NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects and safety of ACZ885 in people with early Alzheimer's disease

Thank you!

Thank you to the participants who took part in the clinical trial for **early Alzheimer's disease**. Every participant helped the researchers learn more about the trial drug **ACZ885**, also called canakinumab.

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: CADPT06A12201

Novartis drug studied: **ACZ885**, also called canakinumab

Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different results.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects and safety of **ACZ885** for people with early Alzheimer's disease.

Alzheimer's disease is a brain condition that causes a slow decline in memory and thinking abilities. Alzheimer's symptoms can start as mild forgetfulness that gets worse over time.

Researchers think that too much **inflammation** could play a role in Alzheimer's disease. They want to learn if lowering inflammation affects memory and thinking abilities in the early stages of Alzheimer's disease.

What is inflammation?
Inflammation is one of the ways the immune system protects the body from disease and infection. Inflammation happens when the immune system brings many cells and proteins to an area of the body. However, too much inflammation can be harmful.

ACZ885 is a drug designed to lower inflammation by blocking a protein called interleukin-1 beta, or **IL-1β**. **ACZ885** is approved in the United States and other countries to treat conditions related to inflammation, like arthritis.

ACZ885 is not approved to treat Alzheimer's disease, but researchers think **ACZ885** might lower harmful inflammation in Alzheimer's disease.

The trial's purpose was to answer these main questions:

- Did ACZ885 change participants' memory and thinking abilities?
- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

How long was this trial?

The trial began in October 2021 and ended in March 2024.

In April 2023, the sponsor decided to stop adding participants and end the trial early. This was a business decision and not related to the safety or effects of **ACZ885** in people with early Alzheimer's disease.

Who was in this trial?

34 participants with early Alzheimer's disease received treatment in this trial – 23 men and 11 women. Participants' ages ranged from 58 to 82 years. Their average age was 72 years.

The number of participants by race is shown below.

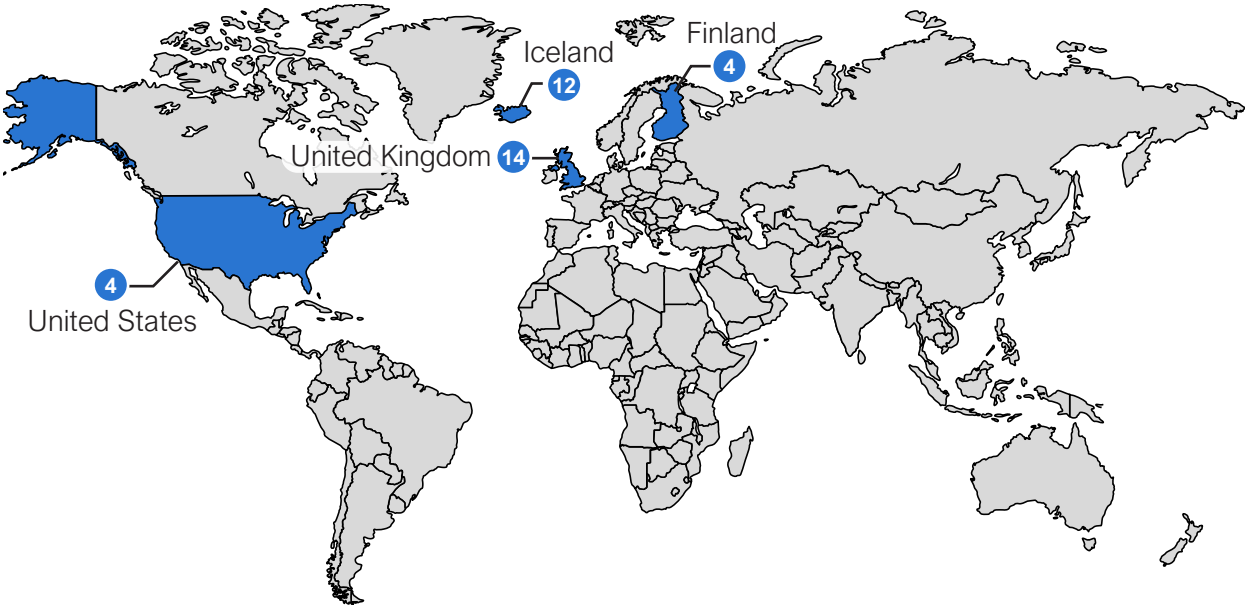
Race

34	White

The participants could take part in this trial if:

- They had mild cognitive impairment, which meant they had mild difficulty in their memory and thinking abilities.
- Their health record showed 6 months of memory and thinking abilities getting worse
- They had a trial partner. The **trial partner** was someone who spends time with the participant most days of the week, went to all trial visits, and could answer questions about participants' memory and thinking abilities.
- They did not have other health conditions that could affect memory and thinking abilities.

34 participants from 4 countries received treatment. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

The treatments in this trial were:

ACZ885, which was received as an injection under the skin every 4 weeks. The first 2 doses were 150 milligrams (mg), and the next 4 doses were 300 mg.

Placebo, which was received as an injection under the skin every 4 weeks. It looks like the trial drug but does not have any trial drug in it. Using a placebo helps researchers better understand the effect of a trial drug.

Participants could continue taking certain medicines for Alzheimer's disease during the trial.

Researchers used a computer to randomly assign participants to their treatment.

The participants, researchers, and trial staff did not know what treatment the participants were receiving. Some trials are done this way because knowing what treatment the participants receive can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.

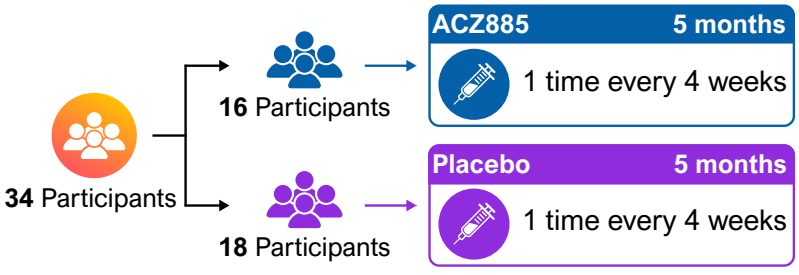
What happened during this trial?

Before treatment — About 2 months

The trial staff checked to make sure the participants could be in this trial.

During treatment — About 5 months

The graphic below shows how many participants were assigned each treatment.



After treatment — About 5 months

Trial staff checked participants for any medical problems for about 5 months after participants' last dose of trial treatment.

Trial staff checked the participants' general health throughout the trial.

What were the main results of this trial?

Did ACZ885 change participants' memory and thinking abilities?

ACZ885 may have changed participants' memory and thinking abilities. Participants who took **ACZ885** could remember and think slightly more than those who took placebo 6 months after starting treatment. However, because the trial ended early, the researchers could not conclude if this change was meaningful.

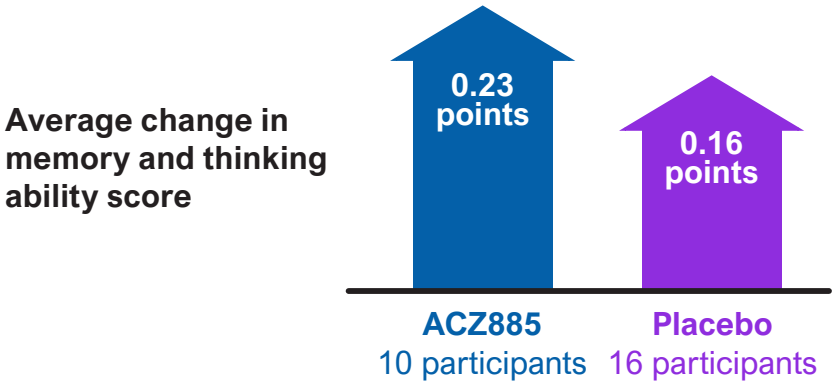
To find this out, each participant and their trial partner completed tasks and answered questions before, during and after trial treatment. The tasks and questions measured participants' memory and thinking, including their ability to:

- Remember a list of words and set of numbers
- Name words within a category, such as animals or foods

Researchers scored participant's answers after treatment based on how much the answers changed from before treatment.

Change in memory and thinking abilities

A **higher** score meant a participant could remember and think **more**.



Participants who received **ACZ885** or placebo could remember and think slightly more than those who took placebo 6 months after starting treatment. However, because the trial ended early, the researchers could not conclude if the difference between the groups was meaningful.

What were the other results of this trial?

Did ACZ885 lower inflammation in participants' brains?

Because the trial ended early, researchers could not conclude if **ACZ885** lowered inflammation in participants' brains.

To measure this, researchers looked at images of participants' brains before and after trial treatment using a PET (positron emission tomography) scan. A **PET** scan is an imaging test that can help doctors find specific cells and inflammation.

Because the trial ended early, there were not enough participants that had a PET scan. Due to this, the researchers could not conclude if **ACZ885** lowered inflammation in participants' brains.

Did ACZ885 change other measures of participants' Alzheimer's disease symptoms?

Because the trial ended early, the researchers could not conclude if **ACZ885** changed other measures of participants' Alzheimer's disease symptoms compared to the placebo.

To find this out, participants and their trial partners answered questions before, during and after treatment to measure changes in the participants':

- Mood and behavior
- Ability to complete everyday tasks
- Other measures of memory and thinking abilities

The researchers also asked the participants' trial partners about distress related to participants' symptoms. Because the trial ended early, the researchers could not conclude if **ACZ885** changed trial partners distress.

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of treatment until about 5 months after the last treatment.

An **adverse event** is:

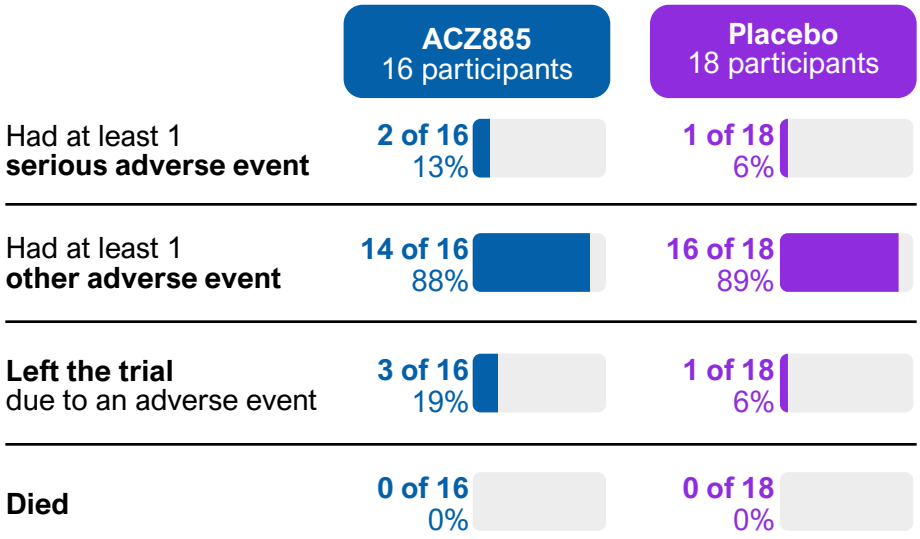
- Any **sign or symptom** that the participants have during a trial
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

Almost all the participants (30 of 34) had adverse events. 3 participants had adverse events that were considered serious. 4 participants left the trial due to an adverse event. No participants died. A similar number of participants who received **ACZ885** and placebo had adverse events.

The researchers concluded there were no new safety concerns for **ACZ885** in this trial.

How many participants had adverse events?



Additional safety measures

Sometimes, medicines used to treat Alzheimer's disease and other diseases can also cause unwanted changes to a person's thoughts, including thoughts of suicide.

To measure this, the trial doctors asked each participant to answer questions about thoughts of suicide. Participants who received **ACZ885** did not have more thoughts of suicide than those who received placebo.

What serious adverse events did the participants have?

3 participants had serious adverse events. No participants died.

The serious adverse events that happened in participants who received **ACZ885** were:

- **Type of cancer** | Transitional cell carcinoma
- **COVID-19**
- **Strep infection** | Streptococcal infections

The serious adverse events that happened in participants who took placebo were:

- **A problem in the brain** | Metabolic encephalopathy

What other adverse events did the participants have?

30 participants had other adverse events.

The table below shows the other adverse events that happened in **3 or more** participants. Additional adverse events happened in fewer participants.

	ACZ885 16 participants	**Placebo** 18 participants
High blood pressure Hypertension	**4 of 16** 25%	**1 of 18** 6%
Back pain	**2 of 16** 13%	**2 of 18** 11%
Possible sign of kidney damage Blood creatinine increased	**1 of 16** 6%	**2 of 18** 11%
Possible sign of pancrease inflammation Lipase increased	**1 of 16** 6%	**2 of 18** 11%
High level of protein in urine Proteinuria	**2 of 16** 13%	**1 of 18** 6%
UTI Urinary tract infection	**1 of 16** 6%	**2 of 18** 11%

What was learned from this trial?

Researchers learned about the effects and safety of **ACZ885** in people with early Alzheimer's disease. The sponsor ended this trial early for business reasons and not for any reason related to the safety or effects of **ACZ885**.

Because the trial ended early, the researchers could not conclude if participants who received **ACZ885** compared to those who received placebo:

- Had meaningful changes in their memory and thinking abilities 6 months after starting treatment
- Had lower inflammation in their brains
- Had changes in other measures of Alzheimer's disease symptoms

The researchers concluded there were no new safety concerns for **ACZ885** in this trial. Participants who received **ACZ885** did not have more thoughts of suicide than those who received placebo.

When this summary was written, the sponsor had no plans for future trials of **ACZ885** in people with early Alzheimer's disease.

Where can I learn more about this trial?

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**

Follow these steps to find the scientific summary:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Accept the terms **I accept** → Search by study number **CADPT06A12201**

For more information about this trial, go to any of these websites:

- **clinicaltrials.gov** – search using the number **NCT04795466**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2020-003966-38**

Other trials of **ACZ885** may appear on the public websites above. When there, search for **ACZ885** or canakinumab.

Full clinical trial title: EXploratory PLatform trial on Anti-INflammatory agents in Alzheimer's Disease (EXPLAIN-AD): A randomized, placebo-controlled, multicenter platform study to evaluate the efficacy, safety, tolerability and pharmacokinetics of various anti-inflammatory agents in patients with mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's disease

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