Clinical Trial Results

NOVARTIS

Research Sponsor:	Novartis
Location of Headquarters:	Basel, Switzerland
Drug Studied:	ACZ885 (Canakinumab)
Protocol #:	CACZ885X2201
Full Trial Title:	A randomized, double-blind, placebo-controlled, multiple-dose study of subcutaneous ACZ885 for the treatment of abdominal aortic aneurysm
Full Scientific Summary:	www.novctrd.com
Trial Date:	December 2013 to October 2015

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.

Thank you for taking part in the clinical trial for the drug ACZ885, also known as canakinumab. You helped researchers learn more about how ACZ885 works in people with an abdominal aortic aneurysm, also called an AAA. This trial started in December 2013 and ended in October 2015.

Novartis, the sponsor of this trial, thanks you for your help and 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 member at your trial site.

What's happened since the trial ended?

This trial was designed to observe each patient for about 1 year, but it took close to 2 years to complete. The trial included 65 patients from 8 sites. Patients were enrolled in sites in Denmark, the Netherlands, Sweden, and the United Kingdom. Of the 65 patients who entered the trial, 1 patient was diagnosed with thrombocytopenia or having a low number of platelets in the blood. This patient did not get any treatment.

This trial stopped early in September 2015 because the trial drug did not have the result that was expected. The last patient completed all of their follow-up appointments for the study in October 2015. 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 were looking for a better way to treat abdominal aortic aneurysms or AAAs. The abdominal aorta is the main blood vessel that supplies blood to the abdomen, pelvis, and legs. An AAA occurs when the abdominal aorta grows very large and can start to bulge or even burst. Researchers have found that a protein called IL-1 beta is found in higher amounts in people with an AAA than in other people.

The trial drug 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, including an AAA.

The main questions researchers asked in the trial were:

- Did ACZ885 reduce the size and growth of the AAA after 12 months of treatment compared to no trial drug at all?
- What medical problems did patients have during the trial?

To answer these questions, researchers asked for the help of men and women like you.

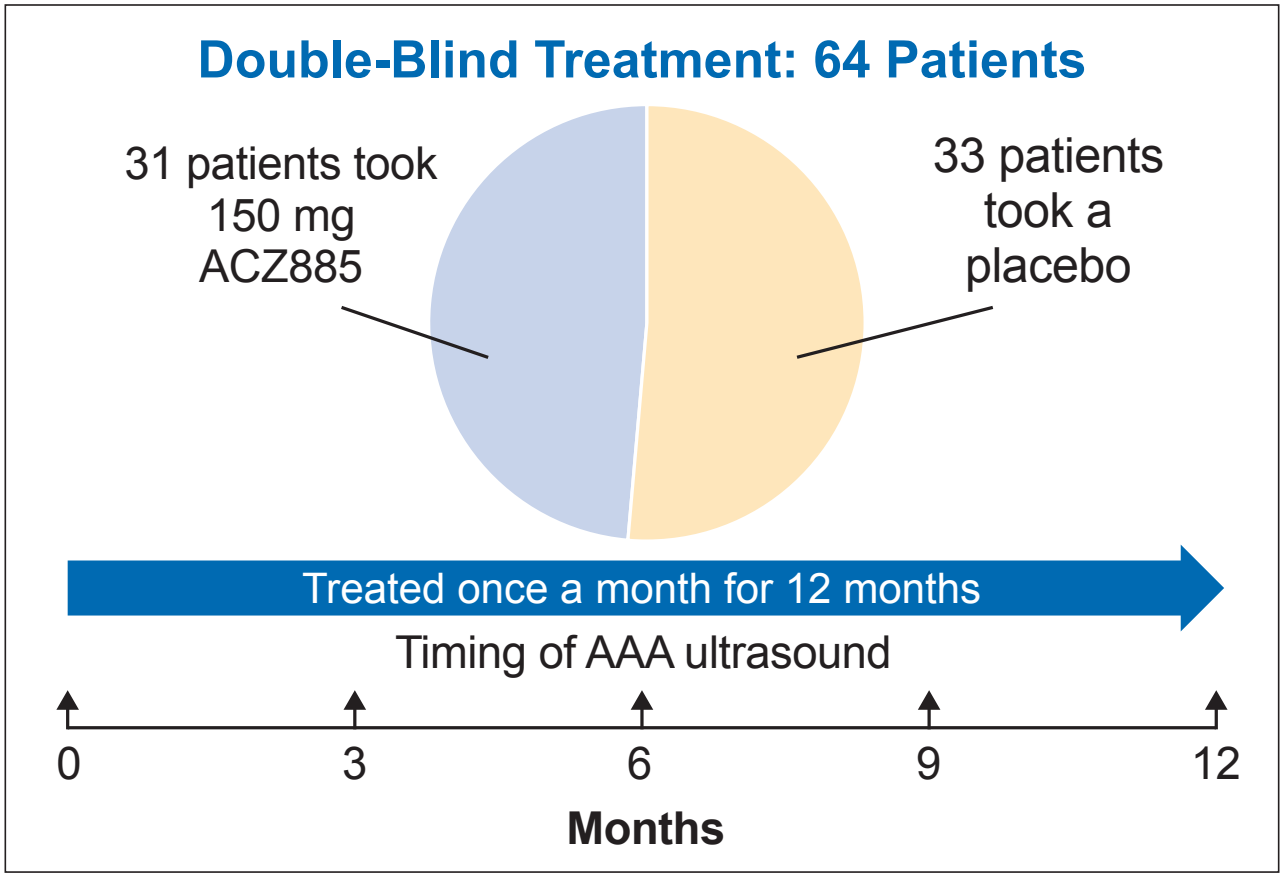
What kind of trial was this?

This trial was “double-blind.” This means that none of the patients, trial doctors, or study staff knew what treatment each patient received. Patients in this trial took either ACZ885 or a placebo. A placebo looks like the trial drug but contains no medicine at all.

Some trials are done this way because knowing what treatment each patient is getting can affect the results of the trial. This way, the results are looked at fairly. When the trial ended, the research sponsor found out which treatment patients took, so they could create a report of the trial results.

What happened during the trial?

The figure below shows how the trial was done.



The patients in this trial were men and women between the ages of 53 and 86 years old who had an AAA. To participate in the trial, the AAA had to be of a certain size. Trial doctors checked the size of patients' abdominal aorta by taking a picture using a medical test called an ultrasound. All patients also had full check-ups and a physical examination to make sure they could take part in the trial. Trial doctors took blood samples and checked patients' height, weight, body temperature, blood pressure, and pulse rate and checked participants' overall heart health using an electrocardiogram, or ECG. Patients with certain conditions, like severe high blood pressure, kidney disease, diabetes, or a history of tuberculosis, were not eligible to join the trial.

The treatment period lasted for 12 months. During the treatment period, patients were randomly assigned, like flipping a coin, to get a monthly injection under the surface of the skin of either a placebo or 150 milligrams (mg) of ACZ885. Throughout the trial, trial doctors checked patients' weight, temperature, blood pressure, and pulse rate and also took blood samples. Trial doctors also did an ECG at many visits to check the patients' heart health. Patients had ultrasounds of their abdominal aorta done every 3 months.

About 1 month after the last injection, patients had a final follow-up visit.

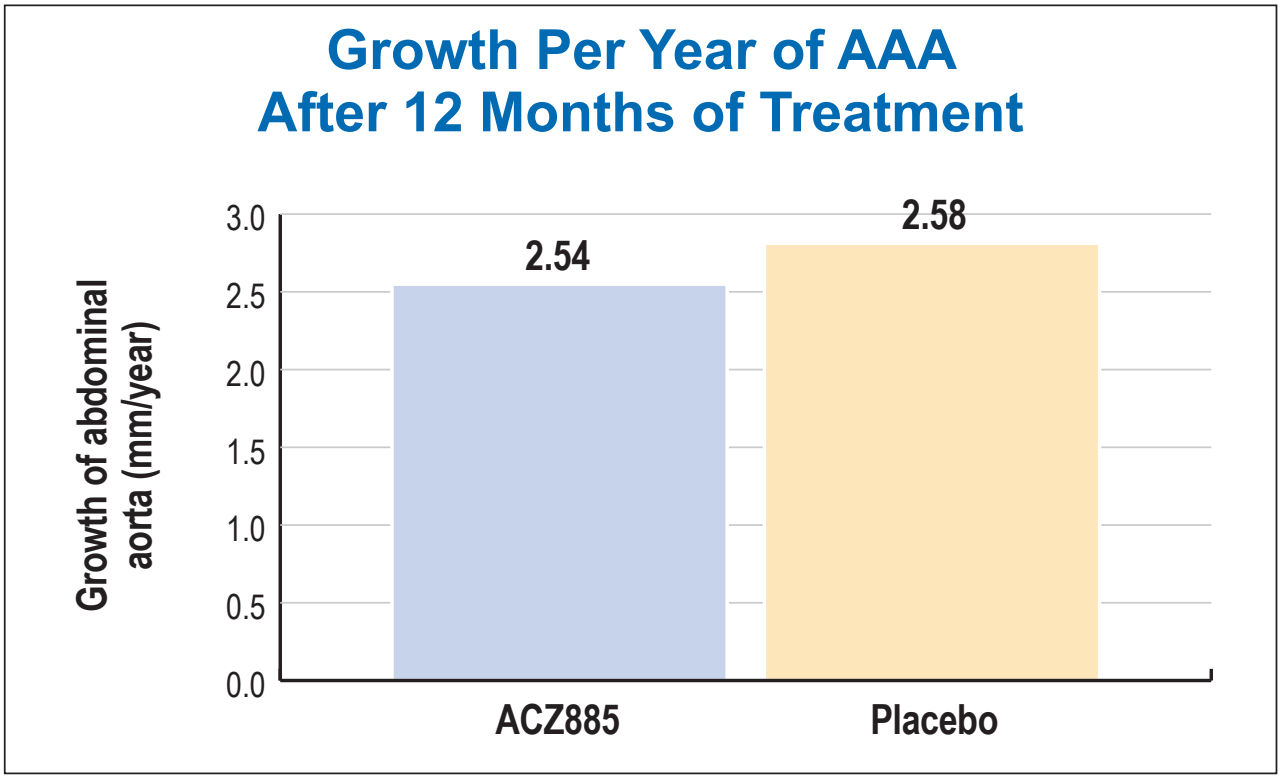
What were the results of the trial?

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 studies 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 reduce the size and growth of the AAA after 12 months of treatment compared to no trial drug at all?

No. Researchers measured the size and growth rate of patients' abdominal aortic aneurysm, or AAA, throughout the trial. Researchers took a picture of the AAA using an ultrasound. They used the picture to measure the size and growth rate of the AAA. At month 12, patients in the ACZ885 group had a growth of 2.54 millimeters (mm) per year in their AAAs, while patients in the placebo group had a growth of 2.58 mm per year. Overall, the results did not show that treatment with ACZ885 was better than the placebo.

The graph below shows the growth in AAA size after 12 months of treatment with ACZ885 or a placebo.



What medical problems did patients have?

A lot of research is needed to know whether a drug causes a medical problem. So when new drugs 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 sign or symptom that may or may not be caused by the trial drug.

How many patients had adverse events during the trial?

A total of 56 (87.5%) patients had adverse events during the trial. Out of all patients who received treatment during the trial, 11 (17.2%) patients stopped taking the trial drug because of adverse events. Patients can stop taking the trial drug at any time during the study, even if their adverse events are not serious. The table below shows how many patients had adverse events during this trial.

Adverse Events in this Trial

	ACZ885 150 mg Out of 31 patients	Placebo Out of 33 patients	Total Out of 64 patients
How many patients had adverse events?	28 (90.3%)	28 (84.8%)	56 (87.5%)
How many patients had serious adverse events?	2 (6.5%)	0 (0.0%)	2 (3.1%)
How many patients stopped taking the trial drug because of adverse events?	7 (22.6%)	4 (12.1%)	11 (17.2%)

Did any patients have serious adverse events?

An adverse event is called “serious” when it is life threatening, causes lasting problems, or leads to hospitalization.

In this trial, 2 patients in the ACZ885 treatment group experienced a serious adverse event. The serious adverse events were a broken hip and pain from an aortic aneurysm. Trial doctors did not think that either of the serious adverse events were related to the trial drug. No patients died during the trial.

What were the most common non-serious adverse events?

The table below shows the most common non-serious adverse events (in at least 6% of all patients) in this trial.

Most Common Non-Serious Adverse Events in this Trial

Adverse Event	ACZ885 150 mg Out of 31 patients	Placebo Out of 33 patients	Total Out of 64 patients
Common cold	5 (16.1%)	3 (9.1%)	8 (12.5%)
Back pain	4 (12.9%)	3 (9.1%)	7 (10.9%)
High blood pressure	4 (12.9%)	3 (9.1%)	7 (10.9%)
Injection site swelling	3 (9.7%)	2 (6.1%)	5 (7.8%)
Abdominal pain	3 (9.7%)	1 (3.0%)	4 (6.3%)
Aortic aneurysm (bulge in the aorta)	2 (6.5%)	2 (6.1%)	4 (6.3%)
Joint pain	2 (6.5%)	2 (6.1%)	4 (6.3%)
Cough	3 (9.7%)	1 (3.0%)	4 (6.3%)
Peripheral edema (swelling in the limbs)	0 (0.0%)	4 (12.1%)	4 (6.3%)

For a full list of the adverse events that occurred in this trial, please refer to the full scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).

Events of Special Interest

Researchers also wanted to see if patients in this trial experienced any heart-related adverse events that may happen to people with AAA. One patient in the ACZ885 group experienced a mini-stroke that may have been caused by a blockage in the blood vessels supplying blood to the brain. Trial doctors did not think that this adverse event was related to the trial drug.

Researchers also wanted to see if patients' immune systems made antibodies against ACZ885 in the blood. If antibodies against ACZ885 form, the drug may not work as well, or it may cause an allergic reaction to the drug - both may happen, or nothing may happen. No patients in this trial developed antibodies against ACZ885 in their blood.

Where can I learn more about this trial?

Researchers look at the results of many trials to decide which drugs work best and are safest for patients. It takes volunteers in many trials all around the world to advance medical science.

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). Once on the site, click **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **CACZ885X2201** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the doctor or staff at your trial site.

This trial was also registered on the following websites:

- https://clinicaltrials.gov/ct2/show/NCT02007252 - **National Clinical Trial #** NCT02007252.
- https://www.clinicaltrialsregister.eu/ctr-search - **EU Clinical Trial #** 2013-002088-25

Thank you

It is said that the greatest gift is one which is given anonymously, giving when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge and benefits public health.

Thank you for the gift of your participation in clinical research.

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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