NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the use of inclisiran in primary care for adults who have or who are at risk of developing heart or blood vessel disease and also have high levels of bad cholesterol

Thank you!

Thank you to the participants who took part in the clinical trial for lowering bad cholesterol. 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: CKJX839A1GB01

Drug studied: Inclisiran, also known as 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 findings.

What was the main purpose of this trial?

The purpose of this trial was to learn if using **inclisiran** along with standard treatment in primary care could help adults with heart or blood vessel disease or who are at risk of developing the disease and also have high levels of bad cholesterol.

High cholesterol is when a person has too much of a type of fat in the blood called **LDL-C** (low-density lipoprotein cholesterol). **LDL-C** is also known as 'bad cholesterol,' and it can collect on the walls of blood vessels. High blood levels of **LDL-C** can increase the chances of heart or blood vessel disease like heart attack or stroke. There are approved treatments for high cholesterol but sometimes people may need more help lowering their **LDL-C**.

Inclisiran is a drug approved for the treatment of high levels of bad cholesterol in the blood. It works by stopping the liver from releasing too much of a protein called **PCSK9**. Too much **PCSK9** can slow down how the body removes bad cholesterol from the blood. If blood levels of **PCSK9** go down, levels of bad cholesterol should also go down.

Trial drug
Inclisiran

Pronounced as
IN kli SIR an

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

- Did **inclisiran** with or without the lifestyle guidance reduce bad cholesterol levels in participants compared to standard treatment with lifestyle guidance by 9 months of treatment?
- What adverse events did the participants have during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial began in July 2021 and ended in January 2023. It was planned for the participants to be in the trial for about 9 months after receiving the trial treatment.

Who was in this trial?

891 participants from the United Kingdom took part in this trial.
844 out of 891 participants received the trial treatment.
Participants' ages ranged from 34 to 89 years. Their average age was 66 years. The number of participants by gender is shown below.

Gender

367 Men	524 Women

Race

23 Asian	6 Black	5 Mixed
848 White	9 Other	

The participants could take part in this trial if they:

- were aged 18 years or older,
- were on a stable dose of medicines to lower bad cholesterol or
- were asked to take medicines to lower bad cholesterol but had side effects after taking them, and
- had high levels of bad cholesterol in their blood.

What treatments did the participants receive?

The treatments in this trial:

Inclisiran 300 mg was given as an injection under the skin on Day 1 and again on Day 90.

Lifestyle guidance: the participants were guided over telephone calls to make better choices with diet, exercise, and medication to better manage their glucose levels. Participants who smoked were suggested to stop smoking to further reduce the risk of heart or blood vessel disease.

Standard treatment: the participants continued to receive locally recommended standard of care medicines for heart or blood vessel disease and for high bad cholesterol levels.

Apart from the trial treatment and the standard treatment, participants could also take medicines for any other medical issues under the trial doctor's observation. The participants, trial doctors, or trial staff knew what treatment the participants were receiving.

What happened during this trial?

Before treatment — 2 weeks

Trial doctors checked the participants' health, their heart or blood vessel disease, and their bad cholesterol levels to make sure they could be in this clinical trial.

During treatment — 9 months

Out of the 891 participants randomly assigned to the 3 treatment groups, 844 received the trial treatment.

- **Standard treatment + lifestyle guidance (290 participants)**
- **Standard treatment + inclisiran 300 mg (273 participants)**
- **Standard treatment + inclisiran 300 mg + lifestyle guidance (281 participants)**

Inclisiran was given as an injection under the skin once on Day 1 and again on Day 90.

Trial doctors monitored the participants' disease condition and general health throughout the trial.

After treatment — 1 month

- Participants returned to the trial site after the treatment period.
- Trial doctors assessed the participants' overall health and wellbeing during this period.

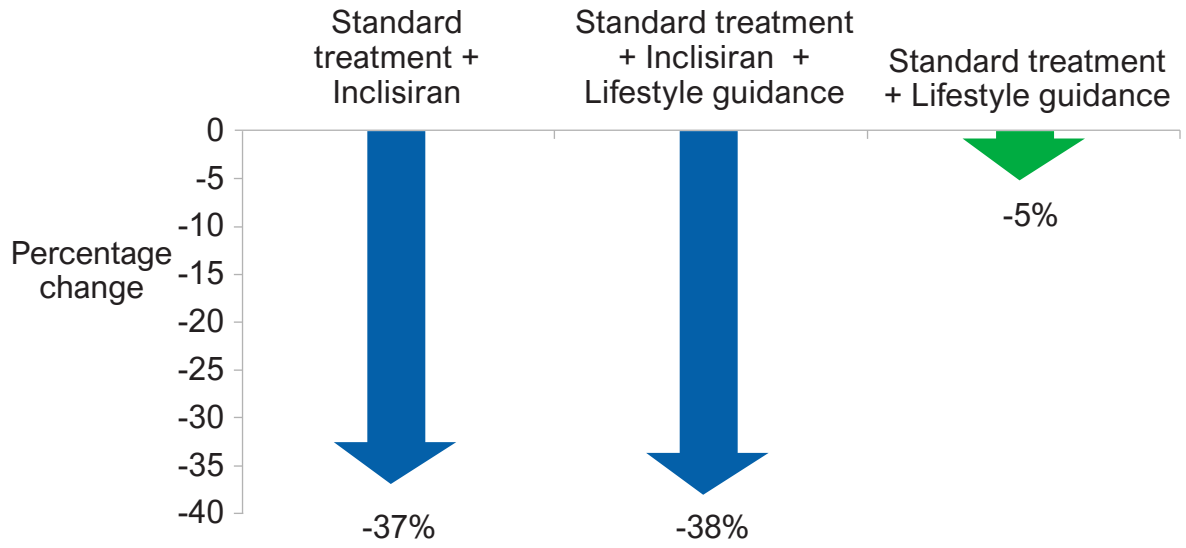
What was the main result of this trial?

Did inclisiran with or without the lifestyle guidance reduce bad cholesterol levels in participants compared to standard treatment with lifestyle guidance by 9 months of treatment?

Yes, **inclisiran** with or without lifestyle guidance, reduced bad cholesterol levels (38% and 37%) in the blood compared to the standard treatment (5%) by 9 months of treatment.

To find this out, trial doctors measured the average change in the level of bad cholesterol in participants' blood. They then compared this change between the participants in the 3 treatment groups.

Percentage change in bad cholesterol level



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 treatment up to 1 month after the end of the trial.

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.

10% of participants (88 of 844) had serious adverse events. 5 participants had other adverse events. 2 participants died. 8 participants left the trial due to an adverse event. The researchers concluded there were no new safety concerns for **inclisiran** in this trial.

How many participants had adverse events?

Participants who:	Inclisiran 300 mg 273 participants	Inclisiran 300 mg + lifestyle guidance 281 participants	Standard treatment + lifestyle guidance 290 participants
Had at least 1 serious adverse event	24 of 273 9%	36 of 281 13%	28 of 290 10%
Had at least 1 other adverse event	3 of 273 1%	2 of 281 1%	0 of 290 0%
Left the trial due to an adverse event	2 of 273 1%	3 of 281 1%	3 of 290 1%
Died during the trial	2 of 273 1%	0 of 281 0%	0 of 290 0%

What serious adverse events did the participants have?

88 participants had serious adverse events. 2 participants died.

The table below shows the most common serious adverse events that happened in **2 or more** participants in any treatment group.

	Inclisiran 300 mg 273 participants	**Inclisiran 300 mg + lifestyle guidance** 281 participants	**Standard treatment + lifestyle guidance** 290 participants
Diabetes Type 2 diabetes mellitus	**3 of 273** 1%	**1 of 281** <1%	**2 of 290** 1%
Heart attack Acute myocardial Infarction	**1 of 273** <1%	**1 of 281** <1%	**2 of 290** 1%
Infection in the urinary system Urinary tract infection	**1 of 273** <1%	**2 of 281** 1%	**0 of 290** 0%
Severe infection that spreads from the urinary tract throughout the body Urosepsis	**1 of 273** <1%	**2 of 281** 1%	**0 of 290** 0%
Irregular heartbeat Atrial fibrillation	**2 of 273** 1%	**5 of 281** 2%	**0 of 290** 0%
Kidney damage Acute kidney injury	**2 of 273** 1%	**2 of 281** 1%	**0 of 290** 0%
Lung infection Pneumonia	**4 of 273** 1%	**1 of 281** <1%	**1 of 290** <1%
Suicidal thoughts Suicidal ideation	**2 of 273** 1%	**0 of 281** 0%	**1 of 290** <1%
Swelling in the colon Diverticulitis	**0 of 273** 0%	**2 of 281** 1%	**0 of 290** 0%

What other adverse events did the participants have?

5 participants had other adverse events.

The table below shows the other adverse events that happened in **1 or more** participants in any treatment group.

	Inclisiran 300 mg 273 participants	**Inclisiran 300 mg + lifestyle guidance** 281 participants	**Standard treatment + lifestyle guidance** 290 participants
Back pain	**1 of 273** <1%	**0 of 281** 0%	**0 of 290** 0%
Feeling dizzy Dizziness	**0 of 273** 0%	**1 of 281** <1%	**0 of 290** 0%
Muscle cramps Muscle spasms	**1 of 273** <1%	**0 of 281** 0%	**0 of 290** 0%
Pain in hands and feet Pain in extremity	**1 of 273** <1%	**0 of 281** 0%	**0 of 290** 0%
Rash	**0 of 273** 0%	**1 of 281** <1%	**0 of 290** 0%
Rashes at the injection site Injection site rash	**1 of 273** <1%	**0 of 281** 0%	**0 of 290** 0%

What was learned from this trial?

Researchers learned about the effects of **inclisiran** in reducing bad cholesterol.

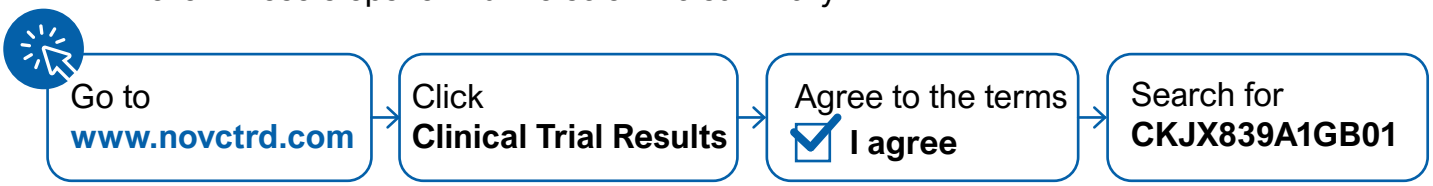
- The researchers found **inclisiran** with or without lifestyle guidance reduced bad cholesterol compared to standard treatment with lifestyle guidance.
- Researchers found no new safety concerns with **inclisiran**.

At the time this report was created, future trials with **inclisiran** were planned.

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 one of these websites:

- **clinicaltrials.gov** – search using the number **NCT04807400**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2020-004401-31**

Other trials will appear on the public websites above. When there, search for KJX839 and/ or inclisiran.

Full clinical trial title: A phase IIIb, multicentre, randomized controlled study to evaluate the implementation, preference and utility for administration of inclisiran sodium in participants with Atherosclerotic Cardiovascular Disease (ASCVD) or ASCVD-risk equivalents and elevated Low Density Lipoprotein Cholesterol (LDL-C) using a primary care models in the NHS.

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

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www.novartis.com/clinicaltrials