

Clinical Trial Results Summary

A trial to learn more about how LNA043 works and about its safety in people with cartilage damage in the knee

Research Sponsor: Novartis

Drug Studied: LNA043

Trial Number: CLNA043X2201

Thank you!



Thank you to the participants who took part in the clinical trial for the trial drug LNA043. All of the participants helped the researchers learn more about how LNA043 works and how safe it is.

Novartis sponsored this trial and reviewed the results of the trial when it ended. We at Novartis believe 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.



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

You can find more information about this trial on the websites listed on the last page of this summary.

Overview of this trial



What was the purpose of this trial?

This clinical trial was designed to learn more about the safety of a trial drug called LNA043. It was also designed to learn about how LNA043 affected knee cartilage. Healthy cartilage has 2 substances called collagen and glycosaminoglycans, also called GAG.

The main questions the researchers wanted to answer in this trial were:

- Did LNA043 increase the amount of collagen and GAG in the knee cartilage?
- Did LNA043 cause other changes to the knee cartilage?
- What medical problems did the participants have during the trial?

Keeping track of the participants' medical problems helped the researchers learn about the safety of LNA043.



Who was in the trial?

- 14 men and women with cartilage damage in their knee participated in this clinical trial.
- Each participant needed a type of knee surgery called autologous chondrocyte implantation, also known as ACI surgery.



What treatments did the participants receive?

During this trial, the participants received LNA043 or a placebo.

A placebo looks like a trial drug but does not have any trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.



What were the main results of the trial?

Overall, the researchers learned that:

- Both treatment groups had an increase in collagen and GAG levels in the knee cartilage after treatment. But, the researchers could not conclude that LNA043 affected the collagen or GAG levels any more than the placebo.
- Yet, more cartilage grew back in the area where the cartilage was removed at Week 4 in the participants who received LNA043 compared to those who received the placebo.
- The newly grown cartilage had similar characteristics compared to healthy cartilage.
- 57.1% of the participants had medical problems during this trial. None of the medical problems were serious and none caused a participant to leave the trial. The most common medical problems were headache and nausea.

What was the purpose of the trial?



Researchers are looking for a better way to treat patients with cartilage damage. Before a treatment can be approved for patients to receive, researchers do clinical trials to find out how safe it is and how it works. In this trial, the researchers studied how the trial drug called LNA043 affected the participants' knee cartilage. The researchers also studied the safety of LNA043.

Cartilage is a layer of firm, smooth tissue found between certain joints in the body, like the knee joint. The knee joint connects the upper leg bone to the lower shin bone. As people get older and put more stress on their bodies, this cartilage loses its smoothness. The 2 bones in the knee joint may start rubbing against each other. This can stiffen the joint and make movement painful.

Healthy cartilage in the knee has 2 substances called collagen and glycosaminoglycans, also called GAG. Collagen provides structure, and GAG helps cushion the joint from impact due to walking or other activities. When cartilage gets damaged, GAG and collagen are also damaged. When this happens, the body helps to fix the damage by making cells that produce new cartilage. But, the body is not always able to fix the damage on its own. The trial drug, LNA043, is designed to act like a protein in the body that helps the cartilage heal by causing cells in the joint to make GAG and collagen. The researchers wanted to find out if LNA043 increased the amount of GAG and collagen found in the participants' knee cartilage.

The main questions the researchers wanted to answer in this trial were:

- Did LNA043 increase the amount of collagen and GAG in the knee cartilage?
- Did LNA043 cause other changes to the knee cartilage?
- What medical problems did the participants have during the trial?

Who was in the trial?



To answer the questions in this trial, the researchers asked for the help of 14 men and women:

- Everyone in the trial was 23 to 46 years old when they joined. The average age of the participants was 34 years.
- Each participant had cartilage damage in their knee.
- Each participant was also scheduled to have autologous chondrocyte implantation surgery, also known as ACI surgery.

The ACI surgery is a procedure doctors sometimes use to repair damaged knee cartilage. The ACI surgery involves removing a small piece of the knee cartilage to help repair the damaged area. In this trial, the researchers wanted to find out if LNA043 could help the cartilage heal in the area where the small piece of cartilage was removed.

The trial took place in Austria.

What treatments did the participants receive?



The clinical trial team used a computer program to randomly assign the treatment each participant received. This helped make sure that comparing the results of the treatments was as fair as possible.

The chart below shows the treatments the participants received.

	LNA043	Placebo
	<ul style="list-style-type: none">9 participants received LNA043 at a dose of 20 milligrams, also known as mg	<ul style="list-style-type: none">5 participants received the placebo
	<ul style="list-style-type: none">Through a needle into the knee joint, also known as an injection	
	<ul style="list-style-type: none">1 time	

A placebo looks like the trial drug but does not have any trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial treatment.

During this trial, none of the participants, trial staff, or sponsor staff knew what treatment each participant received. Some trials are done this way because knowing what treatment the participants are receiving can influence the results. Not knowing what treatment participants receive helps make sure the results are looked at fairly.

What happened during the trial?

The trial started in October 2017 and ended in April 2019. Each participant was in the trial for up to about 34 weeks.

The researchers stopped this trial early because the sponsor had enough information to understand how LNA043 worked in the participants. The decision to stop the trial was not related to safety.

The chart below shows what happened during the trial.



Before the participants received treatment

The trial doctors checked the participants' health to make sure they could be in the trial.

Up to 6 weeks



While receiving treatment

There were 2 parts of the ACI surgery. During the first part of the surgery, the trial doctors:

- removed a small piece of the knee cartilage
- injected either LNA043 or the placebo into the knee joint

1 dose of trial treatment



After the participants received the treatment

The participants had the second part of surgery about 4 weeks later, and the trial doctors took a cartilage sample.

Throughout the trial, the participants:

- had pictures of their knee taken using MRI
- had blood, urine, and joint fluid taken
- had their overall health checked and answered questions about how they were feeling

Up to 28 weeks

What were the results of the trial?

This is a summary of the overall results from this trial. The individual results of each participant might be different and are not in this summary.

The results from several trials are needed to decide which treatments are safest and work best. Other trials may provide new information or different results. Always talk to a doctor before making any changes to your healthcare.

Did LNA043 increase the amount of collagen and GAG in the knee cartilage?



Both treatment groups had an increase in collagen and GAG levels in the knee cartilage after treatment. But, the researchers could not conclude that LNA043 increased the amount of collagen and GAG in the knee cartilage more than the placebo.

To answer this question, the trial doctors took pictures of each participant's knee using magnetic resonance imaging, also known as MRI. In these pictures, the researchers could see how much GAG was in the knee cartilage.

They measured how much GAG was in the area where a small piece of cartilage was removed during the first surgery. This was also where LNA043 was injected during the first surgery. The researchers compared the amount of GAG in that area to the amount of GAG in a healthy part of the cartilage. Increased GAG levels would mean increased regrowth of cartilage in the knee.

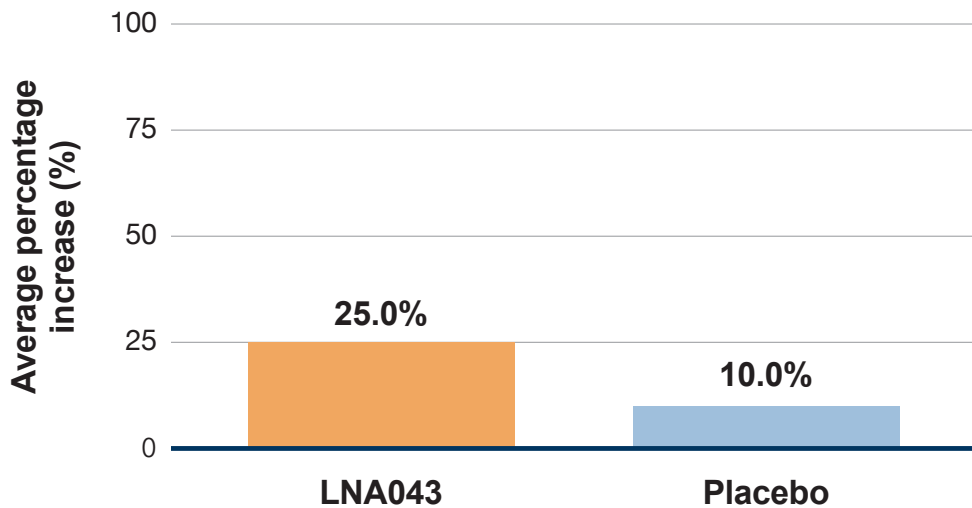
The researchers found that the level of GAG increased in both the participants who received LNA043 and those who received the placebo. But, the difference in the results of each treatment was small. The researchers could not conclude that LNA043 affected the GAG levels any more than the placebo.

The researchers found that 4 weeks after treatment, the GAG levels in the cartilage increased by an average of:

- 25.0% in the participants who received LNA043
- 10.0% in the participants who received the placebo

The chart below shows these results 4 weeks after treatment.

Average percentage increase in GAG levels in the knee cartilage



Researchers checked the levels of GAG again at 12 and 28 weeks after treatment. They found that GAG levels in the participants who received LNA043 were similar to the participants who received the placebo.

The researchers also used MRI pictures to look at how collagen was organized in the cartilage where LNA043 was injected. The researchers compared the collagen in that area to an area of healthy cartilage. This was done several times during the trial, including at 4, 12, and 28 weeks after treatment.

Overall, the researchers found that the MRI pictures did not show a difference in how collagen was organized between the participants who received LNA043 and those who received the placebo.

Did LNA043 cause other changes to the knee cartilage?



The researchers found that more cartilage grew back in the area where the cartilage was removed at Week 4 in the participants who received LNA043 compared to those who received the placebo. Overall, the researchers found that the newly grown cartilage had similar characteristics compared to healthy cartilage.

- The researchers also used MRI pictures to measure how much cartilage grew back in the area where a small piece of cartilage was removed during the first surgery. The amount of cartilage in this area was measured 4, 12, and 28 weeks after treatment. They found that more cartilage grew back in the participants at Week 4 who received LNA043 compared to the participants who received the placebo.
- The researchers looked at different characteristics of the cartilage sample that was taken during the second surgery. They compared this sample to healthy cartilage. For each characteristic the researchers looked at, no difference was found between the cartilage sample and the healthy cartilage. This was true no matter what treatment the participants received.

What medical problems happened during the trial?

Medical problems that happen in 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 it results in death.

Adverse events may or may not be caused by the treatments in the trial. A lot of research is needed to know whether a treatment causes an adverse event. Doctors keep track of all the adverse events that happen in trials, even if they do not think the adverse events might be related to the treatments.

This section is a summary of the adverse events that happened during this trial.



57.1% of the participants had adverse events during this trial. None of the adverse events were serious and none caused a participant to leave the trial. The most common adverse events were headache and nausea.

Participants who had adverse events

Adverse events in this trial					
		LNA043 (Out of 9 participants)		Placebo (Out of 5 participants)	
Adverse events	44.4%	<div><div></div></div>	(4 out of 9)	80.0%	<div><div></div></div> (4 out of 5)
Serious adverse events	0.0%	<div><div></div></div>	(0 out of 9)	0.0%	<div><div></div></div> (0 out of 5)
Left the trial or stopped receiving treatment due to adverse events	0.0%	<div><div></div></div>	(0 out of 9)	0.0%	<div><div></div></div> (0 out of 5)

What were the most common serious adverse events?

During this trial, none of the participants had serious adverse events.




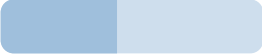

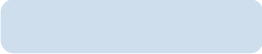

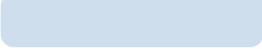

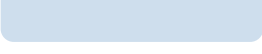





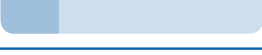



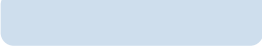




None of the participants died during this trial.

What were the adverse events?

The most common adverse events during this trial were headache and nausea. Both adverse events happened in 14.3% of the participants. This was 2 out of 14 participants for each adverse event.

The table below shows the adverse events that happened in this trial.

Adverse events in this trial

	LNA043 (Out of 9 participants)		Placebo (Out of 5 participants)	
Headache	22.2% (2)		0.0% (0)	
Nausea	0.0% (0)		40.0% (2)	
Joint pain (Arthralgia)	11.1% (1)		0.0% (0)	
Bruise (Contusion)	11.1% (1)		0.0% (0)	
Fall	11.1% (1)		0.0% (0)	
Flu-like illness (Influenza-like illness)	11.1% (1)		0.0% (0)	
Decreased range of motion in the joints	0.0% (0)		20.0% (1)	
Common Cold (Nasopharyngitis)	0.0% (0)		20.0% (1)	
Thyroid lump (Thyroid mass)	0.0% (0)		20.0% (1)	
Deeper bruising from some kind of injury (Traumatic hematoma)	11.1% (1)		0.0% (0)	
Urinary tract infection	0.0% (0)		20.0% (1)	
Suddenly feeling off balance (Vertigo)	11.1% (1)		0.0% (0)	

For more information about the adverse events in this trial, please see the scientific summary that can be found on the websites noted at the end of the summary.

What was learned from this trial?

The information described above helped researchers learn more about LNA043 and its safety in participants with knee cartilage damage who needed ACI surgery. Based on the results of this trial, researchers are continuing to look at whether LNA043 can be a possible treatment for cartilage damage.

More research is needed to figure out which treatments can be used for patients with cartilage damage in the knee. This summary shows only the main results from this one trial. Other trials may provide new information or different results.

Where can I learn more about this trial?



More information about the results of this trial can be found in the scientific results summary available on the Novartis Clinical Trial Results website.

- Go to www.novctrd.com.
- Once on the site, click **“Clinical trial results and trial summary for patients”** at the top right of the page.
- After accepting the terms, go to the bottom left of the page and click **“Search by study number”**.
- Type **“CLNA043X2201”** into the keyword 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 participated in the trial and have questions about the results, please speak with the trial doctor or staff at your trial site.

You can find more information about this trial on the websites listed below.

- www.clinicaltrials.gov Once you are on the website, type “**CLNA043X2201**” into the “**Other terms**” search box, and click “**Search**”.
- www.clinicaltrialsregister.eu Once you are on the website, click “**Home and Search**”, then type “**CLNA043X2201**” in the search box, and click “**Search**”.

If more clinical trials are planned, they will be listed on the above public websites or www.novartisclinicaltrials.com. Search for “**LNA043**” or “**osteoarthritis**”.

Full trial title: A randomized, placebo-controlled, patient and investigator blinded, single dose, Proof of Concept study investigating the safety, tolerability and preliminary efficacy of intra-articular LNA043 in regenerating the articular cartilage of the knee at donor sites in patients undergoing autologous chondrocyte implantation

Protocol number: CLNA043X2201

Thank you!

Clinical trial participants belong to a large community of participants around the world. They help researchers answer important health questions and study new medical treatments.



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