Clinical Trial Results Summary

NOVARTIS

The safety of ACZ885 and its effects on pain from sickle cell anemia in children and young adults

Thank you!

Thank you to the participants who took part in the clinical trial for the trial drug **ACZ885**, also called **canakinumab**. All of the participants helped the researchers learn more about how well ACZ885 works and how safe it is to take.

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: CACZ885X2206
Drug studied: ACZ885 (canakinumab)
Sponsor: Novartis

This trial at a glance

What was the purpose of this clinical trial? Read more on **page 3**

The purpose of this trial was to learn:

- If ACZ885 could lower the pain of children and young adults with sickle cell anemia, also called SCA
- More about the safety of ACZ885

Who was in this trial? Read more on **page 4**

- 49 males and females began this trial
- The participants were 8 to 20 years old and had SCA that regularly caused them pain

What trial treatments did the participants receive? Read more on **pages 4-5**

Each participant was assigned at least one of these treatments:

- ACZ885
- Placebo – looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

The participants received the trial treatments as injections.

What were the main results of this trial? Read more on **pages 5-9**

- Everyone in the trial had slightly less pain after 12 weeks. The participants who received ACZ885 reported about the same level of pain on average compared to those who received the placebo.
- Most participants had medical problems, some of which were considered serious. The number of participants who had medical problems was similar between those who received ACZ885 and those who received the placebo. Many of these medical problems are common for people with SCA, such as pain from sickle cell crisis.

Read about other results of this trial on **page 10**

You can find **more information** about this trial by going to the websites listed on **page 11.**

What was the purpose of this clinical trial?

The purpose of this trial was to learn if the trial drug ACZ885 could lower the pain of children and young adults with **sickle cell anemia**, also called **SCA**. SCA is a life-long condition that causes many red blood cells to change shape and break down faster. Red blood cells carry oxygen to other cells in the body. Because these cells break down faster, the body often can't get enough oxygen. This breakdown can also cause inflammation.

ACZ885 is a drug designed to lower inflammation by blocking a protein that can trigger inflammation. It's approved in some countries to treat certain conditions that involve inflammation.

What is inflammation?

Inflammation involves many cells and proteins that work to protect the body while it heals. Too much inflammation can harm the body and cause pain.

Researchers wanted to learn if ACZ885 could also lower pain and inflammation from SCA. This trial was also designed to learn about the safety of ACZ885. Before a drug can be approved for doctors to prescribe for other conditions, researchers do many trials to find out how safe it is and how it works.

The main questions this trial was designed to answer:

- Did the participants who received ACZ885 report less pain compared to those who received the placebo?
- What medical problems did the participants have during this trial? Keeping track of the medical problems helped to learn about the safety of ACZ885.

How long was this trial?

This trial took place from April 2017 to April 2020. The participants could take part in the trial for up to 15 months.

This trial ended early because the clinical trial team collected enough data about how well ACZ885 worked for children and young adults with SCA. The decision to end the trial early was not related to safety.

Who was in this trial?

49 participants received treatment – 28 males and 21 females. 8 participants did not complete this trial. The participants were 8 to 20 years old. Their average age was 16.

Every participant in this trial had SCA that regularly caused them pain. They also:

- Had pain from a sickle cell crisis that kept them from their normal activities at least 2 times during the past year
- Did not receive blood transfusion therapy on a regular basis or within the past 3 months.
- Did not have other serious medical conditions

This trial took place in Canada, Germany, Israel, South Africa, Turkey, the United Kingdom, and the United States.

Visit novctrd.com for more information about:

- Who could and could not be in this trial
- The participants in this trial, such as their age, gender, and race

Use trial number **CACZ885X2206** to find the scientific summary.

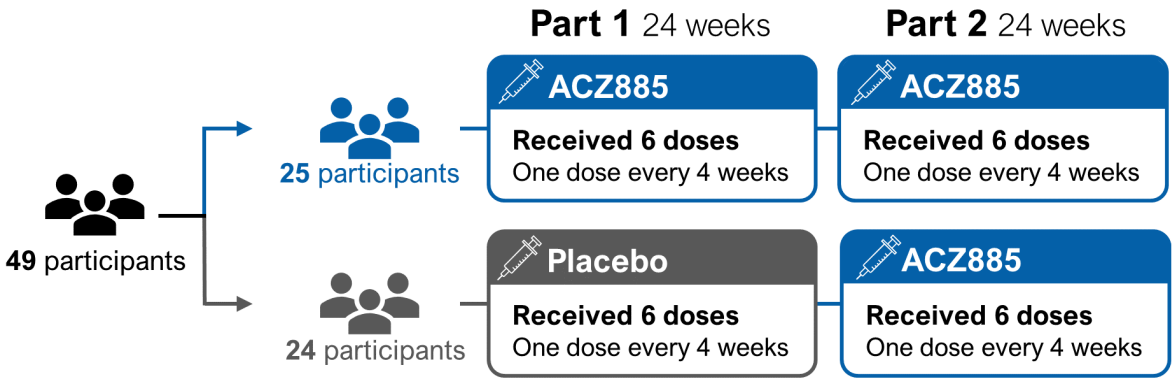
What trial treatments did the participants receive?

A computer program was used to randomly assign each participant to at least one of these treatments:

- **ACZ885:** The participants received up to 300 mg based on their body weight
- **Placebo:** A placebo looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

Using a computer program to assign the treatments helped make sure the team compared the results as fairly as possible.

The graphic below shows the number of participants who received each of these treatments during each part of this trial.



This trial was divided into Part 1 and an optional Part 2:

- In Part 1, the participants and most trial staff did not know what treatment each participant received. Some trials are done this way because knowing what treatment participants receive can influence the results. Not knowing what treatment participants receive helps make sure the results are looked at fairly.
- In Part 2, all participants received ACZ885, so trial staff knew what treatment each participant received. Some trials are done this way to show the safety and effects of a trial drug over a longer period of time.

The trial pharmacists knew the treatment assigned to each participant during both parts of the trial so they could make sure the participants received their assigned treatment.

The participants could continue to take their regular medicines for SCA during this trial.

What were the main results of this trial?

This is a summary of the overall results of this trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results.

Always talk to a doctor before making any changes to your health care.

Did the participants who received ACZ885 report less pain compared to those who received the placebo?

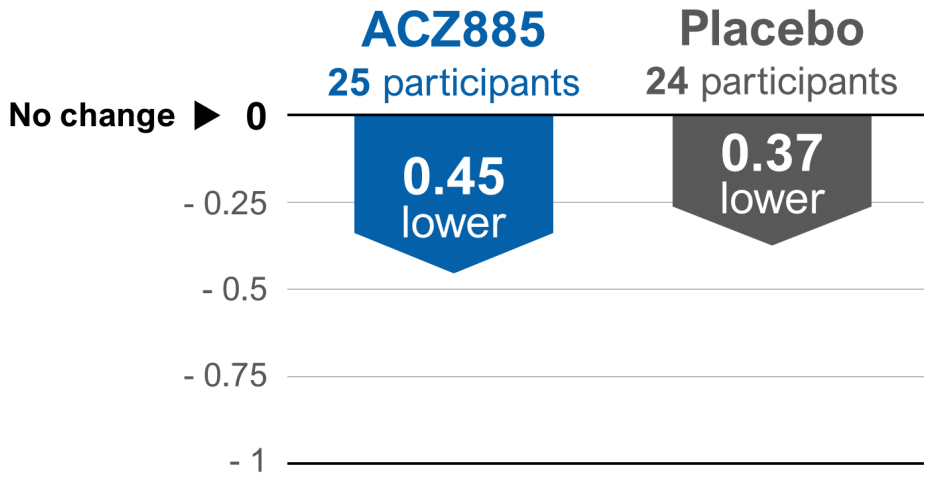
Everyone in the trial had slightly less pain after 12 weeks. The participants who received ACZ885 reported about the same level of pain on average compared to those who received the placebo.

To find this out, each participant received an **eDiary**, an electronic device to report their level of pain before, during, and after treatment. Each day, the participants used their eDiary to report their pain on a scale from 0 (no pain) to 10 (worst pain).

After 12 weeks in Part 1, the participants' reported level of pain went down by **0.45** for those who received ACZ885 and **0.37** for those who received the placebo. The difference between these groups was too small to be meaningful.

Change in reported level of pain

The average change in the participants' reported level of pain from before treatment to after 12 weeks of treatment



The team also looked at the change in reported level of pain after 24 weeks in Part 1 and again in Part 2. From Part 1, they found that the participants who received ACZ885 reported slightly less pain compared to those who received the placebo. This change wasn't enough to be considered meaningful. The changes reported in Part 2 were also not enough to be considered meaningful.

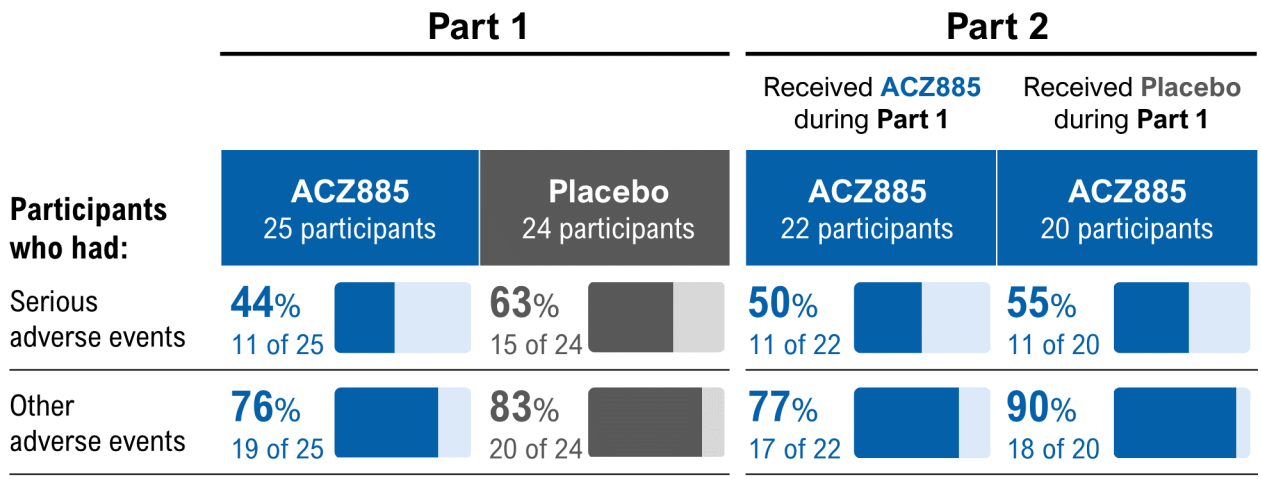
What medical problems did the participants have during the trial?

Medical problems that happen during trials are called “adverse events”. An **adverse event** is any unwanted sign or symptom that the participants have during a trial. An adverse event is 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. Many trials are needed to know if a drug or treatment causes an adverse event. Trial doctors keep track of all adverse events that happen in trials, even if they think the adverse events might not be related to the trial treatments.

Most participants had adverse events, some of which were considered serious. The number of participants who had adverse events was similar between those who received ACZ885 and those who received the placebo. Many of these adverse events are common for people with SCA, such as pain from sickle cell crisis.

Participants who had adverse events



No participants left this trial due to adverse events.

What serious adverse events did participants have?

About half of all participants in this trial had serious adverse events. The table below shows the serious adverse events that happened to **2 or more participants** in a treatment group. Other serious adverse events were reported by fewer participants.

Serious adverse events

	Part 1		Part 2	
			Received **ACZ885** during **Part 1**	Received **Placebo** during **Part 1**
	ACZ885 25 participants	**Placebo** 24 participants	**ACZ885** 22 participants	**ACZ885** 20 participants
Pain from sickle cell crisis	40% 10 of 25	46% 11 of 24	41% 9 of 22	50% 10 of 20
Lung infection Pneumonia	0% 0 of 25	4% 1 of 24	9% 2 of 22	5% 1 of 20
Acute chest syndrome	0% 0 of 25	8% 2 of 24	0% 0 of 22	0% 0 of 20

Acute chest syndrome is when sickle cells block blood flow in the lungs, causing pain and trouble breathing.

What other adverse events did participants have?

Most participants in this trial had adverse events that were not serious. The table below shows the adverse events that happened to **3 or more participants** in a treatment group. Other adverse events were reported by fewer participants.

Other adverse events

	Part 1		Part 2	
			Received ACZ885 during **Part 1**	Received Placebo during **Part 1**
	ACZ885 25 participants	**Placebo** 24 participants	**ACZ885** 22 participants	**ACZ885** 20 participants
Pain	24% 6 of 25	21% 5 of 24	14% 3 of 22	35% 7 of 20
Headache	20% 5 of 25	13% 3 of 24	9% 2 of 22	20% 4 of 20
Upper respiratory tract infection Such as the cold or flu	4% 1 of 25	21% 5 of 24	9% 2 of 22	30% 6 of 20
Back pain	8% 2 of 25	8% 2 of 24	9% 2 of 22	25% 5 of 20
Pain in the arms or legs Pain in extremity	12% 3 of 25	13% 3 of 24	0% 0 of 22	15% 3 of 20
Chest pain, not heart-related	4% 1 of 25	4% 1 of 24	14% 3 of 22	10% 2 of 20
Belly pain Abdominal pain	0% 0 of 25	0% 0 of 24	0% 0 of 22	15% 3 of 20

For more information about the adverse events the participants in this trial had, visit novctrd.com. Use trial number **CACZ885X2206** to find the scientific summary.

What other results were learned?

Did ACZ885 lower the signs of inflammation in the participants' blood?

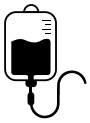
The participants who received ACZ885 had lower signs of inflammation in their blood compared to those who received the placebo.

Did the participants who received ACZ885 miss fewer days of school or work because of their pain?

Researchers noticed a trend of fewer missed days of school or work in the participants that received ACZ885 towards the end of their treatment.

Did the participants who received ACZ885 have less signs of hemolysis?

Hemolysis means the breakdown and death of red blood cells. Sickle cells break down and die more quickly than normal red blood cells. The participants who received ACZ885 had no difference in their signs of hemolysis compared to those who received the placebo.



Did the participants who received ACZ885 have fewer blood transfusions?

Sometimes patients with SCA get transfusions to treat sickle cell symptoms they are currently having. These are called 'rescue transfusions'. Sometimes SCA patients get transfusions to help prevent a SCA crisis. ACZ885 did not make a meaningful difference in the overall number of blood transfusions that the participants had. But the participants who received ACZ885 had fewer rescue blood transfusions on average compared to those who received the placebo.

What was learned from this trial?

This was the first trial to learn about how well ACZ885 works for children and young adults with SCA. The clinical trial team learned that blocking a protein could lower inflammation from SCA. However, it did not meaningfully lower the participants' reported pain. They also found that, on average, the participants who received ACZ885 missed fewer days of school and reported feeling less tired during the day towards the end of their treatment.

The clinical team concluded the safety results for the participants who received ACZ885 were similar to those who received the placebo.

This was one of many trials a drug must go through before it can be approved for doctors to prescribe for people with SCA. This type of trial learns about the safety of a trial drug and how well it works in a small number of participants.

The results presented here are for one trial. One trial cannot give a complete picture of the benefits and risks of a trial drug. The results of many trials are needed to find out which treatments can be used for people with SCA. This summary shows only the main results from this trial. Other trials may provide nev information or different results.

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

You can find detailed results and more information about this clinical trial on the Novartis Clinical Trial Results website:

1. Visit novctrd.com
2. Click on “Clinical Trial Results” at the top right of the page
3. Read and scroll down, then click “I accept” to agree to use the information and the website
4. Select “Study number” from the drop-down menu
5. Type **“CACZ885X2206”** in the search box and click search

If you would like to view the website in a language other than English, you can click the “Google Translate” button on the top right of the page.

If you participated in the trial and have **questions** about the results, please speak with the trial doctors or staff at your trial site.

This trial was registered on the following websites:

- ClinicalTrials.gov – https://clinicaltrials.gov/
  To find this trial, type **CACZ885X2206** in the **Other terms** search box
- European Union Clinical Trials Register – https://www.clinicaltrialsregister.eu/ctr-search
  To find this trial, type **CACZ885X2206** in the search box

Full trial title:

A multiple-dose, subject- and investigator-blinded, placebo-controlled, parallel design study to assess the efficacy, safety and tolerability of ACZ885 (canakinumab) in pediatric and young adult patients with sickle cell anemia

If more trials are planned, they will appear on the public websites listed above. When there, search for **ACZ885** or **canakinumab**.

Thank you!

Novartis would like to thank all of the people who participated in this clinical trial. The participants made this clinical trial possible and helped researchers answer important health questions and learn about a possible medical treatment. Many volunteers and many clinical trials are needed to advance medical science.

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