NOVARTIS

Clinical Trial Results Summary

A trial to learn about the effects of KJX839 in Japanese people with high levels of bad cholesterol and a high risk of developing heart or blood vessel diseases

Protocol number: CKJX839A11201

Thank You!

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.

Thanks to the participants for taking part in this trial for the drug **KJX839**, also known as inclisiran. They helped researchers learn more about how **KJX839** works in people with high levels of bad cholesterol and a high risk of developing heart or blood vessel diseases.

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If the participants have any questions about the trial results, please talk to the doctor or staff at the trial site.

This summary shows the results of a single clinical trial. Other clinical trials may have different findings.

Why was the research needed?

Researchers were looking for a better way to treat Japanese people with hypercholesterolemia including heterozygous familial hypercholesterolemia (HeFH).

Hypercholesterolemia is when a person has high levels of low-density lipoprotein cholesterol (LDL-C), also known as bad cholesterol, in the blood. This is commonly passed on from parent to children and can be affected by diet, lifestyle, or other diseases. HeFH is hypercholesterolemia which is passed on from parent to children.

Statins are a type of medicine given to lower the levels of bad cholesterol. However, the levels may remain high if the patient has heart disease, diabetes, or HeFH.

KJX839 (Inclisiran) is a medicine that was approved in other countries but not in Japan at the start of this trial for the treatment of high levels of bad cholesterol in the blood. **KJX839** reduces the level of bad cholesterol in the blood.

Drug	Pronounced as
Inclisiran	IN kli SIR an

In this trial, researchers wanted to check if **KJX839** can lower bad cholesterol levels in Japanese participants with high levels of bad cholesterol and a high risk of developing heart or blood vessel diseases.

How long was this trial?

This trial started in January 2021 and ended in October 2022. The entire duration, from enrolling the first participant to the last participant completing the trial was around 1 year and 9 months. An individual participant was in this trial for an average of 1 year.

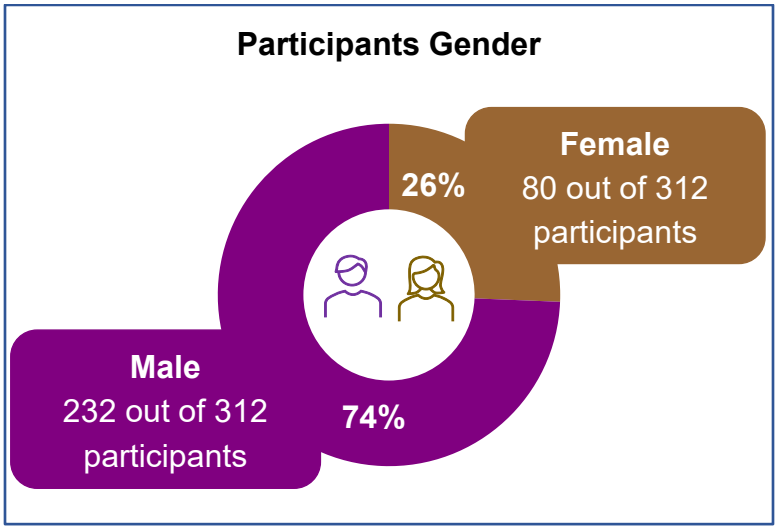
Who was in this trial?

The participants could take part in this trial if they:

- were aged 20 years or older,
- had or were at high risk of developing heart or blood vessel disease,
- were diagnosed with high levels of bad cholesterol and HeFH that cannot be managed by standard treatment,
- were receiving high doses of statins or stopped taking statins due to severe side effects, and
- did not have any major heart problems in the 3 months before starting the trial.

A total of 312 Japanese participants received treatment.

Participants' age ranged from 34 to 85 years. The average age of the participants was 64 years. Most participants were men, 232 out of 312 (74%).



What treatments did the participants receive?

The treatments in this trial were:

	**KJX839** was given as an injection under the skin at a dose of 100 mg, 200 mg, or 300 mg on Day 1, Day 90, and Day 270.
	**Placebo** looked like the trial drug but did not have any medicine in it. Using a **placebo** helps researchers better understand the effect of a trial drug by making sure that the changes were not happening by chance. The placebo was used as a comparator with the treatment drug in this trial.

Along with the treatments above, participants could take other treatments with the trial doctor's agreement.

In this trial, none of the participants, trial doctors, or trial staff knew what treatment the participants were receiving. Some trials are done this way because knowing what treatment each participant is getting can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness towards all treatments.

What happened during this trial?

Before treatment

The trial doctors checked if participants could take part in this trial.

Up to 2 weeks

During treatment

A total of 312 participants took part in this trial. They were randomly assigned to one of the following four treatment groups.

The chance of participants being in the 300 mg and 200 mg groups is double that of the 100 mg and placebo groups. Participants were assigned to groups randomly using a computer.

- **KJX839 300 mg** (99 participants),
- **KJX839 200 mg** (101 participants),
- **KJX839 100 mg** (55 participants), or
- **Placebo** (57 participants).

KJX839 was given as an injection under the skin on Day 1, Day 90, and Day 270 of the trial.

Up to 39 weeks

After the last injection

After the last injection on Day 270, participants' health was monitored for 13 weeks.

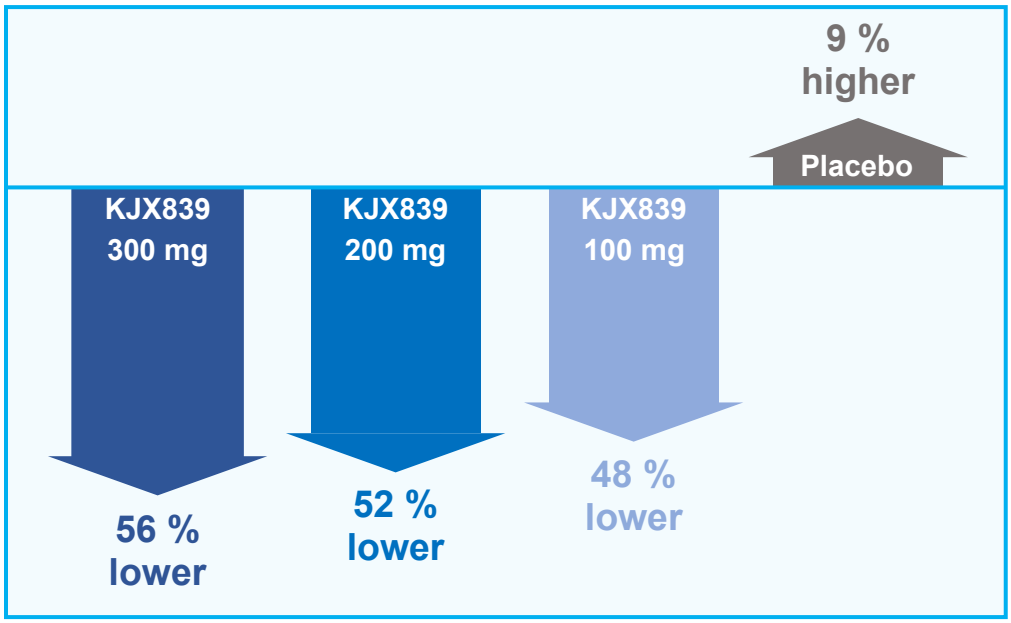
Up to 13 weeks

What was the main result of this trial?

How much did the participants' bad cholesterol levels change after receiving different doses of KJX839 compared with placebo after 180 days of treatment?

After 180 days, levels of bad cholesterol among the participants decreased on average by 56% after receiving **KJX839 300 mg**, 52% after receiving **KJX839 200 mg**, and 48% after receiving **KJX839 100 mg**. Among the participants who received the **placebo**, levels of bad cholesterol increased by 9%.

Change in levels of bad cholesterol after 180 days of treatment



What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "adverse events".

A lot of research is needed to know whether a drug causes an adverse event. **During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug.** When new drugs are being studied, researchers keep track of all adverse events participants have.

This section is a summary of the adverse events that happened during this trial. The website listed at the end of this summary may have more information about all the adverse events that happened in this trial.

An adverse event is any sign, symptom, or disease that participants have during a trial.

An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care. ***These problems may or may not be caused by the trial drug.***

How many participants had adverse events?

The adverse events that happened in the 4 treatment groups during the trial are listed in the table below.

Number of Participants (%) With Adverse Events

	KJX839 300 mg (Out of **99** participants)	**KJX839 200 mg** (Out of **101** participants)	**KJX839 100 mg** (Out of **55** participants)	**Placebo** (Out of **57** participants)
At least 1 serious adverse event	7 (7%)	7 (7%)	2 (4%)	6 (11%)
At least 1 other adverse event	59 (60%)	59 (58%)	38 (69%)	32 (56%)
Stopped drug due to adverse event	1 (1%)	1 (1%)	0 (0%)	0 (0%)
Deaths	0 (0%)	0 (0%)	0 (0%)	1 (2%)

How many participants stopped trial drug due to adverse events?

Two participants discontinued the trial drug due to adverse events. One participant on **KJX839 300 mg** discontinued due to **hives because of an unknown cause** (idiopathic urticaria). And another participant on **KJX839 200 mg** discontinued due to **long-term swelling of the stomach lining** (chronic gastritis).

What were the most common serious adverse events?

The most common serious adverse events that happened in more than 1 participant across the groups were:

- **poorly controlled diabetes** (diabetes mellitus inadequate control) in 1 participant from placebo and another from the **KJX839 200 mg** group.
- **sudden chest pain** (angina unstable) in 1 participant from each of these groups: **placebo**, **KJX839 100 mg**, and **KJX839 300 mg**.

What were the most common other adverse events?

The most common other adverse events that happened in at least 10% (10 out of 100) of participants in any group are presented below.

Number of Participants (%) With Other Adverse Events

	KJX839 300 mg (Out of **99** participants)	**KJX839 200 mg** (Out of **101** participants)	**KJX839 100 mg** (Out of **55** participants)	**Placebo** (Out of **57** participants)
Fever (Pyrexia)	18 (18%)	12 (12%)	8 (15%)	7 (12%)
Poorly controlled diabetes (Diabetes mellitus inadequate control)	15 (15%)	10 (10%)	7 (13%)	9 (16%)
Diabetes (Diabetes mellitus)	12 (12%)	12 (12%)	11 (20%)	5 (9%)
Back pain	8 (8%)	3 (3%)	6 (11%)	5 (9%)
Discomfort (Malaise)	7 (7%)	2 (2%)	1 (2%)	6 (11%)

	KJX839 300 mg (Out of **99** participants)	KJX839 200 mg (Out of **101** participants)	KJX839 100 mg (Out of **55** participants)	Placebo (Out of **57** participants)
Reaction at the injection site (Injection site reaction)	6 (6%)	12 (12%)	3 (6%)	2 (4%)
COVID-19	6 (6%)	5 (5%)	8 (15%)	2 (4%)
Pain at the vaccination site (Vaccination site pain)	5 (5%)	5 (5%)	1 (2%)	8 (14%)

How was this trial useful?

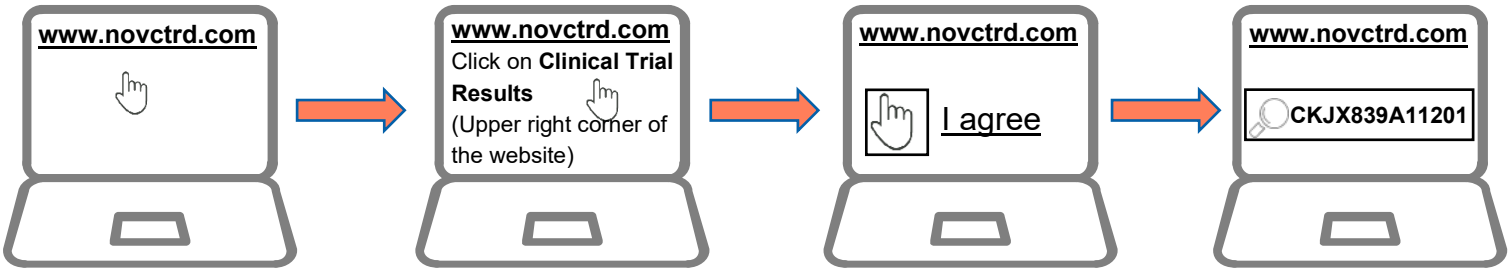
This trial was performed on Japanese participants with hypercholesterolemia including HeFH and a high risk of developing heart or blood vessel diseases. The trial helped researchers understand that **KJX839** is effective in reducing bad cholesterol levels. Each dose showed reductions, the maximum effect was seen in participants taking **KJX839 300 mg**. There was no new safety concern for **KJX839** found in Japanese patients. The result of this trial was used to get approval for use of **KJX839** in Japan.

Some clinical trials (CKJX839B12302 and CKJX839D12303) with **KJX839** are ongoing for hypercholesterolemia including HeFH across the world, including Japan.

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.

Please follow the steps below:



You can find more information about this trial on the following website:

- www.clinicaltrials.gov Use the NCT identifier NCT04666298 in the search field.

Full clinical trial title: A placebo-controlled, double-blind, randomized trial to evaluate the effect of different doses of inclisiran given as subcutaneous injections in Japanese participants with high cardiovascular risk and elevated low-density lipoprotein cholesterol (LDL-C) (ORION-15).

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of people around the world. You helped researchers answer important health questions and test new medical treatments.

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

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