NOVARTIS

Clinical Trial
Results Summary

A clinical trial to learn about the effects of OTQ923 in people with sickle cell disease

Thank you!

Thank you to the participants who took part in the clinical trial for **sickle cell disease**. Every participant helped the researchers learn more about the trial therapy **OTQ923**.

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: CADPT03A12101

Novartis therapy studied:
OTQ923 (ADPT03)

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 of **OTQ923** in people with severe complications of **sickle cell disease**. This was the first time that **OTQ923** had been given to people.

Red blood cells carry a protein called hemoglobin, which helps deliver oxygen to the body. **Sickle cell disease** is a common genetic condition that is passed down from parents. In this condition, there is an abnormality in the genetic code for hemoglobin. This produces abnormal hemoglobin called **sickle hemoglobin** causing red blood cells to become stiff and shaped like a crescent or sickle. These cells can block blood flow, causing pain, fatigue, and low levels of red blood cells (anaemia). Over time, they may damage organs like the lungs, brain, and kidneys, leading to serious problems such as chest pain, stroke, and severe painful episodes (vaso-occlusive crises).

OTQ923 is a trial therapy that works by changing a gene in a person's blood **stem cells.** Doctors collected stem cells from a person's blood. Then they changed (modified) these cells in the laboratory. These modified cells, the **OTQ923**, were given back to the person, which help the body make hemoglobin and increase the amount of **fetal hemoglobin**, a type of blood protein. This extra **fetal hemoglobin** prevents **sickle hemoglobin** from clumping together and blocking blood vessels.

Stem cells are unique cells inside the body that can divide repeatedly and mature into different cell types, including different types of blood cells.

Previous research has shown that people who have higher levels of **fetal hemoglobin**, may have fewer or no symptoms of **sickle cell disease**.

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

- How long did it take for the participants' **neutrophil** count to recover after receiving **OTQ923** therapy?
  - ↳ **Neutrophils** are a type of white blood cell that help the body fight infections.
- How much **fetal hemoglobin** was present in the participants' blood 6 months after receiving **OTQ923** therapy?
- 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 August 2020 and ended early in January 2025. The sponsor decided to stop the trial earlier than planned due to business reasons. The decision was not due to any safety concerns with **OTQ923**.

This trial was designed to have 2 parts:

- **Part 1**: Adult participants received **OTQ923**.
- **Part 2**: Researchers planned to include children in this part. However, the trial ended early, and **Part 2** did not open for participant enrollment.

After this trial ended, participants joined another long-term safety follow-up trial (CADPT03A12001).

Who was in this trial?

4 participants with **sickle cell disease** received treatment in this trial – 2 men and 2 women. Participants' ages ranged from 18 to 24 years. Their average age was 21 years.

The participants could take part in this trial if they:

- had serious complications of **sickle cell disease**, such as 3 or more severe painful episodes (vaso-occlusive crises) in about 2 years
- had taken a medicine called hydroxyurea but it did not work, or were not able to take it due to medical problems, or chose not to take it
- were able to manage self-care and do most of their daily activities

All participants were from the United States and were African American.

What treatment did the participants receive?

The treatment in this trial was **OTQ923**.

Participants received **OTQ923** once as an infusion into a vein.

Before receiving **OTQ923**, participants received standard treatment called a **conditioning regimen**. This treatment helps prepare the body to make new blood cells. The trial doctor chose the **conditioning regimen** to be given to the participants.

The participants, researchers, and trial staff knew that all participants received **OTQ923**.

What happened during this trial?

Before treatment

Up to 1 and a half years

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

Participants taking hydroxyurea, were asked to stop treatment for at least 2 months. They also received monthly red blood cell transfusions, a procedure in which a person is given healthy red blood cells from a donor.

The trial doctor collected stem cells from the participant's blood. These stem cells were sent to a lab where their genes producing **fetal hemoglobin** were modified, to enable them to make **fetal hemoglobin**. After stem cell collection, participants either continued blood transfusions or restarted hydroxyurea based on their doctor's advice.

During treatment

About 2 months

All participants received busulfan, a treatment used to clear out their old **stem cells** in the bone marrow.

After a gap of at least 1 day, participants received **OTQ923**, the modified **stem cells**, as an infusion into a vein.

Participants stayed at the hospital until their blood tests confirmed that participants had started producing new blood cells**,** including **neutrophils**.

After treatment

Up to 2 years

Participants returned to the hospital for weekly check-ups during the first 2 months. They then returned:

- every month during the next 4 months,
- every 2 months during the next 6 months,
- and then every 3 months for the next 1 year.

After about 1 to 2 years in this trial, participants moved into a long-term safety follow-up trial (CADPT03A12001), in which they are being monitored for any medical condition up to a total of 15 years after **OTQ923** administration.

What were the main results of this trial?

How long did it take for the participants' neutrophil count to recover after receiving OTQ923 therapy?

It took an average of **23 days** for participants' **neutrophil** count to recover after receiving treatment with **OTQ923**. Participants' **neutrophils** were considered recovered if their levels stayed above 500 cells per microliter (µL)* of blood for 3 days in a row.

*A **neutrophil** count above 500 µL of blood means that the changed **stem cells** have reached the bone marrow and started making new blood cells.

Neutrophils are a type of white blood cell that help the body fight infections.

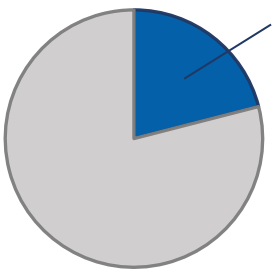
To answer this question, researchers took blood samples from participants after they received **OTQ923** therapy. They checked the participants' **neutrophil** count and how long it took for the body to start making enough **neutrophils** after treatment. This meant the changed **stem cells** had started working.

Participants' neutrophil count recovered on an average by Day 23

How much fetal hemoglobin was present in the participants' blood 6 months after receiving OTQ923 therapy?

Six months after receiving **OTQ923**, participants had an average of 21% **fetal hemoglobin** present in their blood. This means that an increase in **fetal hemoglobin** levels was observed after participants' received **OTQ923**.

To answer this question, researchers measured the levels of **fetal hemoglobin** in participants' blood 6 months after receiving treatment. **Fetal hemoglobin** is a type of hemoglobin. In people with **sickle cell disease**, an increased level of **fetal hemoglobin** helps protect red blood cells and can reduce the severity of sickle cell symptoms.



21% fetal hemoglobin present in participants' blood after 6 months of treatment

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 therapy or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of treatment up to 2 years after receiving **OTQ923** 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.

All participants had adverse events. 3 participants had adverse events that were considered serious. None of the participants died due to an adverse event. The researchers concluded there were no unexpected safety concerns for **OTQ923** in this trial.

How many participants had adverse events?

	OTQ923 4 participants
Had at least 1 **adverse event**	**4 of 4** 100%
Had at least 1 **serious adverse event**	**3 of 4** 75%

What adverse events did the participants have?

The most common adverse events that happened in the participants were:

- **Constipation**
- **Joint pain** (arthralgia)
- **Swelling of the mouth** (stomatitis)
- **Complication of sickle cell disease that happens when sickle red blood cells block blood flow to organs and tissue, causing severe pain** (sickle cell anaemia with crisis)
- **Fever due to low number of neutrophils in the blood** (febrile neutropenia)
- **Low red blood cell count** (anaemia)
- **Decreased number of platelets in the blood** (decreased platelet count)
- **Pain in the hands and feet** (pain in extremity)

What serious adverse events did the participants have?

3 participants had serious adverse events.

The most common serious adverse event that happened in the participants was **complication of sickle cell disease that happens when sickle red blood cells block blood flow to organs and tissue, causing severe pain** (sickle cell anaemia with crisis).

What was learned from this trial?

Researchers learned about the effects of **OTQ923** in people with serious complications of **sickle cell disease**. This trial ended earlier than planned due to business reasons. The decision was not due to any safety concerns with **OTQ923**. After this trial ended, participants moved into a long-term safety follow-up trial (CADPT03A12001), in which they are being monitored for any medical condition up to a total of 15 years after **OTQ923** administration.

Researchers found that:

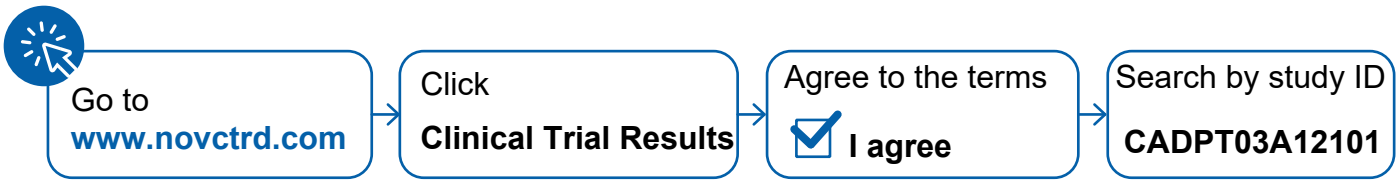
- it took an average of 23 days for a participant's **neutrophil** count to recover (levels above 500 µL of blood for 3 days in a row) after receiving treatment with **OTQ923**.
- participants experienced an increase in **fetal hemoglobin** levels, with an average level of 21% **fetal hemoglobin**, present 6 months after receiving treatment with **OTQ923**.
- there were no unexpected safety concerns for **OTQ923** in this trial.

When this summary was written, a long-term safety follow-up trial (CADPT03A12001) was ongoing for the participants who completed this trial.

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 the following website:

- **clinicaltrials.gov** – search using the number **NCT04443907**

Other trials of **OTQ923** may appear on the public websites above. When there, search for **OTQ923**.

Full clinical trial title: A first-in-patient phase I/II clinical study to investigate the safety and efficacy of genome-edited hematopoietic stem and progenitor cells in subjects with severe complications of sickle cell disease

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