Clinical Trial Results

NOVARTIS

Research Sponsor:	Novartis
Location of Headquarters:	Basel, Switzerland
Drug Studied:	ACZ885 (Canakinumab)
Protocol #:	CACZ885M2201
Full Trial Title:	A multicenter, randomized, double-blind, placebo-controlled study of the safety, tolerability and effects on arterial structure and function of ACZ885 in patients with intermittent claudication
Full Scientific Summary:	www.novctrd.com
Trial Date:	October 2012 to August 2016

Thank you!

Thank you for taking part in the clinical trial for the treatment ACZ885, also known as canakinumab. You helped researchers learn about how ACZ885 works in people with peripheral artery disease who have intermittent claudication, which is pain or discomfort brought on by walking or exercise.

Novartis, the sponsor of this trial, thinks it is important for you to know the results of your trial. 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 have questions about the results, please speak with the doctor, research nurse, or other team members at your trial site.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

What has happened since the trial ended?

You were in this trial for up to a little over 1 year. The whole trial took almost 4 years to complete. The trial included 38 patients from 16 trial sites in Germany, Jordan, and the United States.

Based on an initial review of the data, this trial was stopped early. The trial treatment did not have the results that were expected. After the trial ended early in August 2016, 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, researchers were looking for a better way to help patients with a disease related to blood flow that is called peripheral artery disease, also known as PAD. People with PAD often have reduced blood flow due to “plaque” build up in the arteries in their legs. Plaque contains fat, cholesterol, and other substances. This reduced blood flow may cause “intermittent claudication”, which is discomfort in the leg, buttock, or foot while doing activities like walking.

Researchers have found a protein in the body that might be related to the narrowing of arteries. The protein is called “IL-1 beta”. IL-1 beta can lead to inflammation. The trial treatment, ACZ885, is a type of antibody that can block IL-1 beta. Antibodies are normally made by the body’s immune system to fight off infection. Researchers are now able to use antibodies as medications to treat a variety of conditions.

In this trial, researchers compared ACZ885 to a placebo. A placebo looks like medicine but does not have any real medicine in it. Using a placebo helps researchers better understand the actual effect of a trial treatment.

The main questions researchers asked in the trial were:

- Did ACZ885 change how much plaque was in the wall of the main artery in the leg more than the placebo?
- Did ACZ885 change the amount of 2 different proteins in the blood?
- What medical problems did patients have during the trial?

To answer these questions, researchers asked for the help of women and men like you. The patients in this trial were 47 to 79 years old and had PAD with intermittent claudication.

What kind of trial was this?

This trial was “double-blind”. This means that none of the patients, trial doctors, trial staff, or sponsor staff knew if patients were getting ACZ885 or the placebo.

Some trials are done this way because knowing what treatment each patient is getting can affect the results of the trial. Doing a trial this way helps make sure the results are looked at fairly. After the trial was stopped, the research sponsor found out what all the patients got so they could create a report of the trial results.

What happened during the trial?

Before the trial started:

- You had tests done to check your overall health to find out if you could join the trial.
- Your PAD symptoms were also checked, including looking at how well you could walk and how your blood pressure was in your legs compared to your arms.
- You had images taken of the main artery in your leg using a medical imaging test called “magnetic resonance imaging”, also called an MRI.

During the trial:

- 18 patients got 150 “milligrams”, also known as mg, of ACZ885 through a shot given under the skin once a month.
- 20 patients got the placebo through a shot given under the skin once a month.

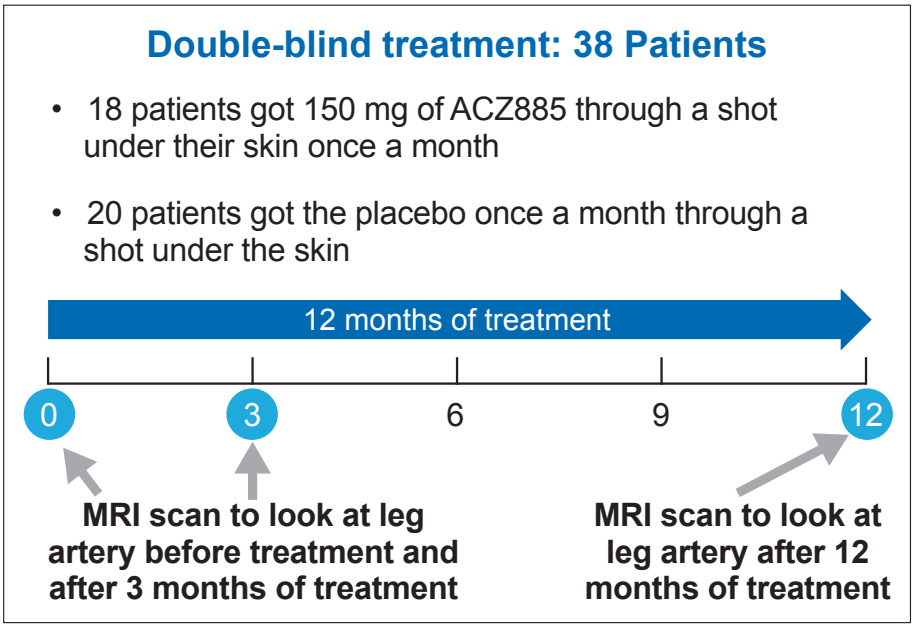
The treatment you got was decided randomly, using a computer program.

To check your health and PAD symptoms:

- You had an MRI scan of the main artery in your leg after 3 months, and again after 12 months.
- You had your overall health checked, the blood pressure in your legs and arms measured and compared, and how well you could walk checked.
- You also gave blood and urine samples and answered questions about any other medicines you were taking and how you were feeling.

You had a final visit 1 month after you got the last shot.

The figure 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. Researchers look at the results of many trials to decide which drugs work best and are safest for patients. Other trials may provide new information or different results. You should not make changes to your treatment based on the results of a single trial without first talking to your doctor.

Did ACZ885 change how much plaque was in the wall of the main artery in the leg more than the placebo?

Overall, the difference between the treatments was too small for researchers to know if ACZ885 changed the narrowing of the main artery in the leg more than the placebo. There was no change in the amount of plaque in the small area of the main artery in either group.

The researchers found out how much plaque patients had by measuring the average area of the main artery. The average area was measured in “square millimeters”, also known as mm^2. The researchers found out how much the average area changed by comparing the patients’ MRIs from before and after treatment.

After 12 months of treatment, patients who got ACZ885 and patients who got placebo had about the same amount of plaque in their main leg artery as before treatment.

Did ACZ885 change the amount of 2 different proteins in the blood?

Overall, researchers found that the difference between patients in the ACZ885 and placebo groups was too small for researchers to know if 1 treatment changed the amount of proteins more than the other after 12 months of treatment.

Researchers measured the amount of 2 proteins in the blood. These proteins help researchers get an idea of how much inflammation is found in each patient. They compared the amount of these proteins before and after treatment. These proteins are called:

- **"Serum amyloid A":** This is also called SAA.
- **"C-reactive protein":** This is also called CRP.

After 12 months, patients in both treatment groups had about the same amount of SAA and CRP in their blood compared to before treatment. But, patients who got ACZ885 did have lower CRP levels at earlier points in the trial, after 2, 7, and 10 months of treatment compared to before treatment.

What medical problems did patients have?

A lot of research is needed to know whether a treatment causes a medical problem. So when new treatments are being studied, researchers keep track of all medical problems that patients have. These medical problems are called "adverse events". An adverse event is any unwanted sign or symptom that may or may not be caused by the trial treatment.

How many patients had adverse events during the trial?

During the trial, adverse events were collected for all patients whether they got ACZ885 or placebo:

- 94.7% of all patients in the trial had adverse events. This was 36 out of the 38 patients.
- 52.6% of all patients in the trial had serious adverse events. This was 20 out of the 38 patients.
- 15.8% of all patients in the trial stopped treatment because of adverse events. This was 6 out of the 38 patients.

The table below shows how many patients in each treatment group had adverse events. Slightly more patients in the placebo group had adverse events compared to the ACZ885 group.

Adverse events during this trial

	ACZ885 150 mg (Out of 18 patients)	Placebo (Out of 20 patients)	Total (Out of 38 patients)
How many patients had adverse events?	88.9% (16)	100.0% (20)	94.7% (36)
How many patients had serious adverse events?	55.6% (10)	50.0% (10)	52.6% (20)
How many patients stopped getting the treatment because of adverse events?	5.6% (1)	25.0% (5)	15.8% (6)

Did any patients have serious adverse events?

During the trial:

- 55.6% of patients who got ACZ885 had serious adverse events. This was 10 out of the 18 patients.
- 50.0% of patients who got the placebo had serious adverse events. This was 10 out of the 20 patients.

An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or leads to hospitalization. During a trial, all serious adverse events are reported and written down, whether or not they are caused by the trial drug.

There was 1 patient who got ACZ885 who died due to a heart attack. The trial doctors did not think this death was related to getting ACZ885.

The serious adverse event that happened most often was reduced blood flow that caused leg pain. This happened in about the same number of patients in both treatment groups. The table below shows the serious adverse events that were reported by at least 2 patients.

Serious adverse events during this trial

Serious adverse event	ACZ885 150 mg (Out of 18 patients)	Placebo (Out of 20 patients)
Reduced blood flow that caused leg pain (peripheral arterial occlusive disease)	16.7% (3)	10.0% (2)
Heart disease due to clogged arteries (coronary artery disease)	11.1% (2)	5.0% (1)
Chest pain not related to the heart (Non-cardiac chest pain)	0.0% (0)	10.0% (2)

For more information about serious adverse events in this trial, please refer to the full scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).

What were the most common non-serious adverse events?

The most common non-serious adverse event was infection of the nose, throat, or airways. This happened in about the same number of patients in both treatment groups.

The table below shows the most common non-serious adverse events that were reported by at least 10% of all patients in the trial.

Most common non-serious adverse events in this trial

Adverse event	ACZ885 150 mg (Out of 18 patients)	Placebo (Out of 20 patients)	Total (Out of 38 patients)
Infection of the nose, throat, or airways (upper respiratory tract infection)	22.2% (4)	20.0% (4)	21.1% (8)
Common cold (nasopharyngitis)	11.1% (2)	20.0% (4)	15.8% (6)
Joint pain (arthralgia)	27.8% (5)	0.0% (0)	13.2% (5)
Reduced blood flow to the limbs that causes leg pain (peripheral arterial occlusive disease)	16.7% (3)	10.0% (2)	13.2% (5)
Tiredness (fatigue)	16.7% (3)	10.0% (2)	13.2% (5)
Chest pain from reduced blood flow to the heart (angina pectoris)	16.7% (3)	5.0% (1)	10.5% (4)
Nausea	16.7% (3)	5.0% (1)	10.5% (4)
Problems falling and staying asleep (insomnia)	16.7% (3)	5.0% (1)	10.5% (4)
Upper abdominal pain	11.1% (2)	10.0% (2)	10.5% (4)

How has this trial helped patients and researchers?

The information described above helped researchers better understand whether ACZ885 works in people with peripheral artery disease who have intermittent claudication. The results presented here are for a single trial. Other trials may provide new information or different results. Researchers look at the results of many trials to decide which treatments work best and are safest for patients. It takes volunteers in many trials all around the world to advance medical science.

Where can I learn more about this trial and future trials?

More information about the results for this trial can be found in the scientific results summary available on the Novartis Clinical Trial Results website (novctrd.com). Once on the site, click **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **CACZ885M2201** 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.

This trial was registered on the following websites:

- Clinical Trials.gov (https://clinicaltrials.gov/) - National Clinical Trial # NCT01731990
- EU clinical register (https://www.clinicaltrialsregister.eu/ctr-search) - EU Clinical Trial # 2012-001427-12

If more clinical trials are planned, they will be listed on the above public websites or www.novartisclinicaltrials.com. Search for **"ACZ885"** or **"canakinumab"**.

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. CISCRP is not involved in recruiting patients for clinical trials, nor is it involved in conducting clinical trials.

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