

# Clinical Trial Results Summary

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A clinical trial to learn more about the effect of starting inclisiran first compared to standard treatment for bad cholesterol in people with heart or blood vessel disease despite receiving statin treatment

## 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:** CKJX839A1US02

**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.

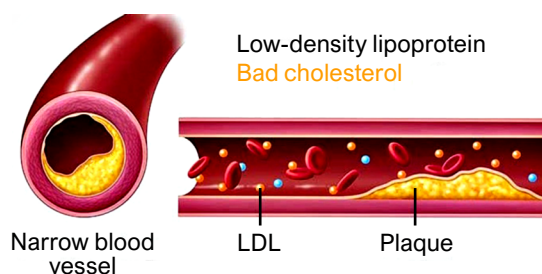
# What was the main purpose of this trial?

The purpose of the trial was to learn about the effects of **inclisiran** compared to **standard treatment** for **bad cholesterol** in people with heart or blood vessel disease in whom the highest doses of statins did not work. Statins are drugs used to prevent heart and blood vessel disease. They are also used to lower **bad cholesterol** levels in the blood.

**Inclisiran first** is **inclisiran** added to the **standard treatment** when the highest tolerated dose of statins failed

Researchers compared the effects of **Inclisiran first**, with that of **standard treatment** alone in lowering **bad cholesterol**.

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



Source: [What is Cholesterol?](#)



**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**



**Standard treatment:** included all cholesterol lowering drugs that a doctor prescribes which includes statins and non-statin drugs.



### The trial purpose was to answer these main questions:

- Did starting **Inclisiran first** help lower bad cholesterol levels in participants compared to the **standard treatment** at Day 330?
- How many participants in the **Inclisiran first** group stopped taking statins compared to the **standard treatment** group at least 1 month before the end of the trial?
- 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 September 2023. It was planned for the participants to be in the trial for about 11 months.

## Who was in this trial?



450 participants from the United States who had heart or blood vessel disease with high **bad cholesterol (LDL-C)** levels received treatment in this trial. Participants' ages ranged from 27 to 89 years. Their average age was 67 years. The number of participants by gender and race is shown below.

### Gender

311

Men

139

Women

### Race

12

Asian

56

Black or African American

1

Multiple races

373

White

8

Unknown

The participants could take part in this trial if they:

- were aged 18 years or older,
- had heart or blood vessel disease,
- had high levels of **bad cholesterol** in their blood,
- had received the most tolerated dose of statins, and
- had side effects after using statins.

## What treatments did the participants receive?

The treatments in this trial were:



**Inclisiran 300 mg:** given as a single injection under the skin on Day 1 and again on Day 90 and Day 270.



**Standard treatment:** included all cholesterol lowering drugs that a doctor prescribes. This includes statins and non-statin drugs to lower **bad cholesterol**.

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.

Researchers assigned participants to treatment groups in a random way using a computer system.

The participants, trial doctors, and trial staff knew what treatment the participants were receiving.

Before the trial started, researchers took participants' permission to collect information about their health, medication, and cholesterol levels. This was needed to understand the effect of bad cholesterol and the treatment on participants' health.

## What happened during this trial?

### Before treatment 1 Month



Trial doctors checked participants' heart or blood vessel disease, cholesterol levels, medications they were taking, and their general health to make sure they could participate in this clinical trial.

### During treatment 11 months



450 participants were randomly and equally assigned to the 2 treatment groups

- **Inclisiran first (225 participants)**
- **Standard treatment (225 participants)**
- Participants in the **Inclisiran first** group received **inclisiran** 300 mg + **standard treatment**.
- **Inclisiran** was given as an injection on Day 1 and again on Day 90 and Day 270.
- The sponsor provided **inclisiran** to the participants in the **Inclisiran first** group until the end of this trial.

### After last dose Up to 2 months



- Participants returned to the trial site 1 time after receiving their last dose of treatment for follow-up visit.
- Participants who completed the trial could continue the **inclisiran** treatment with their doctor's approval.

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

# What were the main results of this trial?

Did starting **Inclisiran first** help lower bad cholesterol levels in participants compared to the **standard treatment** at Day 330?

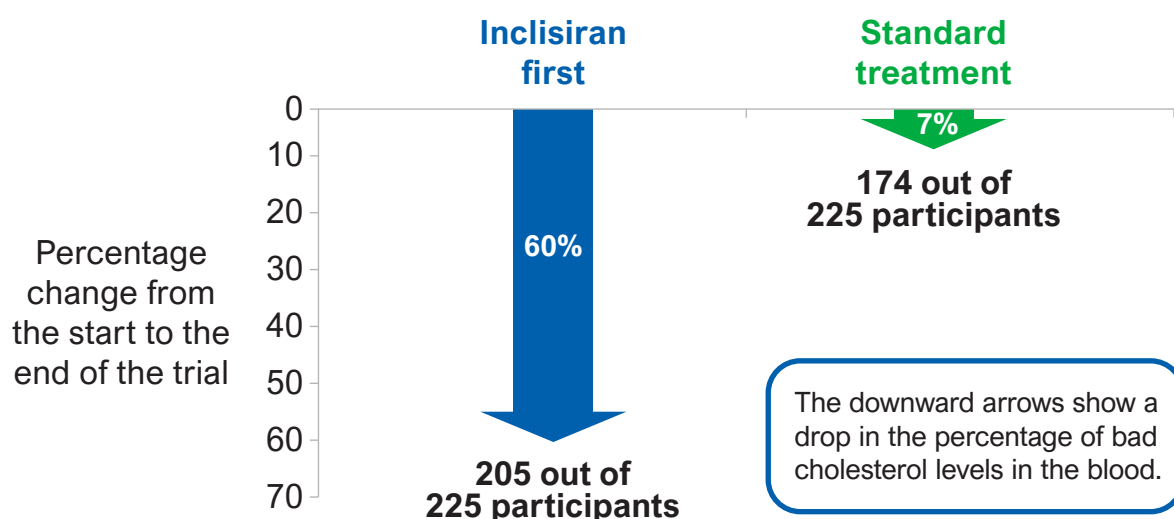


Yes, starting **Inclisiran first** helped lower bad cholesterol levels in participants by 60% compared to a decrease of 7% with **standard treatment** by the end of the trial on Day 330.

To find this out, researchers measured the average change in the levels of **bad cholesterol** in participants' blood throughout the treatment period. They then compared this change between the participants in the 2 treatment groups.

Participants in the **Inclisiran first** group had a bigger drop in bad cholesterol levels compared to participants in the **standard treatment** group.

## Percentage change in bad cholesterol levels

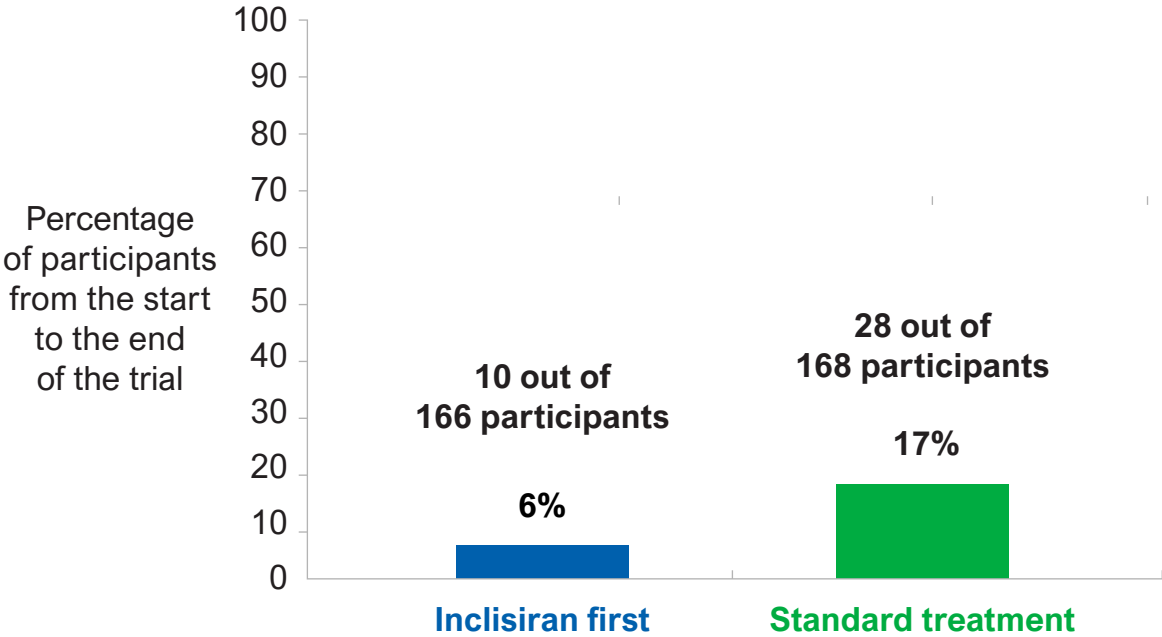


How many participants in the **Inclisiran first** group stopped taking statins compared to the **standard treatment** group at least 1 month before the end of the trial?



6% of participants (10 out of 166) in the **Inclisiran first** group compared to 17% of participants (28 out of 168) in the **standard treatment** group stopped taking statins at least 1 month before the end of the trial. Researchers concluded that there was not much difference in stopping statins with **inclisiran** treatment compared to the **standard treatment**.

Percentage of participants who stopped taking statins



# 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 trial treatment until 2 months after the last dose of the trial 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.



263 out of 450 participants (58%) had adverse events. 56 participants had adverse events that were considered serious. 3 participants left the trial due to an adverse event. 3 participants died.

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

## How many participants had adverse events?

	Inclisiran first 234 participants	Standard treatment 216 participants
<b>Participants who:</b>		
Had at least 1 serious adverse event	27 of 234	29 of 216
Had at least 1 other adverse event	64 of 234	53 of 216
Left the trial due to an adverse event	2 of 234	1 of 216
Died during the trial	2 of 234	1 of 216



## What serious adverse events did the participants have?

56 participants had serious adverse events. 3 participants died, 2 participants in the **Inclisiran first** group and 1 in the **standard treatment** group.

The table below shows the most common serious adverse events that happened in **3 or more** participants.

	Inclisiran first 234 participants	Standard treatment 216 participants
<b>Heart attack</b> Acute myocardial infarction	4 of 234 2%	2 of 216 less than 1%
<b>Lung infection</b> Pneumonia	3 of 234 1%	2 of 216 1%
<b>Fall</b>	3 of 234 1%	1 of 216 less than 1%
<b>Extreme response by the body to an infection</b> Sepsis	3 of 234 1%	1 of 216 less than 1%
<b>Chest pain not caused by heart disease</b> Non-cardiac chest pain	1 of 234 less than 1%	3 of 216 1%
<b>Narrowing of blood vessel in the neck supplying blood to the brain</b> Carotid artery stenosis	0 of 234 0%	3 of 216 1%

## What other adverse events did the participants have?

117 participants had other adverse events.

The table below shows the other adverse events that happened in **5 or more** participants.

	Inclisiran first 234 participants	Standard treatment 216 participants
<b>Pain at the site of injection</b> Injection site pain	18 of 234 8%	0 of 216 0%
<b>Worsening of Covid-19</b> Covid-19	18 of 234 8%	14 of 216 6%
<b>Infection in any part of the urinary tract</b> Urinary tract infection	8 of 234 3%	7 of 216 3%
<b>Fall</b>	3 of 234 1%	9 of 216 4%
<b>Increase in the liver test value of creatine phosphokinase in the blood</b> Blood creatinine phosphokinase increased	10 of 234 4%	13 of 216 6%
<b>Increased blood glucose levels</b> Glycosylated hemoglobin increased	9 of 234 4%	5 of 216 2%
<b>High blood sugar</b> Type 2 diabetes mellitus	8 of 234 3%	10 of 216 5%

## What was learned from this trial?

Researchers learned about the effects of **Inclisiran first** (inclisiran + **standard treatment**) in participants with heart and blood vessel disease and high **bad cholesterol**.



Researchers concluded that, compared to participants who received the **standard treatment**, participants on **Inclisiran first**

- had lower **bad cholesterol** levels
- did not show much difference in participants who stopped taking statins
- had no new safety concerns.

At the time this report was created, there were ongoing trials, and more were being 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](http://www.novctrd.com)

Follow these steps to find the scientific summary:



Go to  
[www.novctrd.com](http://www.novctrd.com)

Click  
**Clinical Trial Results**

Agree to the terms  
☒ **I agree**

Search for  
**CKJX839A1US02**

For more information about this trial, go to the below website:

- [clinicaltrials.gov](http://clinicaltrials.gov) – search using the number **NCT04929249**

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

**Full clinical trial title:** A randomized, multicenter, open-label trial comparing the effectiveness of an “inclisiran first” implementation strategy to usual care on LDL cholesterol (LDL-C) in patients with atherosclerotic cardiovascular disease and elevated LDL-C ( $\geq 70$  mg/dL) despite receiving maximally tolerated statin therapy (VICTORION-INITIATE)



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