Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis

Drug Studied: CFZ533

Protocol #: CCFZ533X2101

Thank you!

Thank you for taking part in the clinical trial for the drug CFZ533. You and all of the participants helped researchers learn more about how CFZ533 works in people with rheumatoid arthritis, also called RA.

Novartis sponsored this trial and thinks it is important to share the results of the trial with you and the public. An independent non-profit organization called CISCRP prepared this summary of the trial results for you. We hope it helps you understand your important role in medical research.

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

What has happened since the trial ended?

You were in this trial for up to about 9 months. But, the entire trial took 4 years to finish. This is because participants started and stopped at different times. The trial started in January 2013 and ended in February 2017.

The trial included 76 participants in the United States and Taiwan. The 76 participants included 56 healthy participants and 20 participants with RA. Eight of the healthy participants were in a separate treatment group. These participants were Chinese. The Chinese healthy participants were included to help researchers learn about CFZ533 in an Asian population.

The sponsor reviewed the data collected when the trial ended and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers are looking for a better way to treat people who have immune system diseases like RA. Before a drug can be approved for patients to take, researchers do clinical trials to find out how well it works and how safe it is. This information is important to know before other trials can be done to find out if CFZ533 improves the health of people with immune system diseases like RA.

In people with immune system diseases like RA, the body's immune system mistakenly attacks the tissues in the body, including the joints. This causes inflammation and swelling that damage the joints and other tissues. Researchers think T-cells and B-cells may be involved in this tissue damage. These cells link together when the immune system needs to fight infections. But in people with RA, these cells link together even when there is no infection. The trial drug CFZ533 may prevent these immune cells from linking together. This may help reduce the symptoms of RA.

In this trial, the researchers wanted to find out what amounts of CFZ533 were safe for participants to take. They also wanted to find out how much CFZ533 got into each participant's blood. To do this, the researchers compared CFZ533 with a placebo. A placebo looks like a drug but does not have any medicine in it. Using a placebo helps researchers better understand the actual effect of a trial drug.

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

- What medical problems did participants have?
- How much CFZ533 got into the participants' blood?
- Did the participants getting CFZ533 have an unwanted immune system response?

What kind of trial was this?

To answer the questions in this trial, the researchers asked for the help of both healthy participants and participants with RA. The participants in this trial were men and women who were 19 to 65 years old.

- This was a "dose escalation" trial. This means that each participant got only 1 dose of the trial treatment. Different groups of participants were given different doses of CFZ533. The researchers looked at the results from each group of participants who were given the same dose before giving the next higher dose to the next group of participants.

- The first 2 healthy participants got CFZ533 as "open-label" treatment. This means that each participant knew what treatment they were getting. The trial staff and sponsor staff also knew what treatment each participant was getting. The researchers did this to make sure CFZ533 was safe for participants to take.

- 54 healthy participants and 20 participants with RA got "double-blind" treatment. This means that none of the participants, trial doctors, or other trial staff, or sponsor staff knew what treatment each participant got. Some trials are done this way because knowing what treatment the participants are getting can affect the results of the trial. Doing a trial this way helps make sure the results are looked at fairly. When the trial ended, the research sponsor found out which treatment participants got so they could create a report of the trial results.

A computer program was used to randomly choose the treatment each participant got. Researchers do this so that comparing the results of each treatment is done as fairly as possible.

What happened during the trial?

Before the trial treatment started, the trial doctors did tests to make sure participants could take part in the trial. Participants gave blood and urine samples. The trial doctors also checked the heart health of participants using an electrocardiogram, also called an ECG. Participants got vaccinations if they needed them. Participants stayed at the trial site the night before treatment started.

This trial was done in 2 parts. Part 1 started first. Then, Part 2 began about halfway through Part 1. Participants were in only 1 part of the trial. Each participant received 1 dose of trial treatment.

Part 1:

- Healthy participants got either CFZ533 or a placebo. Healthy participants got 1 of these through a tube into the vein. This is called an intravenous dose, also called IV.
- After different doses were tested in healthy participants, then the participants with RA joined the trial. Participants with RA got either CFZ533 or a placebo. Each participant with RA got 1 of these through an IV dose.

Part 2:

- Healthy participants in this part got either CFZ533 or a placebo. Healthy participants got 1 of these through a needle under the skin. This is called a subcutaneous dose, also called SC.
- This helped the researchers learn if a different way of giving CFZ533 affected how much CFZ533 got into the blood.

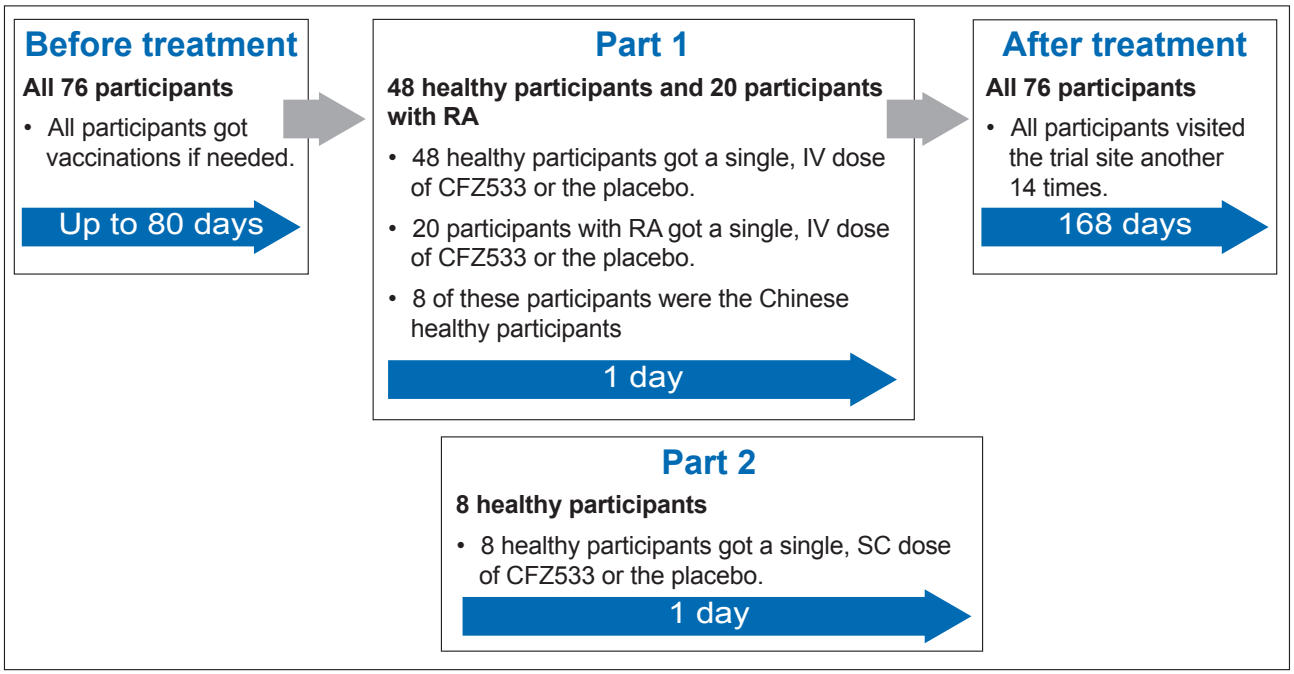
For both parts of the trial, each participant received 1 dose of trial treatment. The dose each participant got was based on which group the participant was assigned to and the participant's body weight. Doses were measured in milligrams per kilogram, also called mg/kg.

Seven different doses of CFZ533 were compared to the placebo in 12 groups:

Treatment	Type of participant	Treatment	Number of participants
Group 1	Healthy participants	0.03 mg/kg CFZ533 by IV	6
Group 2	Healthy participants	0.1 mg/kg CFZ533 by IV	6
Group 3	Healthy participants	0.3 mg/kg CFZ533 by IV	6
Group 4	Healthy participants	1.0 mg/kg CFZ533 by IV	6
Group 5	Healthy participants	3.0 mg/kg CFZ533 by IV	6
Group 6	Healthy participants	3.0 mg/kg CFZ533 by SC	6
Group 7	Healthy participants	Placebo by IV or SC	12
Group 8	Chinese healthy participants	3.0 mg/kg CFZ533 by IV	6
Group 9	Chinese healthy participants	Placebo by IV	2
Group 10	Participants with RA	10.0 mg/kg CFZ533 by IV	6
Group 11	Participants with RA	30.0 mg/kg CFZ533 by IV	4
Group 12	Participants with RA	Placebo by IV	10

After treatment, the participants stayed at the trial site for another 3 days. The trial doctors checked the participants' overall health and heart health. The trial doctors also checked how the participants were feeling and what medications they were taking. The participants visited the trial site another 14 times. At each visit, the trial doctors checked the participants' overall health. The participants gave more blood and urine samples. They may have also gotten another vaccination.

The chart below shows how the trial was done.



What were the results of the trial?

This is a summary of the overall results of your trial, not your individual results. The results presented here are for a single trial. Researchers look at the results of many trials to decide which drugs work best and are safest for patients. Other trials may provide new information or different results. You should not make medical decisions based on the results of a single trial without first talking to your doctor. Always talk to your doctor before making any changes to your medications or treatment plans.

What medical problems did participants have 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. These problems may or may not be caused by the trial drug. A lot of research is needed to know whether a drug causes a medical problem. During a trial, all medical problems are reported and written down, whether or not they are caused by the trial drug. So, when new drugs are being studied, researchers keep track of all medical problems that participants have.

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

How many participants had adverse events?

Adverse events and serious adverse events happened more often in participants with RA compared to the healthy participants. The healthy participants who got CFZ533 through SC had adverse events as often as healthy participants who got CFZ533 through an IV.

None of the healthy participants had serious adverse events. None of the participants left the trial because of an adverse event.

The tables below show how many participants had adverse events during this trial.

Healthy participants

Treatment group	How many healthy participants in the trial had adverse events?
Group 1 (CFZ533)	83.3% (5 out of 6 participants)
Group 2 (CFZ533)	66.7% (4 out of 6 participants)
Group 3 (CFZ533)	100.0% (6 out of 6 participants)
Group 4 (CFZ533)	83.3% (5 out of 6 participants)
Group 5 (CFZ533)	50.0% (3 out of 6 participants)
Group 6 (CFZ533)	83.3% (5 out of 6 participants)
Group 7 (Placebo)	66.7% (8 out of 12 participants)

Chinese healthy participants

Treatment group	How many Chinese healthy participants in the trial had adverse events?
Group 8 (CFZ533)	83.3% (5 out of 6 participants)
Group 9 (Placebo)	0.0% (0 out of 2 participants)

Participants with RA

Treatment group	How many participants with RA in the trial had adverse events?	How many participants with RA in the trial had serious adverse events?
Group 10 (CFZ533)	100.0% (6 out of 6 participants)	0.0% (0 out of 6 participants)
Group 11 (CFZ533)	100.0% (4 out of 4 participants)	25.0% (1 out of 4 participants)
Group 12 (Placebo)	90% (9 out of 10 participants)	10.0% (1 out of 10 participants)

What were the most common serious adverse events?

Overall, 2.6% of participants had serious adverse events. This was 2 out of 76 participants. All serious adverse events reported were in participants with RA. The doctors did not think these serious adverse events were related to CFZ533. The serious adverse events in this trial were:

- Fainting in a participant that got CFZ533
- Confusion in a participant that got CFZ533
- Inflammation in the large intestine in a participant that got placebo

None of the participants died during this trial.

What were the most common adverse events?

Headache was the most common adverse event in healthy participants. Upper respiratory tract infection was the most common adverse event in participants with RA. The tables below and on the next page show the most common adverse events that happened in 10.0% or more of all participants. There were other adverse events, but these happened in fewer participants.

Most common adverse events in this trial in healthy participants

Adverse event	Group 1 CFZ533 (6 participants)	Group 2 CFZ533 (6 participants)	Group 3 CFZ533 (6 participants)	Group 4 CFZ533 (6 participants)	Group 5 CFZ533 (6 participants)	Group 6 CFZ533 (6 participants)	Group 7 Placebo (12 participants)
Headache	50.0% (3)	0.0% (0)	16.7% (1)	16.7% (1)	16.7% (1)	16.7% (1)	50.0% (6)
Pain at the injection site	16.7% (1)	0.0% (0)	33.3% (2)	0.0% (0)	33.3% (2)	0.0% (0)	16.7% (2)
Pain in the throat	16.7% (1)	16.7% (1)	0.0% (0)	0.0% (0)	0.0% (0)	50.0% (3)	8.3 % (1)
Sinus congestion	16.7% (1)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)	33.3% (2)	8.3 % (1)

Most common adverse events in this trial in Chinese healthy participants

Adverse event	Group 8 CFZ533 (6 participants)	Group 9 Placebo (2 participants)
Headache	0.0% (0)	0.0% (0)
High levels of sugar in the blood	33.3% (2)	0.0% (0)
Pain at the injection site	0.0% (0)	0.0% (0)

Most common adverse events in this trial in participants with RA

Adverse event	Group 10 CFZ533 (6 participants)	Group 11 CFZ533 (4 participants)	Group 12 Placebo (10 participants)
Upper respiratory tract infection	33.3% (2)	50.0% (2)	30.0% (3)
Common cold	33.3% (2)	25.0% (1)	0.0% (0)
Vomiting	33.3% (2)	0.0% (0)	0.0% (0)
Headache	16.7% (1)	25.0% (1)	20.0% (2)
Nausea	16.7% (1)	0.0% (0)	20.0% (2)
Low levels of potassium in the blood	16.7% (1)	0.0% (0)	10.0% (1)
Urinary tract infection	16.7% (1)	0.0% (0)	40.0% (4)
Bronchitis	0.0% (0)	0.0% (0)	20.0% (2)

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

How much CFZ533 got into the participants' blood?

The researchers wanted to know how much CFZ533 got into the blood of participants. Overall, the researchers found that:

- In general, the highest amount of CFZ533 in the blood was higher for participants who got higher doses of CFZ533.
- The time it took for CFZ533 to reach its highest amount in the blood was similar in participants with RA compared to healthy participants.
- CFZ533 got into the blood whether given by IV or SC.

Did the participants getting CFZ533 have an unwanted immune system response?

Overall, CFZ533 did not produce an unwanted immune system response in most participants.

The immune system makes proteins called antibodies to find anything that the body does not recognize. This is how the body knows to fight infections caused by bacteria or viruses. Sometimes the immune system makes antibodies against medicines. This might prevent the medicine from working.

The researchers found that 1 healthy participant who got 1mg/kg of CFZ533 through IV had antibodies form against CFZ533. This did not decrease the amount of CFZ533 in the blood and it did not cause any medical problems in this participant.

How has this trial helped patients and researchers?

This trial studied CFZ533 in humans for the first time. The results of this trial helped researchers better understand how the body reacts to different doses of CFZ533 and if CFZ533 can be used in future trials. This research helped doctors understand more about whether CFZ533 could be a treatment for RA and other immune system diseases.

The results from several trials are needed to decide which treatments work best and are safest. 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 (www.novctrd.com). Once on the site, click **"READ MORE"** at the bottom of the page under the heading **"Clinical trial results"**. After agreeing to enter the Novartis website, type **"CCFZ533X2101"** into the keyword search box and click **"Search"**. If you 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 below.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02089087"** into the search box and click **"Search"**.

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

Full Trial Title: A randomized, double-blind, placebo-controlled, single ascending dose first-in-human study to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of CFZ533 in healthy subjects and rheumatoid arthritis patients

Thank you

As a clinical trial participant, you belong to a large community of participants around the world. You helped researchers answer important health questions and test new medical treatments.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation.

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