Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis

Drug Studied: CDZ173

Protocol #: CCDZ173X2203

Thank you!

Thank you for taking part in the clinical trial for the drug CDZ173, also called leniolisib. You and all of the patients helped researchers learn more about how CDZ173 works in people with primary Sjögren's syndrome, also called PSS.

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 the trial for about 5 months. But, the entire trial took almost 1 year to finish. This is because the patients started and stopped at different times. The trial started in June 2016 and ended in May 2017.

The trial included 30 patients in Germany and Hungary. 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 treat people who have PSS. 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. This information is important to know before other trials can be done that help find out if CDZ173 improves the health of people with PSS.

In people with PSS, the body's immune system is overactive. When that happens, the immune system attacks the body, including the glands that make fluids like tears, saliva, or sweat. People with PSS have dryness of the mouth, eyes, and other areas. They also have pain and tiredness that severely affect their daily lives.

Doctors and researchers do not know the cause of PSS. The trial drug, CDZ173, was designed to lower the activity of the immune system by blocking immune cells called B-cells. The researchers in this trial wanted to learn if CDZ173 can help reduce symptoms of PSS.

In this trial, the researchers wanted to find out how CDZ173 works in a small number of patients with PSS. To find this out, the researchers compared CDZ173 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 effects of a trial treatment.

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

- Did CDZ173 decrease the patients' main PSS symptoms?
- Did CDZ173 change other aspects of the patients' PSS?
- How much CDZ173 got into the patients' blood?
- 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 with PSS. The patients in this trial were 26 to 72 years old.

This was a "double-blind" trial. This means none of the patients, doctors, trial staff, or sponsor staff knew what treatment each patient took. Some trials are done this way because knowing what treatment the patients are taking 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 the patients took so they could create a report of the trial results. The sponsor staff did not know the identity of any of the patients.

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

What happened during the trial?

Before treatment started, the trial doctors did tests and checked the health of the patients to make sure the patients could take part in the trial. The patients gave blood, urine, and saliva samples. They also filled out 3 questionnaires about their PSS symptoms. The trial doctors checked the heart health of the patients using an electrocardiogram, also called an ECG.

During treatment, the patients took the treatment twice a day for 12 weeks. Doses were measured in milligrams, also called mg. The patients took capsules of either 70 mg of CDZ173 or the placebo by mouth.

The patients visited their trial site 6 times during treatment. To check the patients' health and PSS symptoms, the trial staff:

- examined the PSS symptoms and heart health of the patients
- asked the patients about their PSS symptoms and how PSS was affecting their lives
- took blood, urine, and saliva samples
- asked the patients how they were feeling and about any other medicines they were taking

The trial doctors used different types of questionnaires to learn about the PSS symptoms of each patient.

Four weeks after treatment, the patients had their final visit at their trial site. The trial doctors checked the overall health and heart health of the patients. The trial doctors also asked how the patients were feeling and what medicines they were taking. The patients gave more blood, urine, and saliva samples.

The chart below shows how the trial was done.

Before treatment	During treatment	After treatment
• 30 patients joined the trial	• 20 patients took CDZ173 twice a day • 10 patients took the placebo twice a day	• The patients visited their trial site 4 weeks after their final dose
Up to 4 weeks	12 weeks	4 weeks

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 without first talking to your doctor. Always talk to your doctor before making any changes to your medicines or treatment plans.

Did CDZ173 decrease the patients' main PSS symptoms?

After 12 weeks of treatment, CDZ173 slightly decreased the patients' main PSS symptoms. But, this difference was too small for the researchers to know if it was caused by the trial drug.

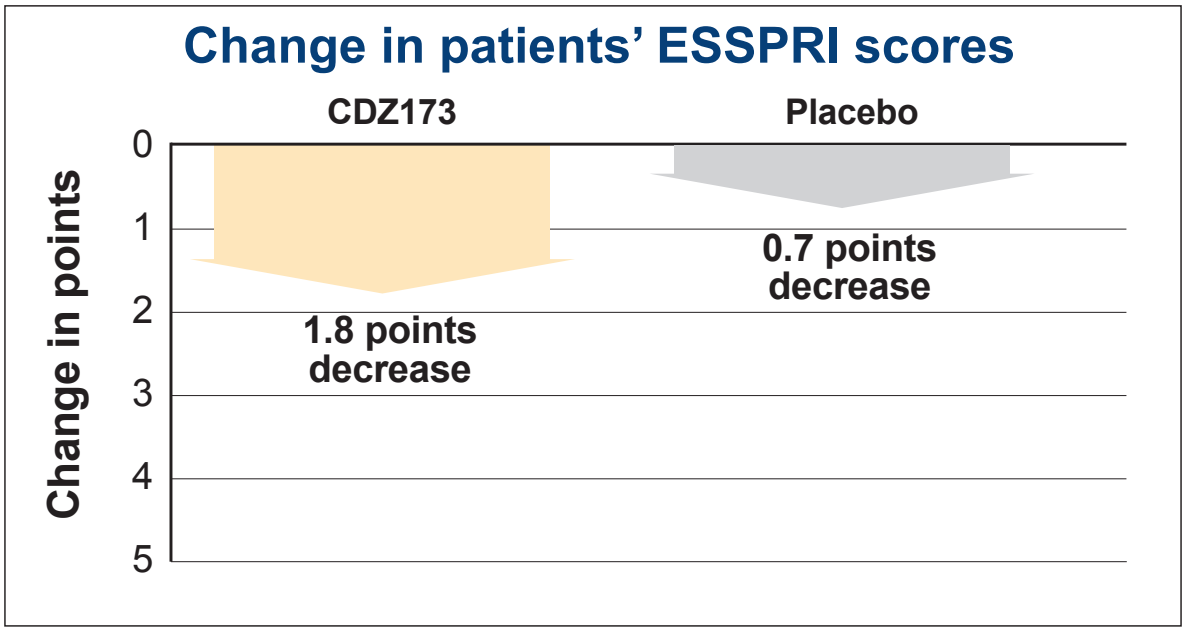
The researchers wanted to know if CDZ173 decreased the patients' main PSS symptoms. To find out, the trial doctors used questions from the EULAR Sjögren's Syndrome Patient Reported Index, also called the ESSPRI. The patients filled out the ESSPRI before, during, and after treatment.

The ESSPRI is a questionnaire that measures how severe patients' main PSS symptoms are. The patients in this trial scored their tiredness, pain, and dryness symptoms each on a scale from 0 to 10. Lower scores meant that the symptoms were less severe.

After 12 weeks of treatment, the researchers found that on average:

- The main symptoms of the patients who took CDZ173 were decreased by 1.8 points.
- The main symptoms of the patients who took the placebo were decreased by 0.7 points.

The chart below shows the change in the patients' ESSPRI scores.



Did CDZ173 change other aspects of the patients' PSS?

Overall, there were changes to other aspects of the patients' PSS in both the CDZ173 and placebo treatment groups. The researchers found that the patients in both treatment groups showed a slight decrease in their PSS symptoms based on each of these questionnaires. But, the differences between the treatment groups were too small for the researchers to know if these differences were caused by the trial drug.

The researchers wanted to know if CDZ173 changed the patients' symptoms. They also wanted to know if the patients' PSS changed throughout the trial. To find out, they used 5 other questionnaires.

The table below shows the questionnaires that were used in the trial.

Name	Description	Completed by
EULAR Sjögren's Syndrome Disease Activity Index (also called the ESSDAI)	Measured how severe the patients' PSS was during the trial	Trial doctor
36-Item Short Form Health Survey (also called the SF-36)	Measured the patients' physical, emotional, and social well-being	Patient
Multidimensional Fatigue Inventory (also called the MFI)	Measured the patients' tiredness	Patient
Visual Analog Scale (also called the VAS)	Measured the patients' overall health	Trial doctor and patient (2 versions)

The patients got these questionnaires before, during, and after treatment. The scores from these questionnaires helped the researchers learn how the patients' symptoms and PSS changed throughout the trial.

How much CDZ173 got into the patients' blood?

To find out how much CDZ173 got into the patients' blood, the trial doctors took blood samples throughout the trial. The researchers learned that in the patients who took CDZ173:

- CDZ173 took an average of 1 hour to reach its highest amount in the blood.
- CDZ173 reached steady and expected levels in the blood.

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.

What medical problems did the 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 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 patients have.

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

How many patients had adverse events?

Most of the patients in this trial had adverse events. Compared to the patients who took the placebo, more patients who took CDZ173 stopped taking the trial drug because of an adverse event. One patient left the trial because of an adverse event.

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

Adverse events during this trial

	CDZ173 (Out of 20 patients)	Placebo (Out of 10 patients)	Total (Out of 30 patients)
How many patients in this trial had adverse events?	100.0% (20)	80.0% (8)	93.3% (28)
How many patients in this trial had serious adverse events?	5.0% (1)	0.0% (0)	3.3% (1)
How many patients stopped taking the treatment because of adverse events?	40.0% (8)	10.0% (1)	30.0% (9)
How many patients left this trial because of adverse events?	5.0% (1)	0.0% (0)	3.3% (1)

What were the most common serious adverse events?

One patient experienced a serious adverse event of a severe rash. This was 3.3% of the patients. The trial doctors thought that this serious adverse event was caused by the trial drug.

None of the patients died during this trial.

What were the most common adverse events?

Rash and upper respiratory tract infection caused by a virus were the 2 most common adverse events during this trial. These adverse events occurred in more patients who took CDZ173 than in patients who took the placebo.

The table below shows the most common adverse events that happened in 10.0% or more of all the patients. There were other adverse events, but these happened in fewer patients.

Most common adverse events during this trial

	CDZ173 (Out of 20 patients)	Placebo (Out of 10 patients)	Total (Out of 30 patients)
Rash	55.0% (11)	10.0% (1)	40.0% (12)
Upper respiratory tract infection caused by a virus	35.0% (7)	40.0% (4)	36.7% (11)
Headache	35.0% (7)	10.0% (1)	26.7% (8)
Diarrhea	25.0% (5)	10.0% (1)	20.0% (6)
Passing gas	5.0% (1)	30.0% (3)	13.3% (4)
Difficulty breathing	15.0% (3)	0.0% (0)	10.0% (3)
Sore throat	15.0% (3)	0.0% (0)	10.0% (3)
Upper respiratory tract infection	15.0% (3)	0.0% (0)	10.0% (3)
Fever	10.0% (2)	10.0% (1)	10.0% (3)
Tiredness	10.0% (2)	10.0% (1)	10.0% (3)

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?

This trial was the first time that CDZ173 was tested in patients with PSS. The information described above helped the researchers better understand if CDZ173 works in people with PSS. The results of many trials are needed to find out which treatments can be used for patients with PSS. This summary shows only the main results from this 1 trial in a small number of patients. 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"** under **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **"CCDZ173X2203"** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the trial doctor or trial 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 **"NCT02775916"** into the search box and click **"Search"**.

- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home & Search"**, then type **"2014-004616-12"** 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 **"CDZ173"** or **"Leniolisib"**.

Full Trial Title: A randomized, double-blind, placebo-controlled, parallel group study to assess the safety, tolerability, pharmacokinetics and preliminary efficacy of CDZ173 in patients with primary Sjögren's syndrome

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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