NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of CFZ533 in people with lupus nephritis

Thank you!

Thank you to the participants who took part in the clinical trial for **lupus nephritis**. Every participant helped the researchers learn more about the trial drug **CFZ533**, also called iscalimab.

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: CCFZ533X2202

Novartis drug studied: CFZ533, also known as iscalimab

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 main purpose of this trial was to learn more about the effects of the trial drug **CFZ533** in people with lupus nephritis.

Lupus is an **autoimmune disease**, which means the immune system attacks healthy cells in the body by mistake. This can cause damage to different parts of the body.

When lupus causes damage to the kidneys, it is called **lupus nephritis**. In people with lupus nephritis, the immune system attacks and damages the kidneys. Damaged kidneys do not work as well to filter the blood. This can lead to blood or protein in the urine, high blood pressure, or cause the kidneys to stop working.

What is the immune system?
The immune system is made up of many cells and proteins that help the body fight off disease and infection.

CFZ533 is a trial drug designed to block a protein in the immune system called CD40. **CD40** makes certain cells in the immune system more active. Researchers think blocking this protein may prevent the immune system from attacking the kidneys.

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

- What medical problems, also called adverse events, did the participants have during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.
- Did CFZ533 lower protein levels in participants' urine?

How long was this trial?

The trial began in September 2018 and ended in June 2023. The participants began this trial on different dates.

Who was in this trial?

57 participants with lupus nephritis received treatment in this trial – 10 men and 47 women. Participants' ages ranged from 20 to 58 years. Their average age was 35 years. The number of participants by race is shown below.

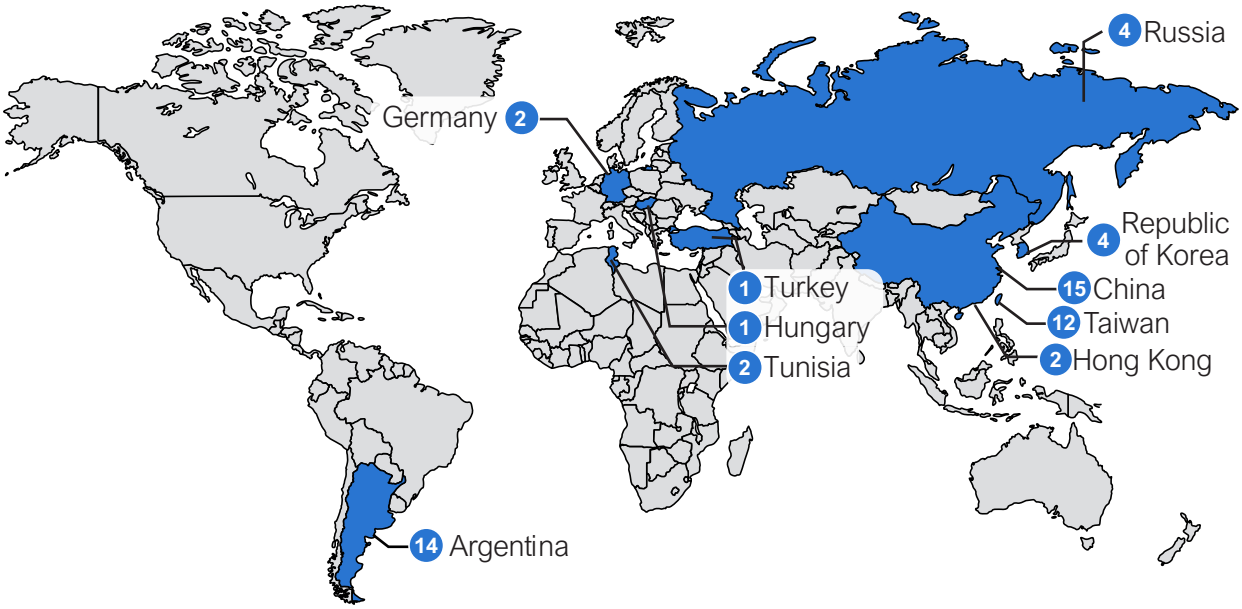
Race

34 Asian	23 White

The participants could take part in this trial if they:

- Had symptoms of lupus nephritis even when receiving standard treatments for lupus nephritis
- Did not receive certain standard treatments for lupus nephritis in the last 3 to 6 months

57 participants from 10 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:

CFZ533 – given based on each participant's weight. Participants received 10 milligrams (mg) for every kilogram of body weight (mg/kg). It was given through a needle in a vein, which is called an intravenous (IV) infusion.

Placebo – given as an IV infusion. A placebo looks like the trial drug but does not have any trial drug in it. Using a placebo helps researchers better understand the effects of a trial drug.

Researchers randomly assigned participants to receive one of the treatments above using a computer.

The participants, 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 the trial, participants could continue taking certain standard treatments for lupus nephritis.

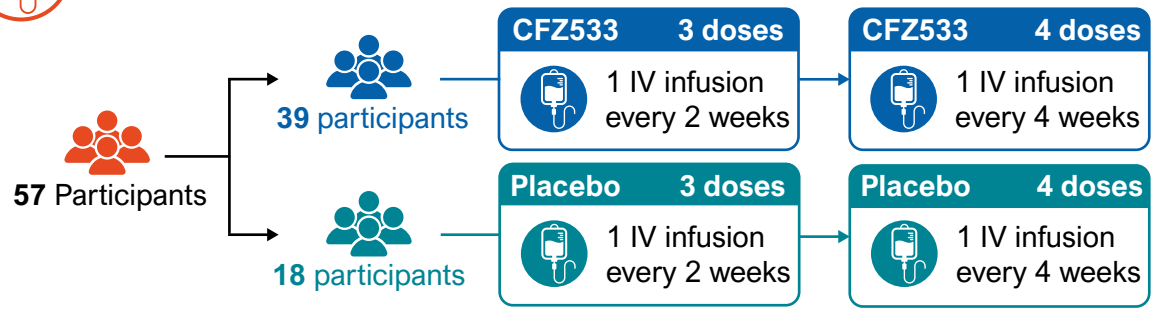
What happened during this trial?

Before treatment — **About 4 weeks**

Trial staff checked the participants' health and lupus nephritis to make sure they could be in this trial.

During treatment — **About 6 months**

Treatments were given as a 1-hour infusion.
The graphic below shows how many participants were assigned each treatment.



Trial staff checked the participants' health and lupus nephritis throughout the trial.

After treatment — **About 6 months**

Participants returned to their trial site up to 7 times after receiving their last dose of treatment for follow-up visits. Trial staff checked the participants' health and lupus nephritis during the follow-up visits.

What were the main results of this trial?

What medical problems, also called 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 up to about 6 months after 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.

Most of the participants (51 of 57) had adverse events. 9 participants had adverse events that were considered serious. 2 participants died in the trial. 4 participants left the trial due to an adverse event. The researchers concluded there were no new safety concerns for CFZ533 in this trial.

How many participants had adverse events?

Participants who:	CFZ533 39 participants	Placebo 18 participants
Had at least 1 **serious adverse event**	6 of 39 15%	3 of 18 17%
Had at least 1 **other adverse event**	32 of 39 82%	18 of 18 100%
Left the trial due to an adverse event	3 of 39 8%	1 of 18 6%
Died during the trial	2 of 39 5%	0 of 18 0%

What serious adverse events did the participants have?

11 serious adverse events happened in 9 participants – 6 participants in the **CFZ533** group, and 3 in the **placebo** group. 2 participants in the **CFZ533** group died during the trial.

In the **CFZ533** group, these serious adverse events happened in 1 participant each:

- **Life-threatening infection of the urinary tract** | Urosepsis
- **Infection in the lung airway** | Bronchitis
- **Stomach flu** | Gastroenteritis
- **UTI** | Urinary tract infection
- **Cytomegalovirus, also known as CMV, infection came back** | Cytomegalovirus infection reactivation
- **Life-threatening immune system activation** | Haemophagocytic lymphohistiocytosis
- **A lung infection** | Pneumonia

In the **placebo** group, these serious adverse events happened in 1 participant each:

- **Redness and swelling of the gallbladder** | Cholecystitis
- **Systemic lupus erythematosus got worse** | Systemic lupus erythematosus
- **Suicidal behavior**
- **Lupus nephritis symptoms got worse** | Lupus nephritis

What other adverse events did the participants have?

50 participants had other adverse events.

The table below shows the other adverse events that happened in **4 or more** participants. Additional adverse events happened in fewer participants.

	CFZ533 39 participants	Placebo 18 participants
Infection in the ear, nose, throat, or airways Upper respiratory tract infection	**7 of 39** 18%	**2 of 18** 11%
COVID-19	**5 of 39** 13%	**3 of 18** 17%
UTI Urinary tract infection	**2 of 39** 5%	**3 of 18** 17%
Shingles Herpes zoster	**3 of 39** 8%	**1 of 18** 6%
Common Cold Nasopharyngitis	**4 of 39** 10%	**0 of 18** 0%

Did CFZ533 lower protein levels in participants' urine?

After about 6 months, participants who received CFZ533 had lower protein levels in urine compared to those who received placebo.

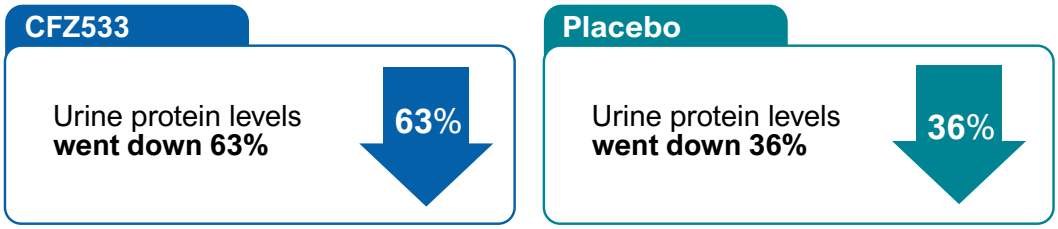
To find this out, the researchers measured protein levels using the **urine protein-creatinine ratio (UPCR)**. People with lupus nephritis have a higher UPCR, which means the kidneys are not working well and are letting too much protein into urine. If the UPCR goes down, it may mean kidney damage is slowing down.

What is UPCR?
UPCR is a test that compares the level of protein in urine to the level of creatinine in urine. Creatinine is a waste product that healthy kidneys filter from the blood into urine in small amounts.

For this test, trial staff collected and tested each participant's urine. They did this before and after about 6 months of treatment. The researchers looked at the average change in protein levels in each participant's urine from before treatment to after treatment.

Change in urine protein levels

The results below show the average change in the level of protein in participants' urine after about 6 months of treatment.



When the urine protein level goes **down**, it may mean kidney damage is **slowing down**.

These results include only those participants who completed their treatment as planned: 20 for CFZ533 and 10 for placebo.

What were the other results of this trial?

Did CFZ533 affect signs of kidney damage after about a year?

Between the CFZ533 and placebo groups, there was no meaningful difference after about a year in the:

- UPCR
- Amount of blood in the urine
- Tiny clumps of cells in the urine

If there is less blood and tiny clumps of cells in the urine, this may mean kidney damage is slowing down.

How many participants had their lupus nephritis go into remission after treatment?

After about 6 months, 13 participants in the CFZ533 group and 4 participants in the placebo group were in remission.

Researchers counted how many participants had lupus nephritis remission after about 6 months. In this trial, **remission** meant a participant had:

- Their UPCR go down to the healthy range
- Higher kidney function
- A normal amount of cells in the urine

Did CFZ533 affect a protein in the immune system called CD40?

Participants' CD40 levels in the blood went up after taking CFZ533 and went back down after stopping CFZ533. This means CFZ533 is working in the way researchers expected.

Sometimes when certain immune proteins are blocked by a drug, the body reacts by producing more of those proteins. In this trial, researchers concluded CD40 levels went up because CFZ533 was blocking CD40 from raising the activity of the immune system.

What was learned from this trial?

Researchers learned about the effects of the trial drug CFZ533 in people with lupus nephritis.

The researchers concluded there were no new safety concerns for CFZ533 in this trial. They also concluded that compared to the placebo group, the CFZ533 group had lower protein levels in urine after about 6 months of treatment.

Researchers also learned that:

- There was no meaningful difference in the UPCR or the amount of blood and tiny clumps of cells in the urine after about a year
- More participants in the CFZ533 group (13) were in lupus nephritis remission compared to the placebo group (4) after about 6 months
- CFZ533 affected CD40 as expected

When this summary was written, the sponsor had no plans for future trials of CFZ533 in people with lupus nephritis.

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 **NCT03610516**
- clinicaltrialsregister.eu/ctr-search/search – search using the number **2017-003230-93**

Full clinical trial title: A randomized, placebo-controlled, patient and investigator blinded, study investigating the safety, tolerability, pharmacokinetics and preliminary efficacy of multiple doses of CFZ533 in patients with moderately active proliferative lupus nephritis

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