NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects and safety of CFZ533 in children and young adults with newly diagnosed type 1 diabetes

Thank you!

Thank you to the participants who took part in the clinical trial for type 1 diabetes. 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: CCFZ533X2207

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 about the effects and safety of **CFZ533** for children and young adults who were newly diagnosed with type 1 diabetes.

Type 1 diabetes is a long-term condition that causes high blood sugar. In type 1 diabetes, the pancreas cannot make enough insulin. This is because the body's **immune system** mistakenly attacks and destroys the cells that make insulin, called beta cells:

- **Insulin** helps the body use sugar for energy. Without enough insulin, blood sugar levels get too high. People with type 1 diabetes need insulin injections to lower their blood sugar levels.
- **Beta cells** are cells in the pancreas that make insulin. The pancreas is an organ near the stomach that makes hormones and helps the body digest food.

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

Type 1 diabetes is most often diagnosed in children and young adults. When newly diagnosed, people may still have some beta cells and can make some insulin on their own.

People who have some beta cells and can make some insulin on their own have better control over their blood sugar levels. This may lower the chance of diabetes-related problems, such as problems with the eyes, kidneys, and nerves in later years. Researchers are looking for treatments to protect and save beta cells after diagnosis.

CFZ533, is a trial drug designed to block a protein in the immune system. Researchers think blocking this protein may prevent the immune system from attacking beta cells.

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

- Did CFZ533 change how much insulin beta cells made after a year of 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 November 2019 and ended in June 2024. Participants started the trial on different dates.

Who was in this trial?

44 participants with type 1 diabetes received the trial treatment in this trial – 29 males and 15 females. Participants' ages ranged from 12 to 21 years. Their average age was 16 years.

The number of participants by race is shown below.

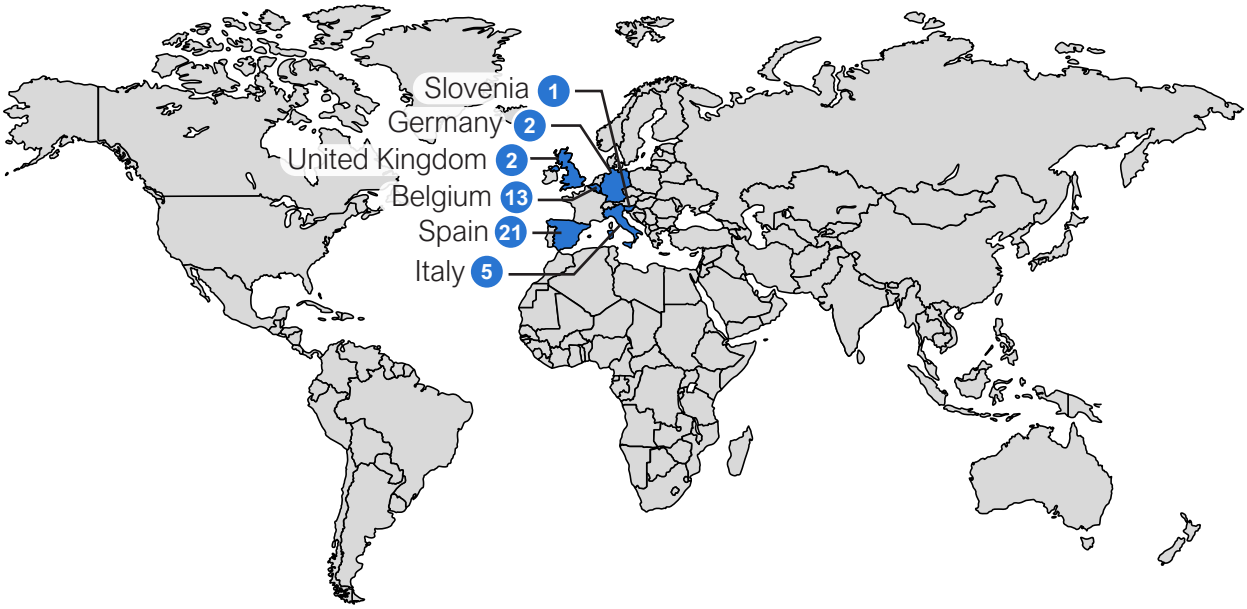
Race

44	White

The participants could take part in this trial if they:

- Were diagnosed with type 1 diabetes within about 3 months before joining the trial
- Had signs that their immune system could be attacking beta cells based on blood tests
- Did not have certain conditions that affect the immune system

44 participants from 6 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, which was received through a needle in a vein, called an intravenous (IV) infusion, on the 1st day. The IV infusion lasted about 30 minutes. Then, **CFZ533** was received as injections under the skin every week. The dose of **CFZ533** that each participant received was based on their body weight.

Placebo, which was received as an IV infusion on the 1st day. The placebo looks like the trial drug but has no trial drug in it. The IV infusion lasted about 30 minutes. Then, placebo was received as injections under the skin every week.

Participants could continue taking insulin to treat type 1 diabetes during this trial. Researchers used a computer to randomly assign participants to their treatment.

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.

What happened during this trial?

Before treatment

About 2 months

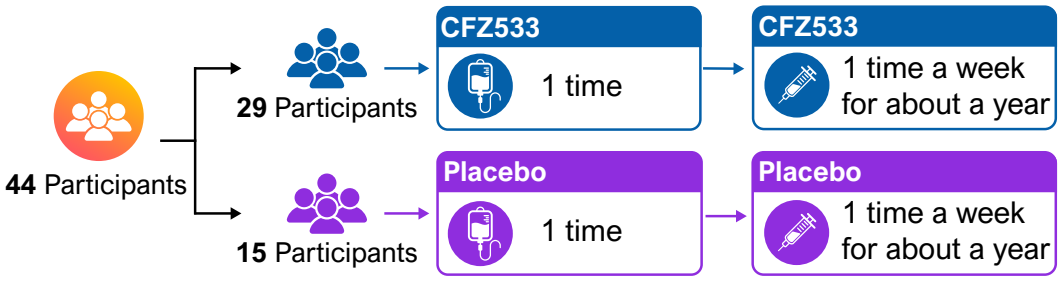
The trial staff checked to make sure the participants could be in this trial.

During treatment

About 1 year

44 participants received either **CFZ533** or placebo one time a week.

The graphic below shows how many participants in each group were assigned each treatment.



The first dose was given as an IV infusion and the rest were given as injections under the skin.

First, a small group of participants from ages 15 to 21 received **CFZ533** or placebo. The researchers checked for any safety concerns before giving the treatments to the rest of the participants.

After treatment

About 5 months

Trial staff checked the participants for:

- Any medical problems for up to about 5 months after their last dose of treatment
- How much insulin their beta cells made until up to 5 months after their last dose of treatment

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

What were the main results of this trial?

Did CFZ533 change how much insulin beta cells made after a year of treatment?

The researchers concluded **CFZ533** may not have changed how much insulin beta cells made compared to placebo after a year of treatment. Researchers could not conclude if any change was meaningful because of the small number of participants in this trial.

To learn this, researchers measured participants' blood samples for C-peptide. They took blood samples before and up to 2 hours after a **mixed meal tolerance test (MMTT)**. The **MMTT** is a test that shows how much insulin the pancreas makes after drinking a liquid meal. Researchers wanted to learn if C-peptide levels went up after the MMTT.

What is C-peptide?
C-peptide is a protein that beta cells make when making insulin. Doctors measure C-peptide levels to see how much insulin the body makes.

A higher level of C-peptide means beta cells are making **more** insulin.

For the **MMTT**, each participant fasted overnight, which means they did not eat or drink anything except water for 8 to 10 hours. In the morning, they drank a liquid meal, like a milkshake. Participants completed the MMTT before starting treatment and several times up to a year of treatment, and after stopping the study drug.

After about a year of treatment, the participants who received **CFZ533** had C-peptide levels that were a little higher than those who received placebo. However, the researchers could not conclude if the difference was meaningful because of the small number of participants in this trial.

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

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events 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 from the start of treatment until up to about 5 months after the last 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.

Almost all the participants (41 of 44) had adverse events. 7 participants had adverse events that were considered serious. 1 participant left the trial due to an adverse event. No participants died. The researchers concluded there were no new safety concerns for **CFZ533** in this trial.

How many participants had adverse events?

	CFZ533 29 participants	**Placebo** 15 participants
Had at least 1 **serious adverse event**	**6 of 29** 21%	**1 of 15** 7%
Had at least 1 **other adverse event**	**27 of 29** 93%	**14 of 15** 93%
Left the trial due to an adverse event	**1 of 29** 3%	**0 of 15** 0%
Died	**0 of 29** 0%	**0 of 15** 0%

What serious adverse events did the participants have?

No participants died. 7 participants had serious adverse events.

6 participants who received **CFZ533** had these serious adverse events:

- **Broken bone from a fall** (traumatic fracture)
- **Fever** (pyrexia)
- **Infection in the colon** (large intestine infection)
- **Low blood sugar** (hypoglycemia)
- **Problems from high blood sugar** (diabetic metabolic decompensation)
- **Seizure** (tonic clonic movements)
- **UTI** (urinary tract infection)
- **Sore throat** (oropharyngeal pain)

1 participant who received placebo had this serious adverse event:

- **Infection in the bone behind the ear** (mastoiditis)

What other adverse events did the participants have?

41 participants had other adverse events.

The table below shows the other adverse events that happened in **7 or more** participants. Additional adverse events happened in fewer participants.

	CFZ533 29 participants	**Placebo** 15 participants
Low blood sugar Hypoglycemia	19 of 29 66%	8 of 15 53%
Common cold Nasopharyngitis	13 of 29 45%	5 of 15 33%
Problems where an injection was given, such as pain, swelling, or redness Injection site reaction	7 of 29 24%	3 of 15 20%
COVID-19	7 of 29 24%	2 of 15 13%
Headache	7 of 29 24%	2 of 15 13%
Fever Pyrexia	5 of 29 17%	3 of 15 20%
Infection in the ear, nose, throat, or airways Upper respiratory tract infection	4 of 29 14%	3 of 15 20%

What were the other results of this trial?

Did CFZ533 change how much insulin beta cells made 5 months after completing treatment?

The researchers concluded **CFZ533** may not have changed how much insulin beta cells made 5 months after participants completed treatment.

To learn this, researchers compared the level of C-peptide in participants' blood during mixed meal tolerance tests before trial treatment and 5 months after their last dose.

Did CFZ533 change how many participants no longer needed insulin or needed very little insulin?

All participants who received either treatment still needed insulin by the end of the trial. The researchers could not conclude if **CFZ533** changed how many participants needed very little insulin after a year of treatment.

To learn this, researchers kept track of how many participants:

- Had HbA1c of 6.5% or less without receiving insulin
- Had insulin dose adjusted A1c of 9% or less with receiving insulin
- Had HbA1c of less than 7% while receiving very little insulin

What is HbA1c?

Hemoglobin A1c, or HbA1c, is a blood test that measures a person's average blood sugar levels over the past 3 months. Lower HbA1c means better control over blood sugar levels. For most people with diabetes, the goal is HbA1c of 7% or less.

What was learned from this trial?

Researchers learned about the effects and safety of **CFZ533** for children and young adults who were newly diagnosed with type 1 diabetes.

The researchers concluded that:

- **CFZ533** may not have changed how much insulin beta cells made after a year of treatment. Researchers could not conclude if any change seen was meaningful because of the small number of participants in this trial.
- There were no new safety concerns for **CFZ533** in this trial.

The researchers also learned that:

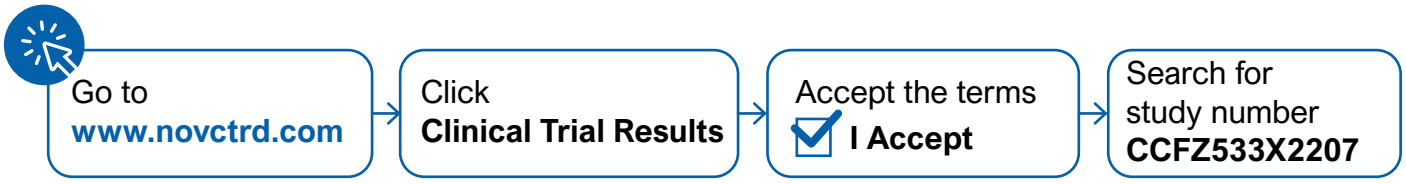
- **CFZ533** may not have changed how much insulin beta cells made 5 months after participants completed treatment.
- All participants who received either treatment still needed insulin by the end of the trial. The researchers could not conclude if **CFZ533** changed how many participants needed very little insulin after a year of treatment.

When this summary was written, the sponsor had no plans for future trials of **CFZ533** in people with type 1 diabetes.

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 **NCT04129528**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2018-004553-25**

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

Full clinical trial title: Investigator- and subject-blinded, randomized, placebo-controlled study to evaluate safety, tolerability, pharmacokinetics and efficacy of CFZ533 in pediatric and young adults with new onset type 1 diabetes mellitus (T1DM)

NOVARTIS

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

1-888-669-6682 (US) | +41-61-324 1111 (EU)

www.novartis.com/clinicaltrials