**Clinical Trial Results**

NOVARTIS

**Research Sponsor:** Novartis
**Drug Studied:** CFZ533
**Protocol Number:** CCFZ533X2204

## *Thank you!*

Thank you for taking part in the clinical trial for the drug CFZ533, also called iscalimab. You and all of the patients helped researchers learn more about how CFZ533 works in people with moderate to severe myasthenia gravis, also called MG.

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 doctor or staff at your trial site.

## What has happened since the trial ended?

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

The trial included 44 patients from 14 trial sites in Denmark, Germany, Taiwan, Canada, and Russia. 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?

In this trial, the researchers wanted to find out if CFZ533 works in a small number of patients with moderate to severe MG. 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 with moderate to severe MG.

MG is an immune system disease. The immune system makes proteins called antibodies to fight anything the body does not recognize. This is how the body fights infections by bacteria and viruses. But sometimes, the immune system makes antibodies that cause it to attack tissues in the body. In most patients with MG, antibodies block chemical signals from the nerves to the muscle cells. This causes muscle weakness and tiredness.

CFZ533 is designed to lower the activity of the immune system. The researchers in this trial wanted to learn if CFZ533 could help the patients' MG symptoms by lowering the activity of the immune system. They also wanted to know more about the safety of CFZ533 in patients with moderate to severe MG. To do this, the researchers compared CFZ533 with a placebo. A placebo looks like the trial 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 the researchers wanted to answer in this trial were:

- Did CFZ533 reduce the patients' MG symptoms?
- Did CFZ533 affect the patients' daily lives in other ways?
- How else did the patients' MG symptoms change during the trial?
- How did CFZ533 affect the patients' immune systems?
- How much CFZ533 stayed in the patients' blood?
- What medical problems did 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 with moderate to severe MG. The patients in this trial were 18 to 74 years old.

This was a "double-blind" trial. This means none of the patients, trial staff, or sponsor staff knew what treatment each patient got. Some trials are done this way because knowing what treatment the patients are getting can affect the results of the trial. Doing a trial this way helps make sure the results are looked at fairly.

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.

When the trial ended, the research sponsor found out which treatment patients got so they could create a report of the trial results. The sponsor staff did not know the identity of any of the patients.

## What happened during the trial?

**Before treatment started,** the trial doctors did tests and 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. The patients kept taking their usual medicines to treat their MG.

**During 24 weeks of treatment,** the patients got up to 6 doses of trial treatment at the trial site. The patients got the trial treatment through a needle into a vein. During the trial:

- 22 patients got CFZ533 every 4 weeks
- 22 patients got the placebo every 4 weeks

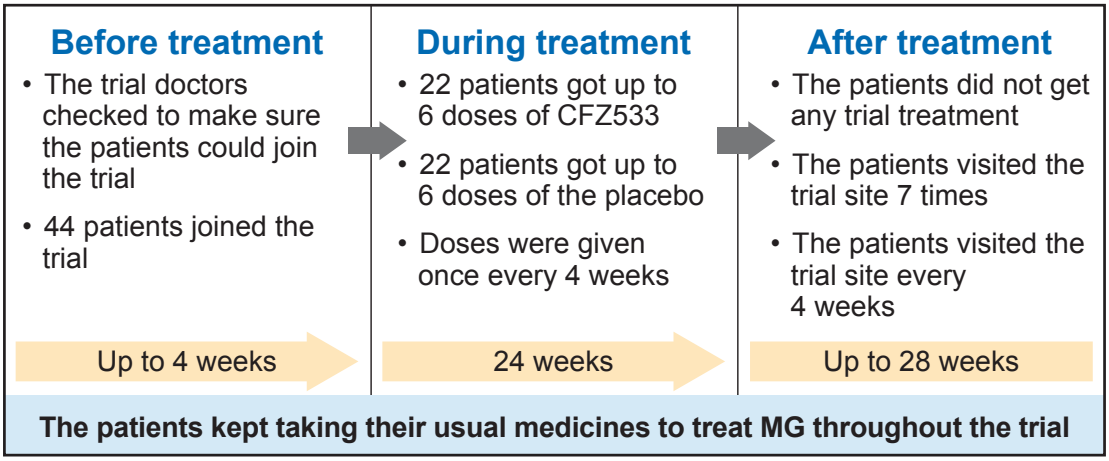
During this time, the trial staff:

- checked the overall health of the patients
- took blood and urine samples
- asked questions about how the patients felt and about any other medicines they were taking

Throughout the trial, the patients kept taking their usual medicines to treat their MG. But, the trial doctors may have asked the patients to stop taking certain medicines or take less of them. The trial doctors did this to make sure that any effects they saw during the trial were due to the trial treatment, and not due to other reasons.

**After treatment,** the patients visited the trial site 7 times for up to 28 weeks. At each visit, the trial doctors checked the overall health of the patients. The trial doctors also checked how the patients were feeling and what medicines they were taking. The trial doctors took more blood and urine samples from each patient.

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. 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.

All 44 patients got at least 1 dose of trial treatment. But, only 34 patients finished the trial. So, the results from the 10 patients who did not finish the trial are not shown in all of the results below.

### Did CFZ533 reduce the patients' MG symptoms?

After 24 weeks of treatment, patients who got CFZ533 had slightly fewer MG symptoms compared to patients who got the placebo. But, the difference between the treatment groups was too small for the researchers to know if CFZ533 reduced the patients' MG symptoms.

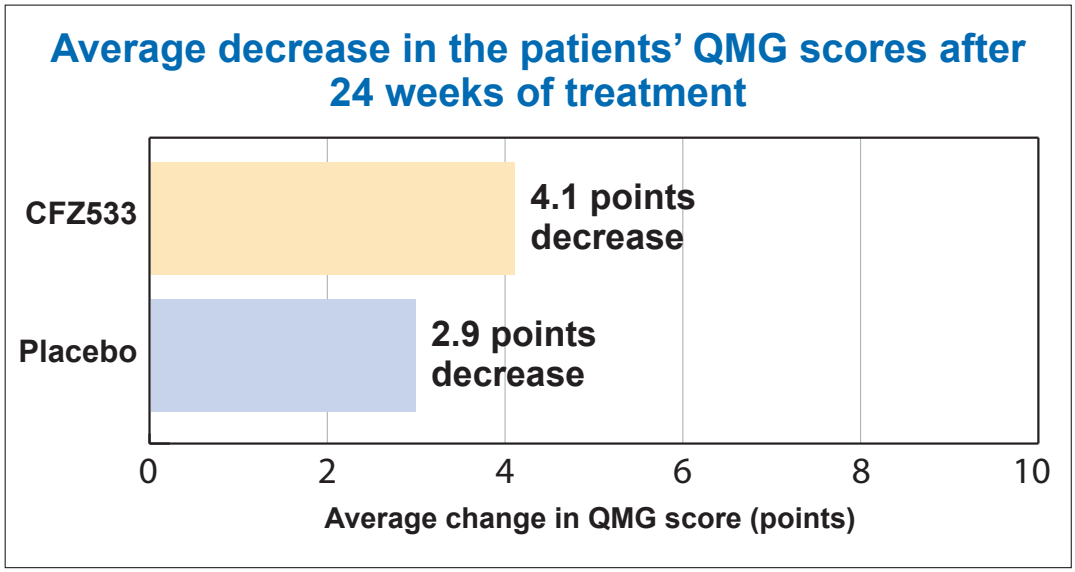
The trial doctors measured the severity of the patients' symptoms before and after 24 weeks of treatment. The trial doctors measured this by testing the patients' muscles using the Quantitative Myasthenia Gravis score, also called the QMG score. A lower score meant that the patient had fewer MG symptoms. A change in a patient's QMG score that was greater than 3 points meant that there was a noticeable effect on the patient's MG symptoms.

After 24 weeks of treatment, the researchers found that patients who got CFZ533 had a slightly greater decrease in the average QMG score than patients who got the placebo.

The researchers learned that the QMG scores:

- decreased by an average of 4.1 points in patients who got CFZ533
- decreased by an average of 2.9 points in patients who got the placebo

The chart below shows the average decrease in QMG score for each treatment group after 24 weeks of treatment.




## Did CFZ533 affect the patients' daily lives in other ways?

Overall, the researchers found that the patients in both treatment groups showed a decrease in how severe their MG symptoms were. Any difference found between the treatment groups was too small for the researchers to know if CFZ533 affected the patients' daily lives.

The researchers wanted to know if CFZ533 affected the patients' daily lives in other ways. To find out, they measured the effect of CFZ533 on the patients' daily lives in 3 different ways.

The table on the next page shows the different measurements. For each of these measurements, a lower score meant that there were fewer or less severe MG symptoms.

| Measurement | Description | Completed by |
|---|---|---|
| Myasthenia Gravis Composite score (also called the "MGC") | Measured the signs and symptoms of the patients' MG to tell the trial doctors about the patients' overall MG status | Trial doctor and patient |
| Myasthenia Gravis-Activities of Daily Living questionnaire (also called the "MG ADL") | Measured how well the patients could do certain daily activities | Patient |
| 15-Item Myasthenia Gravis Quality of Life (also called the "MG QOL-15") | Asked the patient about how MG affects their life | Patient |

For each of these measurements, the differences between the treatment groups were too small for the researchers to know if CFZ533 affected the patients' daily lives.

## How else did the patients' MG symptoms change during the trial?

Overall, the patients' MG symptoms did not get worse during the trial. To find out, the researchers measured the following 5 things:

| Measurement | How it was measured |
|---|---|
| **1.** The patients' average QMG scores after they stopped getting trial treatment | The researchers measured the QMG scores 24 weeks after the last dose. |
| **2.** The number of patients whose MG symptoms got better | The researchers counted how many patients had a decrease of at least 3 points in their average QMG scores throughout the trial. |
| **3.** The number of patients whose MG symptoms got worse | The researchers counted how many patients had an increase of at least 3 points in their average QMG scores throughout the trial. |
| **4.** The number of patients who stopped getting treatment because their MG got worse or the treatment was not having an effect | The researchers counted the number of patients who had to stop getting treatment for these 2 reasons throughout the trial. |
| **5.** The number of patients who had to return to taking their original dose of steroids | The researchers counted how many patients in each treatment group had to return to taking their original dose of steroids throughout the trial. |

**Measurements 1, 2, and 3.** The researchers found that the first 3 measurements showed slight differences between the treatment groups. But, the differences between the treatment groups were too small for the researchers to know if these differences were caused by CFZ533.

**Measurement 4.** The researchers found that none of the patients stopped getting treatment because their MG got worse or because the treatment was not having an effect.

**Measurement 5.** Steroids are a common treatment for MG. But, when steroids are used for a long time, several unwanted effects can happen. So, doctors try to limit their use.

During this trial, the patients could stay on their current steroid treatment for their MG. If the trial doctors thought the patients' MG symptoms were less severe after 12 weeks of treatment, they could slowly decrease the dose of steroids that each patient took. If the patients' MG symptoms got worse, the trial doctors could return the patients to their original dose of steroids. The researchers wanted to know how many patients in each treatment group had to return to taking their original dose of steroids. But, not every patient had less severe MG symptoms after 12 weeks of treatment. So, the trial doctors could not decrease the dose of steroids that most patients took. There were so few patients who returned to taking their original dose of steroids that the researchers could not study these results.

## How did CFZ533 affect the patients' immune systems?

The researchers wanted to know if CFZ533 affected the immune system the way it was designed to. They wanted to find out if CFZ533 blocked an immune system protein called CD40. CD40 is commonly found on immune system cells called B cells. The researchers wanted to learn if CFZ533 blocked CD40 on the B cells and lowered the activity of the immune system. To find out, they measured:

- how much total CD40 was on the B cells
- how much CD40 on the B cells was free to link with other proteins
- how much CD40 was in the blood

Overall, the researchers learned that CFZ533 blocked CD40. They found that at least 90% of the CD40 on the B cells was blocked.

The researchers also wanted to know if the patients' immune systems created antibodies against CFZ533. Usually, the immune system makes antibodies to fight anything the body does not recognize. But sometimes, the immune system makes antibodies against a medicine. This might prevent the medicine from working. The researchers found that none of the patients who got CFZ533 made antibodies against CFZ533.

### How much CFZ533 stayed in the patients' blood?

The researchers wanted to know how much CFZ533 stayed in the blood of patients who got CFZ533. This information is important because it helps the researchers decide when a dose should be given and what dose is safe and effective for patients. To find out, they measured how much CFZ533 was in the patients' blood after 24 weeks of treatment. Overall, the researchers found that:

- the amounts of CFZ533 that stayed in the patients' blood were similar to the amounts that researchers observed in earlier trials of CFZ533
- CFZ533 reached steady and expected levels in the blood during the 24 weeks of treatment

## 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. All 44 patients are included in these results because they all got at least 1 dose of trial treatment.

## How many patients had adverse events?

Most of the patients in this trial had an adverse event. One patient who got CFZ533 stopped getting trial treatment due to an adverse event.

The table below shows how many patients had adverse events during this trial.

**Adverse events in this trial**

| Adverse event | CFZ533 (Out of 22 patients) | Placebo (Out of 22 patients) | Total (Out of 44 patients) |
|---|---|---|---|
| How many patients in this trial had adverse events? | 90.9% (20) | 95.5% (21) | 93.2% (41) |
| How many patients in this trial had serious adverse events? | 31.8% (7) | 18.2% (4) | 25.0% (11) |
| How many patients in this trial stopped taking the trial treatment due to adverse events? | 4.5% (1) | 0.0% (0) | 2.30% (1) |

## What were the most common serious adverse events?

The most common serious adverse event in this trial was MG getting worse. This serious adverse event happened in 2 out of 22 patients who got CFZ533, and 1 out of 22 patients who got the placebo. This was 9.1% of patients who got CFZ533, and 4.6% of patients who got the placebo.

The second most common serious adverse event in this trial was the flu. This serious adverse event happened in 2 out of 22 patients who got CFZ533. This was 9.1% of patients who got CFZ533. None of the patients who got the placebo had this serious adverse event.

There were other serious adverse events, but these happened in only 1 patient each in either treatment group.

There were 2 out of 22 patients who got the placebo who died during this trial. This was 9.1% of patients in the placebo group.

- 1 patient died due to the serious adverse event of hepatitis
- 1 patient died due to the serious adverse event of heart disease

## What were the most common adverse events?

The most common adverse event in this trial was headache. This happened in a similar percentage of patients in both treatment groups. The table below shows the most common adverse events that happened in 4 or more total patients. There were other adverse events, but these happened in fewer patients.

**Most common adverse events in this trial**

| Adverse event | CFZ533 (Out of 22 patients) | Placebo (Out of 22 patients) | Total (Out of 44 patients) |
|---|---|---|---|
| Headache | 18.2% (4) | 13.6% (3) | 15.9% (7) |
| Common cold | 9.1% (2) | 13.6% (3) | 11.4% (5) |
| MG getting worse | 13.6% (3) | 9.1% (2) | 11.4% (5) |
| Nausea | 13.6% (3) | 9.1% (2) | 11.4% (5) |
| Upper respiratory tract infection | 4.5% (1) | 18.2% (4) | 11.4% (5) |
| Dizziness | 9.1% (2) | 9.1% (2) | 9.1% (4) |
| Higher than normal level of hemoglobin in the blood | 9.1% (2) | 9.1% (2) | 9.1% (4) |
| Low level of white blood cells | 9.1% (2) | 9.1% (2) | 9.1% (4) |
| Pneumonia | 13.6% (3) | 4.5% (1) | 9.1% (4) |
| Respiratory tract infection caused by a virus | 9.1% (2) | 9.1% (2) | 9.1% (4) |

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 presented here are for a single trial. The results of this trial helped researchers better understand if CFZ533 can help patients with MG. The results from many trials are needed to find out which treatments can be used for patients with MG. 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. It takes volunteers in many trials all around the world to advance medical science.

If other trials with CFZ533 in patients with MG are planned, you will be able to find them on the websites listed below.

# 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 **"CCFZ533X2204"** 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 **"NCT02565576"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2015-000097-35"** 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"** or **"iscalimab"**.

**Full trial title:** A multi-center, randomized, double-blind, placebo-controlled, parallel group study to preliminarily evaluate the safety, tolerability, pharmacokinetics and efficacy of CFZ533 in patients with moderate to severe myasthenia gravis

## *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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