NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of deferasirox compared with phlebotomy in people with hereditary hemochromatosis

Thank you!

Thank you to the participants who took part in the clinical trial for hereditary hemochromatosis. Every participant helped the researchers learn more about the trial drug **deferasirox**.

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: CICL670F2203

Drug studied: ICL670, also called **deferasirox**

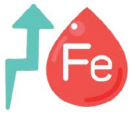
Sponsor: Novartis

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 findings.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of **deferasirox** compared with **phlebotomy** in people with hereditary hemochromatosis. Eye-related adverse events have been associated with the use of **deferasirox** treatment. In this trial, researchers wanted to learn more about whether **deferasirox** is safe for the eyes.



Hereditary hemochromatosis (HH) is a genetic disorder in which the body absorbs too much iron from the gut. Over time, this extra iron builds up in organs like the liver, heart, and pancreas, which can lead to organ damage. In most cases, HH occurs due to changes in a gene known as the 'C282Y' gene.

Phlebotomy is a medical procedure used to draw blood from a participant's veins. In conditions like **HH**, where there is an excess of iron in the blood, **phlebotomy** is used to reduce iron levels by removing blood from the patient. Phlebotomy is a standard treatment for **HH**. But, some people may be unable or unwilling to undergo the procedure due to its painful nature and the need for clinical visits.

Deferasirox works by binding to the iron present in the blood and removing excess iron from the body through stools.

The trial purpose was to answer these main questions:

- How many participants who took **deferasirox** achieved a blood **ferritin** level of 100 micrograms per liter (µg/L) or lower compared to those who underwent **phlebotomy**?
  - ↳ **Ferritin** is a protein that contains iron. Levels of ferritin in the blood indicate the amount of iron in the body.
- What **adverse events** did the participants have during this trial?
  - ↳ An adverse event is any unwanted sign or symptom that participants have after treatment during a trial. Adverse events may or may not be caused by treatments in the trial.

How long was this trial?

This trial began in January 2018 and ended in April 2023.
Researchers decided to stop the trial early because not enough participants joined the trial.

Who was in this trial?

45 participants with **Hereditary hemochromatosis (HH)** received treatment in this trial. Participants' ages ranged from 31 to 71 years. Their average age was 52 years.

The number of participants by gender and race is shown below.

Gender

38 **Men**	7 **Women**

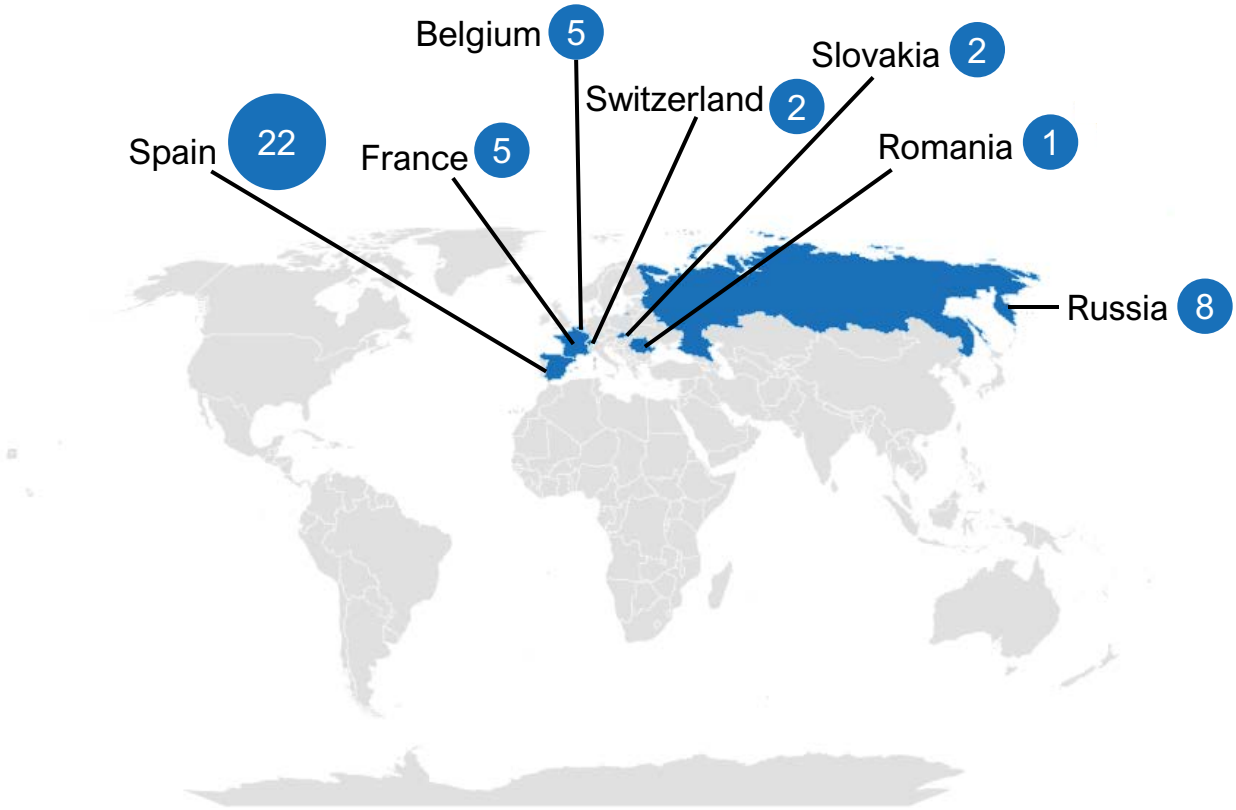
Race

45 **Caucasian**

The participants could take part in this trial if they:

- were at least 18 years of age
- had **HH** with the C282Y mutation and a blood ferritin level of at least 500 µg/L

45 participants from 7 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:

Deferasirox, at a starting dose of 7 milligrams per kilogram (mg/kg) of the participant's body weight, taken by mouth as tablets once every day. The dose of **deferasirox** could be adjusted later during the study.

Phlebotomy, which was done as often as decided by the trial doctors.

In this trial, each participant, the trial doctors, and the trial staff all knew what treatment participants were receiving.

What happened during the trial?

Before treatment — Up to 4 weeks

Trial doctors checked the participants' health to ensure they could take part in this clinical trial.

During treatment — Up to 2 years

Researchers used a computer program to randomly place participants into 2 different groups. This means that each person had an equal chance to end up in either treatment group.

Group 1 (30 participants): Participants took **deferasirox** at a starting dose of 7 mg/kg as tablets by mouth, once every day. The dose of **deferasirox** could be adjusted later during the study.

Group 2 (15 participants): Participants underwent the **phlebotomy** procedure, which was done as often as decided by the trial doctors.

Treatment with **deferasirox** and **phlebotomy** was stopped when the blood ferritin level reached 100 µg/L or below.

After treatment — 30 days after treatment

Participants were checked for adverse events up to 30 days after their last treatment.

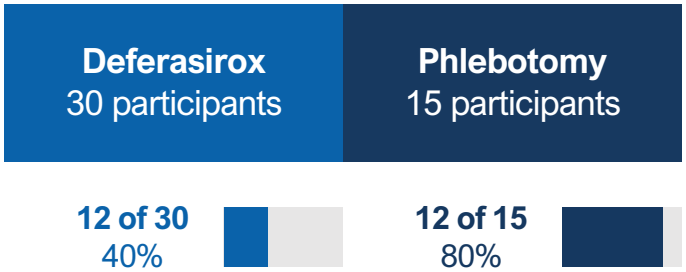
What were the main results of this trial?

How many participants who took deferasirox achieved a blood ferritin level of 100 µg/L or lower compared to those who underwent phlebotomy?

12 out of 30 (40%) participants who took **deferasirox** and 12 out of 15 (80%) participants who underwent **phlebotomy** achieved a blood ferritin level of 100 µg/L or lower.

To answer this question, researchers measured the level of ferritin in the blood. A ferritin level of 100 µg/L or lower indicates that the level of iron in the blood is within the normal range. Maintaining ferritin levels within the normal range is important, especially in conditions like HH, where a high ferritin level can lead to organ damage.

Number of participants (percentage) who achieved a blood ferritin level of 100 µg/L or lower



What adverse events did the participants have?

Trial doctors keep track of all **adverse events** that happen in trials, even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of the treatment up to 30 days after the last study 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.

Almost all the participants (40 of 45) had adverse events. 7 participants had adverse events that were considered serious. 1 participant died. 3 participants left the trial due to an adverse event. The researchers concluded that there were no new safety concerns for **deferasirox** in this trial.

How many participants had adverse events?

Participants who:	**Deferasirox** 30 participants	**Phlebotomy** 15 participants
Had at least 1 serious adverse event	**7 of 30** 23%	**0**
Had at least 1 other adverse event	**28 of 30** 93%	**12 of 15** 80%
Left the trial due to an adverse event	**3 of 30** 10%	**0**
Died during this trial	**1 of 30** 3%	**0**

What serious adverse events did the participants have?

All serious adverse events that were reported during the trial happened in 1 participant each in the **deferasirox** group. These included:

- **Nausea**
- **Sudden death**
- **COVID-19 infection**
- **Skin infection causing redness** (cellulitis)
- **Skin infection causing painful patches on the skin** (erysipelas)
- **Broken leg bone** (lower limb fracture)
- **Increased level of creatinine in the blood** (blood creatinine increased)
- **Increase in liver test value of alanine aminotransferase and aspartate aminotransferase enzyme** (transaminases increased)
- **Bladder cancer** (bladder neoplasm)
- **Pain in shoulder or arm due to compressed nerves and blood vessels near the collarbone** (thoracic outlet syndrome)
- **Decreased kidney function** (renal impairment)

What other adverse events did the participants have?

The table below shows the other adverse events that happened in **10% or more** participants.

	Deferasirox 30 participants	**Phlebotomy** 15 participants
Increased level of creatinine in the blood	**10 of 30** 33%	**1 of 15** 7%
Diarrhoea	**6 of 30** 20%	**2 of 15** 13%
Nausea	**5 of 30** 17%	**0**
Back pain	**4 of 30** 13%	**2 of 15** 13%
Headache	**4 of 30** 13%	**2 of 15** 13%
High blood pressure (hypertension)	**3 of 30** 10%	**3 of 15** 20%
Common cold (Nasopharyngitis)	**2 of 30** 7%	**3 of 15** 20%
Joint pain (Arthralgia)	**1 of 30** 3%	**2 of 15** 13%
Cough	**1 of 30** 3%	**3 of 15** 20%
Feeling dizzy (Dizziness)	**0**	**2 of 15** 13%
Neck pain	**0**	**2 of 15** 13%

What eye-related adverse events did the participants have?

To learn this, researchers kept track of how many participants had eye-related adverse events after treatment.

A total of 9 of 30 (30%) participants who took **deferasirox** had eye-related adverse events. None of the participants who underwent phlebotomy had eye-related adverse events. The most common eye-related adverse events that happened in 2 or more participants who took **deferasirox** were **cloudy lens in the eye** (cataract nuclear) and **high pressure in the eye** (glaucoma).

What was learned from this trial?

Researchers learned about the effects of **deferasirox** in people with **Hereditary hemochromatosis (HH)**. The researchers decided to stop the trial early because not enough participants joined the trial.

The researchers found that:

- **Deferasirox** could be a treatment option for people with **HH** who are not able to or choose not to undergo **phlebotomy**.
- There were no new safety observations with the use of **deferasirox**. Additionally, there were no new eye-related safety observations with the use of **deferasirox**. The safety results were similar to the safety results from previous trials with **deferasirox**.

When this summary was written, the sponsor did not plan to conduct more trials with **deferasirox** in people with **Hereditary hemochromatosis (HH)**. Other trials with **deferasirox** are ongoing.

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:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Agree to the terms **I agree** → Search by study ID **CICL670F2203**

For more information about this trial, go to any of the following websites:

- **www.clinicaltrials.gov** - search using the number **NCT03203850**
- **clinicaltrialsregister.eu/ctr-search/search** - search using the number **2016-002529-12**

Other trials will appear on the public websites above. When there, search for ICL670, **deferasirox**.

Full clinical trial title: A phase II, multicenter, open-label, randomized two-year study to evaluate the efficacy and safety of deferasirox film-coated tablet versus phlebotomy in patients with hereditary hemochromatosis