NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of inclisiran in teenagers with homozygous familial hypercholesterolemia (HoFH)

Thank you!

Thank you to the participants and families who took part in the clinical trial for **homozygous familial hypercholesterolemia (HoFH)**. Every participant helped the researchers learn more about the trial drug **inclisiran**, also called **KJX839**.

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: CKJX839C12302

Novartis drug studied: **inclisiran**, also called **KJX839**

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 more about the effects of **inclisiran** for teenagers with homozygous familial hypercholesterolemia (HoFH). To find this out, researchers compared the effects of **inclisiran** to a **placebo**.

Homozygous familial hypercholesterolemia (HoFH) is a genetic condition passed from both parents to a child that causes high cholesterol. High cholesterol can build up in the blood vessels and block blood flow. This can cause heart attack and stroke.

HoFH is a severe and rare type of familial hypercholesterolemia (FH). It happens when a person gets changed (mutated) genes from both parents. HoFH can cause high cholesterol in childhood.

Inclisiran, also called **KJX839**, is a trial drug created to stop the body from making a **protein called PCSK9**. High levels of the protein PCSK9 can play a role in high LDL cholesterol. It has been approved in certain countries for adults with another type of FH.

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

What is cholesterol?

Cholesterol is a type of fat in the blood. There are 2 main types of cholesterol:

- **LDL cholesterol**, or "bad" cholesterol, which can build up in the blood vessels and cause heart attack and stroke
- **HDL cholesterol**, or "good" cholesterol, which helps the body break down other types of cholesterol and helps protect against heart attack and stroke

Trial drug

Inclisiran also called **KJX839**

Pronounced as

in-kli-sir-an

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

- Did inclisiran lower teenagers' LDL cholesterol from before treatment to 1 year of treatment?
- 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 February 2021 and ended in November 2024. Each participant was in the trial for about 2 years. Participants started the trial on different dates.

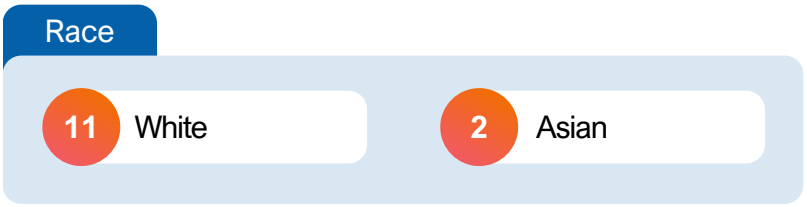
This trial had 2 parts:

- **Part 1** (1 year): Participants received either **inclisiran** or **placebo**
- **Part 2** (1 year): All participants received **inclisiran**

Who was in this trial?

13 teenagers with HoFH received treatment in this trial – 4 boys and 9 girls. Participants' ages ranged from 12 to 17 years. Their average age was 15 years.

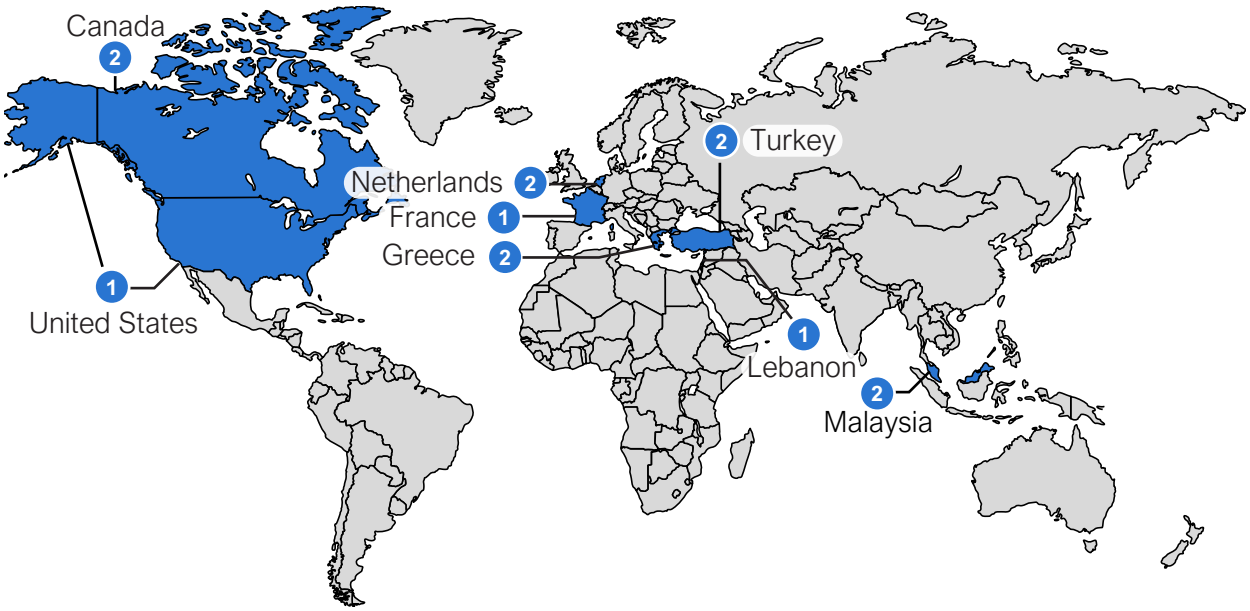
The number of participants by race is shown below.



The participants could take part in this trial if they:

- Had high LDL cholesterol while taking drugs that lower cholesterol
- Did not have another type of familial hypercholesterolemia that was heterozygous (HeFH)

13 participants from 8 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:

Inclisiran, also called **KJX839**, 300 milligrams, which was received as injections under the skin.

Placebo, which was received as injections under the skin. It looks like the trial drug but does not have any drug in it. Using a **placebo** helps researchers better understand the effect of a trial drug.

Along with the treatments above, participants continued taking their regular treatments to lower cholesterol.

Researchers used a computer to randomly assign participants to their treatments in Part 1. Twice as many participants were assigned **inclisiran** compared to **placebo**.

During **Part 1**, the participants and their families, 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.

During **Part 2**, the participants and their families, researchers, and trial staff knew what treatment each teenager received. All participants received **inclisiran**.

What happened during this trial?

Before treatment — 1 month

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

During treatment — 2 years

In Part 1, 13 participants received treatment 3 times in one of these groups:

- Group A: 9 participants received **inclisiran** on Day 1, Month 3, and Month 9
- Group B: 4 participants received **placebo** on Day 1, Month 3, and Month 9

13 participants completed Part 1 and started Part 2. Everyone in Part 2 received **inclisiran** up to 3 times total, on Month 12, Month 15, and Month 21.

After treatment — 1 month after a participant's last trial visit

Trial staff checked participants for any medical problems for up to 1 month after their last trial visit.

At the end of this trial, trial doctors invited participants who benefited from **inclisiran** to join another trial called CKJX839C12001B. This trial was designed to learn about the safety of **inclisiran** over a longer period of time.

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

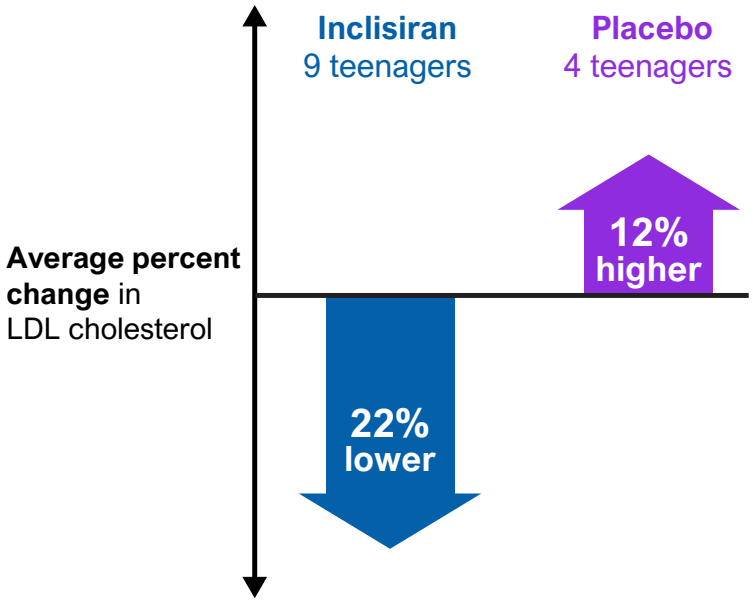
What were the main results of this trial?

Did inclisiran lower teenagers' LDL cholesterol from before treatment to 1 year of treatment?

At 1 year of treatment, the average level of LDL cholesterol was lower in teenagers who received **inclisiran** compared to those who received **placebo** during Part 1.

To learn this, researchers measured the level of LDL cholesterol in participants' blood before and at 1 year of treatment. They compared the change in LDL cholesterol in teenagers who received **inclisiran** to those who received **placebo**.

Average change in LDL cholesterol from before treatment to 1 year of treatment



What were the other results of this trial?

Did inclisiran lower other measures of cholesterol and fats in the blood?

Part 1: Compared to teenagers who received **placebo**, those who received **inclisiran** had lower measures of cholesterol and certain types of fat in the blood at 1 year of treatment.

Part 2: Compared to before treatment, teenagers who received **inclisiran** had lower measures of cholesterol and certain types of fat in the blood at year 2.

To learn this, the researchers looked at different measures of cholesterol and fats in the participants' blood before treatment and at 1 and 2 years of treatment.

Did inclisiran lower the amount of the protein PCSK9 in the blood?

Part 1: Compared to teenagers who received placebo, teenagers who received **inclisiran** had less PCSK9 in the blood at 1 year of treatment.

Part 2: Compared to before treatment, teenagers who received **inclisiran** had less PCSK9 in the blood at year 2 of treatment.

To learn this, the researchers looked at the amount of the protein PCSK9 in the participants' blood before treatment and at 1 and 2 years of treatment. **PCSK9** is a protein that can cause the body to remove less LDL cholesterol from the blood. More PCSK9 can lead to higher LDL cholesterol. **Inclisiran** is designed to stop the body from making PCSK9.

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 drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of treatment until up to 1 month after their last trial visit.

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

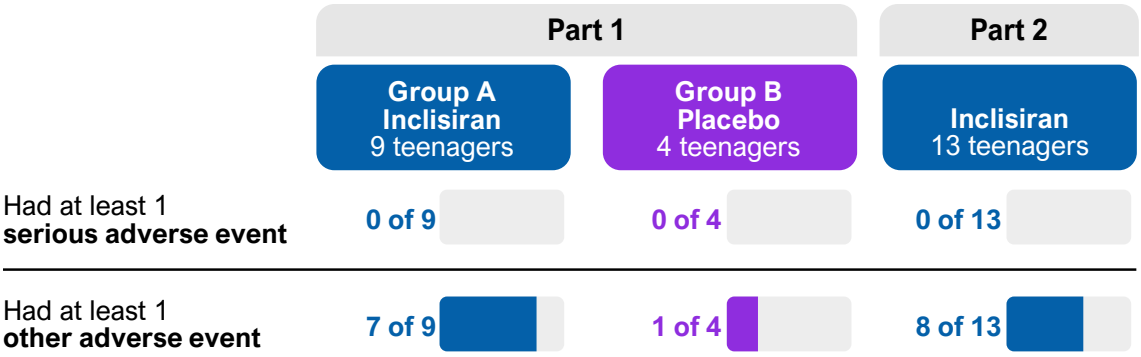
Adverse events **may** or **may not** be caused by treatments in the trial.

In **Part 1**, 8 of 13 teenagers had adverse events. No teenagers had adverse events that were considered serious.

In **Part 2**, 8 of 13 teenagers had adverse events. No teenagers had adverse events that were considered serious.

No teenagers left the trial. No teenagers died during the trial. The researchers concluded there were no new safety concerns for **inclisiran** in this trial.

How many teenagers had adverse events?



What serious adverse events did the teenagers have?

No teenagers in Part 1 or Part 2 had serious adverse events.

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

In **Part 1**, 8 teenagers had other adverse events.

In **Part 2**, 8 teenagers had other adverse events.

The table below shows the most common other adverse events.

	Part 1		Part 2
	Group A Inclisiran 9 teenagers	**Group B Placebo** 4 teenagers	**Inclisiran** 13 teenagers
COVID-19	**4 of 9** 44%	**1 of 4** 25%	**1 of 13** 8%
Upper belly pain Abdominal pain upper	**2 of 9** 22%	**0 of 4** 0%	**1 of 13** 8%
Fever Pyrexia	**2 of 9** 22%	**0 of 4** 0%	**0 of 13** 0%
Flu Influenza	**0 of 9** 0%	**0 of 4** 0%	**2 of 13** 15%
Headache	**0 of 9** 0%	**0 of 4** 0%	**2 of 13** 15%
Reaction, such as redness or pain, where the injection was given Injection site reaction	**2 of 9** 22%	**0 of 4** 0%	**0 of 13** 0%
Stomach flu Gastroenteritis	**1 of 9** 11%	**1 of 4** 25%	**0 of 13** 0%

What was learned from this trial?

Researchers learned about the effects of **inclisiran** for teenagers with homozygous familial hypercholesterolemia (HoFH).

The researchers concluded that, compared to those who received the **placebo**, teenagers who received **inclisiran**:

- Had a lower level of LDL cholesterol at 1 year of treatment during Part 1
- Had lower levels of some other cholesterols and fats in the blood during Part 1 and Part 2
- Had less PCSK9 in the blood during Part 1 and Part 2

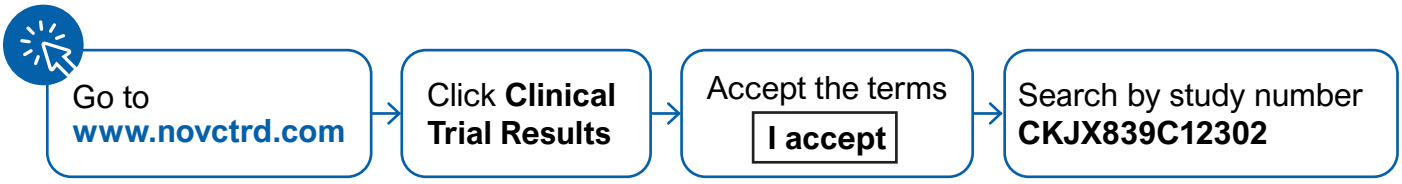
The researchers concluded there were no new safety concerns for **inclisiran** in this trial.

When this summary was written, the extension trial CKJX839C12001B, also called VICTORION-PEDS-OLE, was ongoing for some teenagers who completed this or another 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 any of these websites:

- **clinicaltrials.gov** – search using the number **NCT04659863**
- **clinicaltrialsregister.eu** – search using the number **2020-002755-38**

Other trials of **inclisiran** may appear on the public websites above. When there, search for **inclisiran** or **KJX839**.

Full clinical trial title: Two part (double-blind inclisiran versus placebo [Year 1] followed by open-label inclisiran [Year 2]) randomized multicenter study to evaluate safety, tolerability, and efficacy of inclisiran in adolescents (12 to less than 18 years) with homozygous familial hypercholesterolemia and elevated LDL-cholesterol (ORION-13)

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