NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of canakinumab and pembrolizumab given alone or together before surgery to people with non-small cell lung cancer (NSCLC)

Protocol number: CACZ885V2201C

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.

Thanks to the participants for taking part in this trial for the drug ACZ885 (also known as canakinumab) and pembrolizumab. They helped researchers learn more about how ACZ885 works in people with NSCLC.

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If the participants have any questions about the trial results, please talk to the doctor or staff at the trial site.

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

Why was the research needed?

Non-small cell lung cancer (NSCLC) is a type of lung cancer. This type of cancer, when found only in the lungs, is usually removed by surgery. Standard treatment before surgery includes anti-cancer drugs, radiation, or a combination of both. These treatment options are not always completely successful.

Researchers were looking for a better way to treat NSCLC. A protein in our body called interleukin-1 beta (IL-1β) can cause inflammation in the lungs. This in turn can increase the risk of developing lung cancers such as NSCLC. ACZ885 is a drug that attaches to IL-1β and blocks its action. It is approved in some countries for the treatment of non-cancerous diseases like gouty arthritis (gout), and in conditions where the immune cells target the body's own healthy tissues by mistake. However, it is not approved as a treatment for cancer.

Pembrolizumab is a drug that works by stimulating the body's defense mechanism to recognize and attack cancer cells. It is already approved for the treatment of NSCLC, alone or in combination with chemotherapy.

In this trial, researchers wanted to find out if ACZ885 and pembrolizumab when given alone or in combination have an effect on cancer cells and are safe for participants with NSCLC.

Drug	***Pronounced as***
canakinumab	ca-na-KIN-oo-mab
pembrolizumab	PEM-broe-LIZ-ue-mab
IL-1β	I-L-1 beta

How long was this trial?

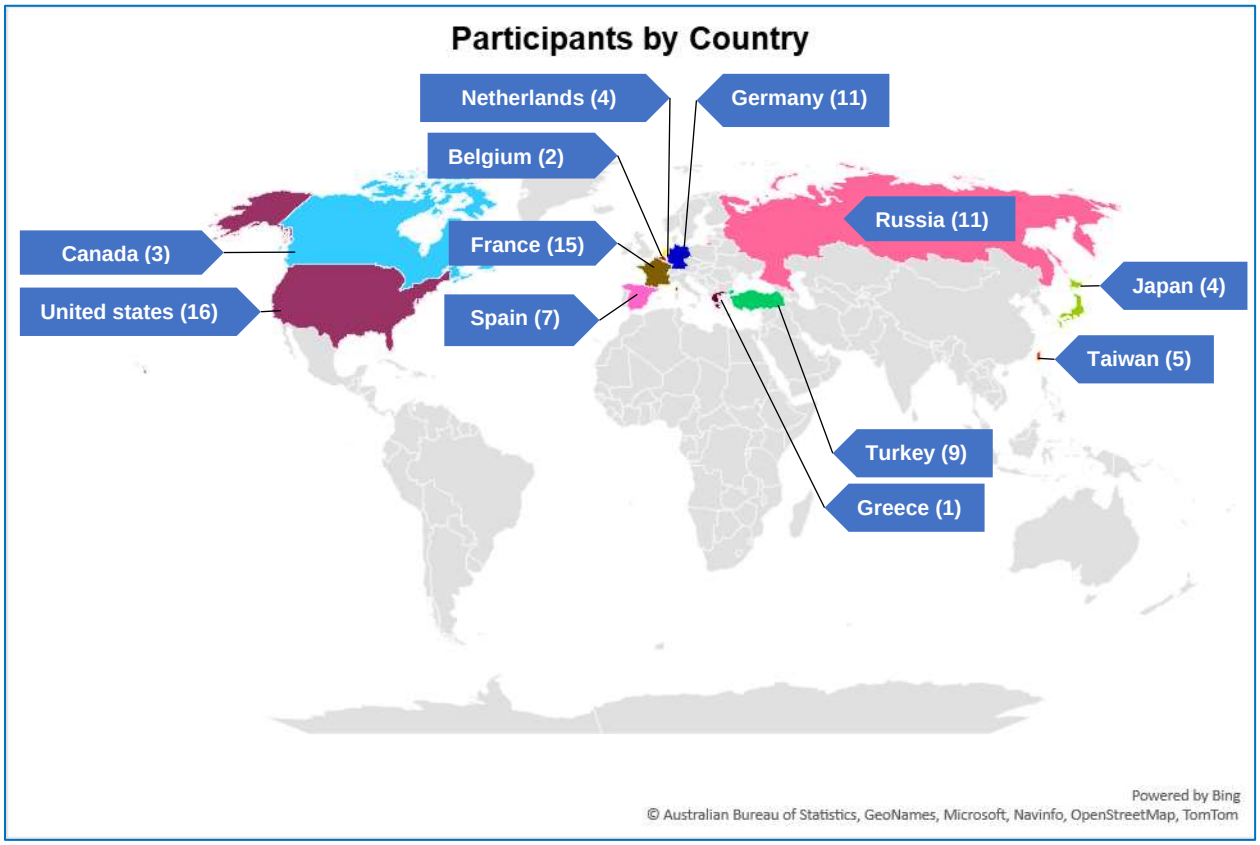
This trial started in November 2019 and ended in August 2022. The entire duration, from enrolling the first participant to the last participant completing the trial was around 2 years and 9 months. An individual participant was in this trial for an average of 7 months.

Who was in this trial?

The participants could take part in this trial if they:

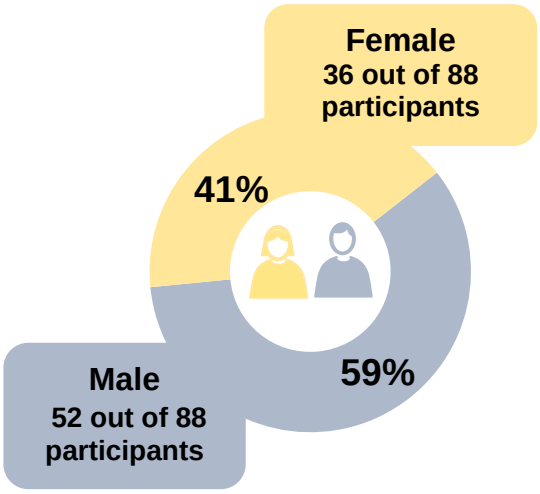
- were at least 18 years,
- had confirmed NSCLC found only in the lungs, which was considered suitable for removal by surgery,
- had surgery planned 4 to 6 weeks after the first dose of the trial drug, and
- had a score of 0 or 1 in their ability to take care of themself, in daily activity, and physical ability measured using the Eastern Cooperative Oncology Group performance scale.

A total of 88 participants from 12 countries took part in this trial. Researchers randomly assigned participants to treatment groups using a computer system. This process is called randomization. It means that each participant could be assigned to any group, and it helps to make sure the groups are distributed fairly. All participants were randomized and received treatment.

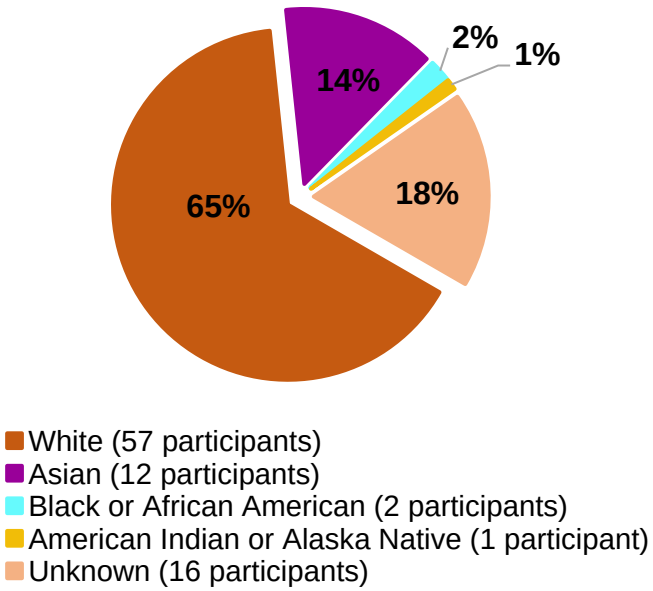


Participants' age ranged from 49 to 83 years. The average age of the participants was 66 years. The majority of participants were men, 52 out of 88 (59%), and white, 57 out of 88 (65%).

Participants' Gender



Participants' Race



What treatments did the participants take?

The treatments in this trial were:

ACZ885, also known as Canakinumab, 200 milligram (mg) was given as an injection under the skin every 3 weeks.

Pembrolizumab, 200 mg was given as an infusion every 3 weeks.

The treatments were given in 2 cycles, with each cycle lasting for 3 weeks.

Along with these treatments, participants could take other treatments for treating symptoms such as vomiting, diarrhea, pain, and other ongoing diseases.

In this trial the participants and clinical trial team knew what treatment each participant took. All participants took either ACZ885 alone, ACZ885 in combination with pembrolizumab or pembrolizumab alone.

What happened during this trial?

Before treatment

The trial doctors checked if participants could take part in this trial.

4 weeks

During treatment

Participants were randomly assigned to receive ACZ885 alone or ACZ885 in combination with pembrolizumab or pembrolizumab alone.

Group 1	**ACZ885** alone	35 participants
Group 2	**ACZ885 with pembrolizumab**	35 participants
Group 3	**Pembrolizumab** alone	18 participants

Subjects were treated for a maximum duration of 6 weeks (2 cycles of treatment).

Up to 6 weeks

After treatment

The participants underwent surgery 4-6 weeks after receiving the first dose.

Researchers closely monitored the overall health of the participants throughout the trial and for about 4 months after the treatment.

Around 19 weeks

What were the main results of this trial?

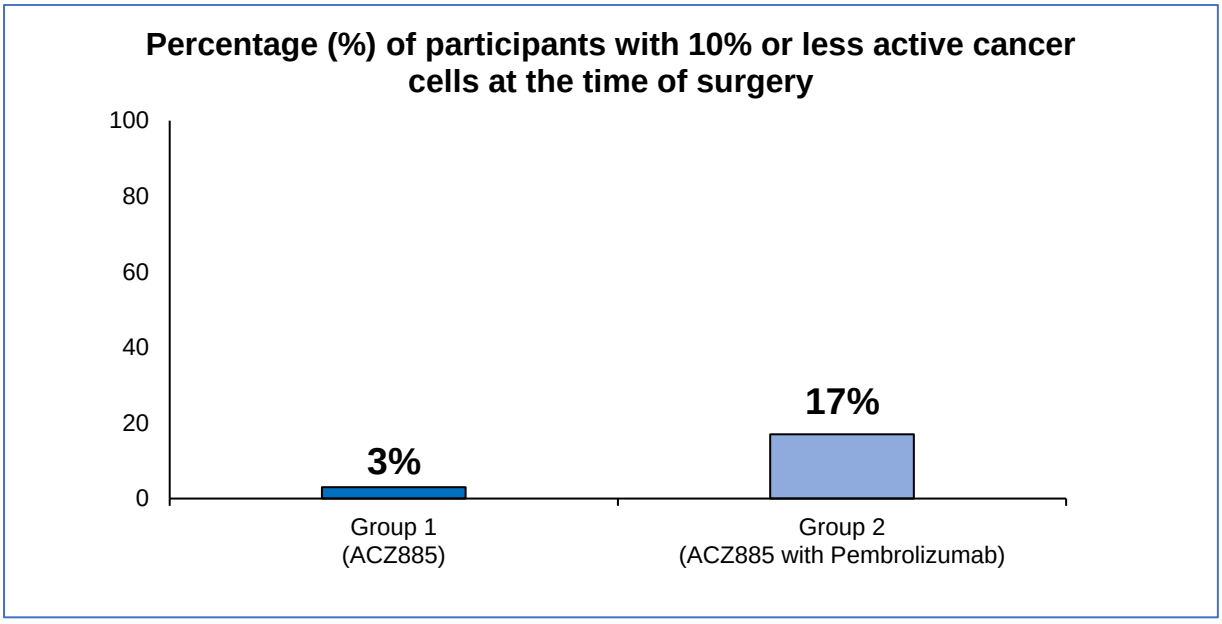
How many participants in Group 1 (ACZ885 alone) or Group 2 (ACZ885 with pembrolizumab) had 10% or less active cancer cells at the time of surgery?

The researchers found that

- 3% (1 out of 35) of participants in Group 1 (ACZ885 alone) and
- 17% (6 out of 35) of participants in Group 2 (ACZ885 with pembrolizumab)

had 10% or less active cancer cells at the time of surgery.

The proportion of participants with 10% or less active cancer cells in each group were not high enough to determine whether the 2 treatments were effective in participants with NSCLC before surgery. In addition, the difference seen between the groups was not found to be significant, as the 14% difference was not large enough to say that this difference was caused by the treatment, rather than by chance.



What were the other results of this trial?

What proportion of participants in Group 3 (pembrolizumab alone) had 10% or less active cancer cells at the time of surgery?

The researchers found that 17% (3 out of 18) of participants in Group 3 (pembrolizumab alone) had 10% or less active cancer cells at the time of surgery.

What proportion of participants in any group (ACZ885 and/or pembrolizumab) had a decrease in tumor size, or had a complete disappearance of all signs of cancer, at the time of surgery?

- 9% (3 out of 35) participants in Group 2 (ACZ885 with pembrolizumab) and
- 11% (2 out of 18) participants in Group 3 (pembrolizumab alone) had a decrease in tumor size at the time of surgery.
- No participants on Group 1 (ACZ885 alone) had a decrease in tumor size or a complete disappearance of all signs of cancer the time of surgery.

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 any 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?

The number of adverse events that happened in the 3 treatment groups during the trial are listed in the following table.

Number of Participants (%) With Adverse Events

	Group 1 **ACZ885** alone (out of **35** participants)	**Group 2** **ACZ885 with pembrolizumab** (out of **35** participants)	**Group 3** **Pembrolizumab** alone (out of **18** participants)
At least 1 adverse event	31 (89%)	32 (91%)	15 (83%)
At least 1 serious adverse event	10 (29%)	9 (26%)	4 (22%)
Stopped drug due to adverse event	0	1 (3%)	1 (6%)
Deaths	3 (9%)	2 (6%)	1 (6%)

How many participants stopped trial drug due to adverse events?

1 out of 18 participants (6%) on pembrolizumab stopped the trial drug due an adverse event of collection of blood in between the chest wall and the lungs. 1 out of 35 participants (3%) on ACZ885 combined with pembrolizumab stopped the trial drug due to an adverse event of increase in liver enzymes.

What were the most common serious adverse events?

The most common serious adverse events that happened in at least 5% (5 out of 100) of participants in any group are listed in the following table.

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

	Group 1 **ACZ885** alone (out of **35** participants)	**Group 2** **ACZ885 with pembrolizumab** (out of **35** participants)	**Group 3** **Pembrolizumab only** (out of **18** participants)
Infection of the lungs (**Pneumonia**)	3 (9%)	1 (3%)	0
COVID (**COVID-19**)	2 (6%)	1 (3%)	1 (6%)
Collection of blood in the space between the chest wall and the lung (**Hemothorax**)	0	0	1 (6%)
Decreased production of thyroid hormone (**Hypothyroidism**)	0	0	1 (6%)
Rash (**Cutaneous eruption**)	0	0	1 (6%)
Bleeding in the stomach (**Upper gastrointestinal hemorrhage**)	0	0	1 (6%)

What were the most common other adverse events?

The most common non-serious adverse events that happened in at least 10% (10 out of 100) of participants in any group are presented below.

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

	Group 1 **ACZ885** alone (out of **35** participants)	**Group 2** **ACZ885 with pembrolizumab** (out of **35** participants)	**Group 3** **Pembrolizumab only** (out of **18** participants)
Low red blood cells (**Anemia**)	9 (26%)	1 (3%)	1 (6%)
Tiredness (**Fatigue**)	9 (26%)	5 (14%)	4 (22%)
Decreased appetite	6 (17%)	1 (3%)	0
Shortness of breath (**Dyspnea**)	5 (14%)	6 (17%)	1 (6%)
Increased liver test value of conjugated bilirubin (**Bilirubin conjugate increased**)	4 (11%)	1 (3%)	1 (6%)
Increased liver test value of bilirubin (**Blood bilirubin increased**)	4 (11%)	0	0
Cough	4 (11%)	6 (17%)	2 (11%)
Low lymphocyte count in blood (**Lymphocyte count decreased**)	4 (11%)	0	1 (6%)
Feeling sick (**Nausea**)	4 (11%)	3 (9%)	3 (17%)
Lung infection (**Pneumonia**)	4 (11%)	1 (3%)	0

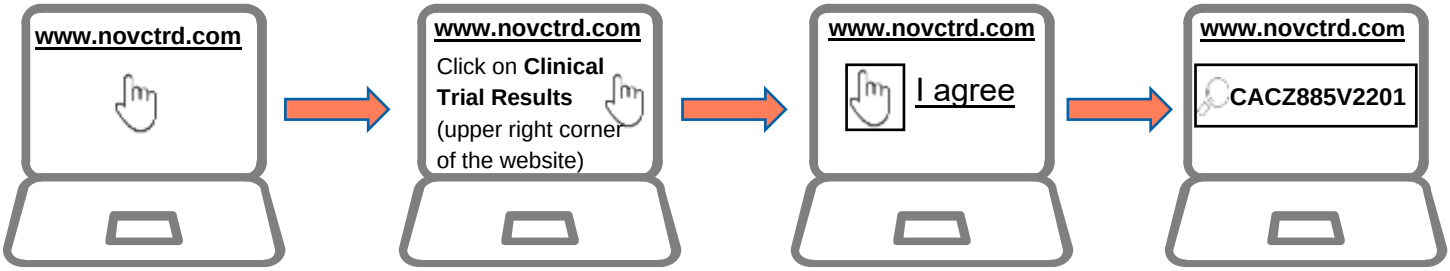
How was this trial useful?

The trial helped researchers to learn about the effects of ACZ885 and pembrolizumab when given alone or together in participants with NSCLC before surgery. Researchers learned that ACZ885 did not work when given alone or in combination with pembrolizumab before surgery. There were no new safety concerns with ACZ885 or pembrolizumab in this trial. Results from this trial may be used in other clinical trials for people with NSCLC. No future trials are planned by Novartis with ACZ885 in participants with NSCLC.

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**.

Please follow the steps below:



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

- **www.clinicaltrials.gov** Use the NCT identifier NCT03968419 in the search field.
- **https://www.clinicaltrialsregister.eu/ctr-search/search** Use the identifier 2018-004813-42 in the search field.

Full clinical trial title: A randomized, open-label, phase II study of canakinumab or pembrolizumab as monotherapy or in combination as neoadjuvant therapy in subjects with resectable non-small cell lung cancer (CANOPY-N)

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.

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

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