NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of LRX712 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 the researchers learn more about the trial drug **LRX712**.

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: CLRX712A12201

Novartis drug studied: LRX712

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 **LRX712** in people with knee osteoarthritis.

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 knee pain and stiffness, especially when moving.

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.

LRX712 is a trial drug designed to repair and grow cartilage.

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

- Did LRX712 change the amount of participants' knee cartilage?
- 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 July 2020 and ended in January 2025. The participants started the trial on different dates.

At the end of this trial, Novartis created a report of the trial results. This summary is based on that report.

Who was in this trial?

45 participants with knee osteoarthritis received treatment in this trial – 25 males and 20 females. Participants' ages ranged from 43 to 75 years.

The number of participants by race is shown below.

Race

2 Asian	43 White

The participants could take part in this trial if they:

- Had mild to moderate knee osteoarthritis based on X-ray results and could walk without assistive devices, such as a cane
- Had knee pain most days of the week
- Did not have certain surgical treatments for their knee osteoarthritis

This trial took place in the Netherlands.

What treatments did the participants receive?

The treatments in this trial were:

LRX712 – received as an injection into 1 knee joint a total of 3 times. The injections were given on day 1, week 4, and week 8. This trial looked at 3 doses of **LRX712**:

- **Low dose LRX712** – 15 milligrams (mg)
- **Medium dose LRX712** – 25 mg
- **High dose LRX712** – 75 mg

Placebo – received as an injection into 1 knee joint a total of 3 times. The injections were given on day 1, week 4, and week 8. The **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.

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

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.

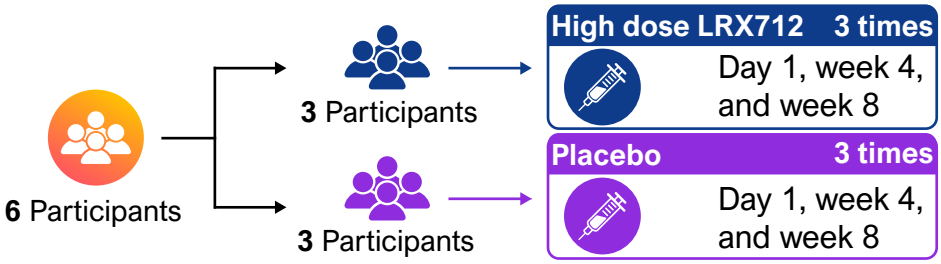
What happened during this trial?

Before treatment — Up to 7 weeks

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

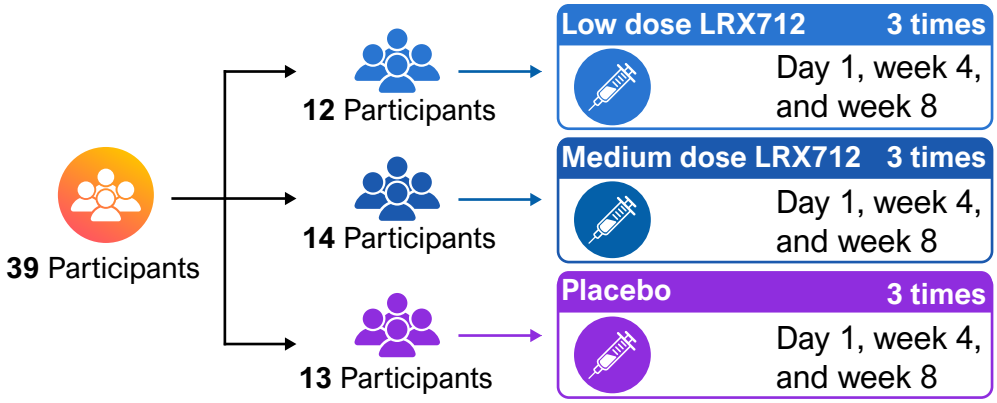
During treatment — About 8 weeks

At the start of this trial, the first 6 participants were assigned to **high dose LRX712** or **placebo**. The graphic below shows how many participants were assigned to each treatment.



Participants who received the **high dose of LRX712** reported more certain medical problems, such as swelling or pain where the injection was given, compared to those who received **placebo**. Because of this, the sponsor paused the trial to review the data and stopped giving participants the **high dose of LRX712**.

When the sponsor restarted the trial, the next 39 participants were assigned to **low dose LRX712**, **medium dose LRX712**, or **placebo**. The graphic below shows how many participants were assigned to each treatment.



After treatment — Up to about 10 months

Trial staff checked participants for up to about 10 months after their last dose of trial treatment for:

- Any medical problems
- Changes in their knee osteoarthritis

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

What were the main results of this trial?

Did LRX712 change the amount of participants' knee cartilage?

The change in the amount of participants' knee cartilage was about the same for those who received the **low dose of LRX712** or **medium dose of LRX712** compared to **placebo**. The researchers concluded the difference between **low dose LRX712** and **medium dose LRX712** compared to **placebo** was not meaningful.

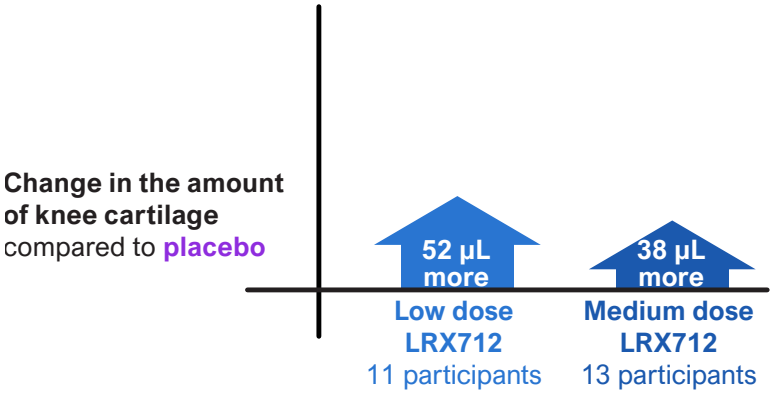
To learn this, researchers looked at images of participants' knee cartilage using MRI. The researchers measured changes in the amount of participants' cartilage in the inner side of the knee from before treatment to about 7 months after starting treatment.

What is MRI?
MRI, also called **magnetic resonance imaging**, takes detailed images of the inside of the body using magnetic fields.

They compared the change for participants who received the **low dose of LRX712** or **medium dose of LRX712** to participants who received **placebo**. Since only a small number of participants received the **high dose of LXR712**, their results were not included.

Change in the amount of participants' knee cartilage compared to placebo

This graph shows the change in the amount of knee cartilage (measured in microliters or µL) from before treatment to about 7 months after starting treatment compared to **placebo**. These results only include participants who had results available.



What were the other results of this trial?

Did LRX712 change other measures of knee osteoarthritis?

Participants who received the **low dose of LRX712** or **medium dose of LRX712** had no change in:

- Signs of knee cartilage health compared to **placebo**
- The amount or thickness of their knee cartilage compared to **placebo**

To learn this, researchers looked at:

- **Changes in the amount of ^{23}Na (sodium) in knee cartilage**, which is a sign of cartilage health. Researchers measured ^{23}Na in participants' MRI images of the knee at about 4, 7, and 12 months after starting treatment. They compared the change for participants who received the **low dose of LRX712** or **medium dose of LRX712** to participants who received **placebo**.
- **Changes in the amount and thickness of the participants' knee cartilage using MRI images**. They compared the change for participants who received the **low dose of LRX712** or **medium dose of LRX712** to participants who received **placebo** at 4, 7, and 12 months after starting treatment.

Since only a small number of participants received the **high dose of LXR712**, their results were not included in these measures.

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 day participants started the trial treatment until about 10 months 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.

Almost all the participants (44 of 45) had adverse events. 3 participants had serious adverse events. No participants died. 1 participant left the trial due to an adverse event. The researchers concluded there were no safety concerns for the **low dose of LRX712** and **medium dose of LRX712** in this trial. Researchers stopped giving participants the **high dose of LRX712** due to certain adverse events such as swelling or pain where the injection was given.

What serious adverse events did the participants have?

3 participants had serious adverse events during the follow-up period after the last dose of treatment.

- **Breast cancer** (**low dose LRX712**)
- **Broken bones** | multiple fractures (**placebo**)
- **Heart attack** | myocardial infarction (**medium dose LRX712**)

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

44 participants had other adverse events.

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

	Treatment				Follow-up			
	Low dose LRX712 12 participants	Medium dose LRX712 14 participants	High dose LRX712 3 participants	Placebo 16 participants	Low dose LRX712 12 participants	Medium dose LRX712 14 participants	High dose LRX712 3 participants	Placebo 16 participants
Headache	5 of 12 42%	8 of 14 57%	1 of 3 33%	12 of 16 75%	0 of 12 0%	1 of 14 7%	0 of 3 0%	2 of 16 13%
Joint pain Arthralgia	5 of 12 42%	2 of 14 14%	0 of 3 0%	4 of 16 25%	3 of 12 25%	2 of 14 14%	0 of 3 0%	4 of 16 25%
Swelling or pain where injection was given Injection site reaction	2 of 12 17%	1 of 14 7%	3 of 3 100%	4 of 16 25%	0 of 12 0%	0 of 14 0%	0 of 3 0%	0 of 16 0%
Joint stiffness	3 of 12 25%	7 of 14 50%	0 of 3 0%	0 of 16 0%	0 of 12 0%	0 of 14 0%	0 of 3 0%	0 of 16 0%
Unpleasant feeling in arm or leg Limb discomfort	1 of 12 8%	2 of 14 14%	0 of 3 0%	3 of 16 19%	0 of 12 0%	0 of 14 0%	0 of 3 0%	0 of 16 0%
Common cold Nasopharyngitis	1 of 12 8%	1 of 14 7%	0 of 3 0%	3 of 16 19%	0 of 12 0%	0 of 14 0%	0 of 3 0%	0 of 0 0%

What was learned from this trial?

Researchers learned about the effects and safety of **LRX712** in people with knee osteoarthritis.

The researchers concluded that, compared to those who received the **placebo**, participants who received the **low dose of LRX712** or **medium dose of LRX712** had:

- No meaningful change in the amount of knee cartilage 7 months after starting treatment
- No change in signs of knee cartilage health up to 12 months after starting treatment
- No change the amount or thickness of knee cartilage up to 12 months after starting treatment

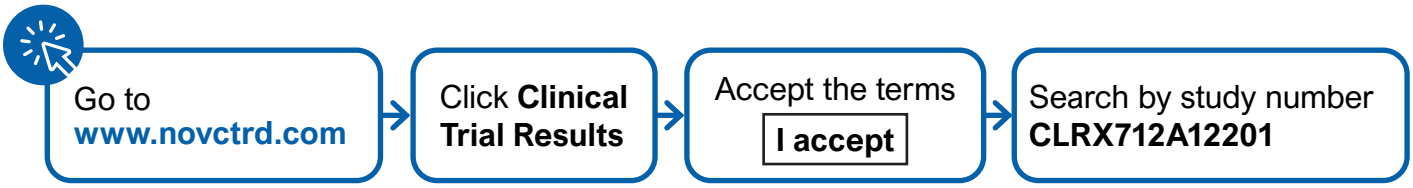
The researchers concluded there were no safety concerns for the **low dose of LRX712** and **medium dose of LRX712** in this trial. Researchers stopped giving participants the **high dose of LRX712** due to certain adverse events such as swelling or pain where the injection was given.

When this summary was written, Novartis had no plans for future trials of **LRX712** in people with knee osteoarthritis.

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 **NCT04097379**
- **clinicaltrialsregister.eu** – search using the number **2019-002963-92**

Other trials of **LRX712** may appear on the public websites above. When there, search for **LRX712**.

Full clinical trial title: A randomized, placebo-controlled, subject and investigator blinded study investigating the safety, tolerability and preliminary efficacy of 8-week treatment with intra-articular LRX712 to regenerate articular cartilage in patients with mild/moderate knee osteoarthritis

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

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