NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of CFZ533 in people who had a liver transplant

Thank you!

Thank you to the participants who took part in the clinical trial after **liver transplant**. 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: CCFZ533A2202

Novartis drug studied: **CFZ533**, also called 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 purpose of this trial was to learn more about the effects of **CFZ533** and if it works as well as the standard treatment to prevent rejection in liver transplant recipients. Standard treatment works to prevent rejection but can have long-lasting side effects, including infections and kidney damage.

Liver transplant is a surgery to place a healthy liver from someone else's body into a person whose liver no longer works. A **recipient** is the person who receives a transplant. After transplant, the recipient may have liver rejection.

Rejection means the body's immune system attacks the transplanted liver. Rejection can lead to failure of the new liver, which means the new liver stops working.

CFZ533 also called iscalimab, is a trial drug designed to prevent liver rejection. **CFZ533** blocks part of the immune system. By blocking this, **CFZ533** may help prevent the immune system from attacking the transplanted liver.

Standard treatment to prevent liver rejection is **tacrolimus (TAC)**. **TAC** is a medicine that lowers the immune system's response to prevent the immune system from attacking the new liver. Standard treatment may be called anti-rejection or immunosuppressive medicine.

Trial drug
CFZ533 also called iscalimab
Pronounced as
is-cal-i-mab

Standard treatment
Tacrolimus
Pronounced as
ta-kruh-lee-muhs

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

- How many participants had liver rejection, liver failure, or died within a year after starting treatment?
- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

How long was this trial?

The trial began in October 2019 and ended early in April 2023. Participants were in the trial for up to 3 and a half years.

The sponsor decided to end this trial early because early analysis showed that **CFZ533** did not prevent liver rejection, liver failure, and death as well as the standard treatment **TAC**.

Who was in this trial?

128 participants who just had a liver transplant were in this trial – 94 men and 34 women. Participants' ages ranged from 25 to 70 years. Their average age was 56 years.

The number of participants by race is shown below.

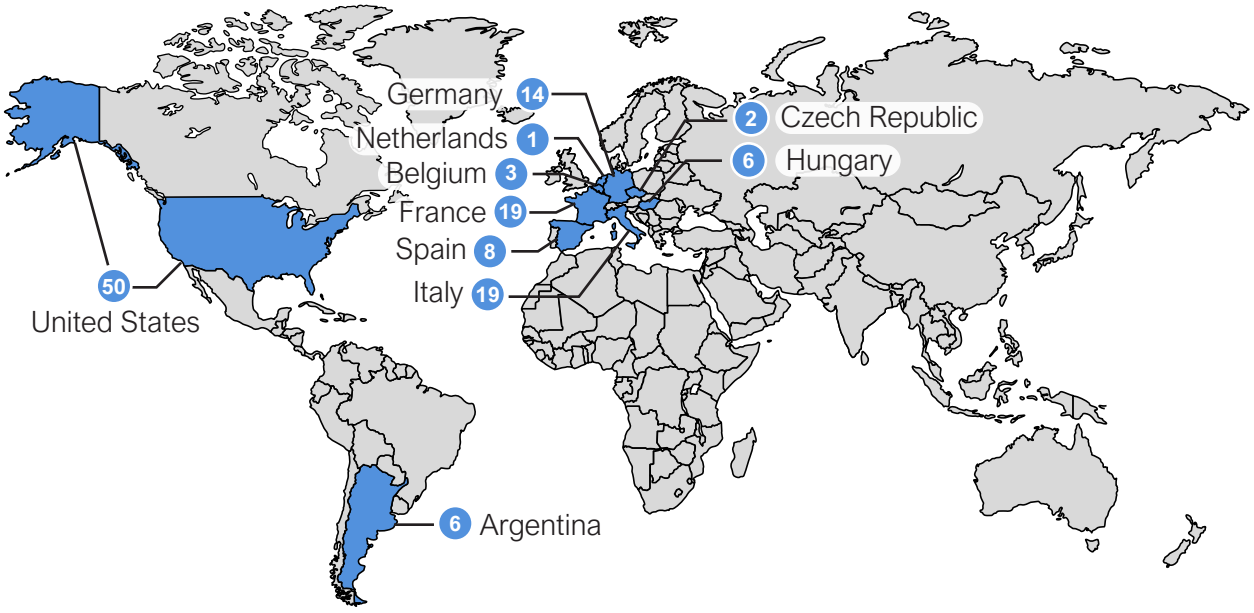
Race

7	Black or African American
120	White
1	Not collected

The participants could take part in this trial if they:

- Had not received any other transplants like a heart, pancreas, or bone marrow transplant
- Had received a liver transplant from a deceased donor – the deceased donor could not have died from heart problems

128 participants from **10** countries were assigned treatment in this trial. 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, which participants first received through a needle in a vein called an intravenous (IV) infusion. Then, they received **CFZ533** as injections under the skin. This trial looked at 2 doses of **CFZ533**:

- **300 milligram (mg)** given as an IV infusion for the first dose, then as injections every 2 weeks
- **600 mg** given as an IV infusion for the first 2 doses, then as injections every 2 weeks

Tacrolimus, which was taken by mouth as tablets or was received as an IV infusion 1 or 2 times a day, as per standard treatment.

Other standard anti-rejection medicines, which were taken by mouth or was received as an IV infusion:

- Mycophenolate mofetil (MMF)
- Corticosteroids

All participants took other standard anti-rejection medicines.

Researchers randomly assigned participants to treatment groups using a computer.

In this trial, the participants and clinical trial team knew what treatment each participant received.

What happened during this trial?

Before treatment **Up to 2 months**

Trial doctors checked each participant's health and liver transplant to make sure they could be in this clinical trial.

During treatment **Up to 3 years**

128 participants were assigned one of these treatments:

- **300 mg CFZ533** 48 participants
- **600 mg CFZ533** 48 participants
- **Tacrolimus (TAC)** 32 participants

All participants also took MMF and corticosteroids, which are other standard anti-rejection medicines.

After treatment **3 months to the end of the trial**

After their last dose of trial treatment, all participants received standard treatments. Trial staff checked the participants':

- Safety for up to about 3 months
- Liver transplant and survival until the end of the trial

Trial doctors checked the participants' general health throughout the trial.

What were the main results of this trial?

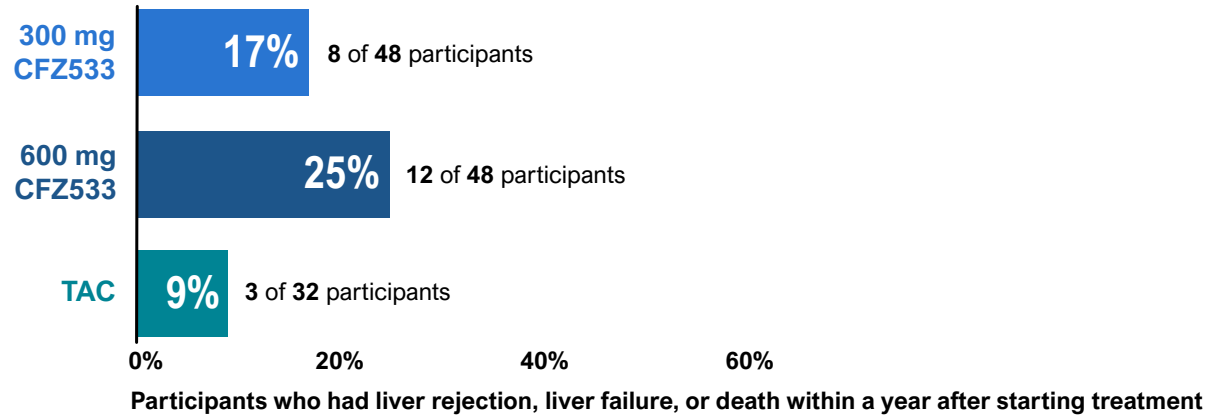
How many participants had liver rejection, liver failure, or died within a year after starting treatment?

A larger number of participants who received **CFZ533** had liver rejection, liver failure, or died compared to those who received **TAC**. The researchers concluded that **CFZ533** did not prevent liver rejection, liver failure, and death as well as the standard treatment **TAC**.

To learn this, the researchers compared how many participants in each group had any of these:

- **Liver rejection** based on a liver biopsy (doctors took a sample of liver tissue to test)
- **The transplanted liver stopped working**, which meant the participant was put back on the list to get another liver, had another liver transplant, or died from liver failure
- **Death** from any cause

Number of participants who had liver rejection, liver failure, or died within a year after starting treatment



What medical problems, also called adverse events, happened during this trial?

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 **during trial treatment**, which was defined as from the first dose to:

- 14 weeks after the last dose of **CFZ533**
- 12 weeks after the last dose of **TAC**

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.

Almost all the participants who received treatment (124 of 127) had adverse events. 79 participants had adverse events that were considered serious. 12 participants left the trial due to an adverse event. 4 participants died.

How many participants had adverse events?

Participants who:	300 mg CFZ533 48 participants	600 mg CFZ533 47 participants	Tacrolimus 32 participants
Had at least 1 **serious adverse event**	30 of 48	29 of 47	20 of 32
Had at least 1 **other adverse event**	45 of 48	42 of 47	30 of 32
Left the trial due to an adverse event	3 of 48	6 of 47	3 of 32
Died	1 of 48	3 of 47	0 of 32

The tables in this section do not include a participant assigned 600 mg **CFZ533** that did not receive any trial treatment.

What serious adverse events did the participants have?

4 participants died – 1 participant in the 300 mg **CFZ533** group and 3 in the 600 mg **CFZ533** group.

79 participants had serious adverse events.

The table below shows the most common serious adverse events that happened in **4 or more** participants in any group. Additional serious adverse events happened in fewer participants.

	300 mg CFZ533 48 participants	600 mg CFZ533 47 participants	Tacrolimus 32 participants
Fever Pyrexia	5 of 48 10%	5 of 47 11%	0 of 32 0%
Immune system attacks the transplanted liver Transplant rejection	4 of 48 8%	2 of 47 4%	2 of 32 6%
COVID-19	4 of 48 8%	2 of 47 4%	2 of 32 6%

What other adverse events did the participants have?

117 participants had other adverse events.

The table below shows the other adverse events that happened in **12 or more** participants in any group. Additional adverse events happened in fewer participants.

	300 mg CFZ533 48 participants	600 mg CFZ533 47 participants	Tacrolimus 32 participants
Low levels of white blood cells Leukopenia	17 of 48 35%	16 of 47 34%	9 of 32 28%
Low levels of a type of white blood cell Neutropenia	14 of 48 29%	10 of 47 21%	4 of 32 13%
Frequent, loose, or watery stool Diarrhea	12 of 48 25%	8 of 47 17%	9 of 32 28%
Swelling in the lower legs or hands Oedema peripheral	12 of 48 25%	6 of 47 13%	4 of 32 13%
COVID-19	15 of 48 31%	15 of 47 32%	8 of 32 25%

What was learned from this trial?

Researchers learned about the effects of **CFZ533** in people who had a liver transplant. The sponsor ended this trial early because data showed that **CFZ533** did not work as well as the standard treatment **TAC** to prevent liver rejection.

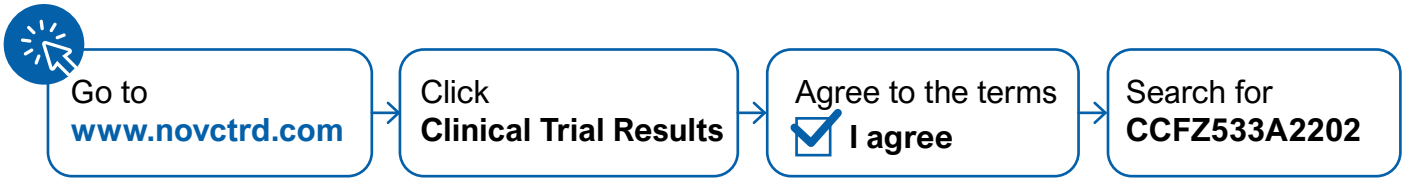
The researchers concluded that, compared to those who received **TAC**, a larger number of participants who received **CFZ533** had liver rejection, liver failure, or died.

When this summary was written, the sponsor had no plans for future trials of **CFZ533** in people who had a liver transplant.

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 **NCT03781414**
- clinicaltrialsregister.eu – search using the number **2018-001836-24**

Other trials of **CFZ533** may appear on the public websites above. When there, search for CFZ533 or iscalimab.

Full clinical trial title: A 12-month, open-label, multicenter, randomized, safety, efficacy, pharmacokinetic (PK) and pharmacodynamic (PD) study of two regimens of anti-CD40 monoclonal antibody, CFZ533 vs. standard of care control, in adult de novo liver transplant recipients with a 12-month additional follow-up and a long-term extension (CONTRAIL I)

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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