

Clinical Trial Results Summary

A clinical trial to learn more about the safety and effects of RHH646 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 to learn more about the trial drug **RHH646**.

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: CRHH646A12201

Novartis drug studied: **RHH646**

Sponsor: Novartis

..... If you were a participant and have any questions about the results, please talk to your 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 more about the safety and effects of **RHH646** for 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 condition causes knee pain and stiffness, especially when moving the knee.

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.



RHH646 is a trial drug created to repair and grow cartilage.



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

- Did RHH646 change the amount of participants' knee cartilage?
- What medical problems, also called adverse events, happened during this trial?

↳ **Adverse events** reported are any sign or symptom that participants had during this trial. Adverse events **may** or **may not** be caused by treatments in this trial.

How long was this trial?



The trial began in May 2023 and ended in February 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?



82 participants with **knee osteoarthritis** received treatment in this trial – 31 males and 51 females. Participants' ages ranged from 42 to 75 years. Their average age was 62 years.

The table below shows the number of participants by race.



The participants could take part in this trial if they:

- Had mild to moderate knee osteoarthritis based on X-ray results
- Had knee pain at least 3 days of the week for 3 months that needed to be treated with medicines, such as ibuprofen or acetaminophen
- Did not have certain surgical treatments for their knee osteoarthritis

82 participants from 5 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:



RHH646 – 75 milligrams (mg) taken by mouth as capsules once a day.



Placebo – taken by mouth as capsules once a day. It 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.

Along with the treatments above, participants could continue to take other medicines for knee osteoarthritis, such as ibuprofen or acetaminophen.

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 6 weeks



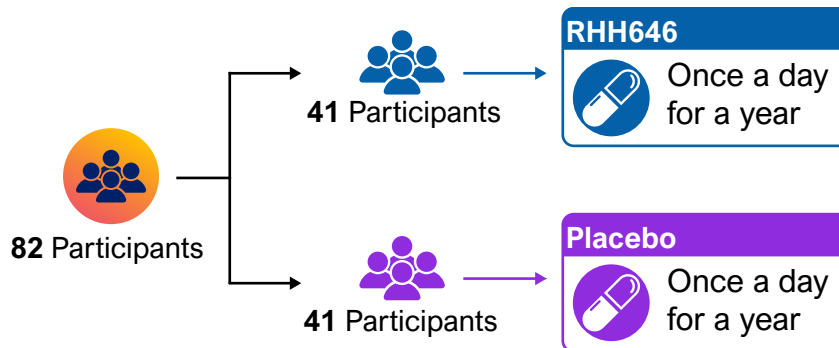
The trial staff checked to make sure the participants could be in this trial.

During treatment

1 year



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



After treatment

About 1 month



Trial staff checked participants for any medical problems for about 1 month after their last dose of trial treatment.

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

What were the main results of this trial?

Did RHH646 change the amount of participants' knee cartilage?



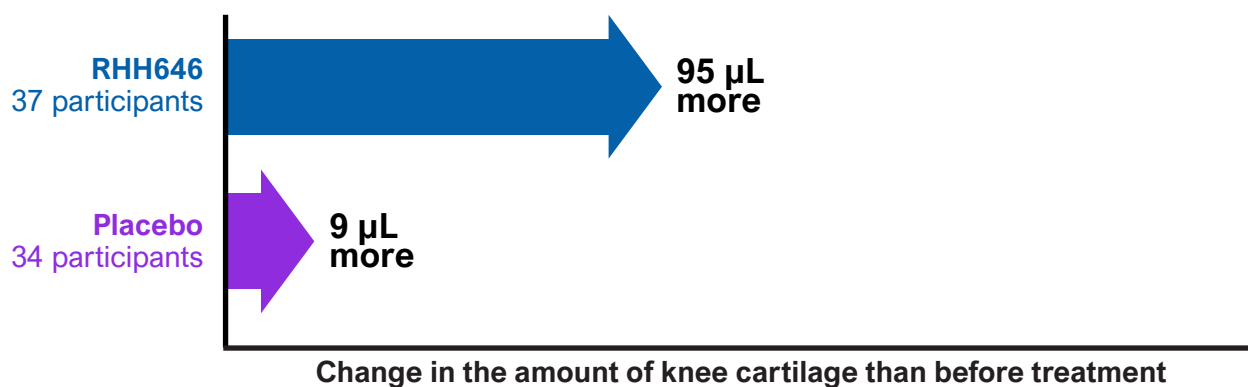
Participants who took **RHH646** had slightly more knee cartilage compared to those who took **placebo**. However, the researchers could not conclude if the difference between the treatment groups was meaningful.

To learn this, researchers used magnetic resonance imaging, or MRI, to look at images of participants' knee cartilage. The researchers measured changes in the amount of participants' cartilage in the inner side of the knee from before treatment to 1 year after starting treatment.

They compared these changes in participants who took **RHH646** to participants who took **placebo**.

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 after 1 year of treatment. These results only include participants who had results available.



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 trial treatment until 1 month after 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, requires hospital care, or results in death

Treatments in the trial **may** or **may not** cause adverse events.

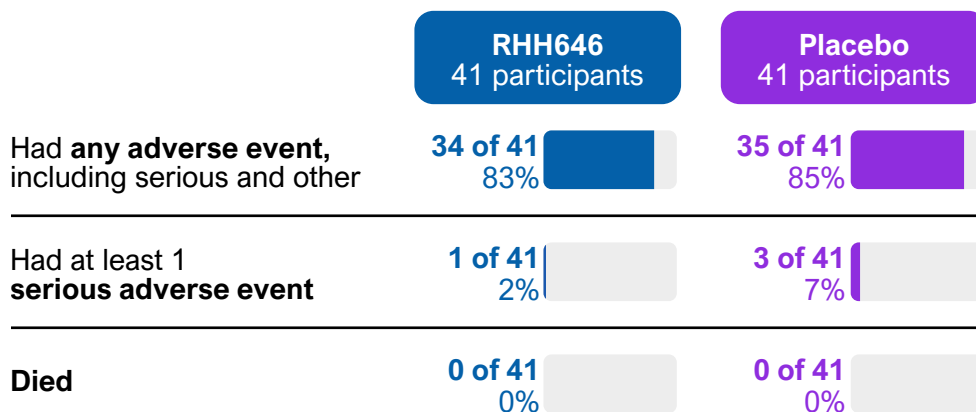


69 out of 82 participants had adverse events, including serious and other adverse events.

- 4 participants had serious adverse events
- No participants died

The researchers concluded there were no new safety concerns for **RHH646** in this trial.

How many participants had adverse events?



What serious adverse events did the participants have?

4 participants had serious adverse events.

1 participant who took **RHH646** had 2 serious adverse events:

- **Injured foot** | Limb injury
- **Infection after surgery** | Post-operative wound infection

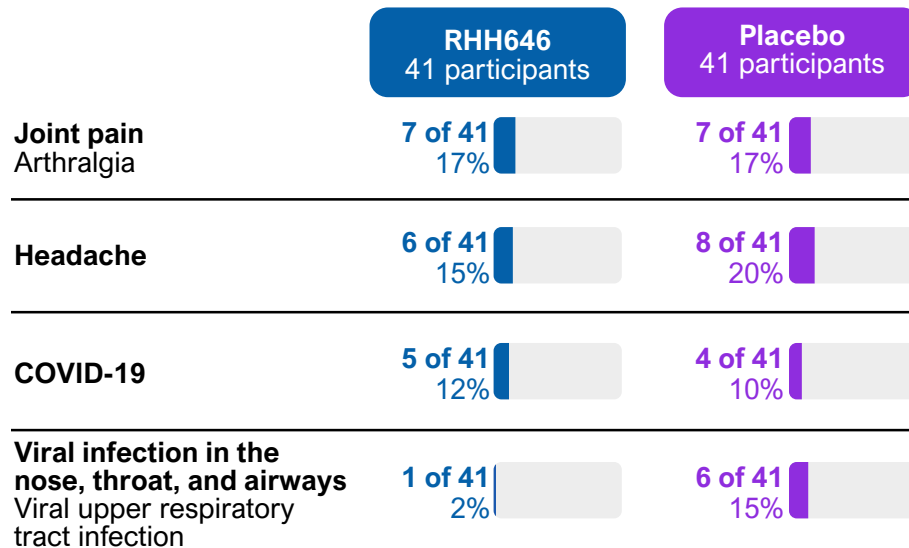
3 participants who took **placebo** had serious adverse events. These serious adverse events happened in 1 participant each:

- **Bacterial skin infection** | Erysipelas
- **Infection in the colon** | Large intestine infection
- **Torn meniscus (cartilage) in the knee** | Meniscus injury

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

69 participants had other adverse events.

The table below shows the most common other adverse events that happened in **7 or more** participants. Additional other adverse events happened in fewer participants.



What were the other results of this trial?

How much RHH646 got into the blood?



Overall, the researchers found that the level of **RHH646** in the blood was what they expected. It took about a month for **RHH646** to reach a steady level in blood.

To learn this, the trial staff took many blood samples from each participant during the trial to measure the level of **RHH646**. This allowed the researchers to learn that the level of **RHH646** in the participants' blood stayed about the same over time until the end of treatment.

Researchers can use these results to decide how often and how much **RHH646** to give in future trials.

What was learned from this trial?

Researchers learned about the safety and effects of **RHH646** in people with **knee osteoarthritis**.



The researchers concluded that:

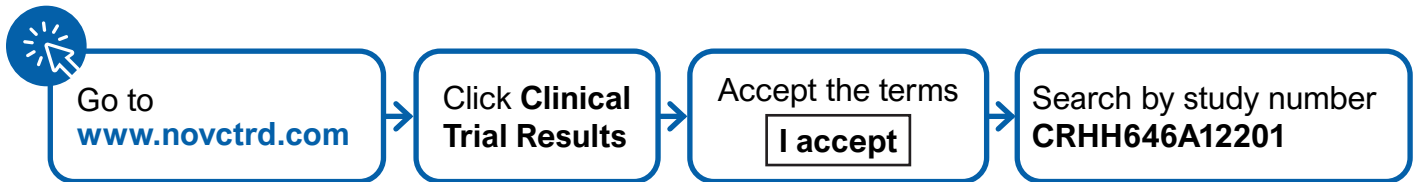
- Participants who took **RHH646** had slightly more knee cartilage compared to those who took **placebo**. However, the researchers could not conclude if the difference between the treatment groups was meaningful.
- There were no new safety concerns for **RHH646** in this trial.
- The level of **RHH646** in the blood was what they expected. It took about a month for **RHH646** to reach a steady level in blood. The level of **RHH646** in the blood stayed about the same over time until the end of treatment.

When this summary was written, Novartis was considering next steps for **RHH646**.

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

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 **NCT05816395**
- euclinicaltrials.eu – search using the number **2022-502821-16**

Other trials of **RHH646** may appear on the public websites above. When there, search for **RHH646**.

Full clinical trial title: A randomized, placebo controlled, investigator and participant-blinded study investigating safety, tolerability, and efficacy of RHH646 in participants with knee osteoarthritis



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

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