Clinical Trial Results Summary

NOVARTIS

A clinical trial to learn about the safety of trial drug LRX712 for people with osteoarthritis

Thank you!

Thank you to the participants who took part in the clinical trial for the drug **LRX712**. All of the participants helped the researchers learn more about how safe LRX712 is to take.

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. An independent organization prepared this summary of the trial results.

We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CLRX712X2101
Drug studied: LRX712
Sponsor: Novartis

You can find **more information** about this trial by going to the websites listed on **page 9** of this summary.

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

This trial at a glance

What was the purpose of this trial? Read more on **page 3**

The purpose of this trial was to learn about the safety of different doses of the trial drug LRX712. This was the first time people received LRX712. LRX712 is designed to be a possible treatment for osteoarthritis, also called OA.

The main question this trial was designed to answer:

- What medical problems did the participants have in this trial? Keeping track of the participants' medical problems helped to learn about the safety of LRX712.

Who was in this trial? Read more on **page 3**

- 42 men and women were in this trial
- Each participant had OA in at least one knee

What treatments did the participants receive? Read more on **page 4**

Participants received one of these treatments as an injection (shot) in one knee:

- **LRX712** – one of 7 dose levels
  - The first participants received the lowest dose of LRX712, and the later participants received higher doses
- **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.

What were the main results of this trial? Read more on **page 6**

The clinical trial team found no serious safety concerns during this trial. Most of the participants who received LRX712 had at least one short-term medical problem. The most common medical problem was pain at the injection site. All participants completed this trial.

This trial had other results along with the main results. Read more on **page 8**

What was the purpose of this trial?

Researchers are looking for better ways to treat **osteoarthritis**. Osteoarthritis, also called OA, is the most common form of arthritis. OA happens when the protective tissue between bones, called cartilage, wears down over time. This can make the joints painful, swollen, and hard to move. Although OA can happen in almost any joint, it's most common in larger joints, such as the hip and knee. Right now, there is no cure for OA, so many patients need joint replacement surgery to help ease the symptoms.

LRX712 is a trial drug designed to possibly help the body repair the cartilage worn down by OA. This trial was the first time people received LRX712. It focused on the safety of LRX712 for people with OA in their knee.

Before a drug can be approved for doctors to prescribe, researchers do many clinical trials to find out how safe it is and how well it works.

This trial was designed to answer these questions:

- What medical problems did the participants have in this trial?
  Keeping track of the participants' medical problems helped to learn about the safety of LRX712.
- How much and how fast did LRX712 get into the participants' blood?

Who was in this trial?

42 participants were in this trial – 29 women and 13 men. Everyone was 30 to 66 years old. Their average age was 57.

Every participant in this trial had mild to moderate OA in at least one knee, based on an x-ray.

This trial took place in the Netherlands.

For more information about who could and could not be in this trial, and the participants in this trial, visit novctrd.com. Use trial number **CLRX712X2101** to find the scientific summary.

What treatments did the participants receive?

A computer program was used to randomly assign each participant to 1 of 7 groups. In each group, they received one of these treatments:

- **LRX712**: one of 7 dose levels
- **Placebo**: a 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.

Using a computer program to assign the treatments helped make sure the results were compared as fairly as possible.

The participants received one dose of their treatment as an injection (shot) in one knee.

The participants, the trial doctor, and the trial nurse did not know what treatment each participant received during each group. Some clinical trials are done this way because knowing what treatment participants get can influence the results. Not knowing what treatment participants get helps make sure the results are looked at fairly.

How did the groups receive the treatments in this trial?

1. In Group 1, the trial doctor gave one participant the lowest dose of LRX712 and one participant the placebo. Neither the participants nor the trial doctor knew who received which treatment.
2. The trial doctor then checked for any safety concerns in these participants.
3. If there were no safety concerns, the rest of the participants in Group 1 received their assigned treatment.
4. The trial doctor checked for safety concerns again before Group 2 started.
5. This continued for all 7 groups.

What happened during this trial?

The trial began in November 2017 and ended in March 2019. All participants completed this trial. The chart on the next page shows how this trial was done.

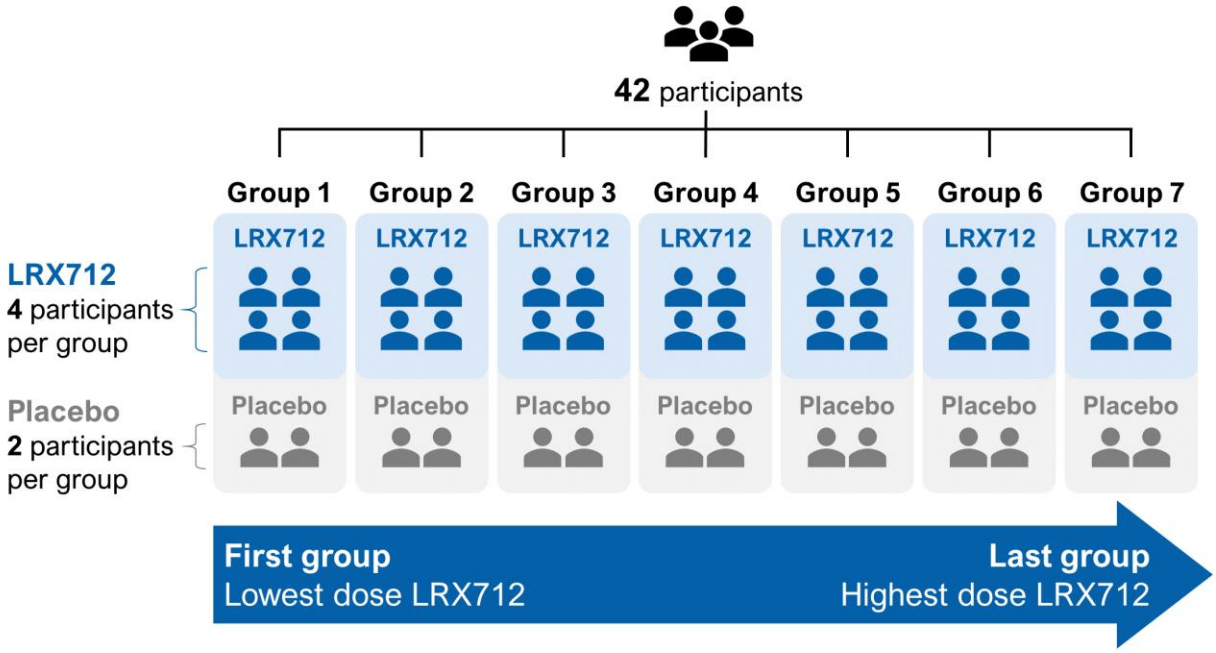
Here's how this trial was done:

Before treatment

- The trial doctor checked participants' health to make sure they could be in this trial
- The participants had an x-ray to measure the severity of OA in their knee

During treatment

- The participants received one dose of their assigned treatment as an injection in one knee
- The trial doctor checked for any safety concerns before the next group received treatment



After treatment

- The participants stayed at the trial site for 4 days so that the trial staff could closely check their health and take blood and urine samples
- The participants visited the trial site 5 times over the next 28 days for trial staff to check their health and take blood and urine samples
- The trial staff checked the participants' health over the phone 60 days after 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.

What medical problems did participants have during the trial?

Medical problems that happen during clinical trials are called “adverse events”. An **adverse event** is any unwanted sign or symptom that participants have during a trial. An adverse event is 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. Many trials are needed to know if a drug or treatment causes an adverse event. Trial doctors keep track of all adverse events that happen in trials, even if they do not think the adverse events might be related to the trial treatments.

The clinical trial team found no serious safety concerns during the trial. Most of the adverse events were short-term. The most common adverse event was pain at the injection site.

Trial doctors looked for any adverse events when the participants visited the trial site and when they checked the participants’ blood and urine samples. The participants also reported adverse events.

Participants who had adverse events during this trial

Participants who had:	LRX712 Groups 1-7 Out of 28 participants	Placebo Groups 1-7 Out of 14 participants
Serious adverse events	0% — 0 of 28	0% — 0 of 14
Non-serious adverse events	96% — 27 of 28	50% — 7 of 14
Left this trial due to adverse events	0% — 0 of 28	0% — 0 of 14

What serious adverse events happened?

During this clinical trial, no serious adverse events were reported, including deaths.

What non-serious adverse events happened?

Most of the participants reported an adverse event that was not serious. The table below shows the adverse events that happened to **3 or more participants**. Other adverse events happened in fewer participants.

For more information about all the adverse events visit novctrd.com. Use clinical trial number **CLRX712X2101** to find the scientific summary.

Non-serious adverse events

Percent of participants: 0% 7% 25% 50% 75%	LRX712 (out of 4 participants per group)							Placebo (out of 14 participants)
	Lowest dose → Highest dose							
	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	Group 7	Groups 1-7
Pain at the injection site (knee)	0	**75%** (3)	**25%** (1)	0	**50%** (2)	**75%** (3)	0	**7%** (1)
Back pain	**25%** (1)	0	**25%** (1)	0	**50%** (2)	0	**50%** (2)	0
Headache	0	**25%** (1)	**25%** (1)	**25%** (1)	0	**25%** (1)	**25%** (1)	**7%** (1)
Trouble moving the joint at the injection site	0	0	0	**25%** (1)	0	**50%** (2)	**50%** (2)	0
Swelling at the injection site	0	**25%** (1)	**25%** (1)	0	0	**50%** (2)	0	**7%** (1)
Feeling sick to the stomach Nausea	0	**25%** (1)	0	**25%** (1)	**25%** (1)	0	0	0
High blood pressure Hypertension	0	0	**25%** (1)	0	**25%** (1)	**25%** (1)	0	0
Joint pain at the injection site	0	0	0	0	0	0	**75%** (3)	0
Joint pain Arthralgia	0	0	0	**25%** (1)	**25%** (1)	0	0	**7%** (1)
Stiff muscles Musculoskeletal stiffness	0	**25%** (1)	0	0	**25%** (1)	0	0	**7%** (1)

What other results were learned?

How much and how fast did LRX712 get into the participants' blood?
To answer this question, trial staff measured the levels of LRX712 when they took samples of the participants' blood throughout the trial.

The clinical trial team found that:

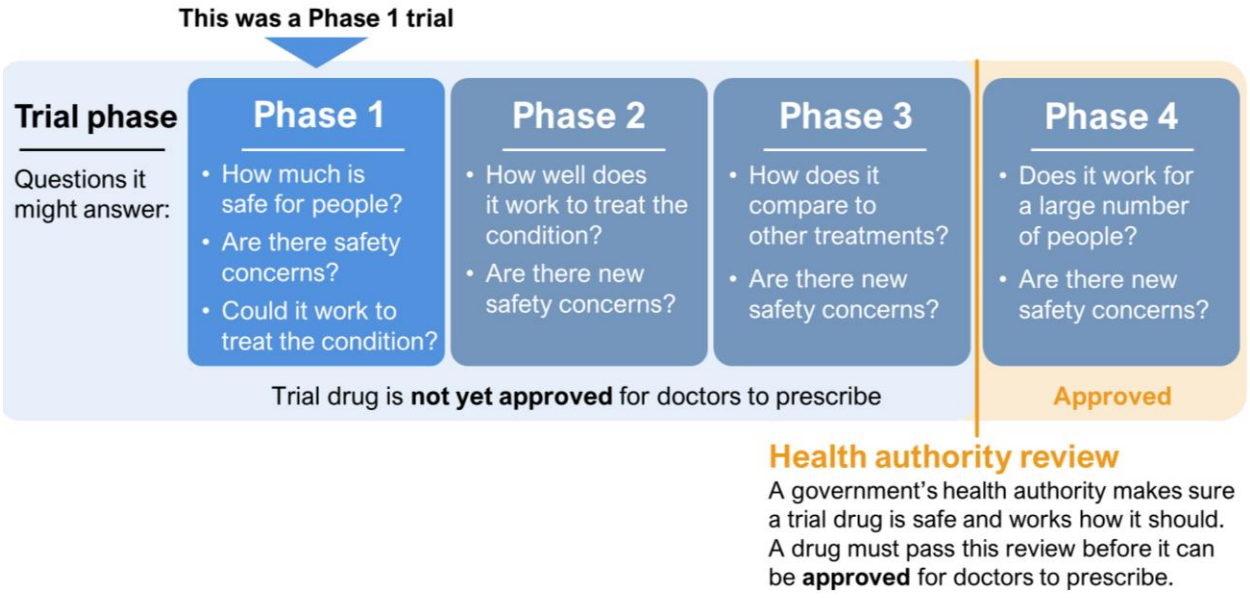
- For the participants who received lower doses (Groups 1 – 3), LRX712 reached its highest level in their blood 4 to 6.5 hours after they received it
- For the participants who received higher doses (Groups 4 – 7), LRX712 reached its highest level in their blood 14 to 24 hours after they received it
- The participants who received higher doses of LRX712 had higher average levels of LRX712 in their blood over 28 days

What was learned from this trial?

This was the first trial to learn about the safety of LRX712 for people. The clinical trial team concluded that LRX712 was safe for the participants in this trial.

The team also learned about how much and how fast LRX712 got into the participants' blood. These results can help to decide how much and how often someone may need to take a treatment.

This was a **Phase 1** clinical trial that was designed to learn about the safety of a trial drug in a small number of people. A drug must go through many phases of clinical trials before it can be approved for doctors to prescribe. The chart below shows these phases and what questions they're designed to answer.



The results presented here are for one clinical trial. One trial cannot give a complete picture of the benefits and risks of a trial drug. The results of many trials are needed to find out which treatments can be used for people with osteoarthritis. This summary shows only the main results from this trial. Other trials may provide new information or different results.

Where can I learn more about this and future clinical trials?

This is a summary of the results for one trial.

You can find detailed results and more information about this trial on the Novartis Clinical Trial Results website:

1. Visit novctrd.com
2. Click on “Clinical trial results and trial summary for patients” at the top right of the page
3. Read and scroll down, then click “I accept” to agree to use the information and the website
4. Select “Search by study number” on the bottom left of the page
5. Type **“CLRX712X2101”** in the search box and click search

If you would like to view the website in a language other than English, you can click the “Google Translate” button on the top right of the page.

If you were in this trial and have questions about the results, please speak with the doctor or staff at your trial site.

This clinical trial was registered on the following website:

- ClinicalTrials.gov: https://clinicaltrials.gov/

  To find this trial, type **CLRX712X2101** in the **Other terms** search box

Full trial title:

A randomized, placebo controlled, subject and investigator blinded, first-in-human single ascending dose study to evaluate the safety, tolerability, and pharmacokinetics after intraarticular injection of LRX712 into the knee of osteoarthritic patients.

If more clinical trials are planned, they will appear on the public websites listed above or at www.novartisclinicaltrials.com. When there, search for **LRX712.**

Thank you!

Novartis would like to thank all of the people who participated in this clinical trial. The participants made this clinical trial possible and helped researchers answer important health questions and learn about a possible medical treatment. Many volunteers and many clinical trials are needed to advance medical science.

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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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