

## Clinical Trial Results Summary

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

## Thank you!

Thank you to the participants who took part in the clinical trial for **knee osteoarthritis**. Every participant helped learn more about the trial drug **LNA043**.

Novartis sponsored this trial. We believe 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:** CLNA043A12202

**Novartis drug studied:** **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.

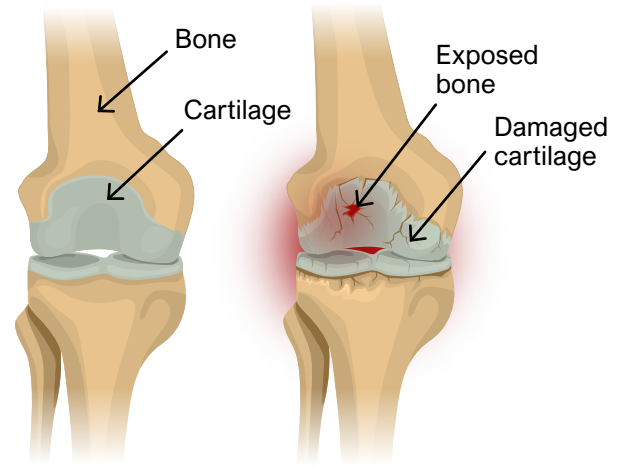
This summary only shows the results of a single clinical trial. Other clinical trials may have different findings.

# What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of **LNA043** in people with **knee osteoarthritis** with moderate to severe pain. To find this out, researchers compared different doses of **LNA043** to a **placebo**.


 **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 rub together, causing swelling, pain and difficulty moving the knee.

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



Normal knee

Knee Osteoarthritis

 **LNA043** is a trial drug designed to help damaged cartilage to grow and heal. It is similar to a protein made by the body called angiopoietin-like 3 that helps cartilage to grow.

A **placebo** looks like the trial drug but does not have any drug in it. Researchers use a **placebo** to better understand the effect of a trial drug.



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

- Did **LNA043** change the knee cartilage thickness of participants after 2 years of treatment compared to placebo?
- 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 May 2021. It was planned that each participant could take part for about 5 years.

However, in November 2024, the sponsor decided to end this trial early after learning that **LNA043** did not show the expected beneficial effects. The decision was not related to any safety concerns with **LNA043**. After this decision was made, the trial officially ended in May 2025.

This trial was designed to have 2 parts:

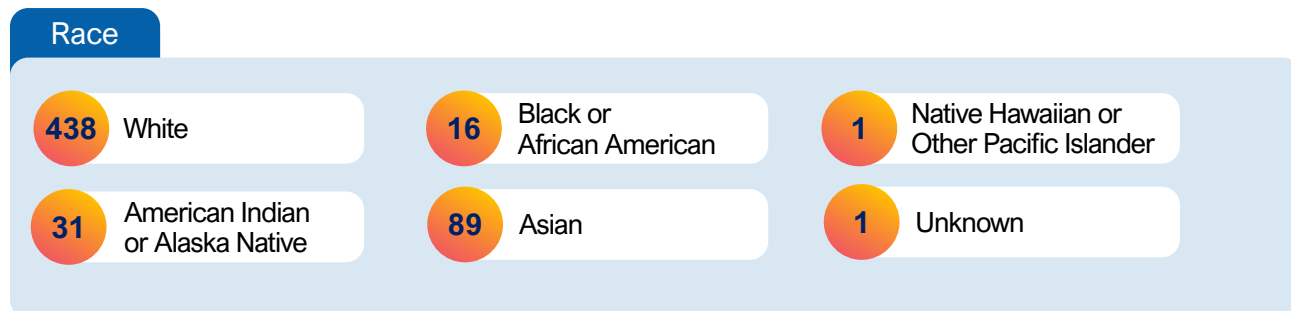
- **Part 1** – participants received either **LNA043** or **placebo** to learn about the effects of **LNA043** over 2 years
- **Part 2** – participants received the same treatment as in Part 1 but less often, to further assess the effects of **LNA043** for an additional 2 years. After the treatment ended, they planned to follow up participants for 1 year. As the trial ended earlier than planned, **Part 2** was not completed

## Who was in this trial?



**576 participants** with **knee osteoarthritis** received treatment in this trial – 222 males and 354 females. Their average age was 60 years.

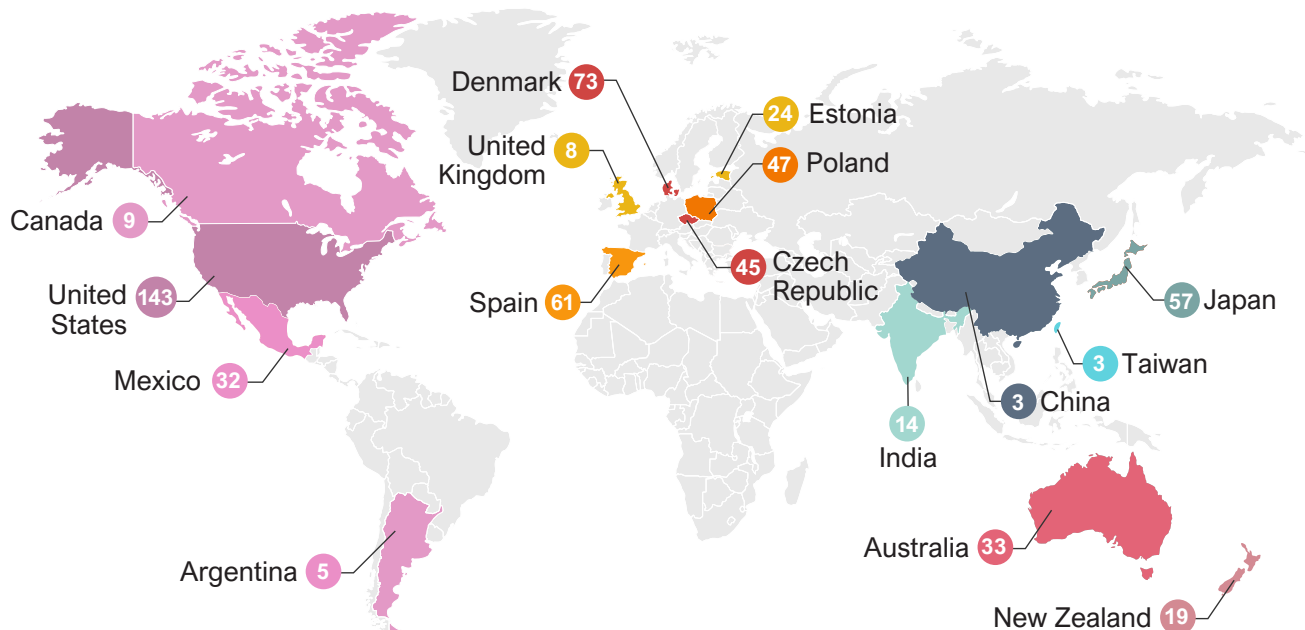
The number of participants by race is shown below:



Participants **could take part** in this trial if they:

- Were aged between 40 and 75
- Had knee osteoarthritis with moderate to severe knee pain for at least 6 months before starting the trial
- Did not have any other problems affecting the knee

**576 participants** from **16 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:



**LNA043:** Participants received **20 or 40 milligrams (mg)** of **LNA043** as injections into the knee joint.



**Placebo:** Received as injections into the knee joint. The **placebo** solution looks like the trial drug but does not have any drug in it. Researchers use a **placebo** to better understand the effect of a trial drug.

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

Researchers used a computer to randomly assign participants to their treatment. Participants were 4 times more likely to receive **LNA043** 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.

# What happened during this trial?

## Before treatment Up to 8 weeks



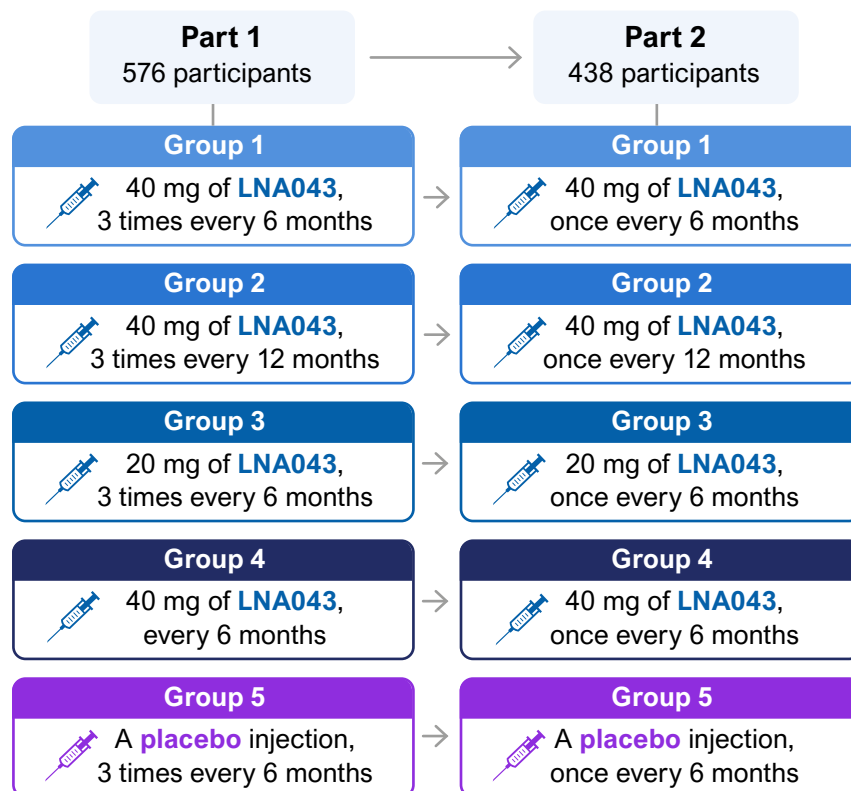
The trial staff checked to make sure the participants could be in this trial.

## During treatment Up to 4 years



A total of 576 participants first entered Part 1 of this trial. They were randomly divided into 5 groups to receive either **LNA043** or **placebo**. The treatment period lasted for 2 years.

At the end of Part 1, participants could join Part 2 of this trial. A total of 438 participants entered Part 2. They continued to receive the same treatment as in Part 1 for another 2 years, given at a different frequency.



All participants received the same number of injections. So, to keep the trial assignments hidden, participants who received **LNA043** in Groups 2 and 4, also received **placebo** on certain days. This helped make sure that no one knew which treatment they were getting, since certain groups were given **LNA043** more often than others.

None of the participants completed 4 years of treatment as the trial ended earlier than planned.

## After treatment 6 months



Trial staff checked participants' general health and for any medical problems for at least 6 months after their last dose of trial treatment.

Trial staff checked participants for their overall health throughout the trial.

# What are the main results of this trial?

## Did LNA043 change the knee cartilage thickness of participants after 2 years of treatment compared to placebo?



The researchers concluded that **LNA043** did not change the participants' knee cartilage thickness, compared to **placebo**.

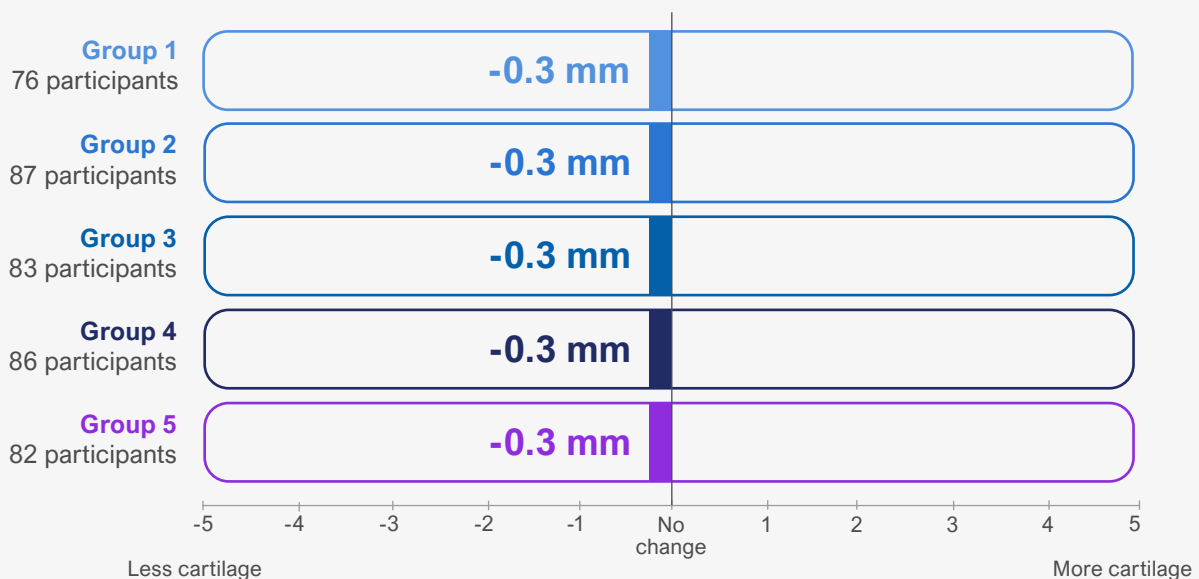
To learn this, researchers looked at images of participants' knee cartilage using magnetic resonance imaging (MRI). They measured changes in the participants' cartilage thickness in the central part of the inner side of the knee from before treatment to 2 years after they started treatment.

Researchers expected to see an increase in the thickness of the knee cartilage after 2 years of treatment, or a reduction in the cartilage loss compared to **placebo**. However, they found that all groups had a similar reduction in the thickness of the knee cartilage after 2 years of treatment.

### Changes in the thickness of participants' knee cartilage

This graph shows the change in the knee cartilage thickness (measured in millimetres or mm) from before treatment to 2 years after they started treatment. These results only include participants who had results available.

Change in thickness of participants' knee cartilage in mm



# 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 do this even if they think the adverse events are not related to the trial treatments.

Researchers need results from many trials to decide if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the day participants started the treatment until up to 6 months 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.



**417 out of 576 participants** had adverse events, including serious and other adverse events.

- **67 participants** had serious adverse events.
- **3 participants** died. These were not considered related to the trial treatment by the trial doctor

The researchers concluded there were no unexpected safety concerns for **LNA043** in this trial.

## What serious adverse events did the participants have?

67 participants had serious adverse events.

The table below shows the most common serious adverse events.

	Group 1 114 participants	Group 2 117 participants	Group 3 116 participants	Group 4 114 participants	Group 5 115 participants
<b>Worsening of osteoarthritis</b>	2 of 114 (2%) 	0 of 117 (0%) 	0 of 116 (0%) 	2 of 114 (2%) 	1 of 115 (1%) 
<b>Bowel cancer</b> Adenocarcinoma of the colon	0 of 114 (0%) 	1 of 117 (1%) 	0 of 116 (0%) 	1 of 114 (1%) 	1 of 115 (1%) 
<b>Breast cancer</b>	0 of 114 (0%) 	1 of 117 (1%) 	1 of 116 (1%) 	0 of 114 (0%) 	1 of 115 (1%) 
<b>Kidney stones</b> Nephrolithiasis	1 of 114 (1%) 	0 of 117 (0%) 	0 of 116 (0%) 	1 of 114 (1%) 	1 of 115 (1%) 

## What other (not including serious) adverse events did the participants have?

The table below shows the most common other adverse events.

	Group 1 114 participants	Group 2 117 participants	Group 3 116 participants	Group 4 114 participants	Group 5 115 participants
<b>Joint pain</b> Arthralgia	17 of 114 (15%) 	24 of 117 (21%) 	21 of 116 (18%) 	28 of 114 (25%) 	27 of 115 (23%) 
<b>COVID-19</b>	27 of 114 (24%) 	20 of 117 (17%) 	16 of 116 (14%) 	15 of 114 (13%) 	14 of 115 (12%) 
<b>Inflammation of the nose and throat</b> Nasopharyngitis	13 of 114 (11%) 	22 of 117 (19%) 	19 of 116 (16%) 	14 of 114 (12%) 	14 of 115 (12%) 
<b>Swelling at the site of injection</b> Injection site joint swelling	10 of 114 (9%) 	9 of 117 (8%) 	8 of 116 (7%) 	8 of 114 (7%) 	3 of 115 (3%) 
<b>Pain at the site of injection</b> Injection site joint pain	6 of 114 (5%) 	8 of 117 (7%) 	9 of 116 (8%) 	6 of 114 (5%) 	4 of 115 (4%) 
<b>Back pain</b>	6 of 114 (5%) 	8 of 117 (7%) 	9 of 116 (8%) 	6 of 114 (5%) 	4 of 115 (4%) 

## What was learned from this trial?

Researchers learned about the effects of **LNA043** in people with **knee osteoarthritis** with moderate to severe pain. The trial ended earlier than planned after researchers learned that **LNA043** did not show the expected benefits. The decision was not related to any safety concerns.

The researchers concluded that:



- **LNA043** did not change the participants' knee cartilage thickness compared to **placebo**
- There were no unexpected safety concerns for **LNA043** in this trial

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

## Where can I learn more about this trial?

To learn more about the results and adverse events in this trial, read the scientific summary of the results. It is available on the Novartis Clinical Trial Results website [www.novctrd.com](http://www.novctrd.com)

Follow these steps to find the scientific summary:



Go to  
[www.novctrd.com](http://www.novctrd.com)



Click  
**Clinical Trial Results**



Accept the terms  
 **I accept**



Search for  
**CLNA043A12202**

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

[clinicaltrials.gov](http://clinicaltrials.gov) – search using the number **NCT04864392**

[euclinicaltrials.eu](http://euclinicaltrials.eu) – search using the number **2023-509937-37-00**

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

**Full clinical trial title:** A 5-year, randomized, double-blind, placebo-controlled, multi-center study assessing the efficacy, safety, and tolerability of intra-articular regimens of LNA043 versus placebo in patients with symptomatic knee osteoarthritis (ONWARDS)



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1-888-669-6682 (US); +41-61-324 1111 (EU)

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