Clinical Trial Results Summary

Research Sponsor: Novartis

Drug Studied: CFZ533 (iscalimab)

Trial Number: CCFZ533X2203

Plain Language Title: A trial to learn more about how CFZ533 works and about its safety in participants with primary Sjögren's syndrome

Thank you!

Thank you to the participants who took part in the clinical trial for the drug CFZ533, also known as iscalimab. All of the participants helped the researchers learn more about how CFZ533 works and how safe it is to take.

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. Novartis reviewed the results of the trial when it ended. An independent organization prepared this summary of the trial results.

We hope this helps the participants understand their important role in medical research.

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

You can find more information about this trial on the website listed on the last page of this summary.

Overview of this trial

What was the purpose of this trial?

In this clinical trial, the researchers studied how a drug called CFZ533 affected the severity of symptoms in participants with primary Sjögren's syndrome, also known as PSS.

The researchers also studied the safety of CFZ533 in these participants.

What treatments did the participants take?

During this trial, the participants received CFZ533 or a placebo.

A 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.

Who took part in the trial?

69 men and women with PSS participated in this clinical trial.

What did the researchers want to learn?

The main questions the researchers wanted to answer in this trial were:

- Did CFZ533 make the participants' PSS symptoms less severe?
- What medical problems did the participants have during the trial?

Keeping track of the participants' medical problems helped the researchers learn about the safety of CFZ533.

What were the main results of the trial?

Overall, the researchers learned that:

- CFZ533 helped reduce the severity of the participants' PSS symptoms more than the placebo when given through a needle put into a vein called an IV infusion.
- Most of the participants had medical problems during this trial, and some of the medical problems were serious. The number of medical problems was about the same in the participants who received CFZ533 as those who received the placebo. The most common medical problem was an infection of the upper airways of the lungs.

Why was the research needed?

Researchers are looking for a better way to treat patients with primary Sjögren's syndrome, also known as PSS. Before a drug can be approved for patients to take, researchers do clinical trials to find out how safe it is and how it works. In this trial, the researchers studied how the trial drug called CFZ533 affected the severity of the participants' symptoms. The researchers also studied the safety of CFZ533.

In people with PSS, the body's immune system is overactive. When that happens, the immune system attacks the body, including the glands that make fluids like tears, saliva, or sweat. PSS may also affect other parts of the body, like the joints and lungs. People with PSS have dryness of the mouth, eyes, and other areas. They also have pain and tiredness that severely affect their daily lives.

Doctors and researchers do not know what causes PSS. The trial drug, CFZ533, was designed to lower the activity of the immune system by blocking the function of immune cells that have a protein called CD40. The researchers in this trial wanted to learn if CFZ533 could help reduce the severity of the participants' PSS symptoms.

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What treatments did the participants receive?

There were 3 treatment groups in this trial.

- Groups 1 and 2: doses of CFZ533 were measured in milligrams per kilogram of body weight, also called mg/kg.
- Group 3: doses of CFZ533 were measured in both mg/kg and milligrams, also called mg.

Groups 1 and 2

The researchers used a computer program to randomly choose the treatment each participant received. This helped make sure the treatments were chosen fairly and comparing the results of the treatments was as accurate as possible. None of the participants, trial staff, or sponsor staff knew what treatment each participant received for the first 12 weeks.

Some trials are done this way because knowing what treatment the participants are receiving can influence the results. Not knowing what treatment participants receive helps make sure the results are looked at fairly.

- For the first 12 weeks, the participants in Groups 1 and 2 received CFZ533 or a placebo.
  - A 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.
- After the first 12 weeks, each participant found out what they were receiving. The trial staff and sponsor staff also found out what each participant was receiving.
  - All of the participants in Groups 1 and 2 received CFZ533 for another 12 weeks.

Group 3

Each participant knew what they were receiving the whole time. The trial staff and sponsor staff also knew what each participant was receiving. All of the participants in Group 3 received CFZ533.

The participants received the treatments through either:

- a needle under the skin, also called an injection
- a needle put into a vein, also called an IV infusion, followed by an injection

The chart below shows the treatments the participants received.

Group 1	Group 2	Group 3
8 participants received 3.0 mg/kg of CFZ533 8 doses over 24 weeks through an injection under the skin	21 participants received 10.0 mg/kg of CFZ533 8 doses over 24 weeks through an IV infusion	13 participants received 4 doses of 600 mg of CFZ533 over 4 weeks Then they received 9 doses of 300 mg of CFZ533 once a week for 9 weeks All doses were through an injection under the skin
4 participants received 4 doses of the placebo over 12 weeks Then they received 4 doses of 3.0 mg/kg of CFZ533 over 12 weeks All doses were through an injection under the skin	11 participants received 4 doses of the placebo over 12 weeks Then they received 4 doses of 10.0 mg/kg of CFZ533 over 12 weeks All doses were through an IV infusion	12 participants received 1 dose of 10.0 mg/kg CFZ533 as an IV infusion during week 1 Then they received 300 mg of CFZ533 once a week for 12 weeks as an injection under the skin

Who took part in the trial?

The researchers asked for the help of participants with PSS. Everyone in the trial was 23 to 74 years old when they joined. The average age of the participants was about 53 years old.

The trial included 69 participants in 5 countries: Germany, Hungary, Switzerland, the United Kingdom, and the United States.

What happened during the trial?

Each participant was in the trial for up to about 36 weeks. The trial lasted several years. It started in October 2014 and ended in June 2018.

The chart below shows what happened during the trial.

Before the participants received the treatment

The trial doctors checked the participants' health to make sure they could be in the trial.

During the trial

69 participants received treatments in 1 of 3 groups.

Group 1

- The participants received CFZ533 injections or the placebo for the first 12 weeks.
- All the participants received CFZ533 injections for the next 12 weeks.

Group 2

- The participants received CFZ533 or the placebo through an IV infusion for the first 12 weeks.
- All the participants received CFZ533 through an IV infusion for the next 12 weeks.

Group 3

- The participants received a CFZ533 injection once a week for 13 weeks.

or

- The participants received CFZ533 through an IV infusion once, then received CFZ533 injections for 12 weeks.

Up to 24 weeks

Up to 13 weeks

After the participants received the last dose

The trial doctors checked the participants' health.

Over a period of 8 weeks

What did researchers learn from the results of the trial?

This is a summary of the overall results from this trial. The individual results of each participant might be different and are not in this summary.

Other trials may provide new information or different results. Always talk to a doctor before making any healthcare decisions.

Did CFZ533 make the participants' PSS symptoms less severe?

Yes. The researchers found that CFZ533 helped reduce the severity of the participants' PSS symptoms more than the placebo when given through an IV infusion.

To answer this question, the trial doctors measured how severe the participants' PSS symptoms were before receiving the trial drug, and 12 weeks after starting treatment. They did this using the European League Against Rheumatism Sjögren's Syndrome Disease Activity Index, also called the ESSDAI. Lower scores meant the PSS symptoms were less severe.

The researchers compared the scores for the participants who received CFZ533 and the participants who received the placebo. They did this in Group 1 and in Group 2.

After 12 weeks of treatment, the researchers found that:

- In Group 1, the participants who received CFZ533 had a similar decrease in their ESSDAI score compared to those who received the placebo.
- In Group 2, the participants who received CFZ533 had a larger decrease compared to those who received the placebo.

The researchers also found that:

- In Group 2, the participants who received 10.0 mg/kg of CFZ533 through an IV infusion had less severe symptoms compared to those who received the placebo.
- In Group 1, the difference between the participants who received 3.0 mg/kg of CFZ533 through an injection and those who received the placebo was small. The difference was too small for the researchers to conclude that CFZ533 given through an injection made the participants' PSS symptoms less severe than the placebo.

In Group 1, the researchers found that the ESSDAI scores decreased by an average of:

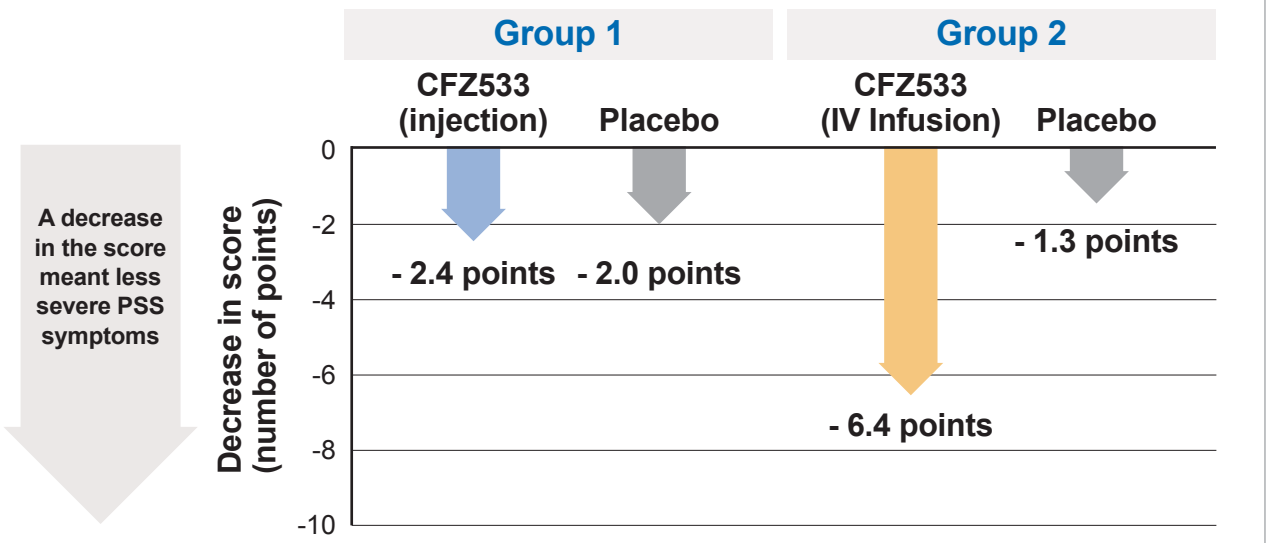
- 2.4 points in the participants who received CFZ533
- 2.0 points in the participants who received the placebo

In Group 2, the researchers found that the ESSDAI scores decreased by an average of:

- 6.4 points in the participants who received CFZ533
- 1.3 points in the participants who received the placebo

The chart below shows these results.

Average decrease in ESSDAI scores after 12 weeks of treatment



The clinical team used the results from groups 1 and 2 to answer the above question as accurately as possible. This is because nobody knew what treatment the participants were receiving, and the researchers could compare CFZ533 to the placebo.

The researchers also wanted to know if there was a difference in ESSDAI scores in Group 3. But, this was not the main question the trial was designed to answer. In Group 3, the researchers compared the scores for the participants who received a CFZ533 injection and those who received a CFZ533 infusion. But, the clinical team had to look at the Group 3 ESSDAI results with caution. This is because this group of participants knew what treatment they were receiving, and the researchers could not compare CFZ533 to a placebo. Using a placebo helps researchers be sure that the changes seen are not just due to chance.

Overall, the researchers found that there was no difference in the ESSDAI scores between the participants who received a CFZ533 injection compared to those who received a CFZ533 infusion after 13 weeks of treatment.

What medical problems happened during the trial?

Medical problems that happen in clinical trials are called “adverse events”. An **adverse event** is any unwanted sign or symptom 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.

Adverse events may or may not be caused by the treatments in the trial. A lot of research is needed to know whether a treatment causes an adverse event. Trial doctors keep track of all the adverse events that happen in trials, even if they do not think the adverse events may be related to the treatments.

This section is a summary of the adverse events that happened during this trial.

The number of adverse events was about the same in the participants who received CFZ533 as those who received the placebo. The most common adverse event was an infection of the upper airways.

How many participants had adverse events?

The table below shows how many participants in each group had adverse events in this trial.

Adverse events in this trial

	Group 1		Group 2		Group 3	
	CFZ533 injection (Out of 8 participants)	Placebo (Out of 4 participants)	CFZ533 IV infusion (Out of 21 participants)	Placebo (Out of 11 participants)	CFZ533 injection (Out of 13 participants)	CFZ533 IV infusion (Out of 12 participants)
How many participants had adverse events?	100.0% (8)	100.0% (4)	52.4% (11)	63.6% (7)	92.3% (12)	100.0% (12)
How many participants had serious adverse events?	12.5% (1)	0.0% (0)	4.8% (1)	0.0% (0)	0.0% (0)	8.3% (1)
How many participants left the trial because of adverse events?	0.0% (0)	25.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)

What were the most common serious adverse events?

During this trial, 5 serious adverse events happened in 3 participants:

- pink eye caused by bacteria in a participant who received CFZ533 in Group 1
- irregular or quick heartbeat in a participant who received CFZ533 in Group 2
- bleeding into a joint in a participant who received CFZ533 in Group 3
- worsening knee pain in a participant who received CFZ533 in Group 3
- worsening knee swelling in a participant who received CFZ533 in Group 3

During this trial, none of the participants died due to serious adverse events.

What were the most common adverse events?

The most common adverse event during this trial was infection of the upper airways.

The adverse events below and on the next page happened in 3 or more participants in each group during the trial. There were other adverse events, but these happened in fewer participants.

Most common adverse events in Group 1

	CFZ533 injection (Out of 8 participants)	Placebo (Out of 4 participants)	Total (Out of 12 participants)
Infection of the upper airways	25.0% (2)	50.0% (2)	33.3% (4)
Joint pain	25.0% (2)	25.0% (1)	25.0% (3)
Dizziness	25.0% (2)	25.0% (1)	25.0% (3)
Infection of the lower airways	25.0% (2)	25.0% (1)	25.0% (3)
Rash	25.0% (2)	25.0% (1)	25.0% (3)

Most common adverse events in Group 2

	CFZ533 IV infusion (Out of 21 participants)	Placebo (Out of 11 participants)	Total (Out of 32 participants)
Infection of the upper airways	9.5% (2)	18.2% (2)	12.5% (4)
Bruise	9.5% (2)	9.1% (1)	9.4% (3)
Diarrhea	9.5% (2)	9.1% (1)	9.4% (3)
Headache	9.5% (2)	9.1% (1)	9.4% (3)

Most common adverse events in Group 3

	CFZ533 injection (Out of 13 participants)	CFZ533 IV infusion (Out of 12 participants)	Total (Out of 25 participants)
Headache	15.4% (2)	33.3% (4)	24.0% (6)
Infection of the upper airways	30.8% (4)	16.7% (2)	24.0% (6)
Common cold	7.7% (1)	33.3% (4)	20.0% (5)

For more information about the adverse events in this trial, please see the scientific summary that can be found on the websites noted at the end of the summary.

What was learned from this trial?

The information described above helped researchers learn if CFZ533 helped reduce the severity of symptoms and about its safety in participants with PSS.

More research is needed to find out which treatments can be used for patients with PSS. This summary shows only the main results from this one trial. Other trials may provide new information or different results.

Where can I learn more about this trial?

More information about the results of this trial can be found in the scientific results summary available on the Novartis Clinical Trial Results website.

- Go to www.novctrd.com.
- Once on the site, click **"Clinical trial results and trial summary for patients"** at the top right of the page.
- After accepting the terms, go to the bottom left of the page and click **"Search by study number"**.
- Type **"CCFZ533X2203"** into the keyword search box and click **"Search"**.

If you would like to view the website in a language other than English, you can click the **"Google Translate"** button on the top right of the page.

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

If more clinical trials are planned, they will be listed on the above public websites or www.novartisclinicaltrials.com. Search for **"CFZ533"**, **"iscalimab"**, or **"primary Sjögren's syndrome"**.

You can find more information about this trial on the websites listed below.

- www.clinicaltrials.gov Once you are on the website, type **"CCFZ533X2203"** into the **"Other terms"** search box, and click **"Search"**.
- www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"CCFZ533X2203"** in the search box, and click **"Search"**.

Full trial title: A multi-center, randomized, double-blind, placebo-controlled, parallel group study to assess the safety, tolerability, pharmacokinetics and preliminary efficacy of CFZ533 in patients with primary Sjögren's syndrome

Protocol number: CCFZ533X2203

Thank you!

Clinical trial participants belong to a large community of participants around the world. They help researchers answer important health questions and study 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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