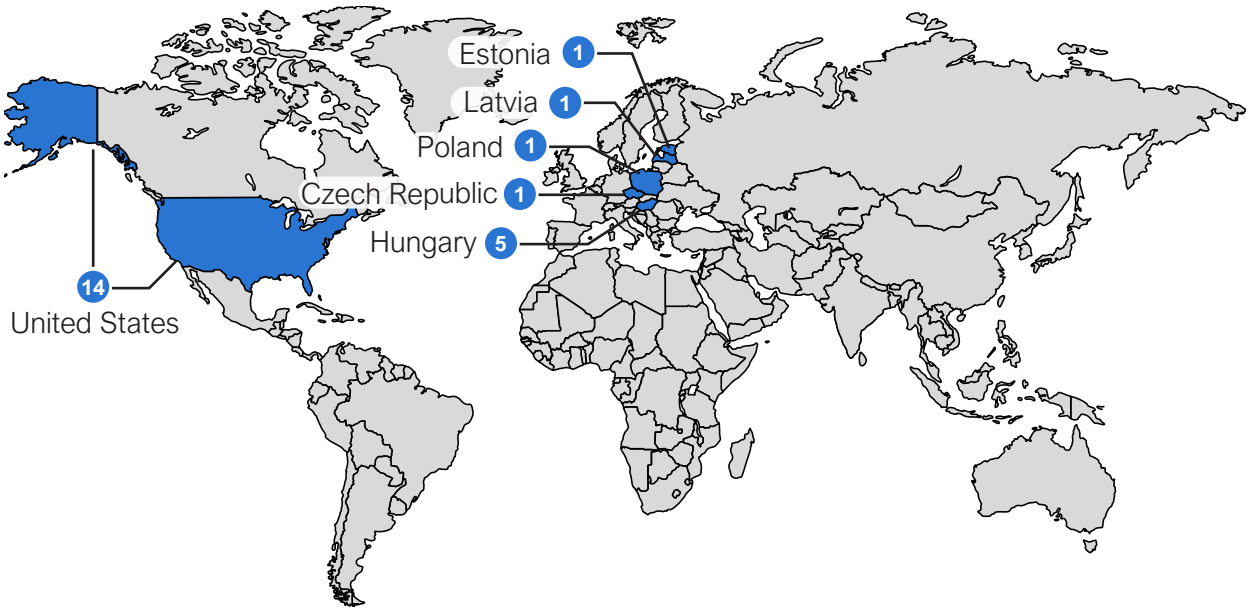
**Race**

| | |
|---|---|
| 1 | Black or African American |
| 1 | Native Hawaiian or other |
| 21 | White |

The participants could take part in this trial if they:

- Had moderate to severe knee pain
- Had a certain level of osteoarthritis visible on x-ray
- Had inflammation in the knee based on magnetic resonance imaging, also called MRI

23 participants from 6 countries received treatment. 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:

**ACZ885** – 600 milligrams (mg) received as an injection into 1 knee joint 1 time on the first day.

**LNA043** – 40 mg received as an injection into 1 knee joint a total of 3 times. The injections were given on weeks 2, 6, and 10.

**Placebo** – received as an injection into 1 knee joint 1 time on the first day of treatment. The **placebo** in this trial looked like **ACZ885** but did not have any drug in it. Using a placebo helps researchers better understand the effect of a trial drug.

All participants could continue to take certain medicines for knee pain, such as acetaminophen, during the trial.

Researchers used a computer to randomly assign participants to a treatment group.

The participants, researchers, and trial staff did not know if the participants were receiving **ACZ885** or **placebo**. 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.

The participants, researchers, and trial staff knew if a participant received **LNA043**. This was because the trial did not include a **placebo** for **LNA043**. The trial was done this way to limit how many injections into the knee joint participants received.

# What happened during this trial?

## Before treatment

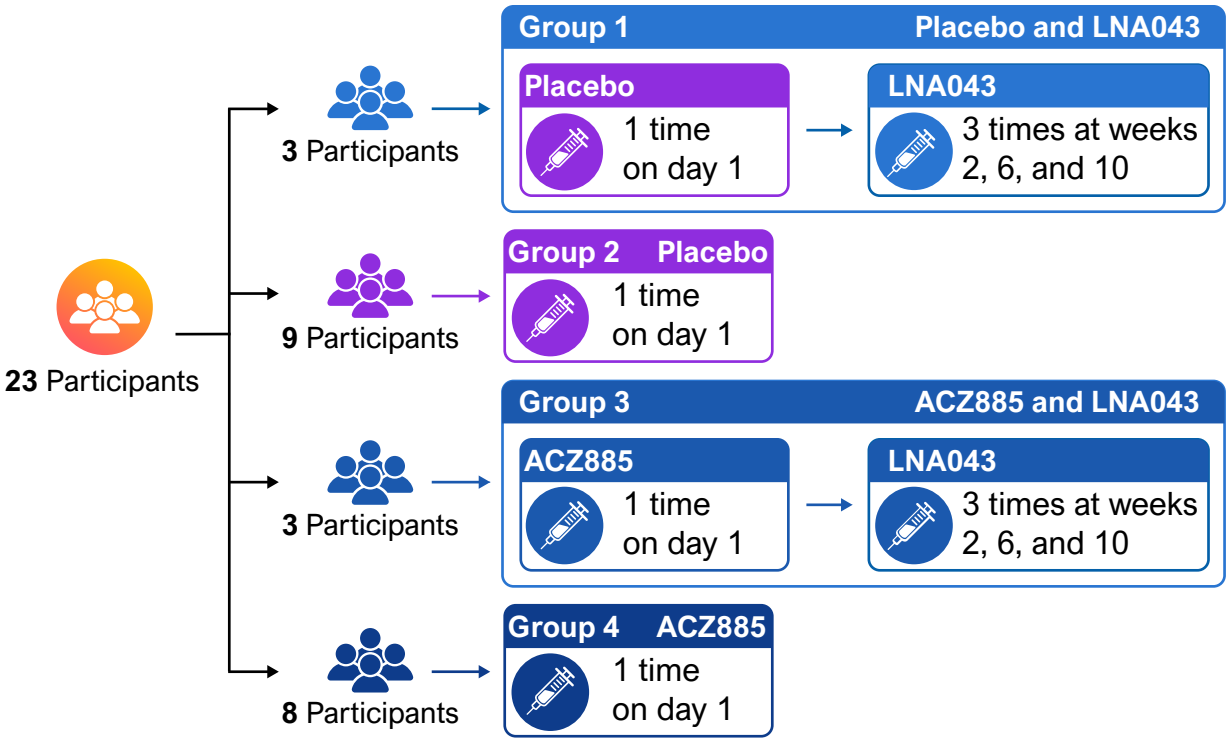
About 6 weeks

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

## During treatment

Up to about 10 weeks

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




## After treatment

Up to about 1 year

Trial staff checked the participants for any medical problems and changes in their knee osteoarthritis for about 1 year after they started treatment.

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

# What were the main results of this trial?

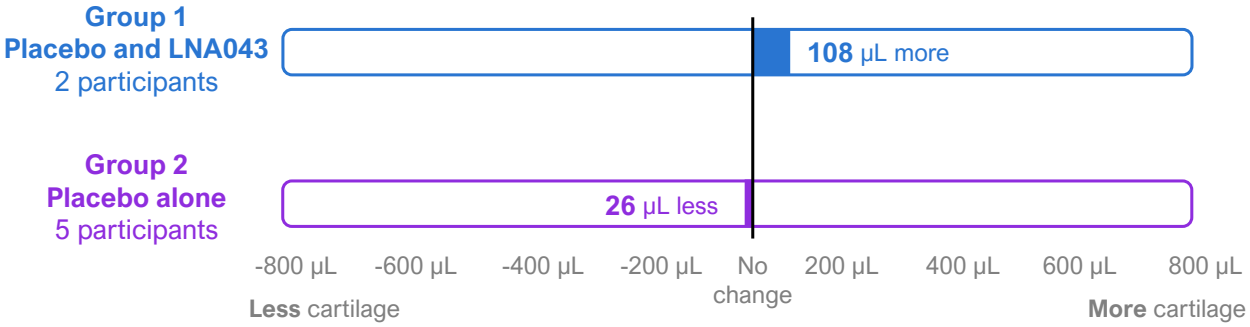
## Did LNA043 change the amount of participants' knee cartilage?

Because the trial ended early, researchers could not conclude if **LNA043** changed the amount of participants' knee cartilage, compared to **placebo** alone.

To learn this, researchers looked at images of participants' knee cartilage using MRI. The researchers measured changes in the amount of participants' cartilage in the inner side of the knee from before treatment to about 6 months after they started treatment. However, there were too few participants for researchers to conclude if **LNA043** changed the amount of participants' knee cartilage.

### Change in the amount of participants' knee cartilage

This graph shows the change in the amount of knee cartilage (measured in microliters or µL) from before treatment to about 6 months after treatment. These results only include participants who had results available.




Because there were too few results, the researchers could not conclude if the change in the amount of knee cartilage was meaningful.

# Did ACZ885 change participants' knee pain?

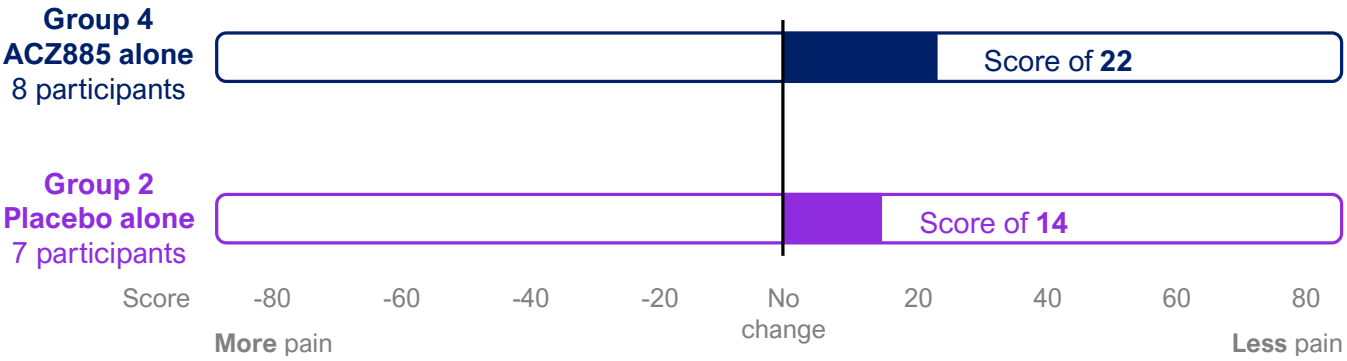
Because the trial ended early, researchers could not conclude if **ACZ885** changed participants' knee pain, compared to **placebo** alone.

To learn this, participants answered questions about their knee pain over the past week at many time points during the trial. Based on their answers, researchers gave them a score. **A higher score meant less knee pain**.

Then, researchers compared the change in each participant's knee pain score based on their answers from before treatment to about 3 months after starting treatment. However, there were too few participants for researchers to conclude if **ACZ885** changed participants' knee pain.

## Change in participants' knee pain score

This graph shows the change in knee pain score from before treatment to about 3 months after treatment. These results only include participants who had results available.




Because there were too few results and results varied, the researchers could not conclude if the change in knee pain score was meaningful.

# What were the other results of this trial?

## Did LNA043, ACZ885, or both affect other measures of participants' knee osteoarthritis?

Because the trial ended early, researchers could not conclude if **LNA043** or **ACZ885** affected other measures of knee osteoarthritis compared to the **placebo** alone. They also could not conclude if **ACZ885 and LNA043** affected certain measures of knee osteoarthritis compared to **placebo** and **LNA043** or **ACZ885** alone.

To learn this, researchers looked at other measures of knee osteoarthritis before and after treatment:

- Knee cartilage amount and thickness using MRI images up to a year after starting treatment
- Participants' answers to questions about their knee pain and ability to complete daily tasks that involved using their knee up to a year after starting treatment
- Inflammation in the knee using a certain type of MRI images 3 months after starting treatment

# 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 up to about 1 year after the start of 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.

Some of the participants (8 of 23) had adverse events. No participants had adverse events that were considered serious. No participants left the trial due to an adverse event. No participants died. The researchers concluded there were no new safety concerns for **ACZ885** and **LNA043** in this trial.

## How many participants had adverse events?

| | Group 1 Placebo and LNA043 3 participants | Group 2 Placebo 9 participants | Group 3 ACZ885 and LNA043 3 participants | Group 4 ACZ885 8 participants |
|---|---|---|---|---|
| Had **any adverse event** | 1 of 3 33% | 2 of 9 22% | 1 of 3 33% | 4 of 8 50% |
| Had at least 1 **serious adverse event** | 0 of 3 0% | 0 of 9 0% | 0 of 3 0% | 0 of 8 0% |
| Had at least 1 **other adverse event** | 1 of 3 33% | 2 of 9 22% | 1 of 3 33% | 4 of 8 50% |
| **Left the trial** due to an adverse event | 0 of 3 0% | 0 of 9 0% | 0 of 3 0% | 0 of 8 0% |
| **Died** | 0 of 3 0% | 0 of 9 0% | 0 of 3 0% | 0 of 8 0% |

## What serious adverse events did the participants have?

No participants had serious adverse events. No participants died.

## What other adverse events did the participants have?

8 participants had other adverse events.

The most common type of other adverse events that happened were infections by bacteria, viruses, or fungus. These occurred in **6** participants, and are shown in the table below. Additional types of other adverse events happened in fewer participants.

| | Group 1 Placebo and LNA043 3 participants | Group 2 Placebo 9 participants | Group 3 ACZ885 and LNA043 3 participants | Group 4 ACZ885 8 participants |
|---|---|---|---|---|
| **Cold sore** Oral herpes | 0 of 3 0% | 0 of 9 0% | 0 of 3 0% | 1 of 8 13% |
| **Common cold** Nasopharyngitis | 0 of 3 0% | 0 of 9 0% | 0 of 3 0% | 1 of 8 13% |
| **COVID-19** | 0 of 3 0% | 0 of 9 0% | 1 of 3 33% | 0 of 8 0% |
| **Infection in the nose, throat, and airways** Upper respiratory tract infection | 0 of 3 0% | 1 of 9 11% | 0 of 3 0% | 0 of 8 0% |
| **Pus filled lump on arm or leg** Abscess limb | 0 of 3 0% | 0 of 9 0% | 0 of 3 0% | 1 of 8 13% |
| **Rash caused by a fungal infection of the skin** Body tinea | 0 of 3 0% | 1 of 9 11% | 0 of 3 0% | 0 of 8 0% |
| **Stuffy nose** Rhinitis | 0 of 3 0% | 0 of 9 0% | 0 of 3 0% | 1 of 8 13% |
| **UTI** Urinary tract infection | 0 of 3 0% | 0 of 9 0% | 0 of 3 0% | 1 of 8 13% |

# What was learned from this trial?

Researchers learned more about the effects and safety of **ACZ885** and **LNA043** when taken alone or together in people with knee osteoarthritis with inflammation.

Because the trial ended early, researchers could not conclude if:

- **LNA043** changed the amount of participants' knee cartilage compared to the **placebo** alone.
- **ACZ885** changed the participants' knee pain compared to the **placebo** alone.
- **LNA043** or **ACZ885** affected other measures of knee osteoarthritis compared to the **placebo** alone.
- **ACZ885 and LNA043** affected certain measures of knee osteoarthritis compared to those who received **placebo** and **LNA043** or **ACZ885** alone.

The researchers concluded there were no new safety concerns for **ACZ885** and **LNA043** in this trial.

When this summary was written, the sponsor had no plans for future trials of **ACZ885** and **LNA043** in people with knee osteoarthritis with inflammation.

# 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:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Accept the terms **I accept** → Search by study number **CLNA043A12203**

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

- **clinicaltrials.gov** – search using the number **NCT04814368**
- **clinicaltrialsregister.eu** – search using the number **2020-003631-21**

Other trials of **ACZ885** and **LNA043** may appear on the public websites above. When there, search for **ACZ885**, canakinumab, or **LNA043**.

**Full clinical trial title:** A randomized, four-arm, canakinumab placebo-controlled, participant, investigator and sponsor-blinded study investigating the safety, tolerability and efficacy of intra-articular canakinumab followed by intra-articular LNA043 in patients with knee osteoarthritis

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