NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects and safety of QUC398 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 **QUC398**.

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: CQUC398A12201

Novartis drug studied: QUC398

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 about the effects and safety of **QUC398** 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. This can cause knee pain and stiffness, especially when moving.

Cartilage is the flexible 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.

QUC398 is a trial drug created to block a protein that breaks down cartilage. By blocking this protein, the trial drug could slow cartilage damage and lessen knee pain.

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

- Did QUC398 change participants' knee pain?
- 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 November 2022 and ended in April 2025. The participants started the trial on different dates.

The trial ended earlier than planned due to a business decision. This decision was because there was enough data for researchers to know that **QUC398** did not have enough of an effect on participants' knee pain. This decision was not due to safety concerns with **QUC398**.

Even though the trial ended early, Novartis is committed to providing a report of results. This summary is based on that report.

Who was in this trial?

101 participants with **knee osteoarthritis** received treatment in this trial – 43 males and 58 females. Participants' ages ranged from 40 to 78 years. Their average age was 64 years.

The table below shows the number of participants by race.

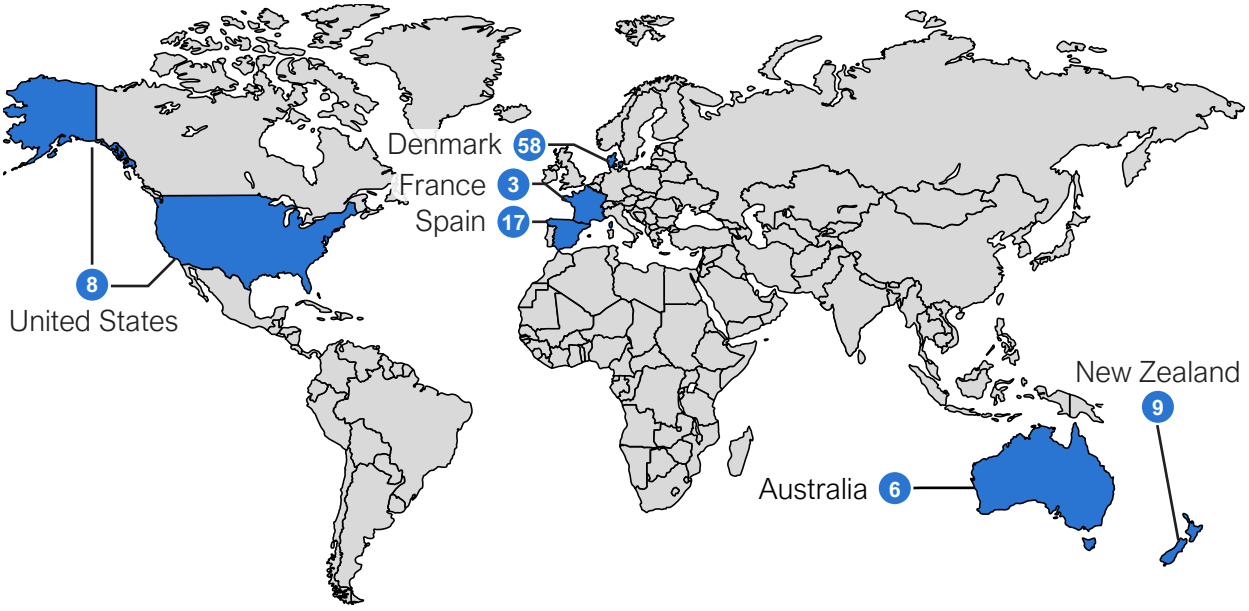
Race

3	Black or African American	1	Native Hawaiian or Other Pacific Islander	97	White

The participants could take part in this trial if they:

- Had knee osteoarthritis based on X-ray results
- Had moderate to severe knee pain for most days in the past 3 months before they joined the trial
- Did not have certain heart problems

101 participants from 6 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:

QUC398 – 300 milligrams (mg), which was received as injections under the skin once every month.

Placebo – which was received as injections under the skin once every month. It looks like the trial drug but does not have any trial drug in it. Researchers use a placebo to better understand the effect of a trial drug.

Along with the treatments above, participants could take acetaminophen, also known as paracetamol, with or without codeine for their knee pain. Participants could also take anti-inflammatory medicines, such as ibuprofen, at certain times during the trial if needed.

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

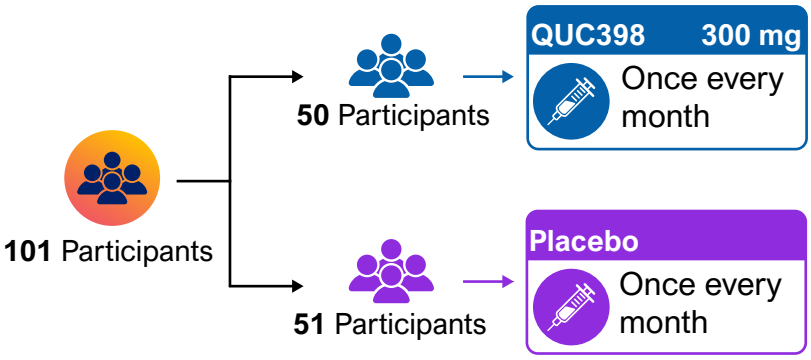
About 6 weeks

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

During treatment

Up to 1 year

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



After treatment

About 2 months

Trial staff checked participants for any medical problems for up to 2 months 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 QUC398 change participants' knee pain?

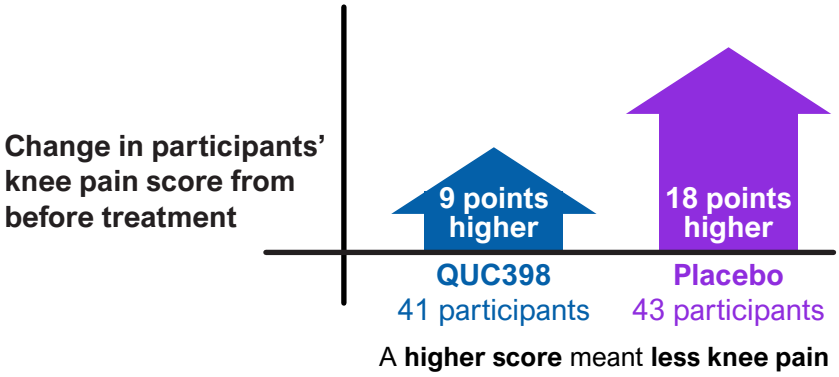
Researchers concluded that **QUC398** did not have enough of an effect on participants' knee pain compared to **placebo** after 3 months of treatment. Because of this, the trial ended early.

To learn this, participants answered questions about their knee pain at many time points during the trial. Based on their answers, researchers scored their pain level. **A higher score meant less knee pain**.

Then, researchers compared the change in each participant's knee pain score from before treatment to after 3 months of treatment.

Change in participants' knee pain score from before treatment to after 3 months of treatment

The graph below only shows results from participants who met all of the trial requirements.



What were the other results of this trial?

Did QUC398 affect other measures of knee osteoarthritis?

Researchers concluded that **QUC398** did not have enough of an effect on other measures of participants' knee pain and knee osteoarthritis symptoms compared to **placebo**.

Because the trial ended early, researchers could not fully conclude if **QUC398** affected the amount of cartilage in participants' knees.

To learn this, researchers looked at the participants' and trial doctors' answers to questions about participants':

- Knee pain severity and how often they felt it
- Other knee symptoms, such as stiffness and swelling
- Ability to complete daily tasks, such as climbing stairs and sitting
- Ability to play sports or do other activities
- Quality of life, including mental health

They measured how much the participants' answers changed over time.

They also looked at MRI images to measure the amount of cartilage in participants' knees. **MRI**, also called **magnetic resonance imaging**, takes detailed images of the inside of the body using magnetic fields.

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 start of treatment until about 2 months after each participant's 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, requires hospital care, or results in death

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

91 out of 101 participants had adverse events, including serious and other adverse events.

- 6 participants had serious adverse events
- No participants died

The researchers concluded there were no safety concerns for **QUC398** in this trial.

What serious adverse events did the participants have?

6 participants had 1 or more serious adverse events.

The table below shows the serious adverse events that happened.

	QUC398 50 participants	Placebo 51 participants
Broken bone in the leg Lower limb fracture	**0 of 50** 0%	**1 of 51** 2%
Chest pain	**0 of 50** 0%	**1 of 51** 2%
Fainting Syncope	**1 of 50** 2%	**0 of 51** 0%
Heart attack Acute myocardial infarction	**0 of 50** 0%	**1 of 51** 2%
Lung cancer that spread Lung cancer metastatic	**1 of 50** 2%	**0 of 51** 0%
Tear in the large intestine Diverticular perforation	**0 of 50** 0%	**1 of 51** 2%
Type of skin cancer Basal cell carcinoma	**0 of 50** 0%	**1 of 51** 2%
Type of skin cancer Squamous cell carcinoma	**0 of 50** 0%	**1 of 51** 2%

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

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.

	QUC398 50 participants	Placebo 51 participants
Pain or swelling where the injection was given Injection site reaction	**23 of 50** 46%	**5 of 51** 10%
Common cold Nasopharyngitis	**7 of 50** 14%	**11 of 51** 22%
Flu Influenza	**6 of 50** 12%	**10 of 51** 20%
Joint pain Arthralgia	**3 of 50** 6%	**10 of 51** 20%
Flu-like illness Influenza like illness	**8 of 50** 16%	**4 of 51** 8%
Knee osteoarthritis that got worse Osteoarthritis	**10 of 50** 20%	**2 of 51** 4%
Headache	**4 of 50** 8%	**3 of 51** 6%

What was learned from this trial?

Researchers learned about the effects and safety of **QUC398** in people with **knee osteoarthritis**.

The trial ended earlier than planned due to a business decision. This decision was because there was enough data for researchers to know that **QUC398** did not have enough of an effect on participants' knee pain. This decision was not due to safety concerns with **QUC398**.

Based on early results from this trial, researchers concluded that **QUC398** did not have enough of an effect on:

- Knee pain compared to **placebo**
- Other measures of knee osteoarthritis symptoms and knee pain compared to **placebo**

Because the trial ended early, researchers could not conclude if **QUC398** affected the amount of cartilage in participants' knees.

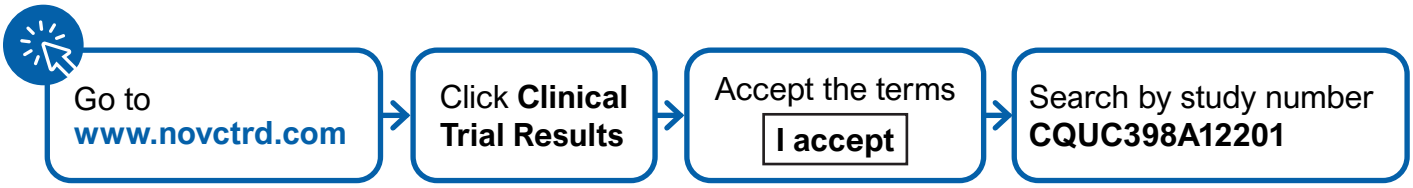
The researchers concluded there were no safety concerns for **QUC398** in this trial.

When this summary was written, the sponsor had no plans for future trials of **QUC398** 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**

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 **NCT05462990**
- **euclinicaltrials.edu** – search using the number **2023-509274-28**

Other trials of **QUC398** may appear on the public websites above. When there, search for **QUC398**.

Full clinical trial title: A randomized, two-arm, placebo-controlled, participant, investigator and sponsor-blinded, proof-of-concept study investigating the efficacy, safety and tolerability of QUC398 in patients with symptomatic knee osteoarthritis

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