NOVARTIS

# The effects and safety of KJX839 in Chinese participants with high cholesterol

## Thank you!

Thank you to the participants who took part in the clinical trial for high cholesterol. Every participant helped the researchers learn more about **KJX839,** also called inclisiran.

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:** CKJX839A12105
**Drug studied:** KJX839
**Sponsor:** Novartis

## What was the main purpose of this trial?

The purpose of this trial was to learn about the safety and effects of KJX839 in Chinese participants with high cholesterol. The researchers also wanted to learn how much and how fast KJX839 got into the blood.

**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 can collect in the walls of blood vessels. High blood levels of LDL-C can increase the chances of serious conditions like heart attack or stroke. There are approved treatments for high cholesterol but sometimes people may need more help lowering their LDL-C.

**KJX839** is a trial drug designed to stop the liver from releasing too much of a protein called PCSK9 into the blood. Too much PCSK9 can slow down how the body removes LDL-C from the blood. If blood levels of PCSK9 go down, levels of LDL-C should also go down.

**The main questions this trial was designed to answer:**

- How much and how fast did KJX839 get into the blood?
- Did KJX839 change the blood levels of PCSK9?
- Did KJX839 change the blood levels of LDL-C?
- What medical problems did the participants have during this trial?
  Keeping track of the medical problems helped to learn about the safety of KJX839.

**Main results:** The researchers found that KJX839 reached its highest level in the blood after 6 to 8 hours. KJX839 was gone from the blood after about 1 and a half days. The amount of KJX839 in the blood went up as the dose went up.

They also found that KJX839 lowered blood levels of PCSK9 and LDL-C. The PCSK9 and LDL-C levels were lower throughout the 3 months after treatment.

The researchers concluded there were no new safety concerns for KJX839 in this trial.

## How long was this trial?

The trial began in February 2021 and ended in October 2021. It was planned for the participants to be in the trial for about 4 months.

## Who was in this trial?

40 participants were in this trial – 11 men and 29 women. The participants were 38 to 74 years old. Their average age was 60.

Every participant in this trial had high blood levels of LDL-C and:

- Were receiving high doses of statins, a type of cholesterol-lowering medicine. Or, were not able to take statins
- Had normal to high levels of another type of fat in the blood called triglycerides
- Did not have any major heart problems in the 3 months before starting the trial

This trial took place in China.

Visit **novctrd.com** for more information about:

- Who could and could not be in this trial
- Which medicines they could or could not take

Use trial number **CKJX839A12105** to find the scientific summary.

## What trial treatments did the participants receive?

The participants were randomly assigned to receive 1 of the following treatments 1 time:

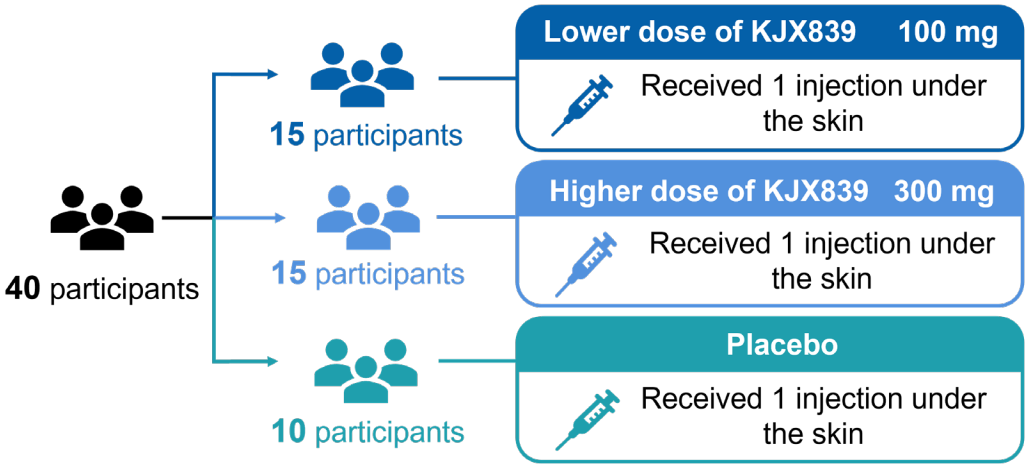
- **KJX839 100 milligrams (mg)**
- **KJX839 300 mg**
- **Placebo** - looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

The participants received their assigned treatment as an injection under the skin. All participants could continue taking certain cholesterol-lowering medicines, like statins.

A computer program was used to randomly assign the treatments. This helped make sure the researchers compared the results as fairly as possible.

The participants, sponsor staff, and trial staff did not know what treatment each participant received during the trial. Some trials are done this way because knowing what treatment participants take can influence the results. Not knowing what treatment participants take helps make sure the results are looked at fairly.

The graphic below shows how many participants were assigned to each treatment.



# What were the main results of this trial?

This is a summary of the overall results of this trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results.

Always talk to a doctor before making any changes to your health care.

## How much and how fast did KJX839 get into the blood?

The researchers found that KJX839 reached its highest level in the blood after 6 to 8 hours. KJX839 was gone from the blood after about 1 and a half days. The amount of KJX839 in the blood went up as the dose went up.

The trial staff took many blood samples from each participant during the trial. This allowed the researchers to learn how much and how fast KJX839 was in the participants' blood over time.

The researchers found that after receiving either dose of KJX839, the amount of KJX839 in the participants' blood:

Was highest
**6 to 8 hours**
after receiving the dose

Was gone from
the blood after about
**1 and a half days**

**Went up** as the
**dose went up**

## Did KJX839 change the blood levels of PCSK9?

Yes. After receiving either dose of KJX839, the blood levels of PCSK9 went down compared to levels before taking KJX839. The PCSK9 levels stayed lower throughout the 3 months after treatment.

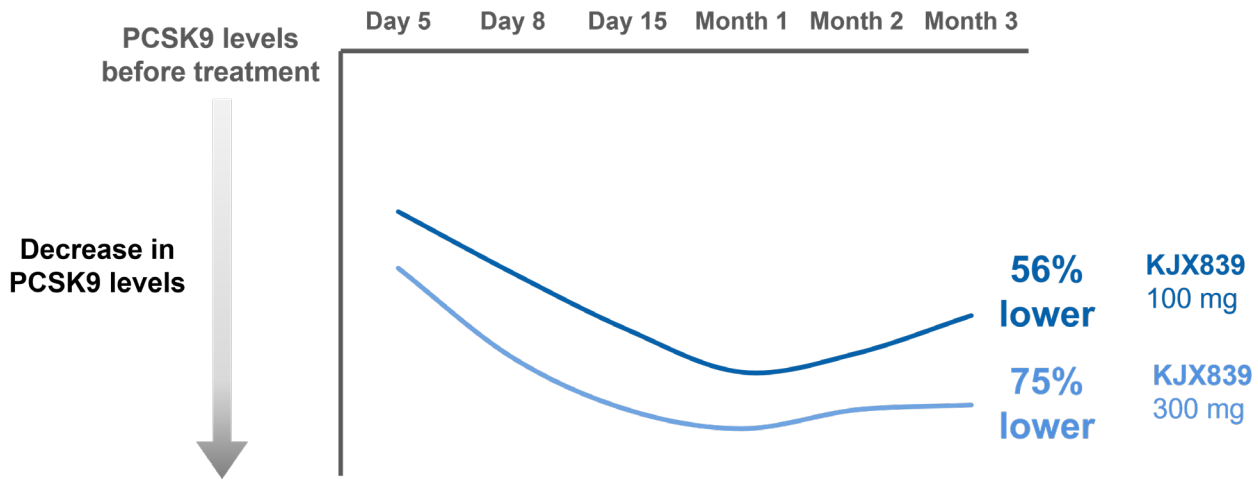
To find this out, the researchers measured how much PCSK9 was in the blood before and at different times after participants received either dose of KJX839. If the levels of PCSK9 lower, then the levels of LDL-C should also lower.

Overall, the researchers found that after receiving either dose of KJX839, the blood levels of PCSK9:

- Were lower compared to levels before taking KJX839
- Stayed lower throughout the 3 months after treatment

### Change in blood levels of PCSK9 after receiving KJX839

The graph below shows the percent change in PCSK9 levels throughout the 3 months after receiving KJX839.




## Did KJX839 change the blood levels of LDL-C?

Yes. After receiving either dose of KJX839, the blood levels of LDL-C went down compared to levels before taking KJX839. The LDL-C levels stayed lower throughout the 3 months after treatment.

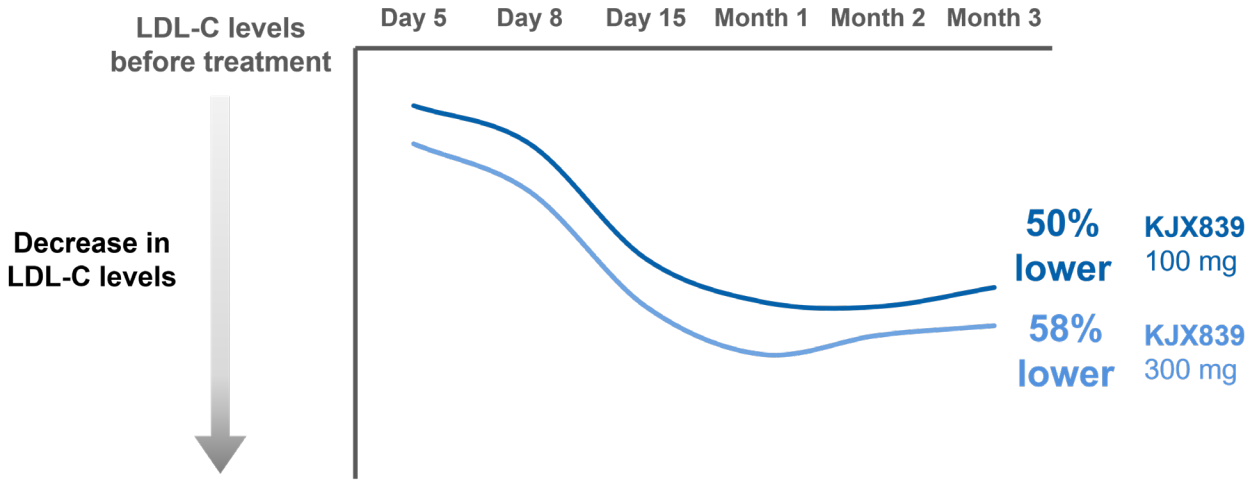
To find this out, the researchers measured how much LDL-C was in the blood before and at different times after participants received either dose of KJX839.

Overall, the researchers found that after receiving either dose of KJX839, the blood levels of LDL-C:

- Were lower compared to levels before taking KJX839
- Stayed lower throughout the 3 months after treatment

### Change in blood levels of LDL-C after receiving KJX839

The graph below shows the percent change in LDL-C levels throughout the 3 months after receiving KJX839.



## What other results were learned?

**Did KJX839 change the blood levels of PCSK9 and LDL-C compared to placebo?**

The researchers also compared changes in blood levels of PCSK9 and LDL-C between the different doses of KJX839 and the placebo.

Throughout the 3 months after treatment, either dose of KJX839:

- Lowered PCSK9 levels more than placebo
- Lowered LDL-C levels more than placebo

The higher dose of KJX839 lowered blood levels of PCSK9 and LDL-C the most compared to placebo.

## What medical problems did the participants have during this trial?

Medical problems that happen during trials are called “adverse events”.

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.

**An adverse event is:**

- Any **unwanted 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.

The adverse events in this section include those that happened during treatment and up to 3 months after treatment.

More than half of the participants reported adverse events (24 out of 40 participants). None of the participants reported adverse events that were considered serious. The most common type of adverse event was high levels of uric acid in the blood which can be common in some people with high cholesterol.

The researchers concluded there were no new safety concerns for KJX839 in this trial.

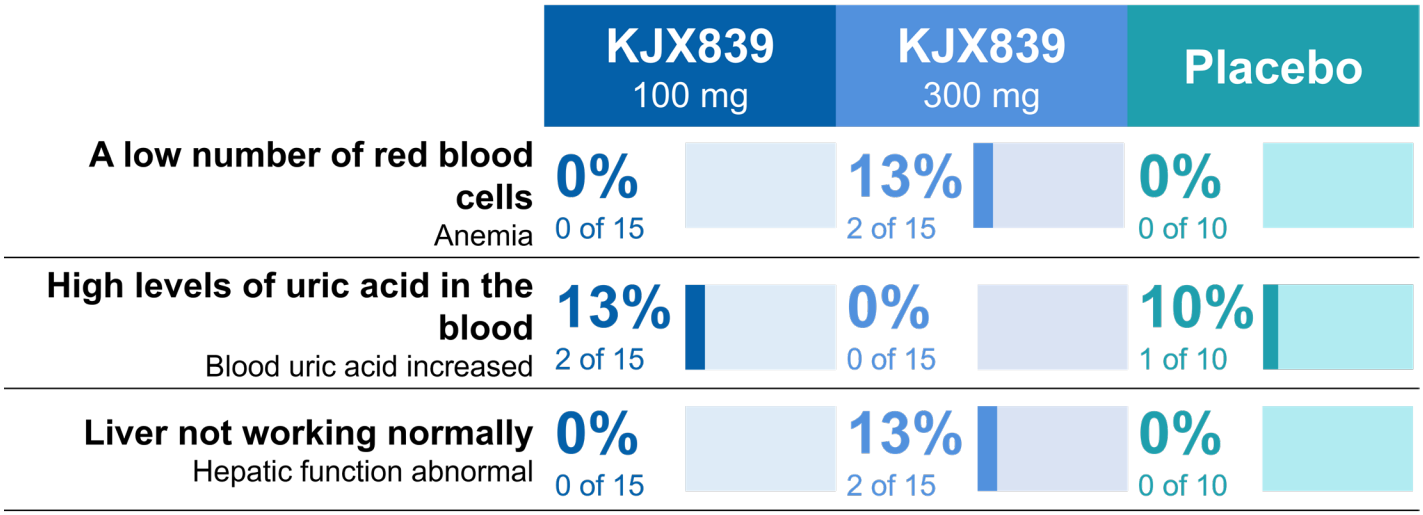
**What serious adverse events did the participants have?**

None of the participants had serious adverse events, including no deaths.

**What other adverse events did the participants have?**

- **KJX839 100 mg** – 7 of 15 participants, or 47%, had an adverse event
- **KJX839 300 mg** – 12 of 15 participants, or 80%, had an adverse event
- **Placebo** – 5 of 10 participants, or 50%, had an adverse event

The table below shows the adverse events that happened in **2 or more participants.** Additional adverse events were reported by fewer participants.




## What was learned from this trial?

This trial helped the researchers learn about the effects and safety of KJX839 in Chinese people with high cholesterol. The researchers concluded that KJX839 reached its highest level in the blood after 6 to 8 hours. KJX839 was gone from the blood after about 1 and a half days. The amount of KJX839 in the blood went up as the dose went up.

They also found that KJX839 lowered blood levels of PCSK9 and LDL-C. The levels stayed lower throughout the 3 months after treatment. The higher dose of KJX839 lowered the levels the most compared to placebo.

The researchers found no new safety concerns for KJX839 in this trial.

These are the results of a single trial. Other trials may have different results. This was one of many trials a drug goes through. This type of trial helped researchers learn about the effects and safety of a trial drug in a small number of participants.

## Where can I learn more about this and future trials?

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

- **novctrd.com** – search using the study number **CKJX839A12105**
- **clinicaltrials.gov** – search using the number **NCT04774003**

If more trials are planned, they will appear on the public websites above. When there, search for **KJX839, inclisiran, or LDL-C.**

**Full trial title:**
A placebo-controlled, participant, investigator and sponsor blinded, randomized study to evaluate the pharmacokinetics and pharmacodynamics of inclisiran treatment given as single subcutaneous injection in Chinese participants with elevated low-density lipoprotein cholesterol (LDL-C) despite treatment with LDL-C lowering therapies (ORION-14)

If you participated in the trial and have **questions** about the results, please speak with the trial doctors or staff at your trial site.

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