Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis
Drug Studied: CFZ533
Protocol Number: CCFZ533X2201

Thank you!

Thank you for taking part in the clinical trial for the drug CFZ533. You and all of the patients helped researchers learn more about how CFZ533 works in patients who got a kidney transplant.

Novartis sponsored this trial and believes 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 trial doctor or staff at your trial site.

What has happened since the trial ended?

You were in this trial for up to about 1 year. But, the entire trial took about 2 years and 10 months to finish. This is because patients started and stopped at different times. The trial started in February 2015 and ended in November 2017.

At first, the researchers planned this trial in 3 parts. But after the trial started, they decided to take out Part 3 and make it a separate trial. So, this trial included only 2 parts.

The trial included 59 patients from 14 trial sites in Brazil, Germany, the Netherlands, and the United States. After the trial ended, the sponsor reviewed the data 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 help patients who get a kidney transplant. Before a drug can be approved for patients to take, researchers do clinical trials to find out how safe it is and how well it works. The information collected from many clinical trials is needed to find out if CFZ533 improves the health of people who get a kidney transplant.

The researchers wanted to learn if CFZ533 could help prevent transplant rejection in a small number of patients who got a kidney transplant. In this trial, the patients got a standard therapy with CFZ533 or with tacrolimus. Tacrolimus is a standard therapy that is also called Tac. A treatment is considered a “standard therapy” when the medical community thinks it is the appropriate and widely used treatment for a condition. Giving patients a standard therapy helps doctors make sure that all patients in the trial get a form of treatment.

CFZ533 is designed to lower the activity of the immune system. It does this by blocking certain proteins from causing an immune system response that can damage the transplanted kidney. The researchers wanted to find out if CFZ533 could help patients who got a kidney transplant by reducing this immune system response. They also wanted to know more about the safety of CFZ533 in patients who got a kidney transplant.

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

- Did the patients in each treatment group have a similar number of rejection events?
- How much CFZ533 stayed in the patients' blood after one IV dose?
- What medical problems did the patients have?

What kind of trial was this?

To answer the questions in this trial, the researchers asked for the help of men and women who needed a kidney transplant. The patients in this trial were 19 to 78 years old.

This was an "open-label" trial. This means each patient knew what they were getting. The trial staff and sponsor staff also knew what the patient was getting. The sponsor staff did not know the identity of any of the patients.

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

What happened during the trial?

This trial was done in 2 parts. Part 1 ended before Part 2 started. None of the patients in Part 1 were included in Part 2.

Part 1 helped the researchers choose the best dose for the patients to get in Part 2. Part 2 helped the researchers find out if CFZ533 lowered the activity of the patients' immune systems enough to prevent rejection of the transplanted kidneys. The researchers wanted to learn if CFZ533 could lower the patients' immune system activity as much as Tac.

Before treatment started in each part, the trial doctors checked the health of the patients to make sure they could take part in the trial. The trial doctors took blood and urine samples from each patient.

During treatment in each part, the patients got their first dose of CFZ533 either before or during their kidney transplant. The dose each patient got was based on his or her body weight. Doses were measured in milligrams per kilogram of body weight, also called mg/kg.

Part 1

There were 7 patients in Part 1. All 7 patients got 3 mg/kg of CFZ533 and the Part 1 standard therapy.

- At the first dose, the patients got CFZ533 through a needle into a vein. This is called an intravenous dose, also called an IV dose.
- At the next 4 doses, the patients got CFZ533 through a needle under the skin. The patients got 4 doses over the course of 3 months.

The Part 1 standard therapy included 3 medicines. These were mycophenolate mofetil, also called MMF, corticosteroids, and Tac. The patients got the standard therapy by mouth.

Part 2

Part 2 started after all 7 patients in Part 1 finished Part 1. There were 52 patients in Part 2.

- 34 patients got 10 mg/kg CFZ533 as an IV dose and the Part 2 standard therapy
- 18 patients got Tac by mouth and the Part 2 standard therapy

The patients who got CFZ533 in Part 2 got up to 17 treatments. The Part 2 standard therapy included 3 medicines. These were MMF, corticosteroids, and basiliximab. The patients got the standard therapy either by mouth or as an IV dose.

The dose of the standard therapy in Part 1 and Part 2 and how often it was given to patients were based on the common practice of the trial site in the patient's country.

Throughout the trial, the trial staff:

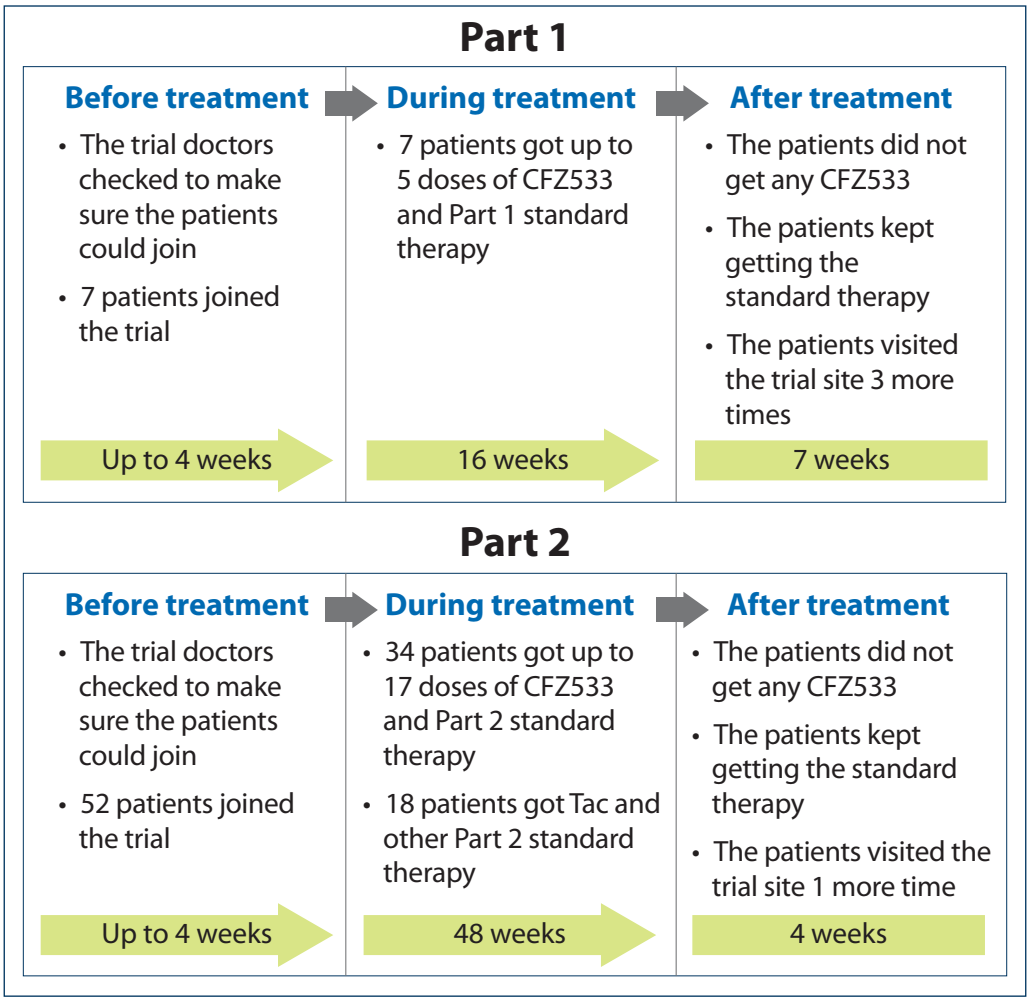
- Checked the overall health of the patients
- Took blood and urine samples
- Asked questions about how the patients felt and about any other medications they were taking

After treatment:

- The patients in Part 1 visited the trial site 3 more times. After the last dose of CFZ533, the patients kept getting the standard therapy based on the common practice in their country.
- The patients in Part 2 visited the trial site at least 1 more time after the last dose.

At these visits, the trial doctors checked the overall health of the patients. The trial doctors also checked how the patients were feeling and what medications they were taking. The patients gave more blood and urine samples.

The chart below shows how the trial was done.



What were the results of the trial?

This is a summary of the main overall results of your trial, not your individual results. The results presented here are for a single trial. Other trials may provide new information or different results. You should not make medical decisions based on the results of a single trial. Always talk to a doctor before making any changes to your medications or treatment plans.

There were 6 out of 7 patients who finished Part 1. There were 43 out of 52 patients who finished Part 2. Most of the patients who stopped getting the trial treatment early did this because:

- the trial doctors decided it was in the interest of the patient's safety
- the patient chose to stop getting treatment

There was 1 patient who got CFZ533 and standard therapy who left Part 2 before getting a kidney transplant. So, only 33 patients are included in the results for the question below.

Did the patients in each treatment group have a similar number of rejection events?

Yes, the number of rejection events was similar in each treatment group. If a patient showed signs of rejecting the kidney transplant, this was called a "rejection event". The researchers wanted to know if the patients who got CFZ533 and standard therapy had a similar number of rejection events compared with patients who got Tac and standard therapy. To find out, the researchers counted the number of rejection events throughout Part 2.

After 12 months of treatment, the researchers found that the patients who got CFZ533 had a similar number of rejection events as the patients who got Tac. The table below shows how many rejection events happened in each treatment group during 12 months of treatment in Part 2.

Number of rejection events in each treatment group in Part 2

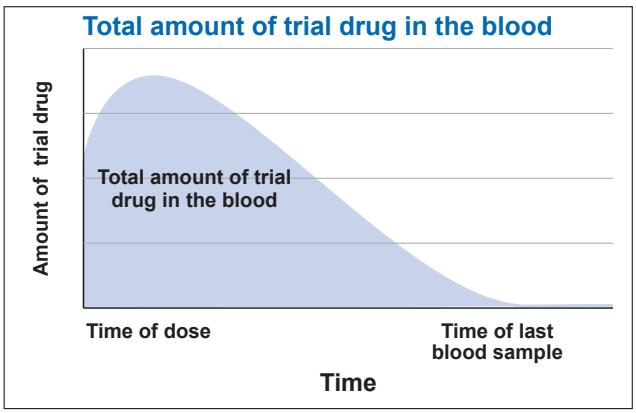
Month	CFZ533 and standard therapy (Out of 33 patients)	Tac and standard therapy (Out of 18 patients)
Month 3	18.2% (6)	11.1% (2)
Month 6	21.2% (7)	16.7% (3)
Month 9	21.2% (7)	16.7% (3)
Month 12	21.2% (7)	16.7% (3)

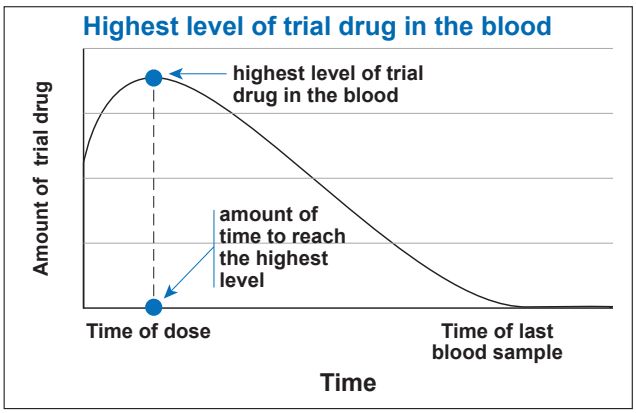
How much CFZ533 stayed in the patients' blood after one IV dose?

The researchers wanted to know how much CFZ533 stayed in the patients' blood after they got a single 3 mg/kg IV dose of CFZ533. To find out, they measured how much CFZ533 was in the patients' blood after the first dose. This helped the researchers to find:

- The average highest level of CFZ533 that stayed in the patients' blood. This was measured in micrograms per milliliter, also called µg/mL.
- The average amount of time it took to reach the highest level of CFZ533. This was measured in days.
- The average total amount of CFZ533 measured in the patients' blood. This was measured in days multiplied by micrograms per milliliter, also called day•µg/mL.

The graphs below show an example of how the amount of a trial drug in the blood can change over time. They do not show the actual results from this trial.





This trial was the first time that the researchers measured the level of CFZ533 in patients who got a kidney transplant. The researchers compared the levels of CFZ533 found in patients who got a kidney transplant with the levels of CFZ533 found in healthy volunteers in earlier CFZ533 trials. The information the researchers collected in Part 1 helped them to decide how much CFZ533 to give to patients in Part 2.

Overall, the researchers found that the average highest level of CFZ533 that stayed in the patients' blood after one IV dose was lower in patients who got a kidney transplant compared with the levels that had been observed in healthy volunteers.

The table below shows the results in the patients who got a kidney transplant.

Measurements of CFZ533 in the patients' blood after one IV dose

Measurement in the patients' blood	Average amount
Highest level of CFZ533	66.3 µg/mL
Amount of time it took to reach the highest level of CFZ533	0.24 day, or about 6 hours
Total amount of CFZ533	367 day•µg/mL

For more information about the results described above, please see the scientific summary that can be found on the websites noted at the end of this summary.

What medical problems did patients have?

Medical problems that happen in clinical trials are called "adverse events". An adverse event is any unwanted sign or symptom that patients have during a trial. An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the patient needs hospital care. These problems may or may not be caused by the trial treatment.

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 treatment. So, when new drugs are being studied, researchers keep track of all medical problems that patients have.

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

How many patients had adverse events?

The table below shows how many patients had adverse events during Part 1. In Part 1, all of the patients had at least 1 adverse event. There was 1 patient who stopped getting trial treatment due to adverse events after getting 4 out of the 5 doses of CFZ533.

Adverse events in Part 1 of this trial

	How many patients in this trial had adverse events?	How many patients in this trial had serious adverse events?	How many patients stopped getting trial treatment because of adverse events?
CFZ533 and standard therapy (Out of 7 patients)	100.0% (7)	57.1% (4)	14.3% (1)

The table below shows how many patients had adverse events during Part 2. In Part 2, a similar percentage of patients in each treatment group stopped getting treatment due to adverse events. A similar percentage of patients in each treatment group had serious adverse events.

Adverse events in Part 2 of this trial

	How many patients in this trial had adverse events?	How many patients in this trial had serious adverse events?	How many patients stopped getting trial treatment because of adverse events?
CFZ533 and standard therapy (Out of 34 patients)	97.1% (33)	61.8% (21)	29.4% (10)
Tac and standard therapy (Out of 18 patients)	100.0% (18)	66.7% (12)	33.3% (6)
Total (Out of 52 patients)	98.1% (51)	63.5% (33)	30.8% (16)

What were the most common serious adverse events?

Part 1

- In Part 1, there were 17 serious adverse events that happened in 4 patients. This was 57.1% of the patients in Part 1.
- The most common serious adverse event in Part 1 was vomiting. This happened in 2 out of 7 patients. This was 28.6% of the patients in Part 1.

All other serious adverse events in Part 1 happened in only 1 patient.

None of the patients died during Part 1.

Part 2

The most common serious adverse event in Part 2 was rejection event of the transplanted kidney. This happened in 6 out of 52 patients. This was 11.5% of the patients in Part 2. There were 5 of these 6 patients who were getting CFZ533. All 5 patients stopped getting CFZ533 and switched to Tac.

None of the patients died during Part 2.

The table below shows the most common serious adverse events that happened in 3 or more total patients in Part 2. There were other serious adverse events, but these happened in fewer patients.

Most common serious adverse events in Part 2 of this trial

Serious adverse event	CFZ533 and standard therapy (Out of 34 patients)	Tac and standard therapy (Out of 18 patients)	Total (Out of 52 patients)
Rejection event of the transplanted kidney	14.7% (5)	5.6% (1)	11.5% (6)
Infection by Cytomegalovirus	8.8% (3)	11.1% (2)	9.6% (5)
Kidney damage related to viral infection	11.8% (4)	5.6% (1)	9.6% (5)
Kidney infection caused by a urinary tract infection	5.9% (2)	16.7% (3)	9.6% (5)
Problems related to the kidney transplant	2.9% (1)	11.1% (2)	5.8% (3)

There were 2 patients in Part 2 who got Tac and standard therapy who stopped getting treatment because their transplanted kidney stopped working.

This was a serious adverse event that happened in:

- 11.1% of the patients who got Tac and standard therapy in Part 2
- 3.8% of total patients in Part 2

What were the most common adverse events?

Part 1

The most common adverse events in Part 1 were lower than normal levels of phosphate in the blood, nausea, and vomiting. Each of these adverse events happened in 71.4% of patients in Part 1. This was 5 out of 7 patients in Part 1.

The table below shows the most common adverse events that happened in 3 or more patients in Part 1. There were other adverse events, but these happened in fewer patients.

Most common adverse events in Part 1 of this trial

Adverse event	CFZ533 and standard therapy (Out of 7 patients)
Lower than normal levels of phosphate in the blood	71.4% (5)
Nausea	71.4% (5)
Vomiting	71.4% (5)
Higher than normal levels of sugar in the blood	57.1% (4)
BK virus infection	42.9% (3)
Diarrhea	42.9% (3)
Difficulty breathing	42.9% (3)
Pain where the incision was made for the transplant	42.9% (3)
Discharge where the incision was made for the transplant	42.9% (3)

Part 2

The most common adverse event in Part 2 was constipation. This adverse event happened in a similar percentage of patients in each treatment group. The table below shows the most common adverse events that happened in 14 or more of total patients in Part 2. There were other adverse events, but these happened in fewer patients.

Most common adverse events in Part 2 of this trial

Adverse event	CFZ533 and standard therapy (Out of 34 patients)	Tac and standard therapy (Out of 18 patients)	Total (Out of 52 patients)
Constipation	41.2% (14)	44.4% (8)	42.3% (22)
Diarrhea	26.5% (9)	55.6% (10)	36.5% (19)
High blood pressure	38.2% (13)	33.3% (6)	36.5% (19)
Nausea	29.4% (10)	50.0% (9)	36.5% (19)
Problems with wound healing	32.4% (11)	44.4% (8)	36.5% (19)
Lower than normal levels of white blood cells in the blood	38.2% (13)	22.2% (4)	32.7% (17)
BK virus infection	29.4% (10)	33.3% (6)	30.8% (16)
Difficulty sleeping	32.4% (11)	27.8% (5)	30.8% (16)
Lower than normal levels of phosphate in the blood	32.4% (11)	27.8% (5)	30.8% (16)
Urinary tract infection	23.5% (8)	38.9% (7)	28.8% (15)
Common cold	29.4 (10)	22.2% (4)	26.9% (14)
Higher than normal levels of potassium in the blood	26.5% (9)	27.8% (5)	26.9% (14)

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 this summary.

How has this trial helped patients and researchers?

The results of this trial helped researchers better understand if CFZ533 can help patients who got a kidney transplant. The results from many trials are needed to find out which treatments can be used for patients who get a kidney transplant. This summary shows only the main results from this 1 trial. This trial was done in a small number of patients over a short time period. Other trials may provide new information or different results.

If more clinical trials are planned, they will be listed on the websites below by searching **"CFZ533"**.

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"** under **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **"CCFZ533X2201"** 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 websites listed below.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02217410"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2015-000925-36"** in 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 12-month randomized, multiple dose, open-label study evaluating safety, tolerability, pharmacokinetics/pharmacodynamics (PK/PD) and efficacy of an anti-CD40 monoclonal antibody, CFZ533, in combination with mycophenolate mofetil (MMF) and corticosteroids (CS), with and without tacrolimus (Tac), in de novo renal transplant recipients

Thank you

As a clinical trial patient, you belong to a large community of patients 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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