NOVARTIS

# Clinical Trial Results Summary

# A clinical study to learn about the effects and safety of canakinumab in participants hospitalized with pneumonia caused by COVID-19

**Protocol number:** CACZ885D2310

## Thank You!

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. Thank you for taking part in this trial for the drug ACZ885, also known as canakinumab. You helped researchers learn more about how canakinumab works in people with pneumonia in COVID-19.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings. Researchers and health authorities, such as the Food and Drug Administration (FDA) in the United States and the European Medicines Agency (EMA) in Europe, look at the results of many clinical trials to understand which drugs work and if they are safe. Websites listed at the end of the summary may have more information about this trial. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

# Why was the research needed?

Researchers were looking for a better way to treat pneumonia in coronavirus disease (COVID-19). COVID-19 is a highly infectious disease caused by a virus. People infected with the virus can be without any symptoms or can have flu-like symptoms. It can also lead to pneumonia. In pneumonia, there is inflammation of one or more parts of the lungs. This can cause difficulty in breathing and may require the help of machines (mechanical ventilators) to breathe. At the time of the trial, no approved treatment was available for pneumonia caused by COVID-19.

**The main question researchers wanted to answer in this trial was:**

**How many participants survived without any life support* from Day 3 to Day 29 when treated with canakinumab along with standard treatment compared to placebo?**

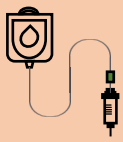
****Life support in COVID-19 treatment may include the use of a mechanical ventilator to support breathing*.**

**The other question researchers wanted to explore in this trial was:**

- How many participants died due to COVID-19 related causes during the 1-month period after treatment with the trial drug?

## Trial drugs

The drugs given in this trial were:



**Canakinumab (can-a-KIN-oo-mab)**: A drug that has been approved in many countries for the treatment of medical problems such as swelling of the joints in children and adults. It works by preventing the release of chemicals in the body that cause inflammation. Canakinumab is an IV drug (drug given as an infusion into the vein). Canakinumab is now being tested in this study for the treatment of pneumonia due to COVID-19.

**Placebo**: This looked like the trial drug but did not have any medicine in it. Using a placebo helps researchers better understand the effect of a trial drug by making sure that the changes were not happening by chance. In the present trial, placebo is given as an infusion into the vein to appear the same as canakinumab.

Throughout the trial, the participants were allowed to continue taking the standard treatment that they were prescribed. These included antibiotics, antiviral drugs, low dose steroid medications, and any other required treatment and supportive care, as decided by their doctors.

# Who was in this trial?

The participants could take part in this trial if they:

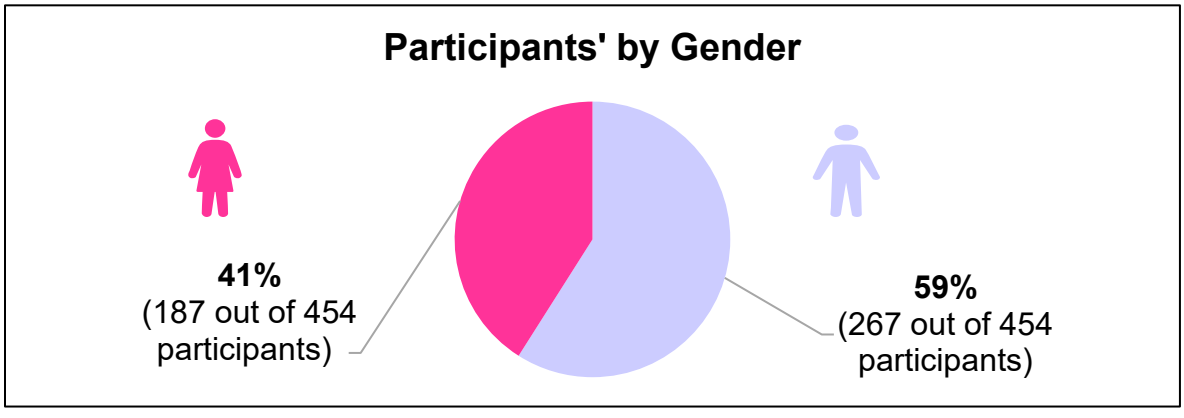
- were aged 12 years or older,
- had at least 40 kg (88 lbs.) body weight,
- had tested positive for COVID-19,
- were hospitalized with pneumonia due to COVID-19 confirmed by a chest scan or X-ray and
- had decreased oxygen in their blood.

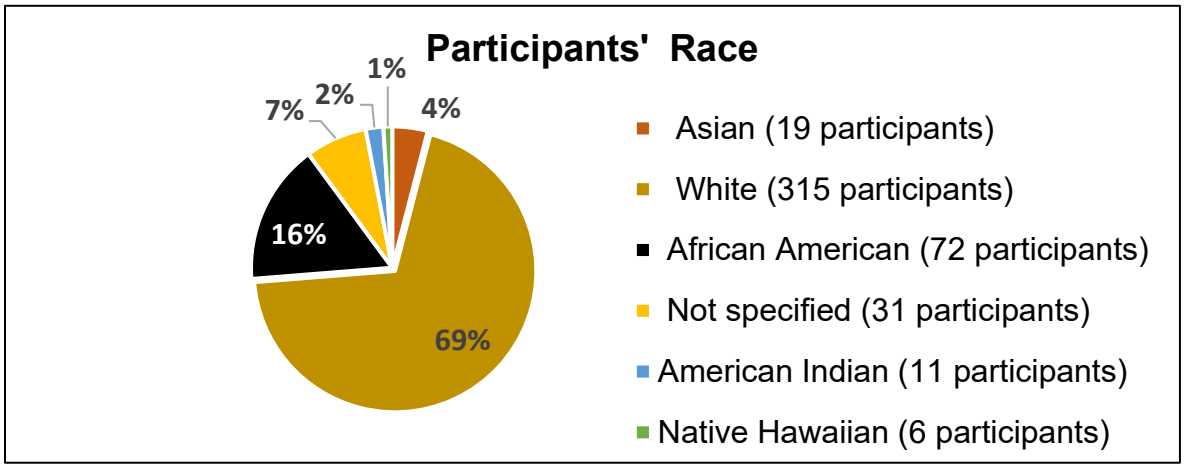
This trial included 454 participants from 6 countries.

| Country | Number of participants (%) |
|---|---|
| **France** | 1 (<1%) |
| **Italy** | 2 (<1%) |
| **Russia** | 153 (34%) |
| **Spain** | 34 (7%) |
| **United Kingdom** | 11 (2%) |
| **United States of America** | 253 (56%) |

The average age of participants was 58 years. Participants' age ranged from 18 to 98 years.

The majority of participants were men, as shown below:






# What happened during this trial?

**Before Treatment (1 Day):**

The trial doctors verified that participants could take part in this trial.

**During Treatment (29 Days):**

Eligible participants were randomly assigned to 2 groups.

| Canakinumab + standard treatment | Placebo + standard treatment |
|---|---|
| 227 participants | 227 participants |

Each participant had an equal chance of receiving canakinumab or placebo. None of the participants, trial doctors, or trial staff knew what treatment participants were receiving.

Along with standard treatment for COVID-19, participants received canakinumab or placebo, one time as an infusion into the vein on Day 1. Researchers monitored participants' health from Day 1 to Day 29 or until their discharge from the hospital. Participants discharged before 29 days were contacted via phone calls.

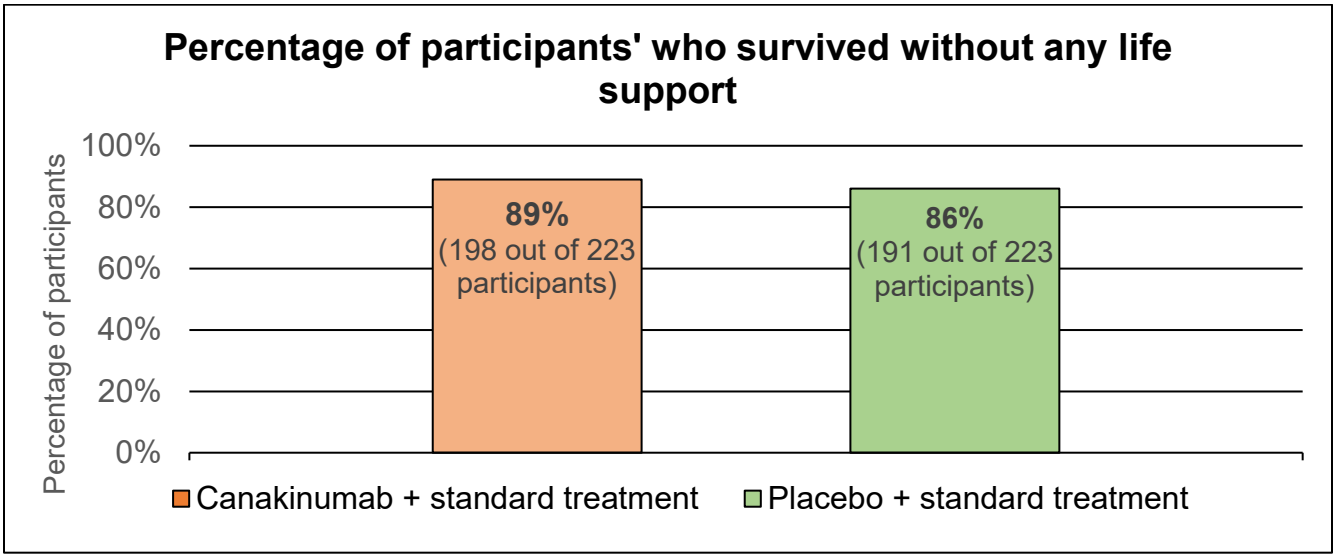
**After Treatment (4 months)**

After Day 29, participants were followed-up over phone calls for additional 4 months.

Researchers completed this trial as planned.

# What were the key results of this trial?

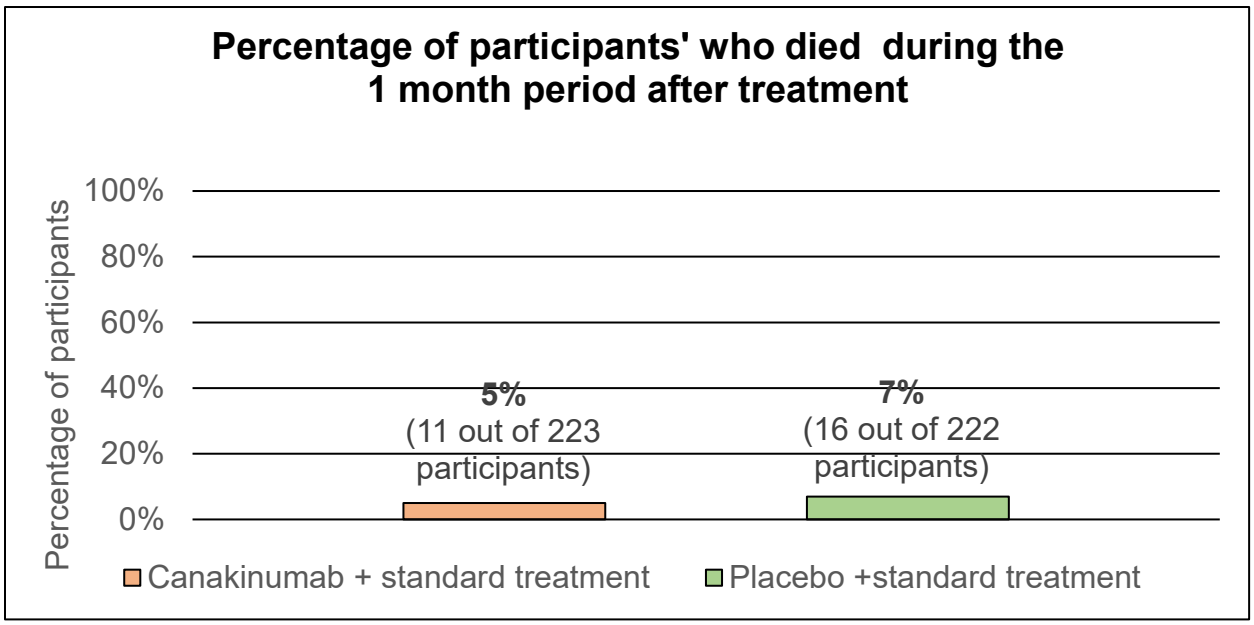
## How many participants survived without any life support (being put on a ventilator) from Day 3 to Day 29 when treated with canakinumab along with standard treatment compared to placebo?




The number of participants who survived without any life support (being put on a ventilator) was slightly more in the canakinumab + standard treatment group compared with the placebo + standard treatment group. However, **this difference between the groups could be by chance rather than a difference caused by the treatment**.

# What were the other results of this trial?

## How many participants died due to COVID-19 related causes during the 1 month period after treatment?




The number of participants who died was slightly less in the group treated with canakinumab along with standard treatment, but **this difference between the groups could be caused by chance rather than as a result of the treatment**.

# What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "adverse events".

A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. When new drugs are being studied, researchers keep track of all adverse events participants have.

This section is a summary of the adverse events that happened during this trial. The websites listed at the end of this summary may have more information about all the adverse events that happened in this trial.

*An adverse event is an unwanted sign, symptom, or disease that participants have during a trial.*
*An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care.*
*These problems may or may not be caused by the trial drug.*

## How many participants had adverse events?

281 out of 448 participants (63%) had one or more adverse events. During the trial, 1 out of 448 participants (1%) stopped the drug early because of an adverse event. Serious adverse events happened in 100 out of 448 participants (22%) in the trial. 48 participants died during this trial.

**Number of Participants (%) experiencing any Adverse Events**

| | **Canakinumab** (Out of 225 participants) | **Placebo** (Out of 223 participants) |
|---|---|---|
| At least 1 adverse event | 141 (63%) | 140 (63%) |
| At least 1 serious adverse event | 47 (21%) | 53 (24%) |
| Stopped drug due to an adverse event | 1 (1%) | 0 |
| Death | 22 (10%) | 26 (12%) |

## What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 5% of participants in any group are presented below.

**Number of Participants (%) With Most Common Non-Serious Adverse Events**

| | Canakinumab Out of 225 participants | Placebo Out of 223 participants |
|---|---|---|
| Low red blood cell count **(Anemia)** | 6 (3%) | 12 (5%) |
| Low blood pressure **(Hypotension)** | 12 (5%) | 10 (4%) |

## What were the most common serious adverse events?

The most common serious adverse events that happened in at least 1% of participants in any group are shown below.

**Number of Participants (%) with most common Serious Adverse Events**

| | Canakinumab Out of 225 participants | Placebo Out of 223 participants |
|---|---|---|
| Kidney damage **(Acute kidney injury)** | 3 (1%) | 7 (3%) |
| Sudden difficulty in breathing **(Acute respiratory distress syndrome)** | 6 (3%) | 3 (1%) |
| Sudden inability to breathe enough oxygen **(Acute respiratory failure)** | 12 (5%) | 13 (6%) |
| Worsening of COVID-19 **(COVID-19)** | 2 (1%) | 3 (1%) |

| | Canakinumab Out of 225 participants | Placebo Out of 223 participants |
|---|---|---|
| Worsening of chest infection due to COVID virus **(COVID-19 pneumonia)** | 1 (1%) | 3 (1%) |
| Difficulty in breathing **(Dyspnea)** | 1 (1%) | 3 (1%) |
| Low blood pressure **(Hypotension)** | 2 (1%) | 3 (1%) |
| Too little oxygen in the body **(Hypoxia)** | 2 (1%) | 4 (2%) |
| Worsening of chest infection **(Pneumonia)** | 2 (1%) | 3 (1%) |
| Collapsed lungs **(Pneumothorax)** | 2 (1%) | 3 (1%) |
| Inability to breathe enough oxygen **(Respiratory failure)** | 8 (4%) | 8 (4%) |
| Extreme response by the body to infection **(Sepsis)** | 3 (1%) | 2 (1%) |
| Severely low blood pressure due to infection **(Septic shock)** | 3 (1%) | 5 (2%) |

## How many participants stopped trial drug due to adverse events?

During the trial, 1 out of 225 (1%) participants stopped canakinumab early due to redness of the skin (**erythema**).

## How was this trial useful?

Researchers learned about the effect of canakinumab in participants with pneumonia caused by COVID-19. At the end of the study, it was clear that canakinumab was no more effective than placebo, when given in combination with standard treatment, in treating pneumonia in COVID-19. No safety concerns were observed in participants with COVID-19 who received canakinumab.

Results from this trial may be used in other clinical trials for people with COVID-19. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

## 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).

You can find more information about this trial on the following websites:

- www.clinicaltrials.gov – Use the NCT04362813 identifier in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search/search – Use the EudraCT identifier 2020-001370-30 in the search field.

**Full clinical trial title:** Phase 3 multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of canakinumab on cytokine release syndrome in patients with COVID- 19-induced pneumonia (CAN-COVID)

**Trial Dates:** The trial started in April 2020 and ended in December 2020.

## Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of people around the world. You helped researchers answer important health questions and test new medical treatments.

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

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