Clinical Trial Results Summary

NOVARTIS

The effects on breathing and the safety of canakinumab for people with pulmonary sarcoidosis

Thank you!

Thank you to the participants who took part in the clinical trial for the drug **canakinumab**, also called ACZ885. All of the participants helped the researchers learn more about how canakinumab 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. An independent organization prepared this summary of the trial results.

We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CACZ885X2205
Drug studied: canakinumab
(can-a-KIN-ue-mab)
Sponsor: Novartis

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

? 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 at a glance

What was the purpose of this trial?

Read more on **page 3**

This trial was designed to find out if canakinumab could help people with pulmonary sarcoidosis breathe easier. Pulmonary sarcoidosis is a long-term disease that affects the lungs and can make it hard to breathe. Canakinumab is a drug that has been approved to treat other diseases.

This trial was designed to answer these questions:

- Did canakinumab change how well the participants could breathe?
- What medical problems did the participants have in this trial?
  Keeping track of the medical problems helped to learn about the safety of canakinumab.

Who was in this trial?

Read more on **page 4**

- 40 men and women were in this trial
- Every participant was 29 to 67 years old and had pulmonary sarcoidosis

What treatments did the participants receive?

Read more on **page 4**

Each participant was assigned one of these treatments:

- Canakinumab
- 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.

Participants received their assigned treatment through an injection under the skin.

What were the main results of this trial?

Read more on **page 6**

Canakinumab did not make a meaningful difference in how well the participants could breathe compared to the placebo.

Most of the participants had medical problems during this trial, and some of the medical problems were serious. The participants who received canakinumab had a similar number of medical problems as those who received the placebo. The most common medical problems were feeling tired and the common cold.

This trial had other results in addition to the main results.

Read more on **page 9**

What was the purpose of this clinical trial?

Researchers are looking for better ways to treat sarcoidosis in the lungs, also called pulmonary sarcoidosis. **Sarcoidosis** is a rare, long-term disease that affects many organs in the body, most often the lungs. When it affects the lungs, it can cause coughing, shortness of breath, and wheezing.

Researchers aren't sure what causes sarcoidosis. They suspect it may happen when irritants in the air trigger the body's immune system.
The immune system is made of cells and proteins that protect the body from harm. When the immune system detects something harmful, one way it responds is with **inflammation**.

What is inflammation?

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

For people with sarcoidosis, their immune system overreacts to these irritants. Their inflammation response causes small groups of immune cells to grow in the body. These groups of cells are often called **nodules** or granulomas. When these nodules grow in the lungs, they can block the airways and make it hard to breathe.

Researchers have found that these nodules have high levels of an inflammation protein called **IL-1β**, which stands for interleukin-1 beta.
Canakinumab (can-a-KIN-ue-mab), also called ACZ885, is a drug designed to block IL-1β and is approved to treat other diseases that involve inflammation. Researchers wanted to learn if blocking IL-1β would break up the nodules and help people breathe easier.

Canakinumab is not approved to treat sarcoidosis. Before a drug can be approved to treat sarcoidosis, researchers do many trials to find out how safe it is and how it works.

This trial was designed to answer these questions:

- Did canakinumab change how well the participants could breathe?
- What medical problems did the participants have in this trial?
  Keeping track of the medical problems helped to learn about the safety of canakinumab.

Who was in this trial?

40 participants were in this trial – 28 men and 12 women. Everyone was 29 to 67 years old. Their average age was 50.

Every participant in this trial:

- Had sarcoidosis in their lungs for at least one year
- Had trouble breathing due to sarcoidosis
- Was in otherwise good overall health

Participants could continue their regular sarcoidosis treatments during the trial.

This trial took place in Germany, the Netherlands, and the United States.

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

Follow the instructions on **page 11** to find the scientific summary

What treatments did the participants receive?

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

- **Canakinumab:** 300 mg (milligrams) per dose
- **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 clinical trial team compared the results as fairly as possible.

Participants received their assigned treatment through an injection under the skin every 4 weeks.

The participants and trial staff did not know what treatment each participant received during the trial. 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.

What happened during this trial?

The trial began in December 2016 and ended in March 2019. 7 participants did not complete this trial.

The trial staff measured how well the participants could breathe during certain visits to the trial site. They also looked at the sarcoidosis nodules in participants' lungs. To do this, the staff used 2 types of imaging scans:

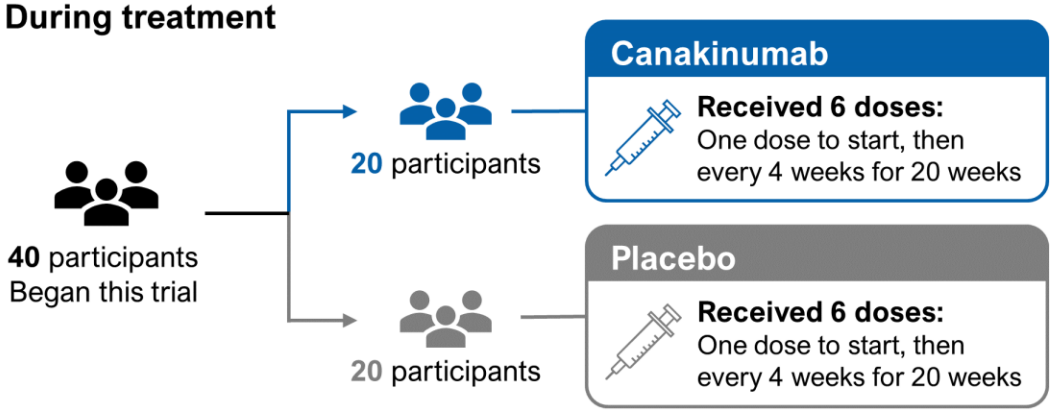
- **PET/CT scan**: measured inflammation in the sarcoidosis nodules
- **HRCT scan**: created a detailed picture of the lungs

Here's how this trial was done:

Before treatment

- The trial doctors checked each participant's health to make sure they could be in this trial
- The trial staff measured how well each participant could breathe
- The trial staff also looked at the sarcoidosis nodules in each participant's lungs using PET/CT and HRCT scans
- Participants could continue their regular sarcoidosis treatments during the trial

During treatment



During certain trial visits, the trial staff measured:

- How well the participant could breathe
- The size and inflammation of the participant's sarcoidosis nodules with PET/CT and HRCT scans

After treatment

- 12 weeks after their last dose, each participant had a final trial site visit for the trial doctors to check their health

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 canakinumab change how well the participants could breathe?

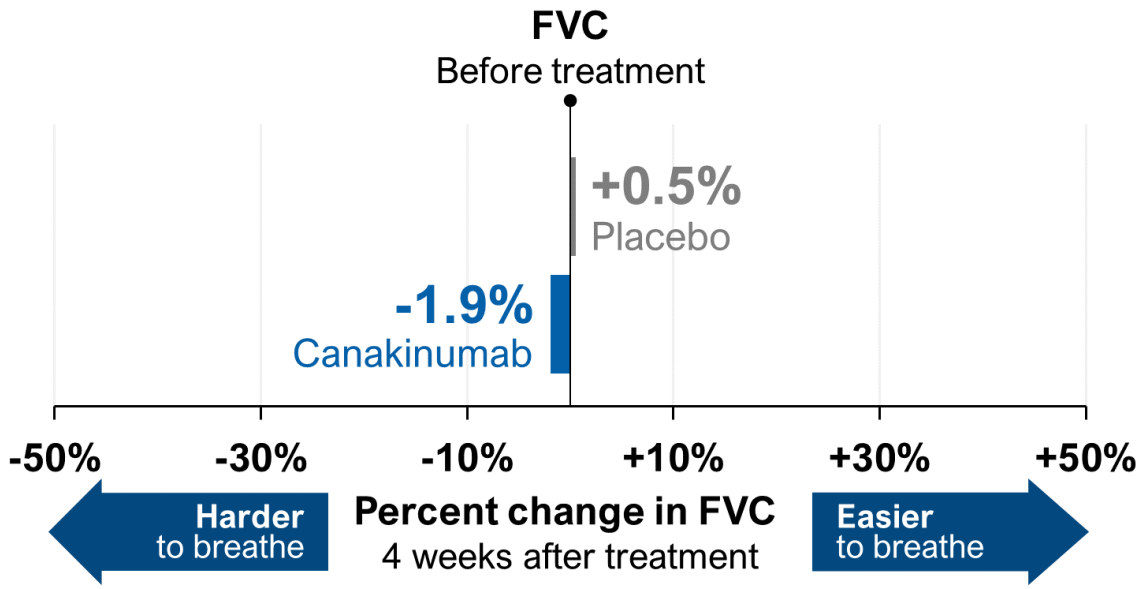
Canakinumab did not make a meaningful difference in how well the participants could breathe compared to the placebo.

To find this out, the trial staff measured the participants' forced vital capacity, also called FVC. A person's **FVC** is how much air they can breathe out after taking a very deep breath.

A higher FVC means that a person can breathe easier.

The clinical trial team compared participants' FVC before treatment to their FVC 4 weeks after treatment. They found that participants who received either canakinumab or the placebo had about the same FVC before and after treatment.

The participants' average change in FVC from before to after treatment



What medical problems did the participants have during the trial?

Medical problems that happen during clinical trials are called **adverse events**. Trial doctors looked for any adverse events when they checked the participants' health during the trial. The participants also reported adverse events.

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 do not think the adverse events might be related to the trial treatments.

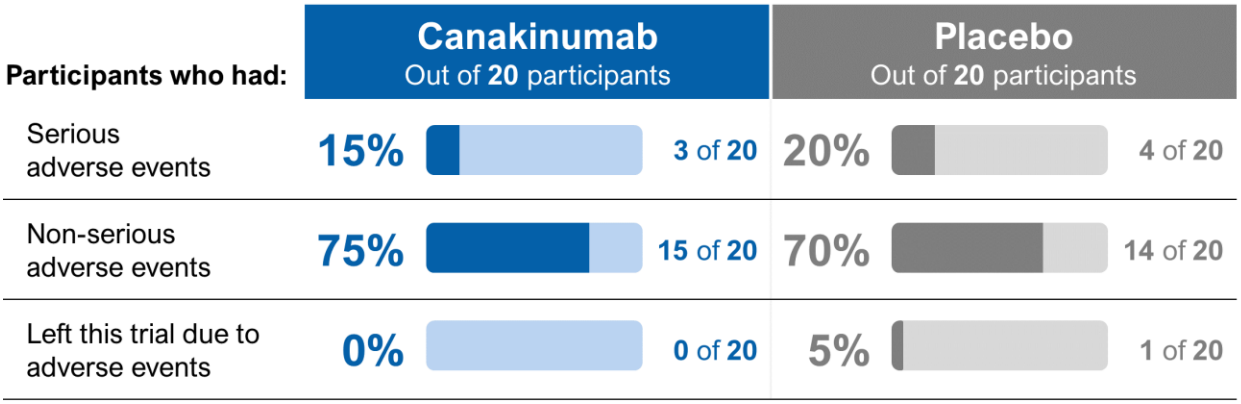
What is an adverse event?

- An **adverse event** is any unwanted sign or symptom that participants have during a trial
- It 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

The clinical trial team concluded there was no meaningful difference in the safety of canakinumab compared to the placebo. The most common adverse events were tiredness and the common cold.

Trial doctors looked for adverse events when they checked the participants' health at the trial site. The participants also reported adverse events.

Participants who had adverse events



What serious adverse events did participants have?

Canakinumab 20 participants	Placebo 20 participants
3 participants had a total of 3 serious adverse events during this trial. These were: • **Irregular heartbeat** (Atrial fibrillation) • **Blocked or narrowed blood vessels in the heart** (Coronary artery disease) • **The flu** (Influenza)	4 participants had a total of 5 serious adverse events during this trial. These were: • **A small lump in the large intestines** (Large intestine polyp) • **A burst appendix** (Appendicitis) • **An infection in the belly caused by the burst appendix** (Peritonitis) • **Bacterial infection** (Atypical mycobacterium test positive) • **Blood clot in the lungs** (Pulmonary embolism)

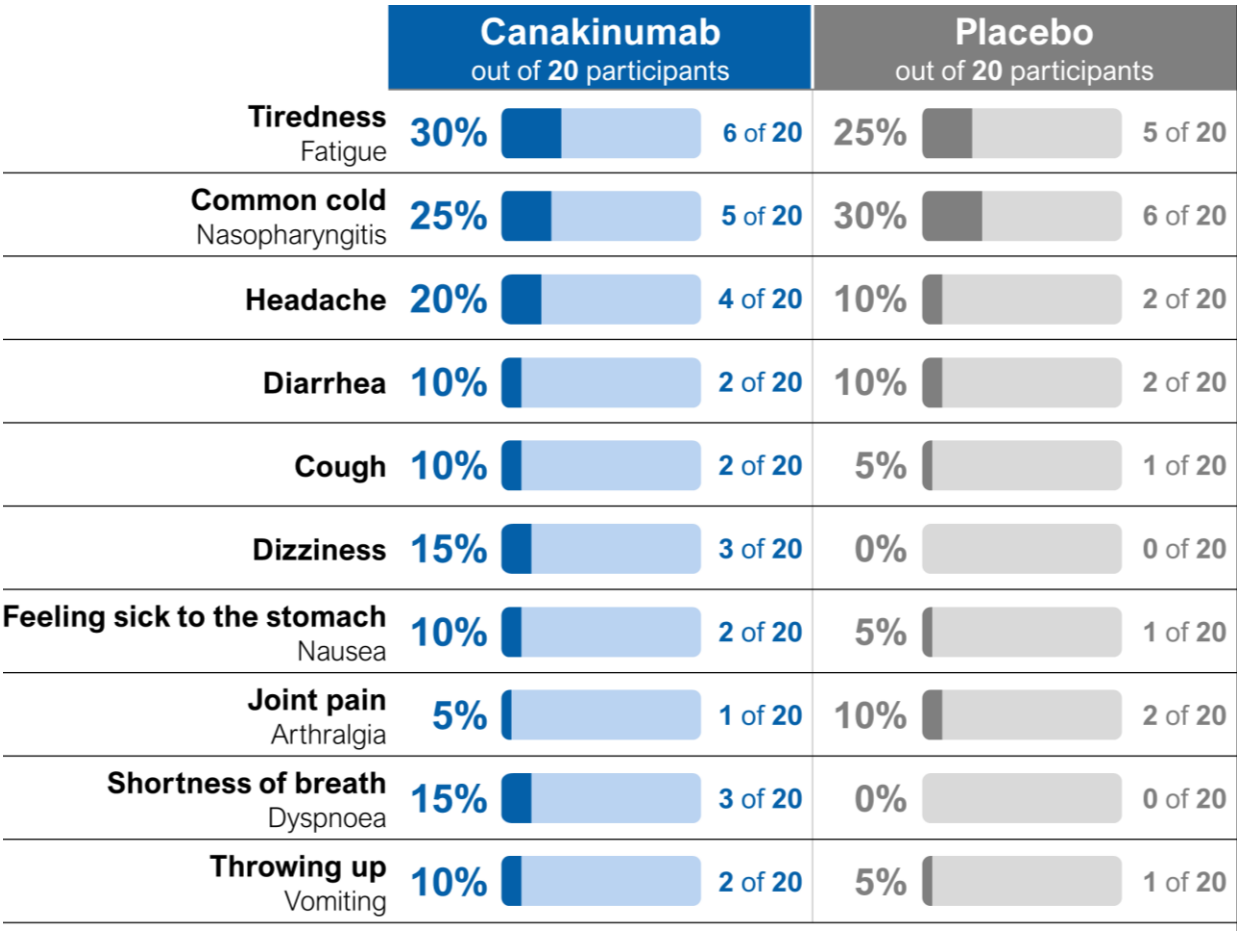
During this trial, no other serious adverse events were reported, including deaths.

What non-serious adverse events did participants have?

90% of the participants (36 of the 40 participants) had adverse events that were not serious. The table on the next page shows the adverse events that were reported by **3 or more participants**. Other adverse events were reported by fewer participants.

For more information about all the adverse events reported by participants in this trial, visit novctrd.com. Use trial number **CACZ885X2205** to find the scientific summary.

Non-serious adverse events



What other results were learned?

The trial staff looked at the size and inflammation of the sarcoidosis nodules in participants' lungs using the PET/CT and HRCT scans. They also measured how far the participants could walk in 6 minutes and took other breathing measures.

The clinical trial team learned that, compared to the placebo, participants who received canakinumab:

- Had slightly less inflammation in their lungs
- Were able to walk farther in 6 minutes

However, the team concluded that more research is needed to know if these results are meaningful.

The team also found that canakinumab had no meaningful effect on:

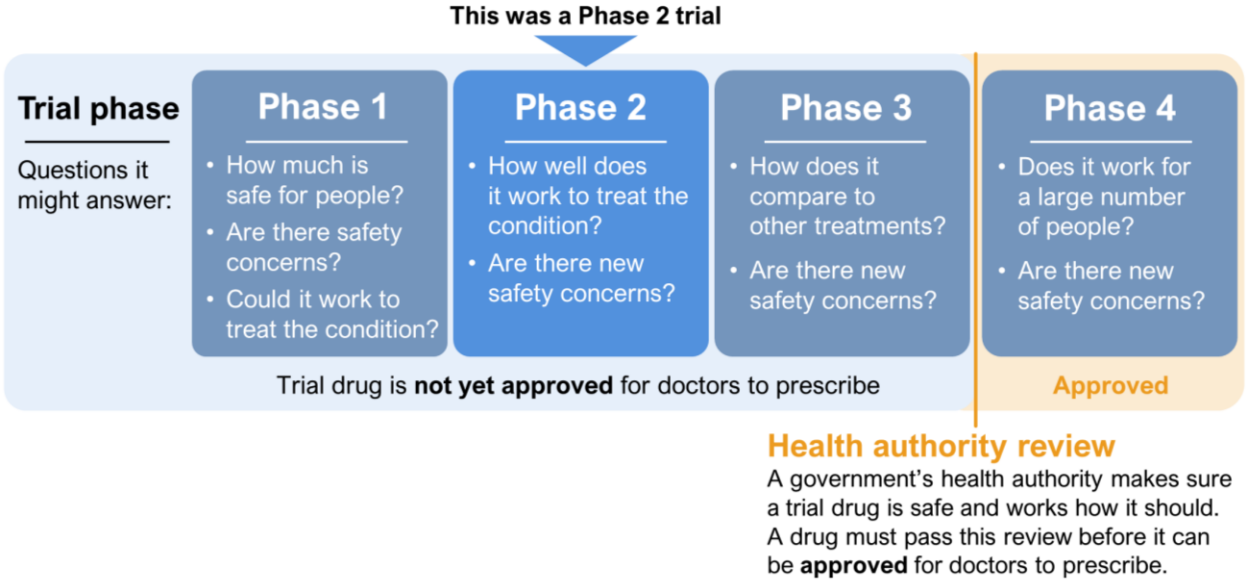
- The size of the sarcoidosis nodules in the participants' lungs
- The other measures of the participants' breathing

What was learned from this trial?

The clinical trial team learned that canakinumab was safe for the participants in this trial and blocked the immune protein IL-1β as expected.

The team also learned that blocking only IL-1β was not enough to change how well the participants could breathe. With this information, other research may find out if blocking additional immune proteins could possibly treat sarcoidosis.

This was a Phase 2 trial that learned about the safety of a trial drug and how well it worked in a small number of participants. This is one of many trials a drug must go through before it can be approved for doctors to prescribe to people with pulmonary sarcoidosis. The chart below shows these phases and what questions each phase might answer.



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 pulmonary sarcoidosis. This summary shows only the main results from this trial. Other trials may provide new information or different results.

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

This is a summary of the results for one trial.

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 and trial summary for patients” 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 “Search by study number” on the bottom left of the page
5. Type **“CACZ885X2205”** 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 were in this trial and have questions about the results, please speak with the doctor or staff where you took part in this clinical trial.

This trial was registered on the following websites:

- ClinicalTrials.gov – https://clinicaltrials.gov/
  To find this trial, type **CACZ885X2205** in the **Other terms** search box
- European Union Clinical Trials Register – https://www.clinicaltrialsregister.eu/ctr-search
  To find this trial, type **CACZ885X2205** 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 patients with pulmonary sarcoidosis

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.

NOVARTIS

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

1-888-669-6682 (USA)
+41-61-324 1111 (EU)
www.novartisclinicaltrials.com