NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects and safety of canakinumab plus docetaxel compared with placebo plus docetaxel in participants with advanced non-small cell lung cancer for whom previous treatments had been unsuccessful

Protocol number: CACZ885V2301

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 participants for taking part in this trial for the drug canakinumab, also known as ACZ885. They helped researchers learn more about how canakinumab works in people with advanced non-small cell lung cancer.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings. If trial participants have any questions about the trial results, please talk to the doctor or staff at the trial site.

How long was this trial?

This trial started in January 2019 and ended in December 2021. The entire duration of the trial was around 2 years and 11 months. An individual participant was in this trial for an average of 7 months, after which they followed up every 3 months until they withdrew consent, lost contact during follow-up, or passed away.

The sponsor ended this trial early because the results did not show any benefit from using the trial drug. When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Why was the research needed?

Non-small cell lung cancer (NSCLC) is a type of cancer that starts in the lungs. The cancer cells in the lungs divide rapidly and can spread to other parts of the body, at which stage the cancer is called 'advanced'.

Currently available treatments for advanced NSCLC mainly include anti-cancer drugs, high doses of radiation, or a combination of these. However, these treatment options are not completely successful. Therefore, new methods for treating advanced NSCLC are needed.

Drug / term	***Pronounced as***
canakinumab	kan-a-KIN-oo-mab
docetaxel	do-se-TAX-el
IL-1β	I-L-1 Beta

Researchers were looking for a better way to treat advanced NSCLC. They believe a naturally occurring agent called interleukin-1 beta (IL-1β), which causes inflammation, may play an important role in the development of NSCLC. Canakinumab is a drug that can bind and block IL-1β, eventually helping the immune system to fight NSCLC. Researchers believe that the effect of chemotherapy increases when combined with these types of drugs.

Canakinumab is approved in some countries for the treatment of non-cancerous diseases. However it is not approved as a treatment for cancer, and given its action in blocking IL-1β, researchers wanted to find out if canakinumab could be effective in treating individuals with NSCLC. Researchers included the participants that had previously been treated unsuccessfully with PD-(L)1 inhibitors and platinum-based chemotherapy.

Who was in this trial?

The participants could take part in this trial if they:

- were at least 18 or older
- were diagnosed with stage 3 or stage 4 NSCLC, also known as advanced NSCLC
- had worsening of cancer following prior treatment.
- were either fully active or physically restricted but able to carry out light work

A total of 352 participants from 26 countries were screened to participate in this trial. Out of those, 245 participants were assigned to receive study treatment.

Researchers performed this trial in two parts.

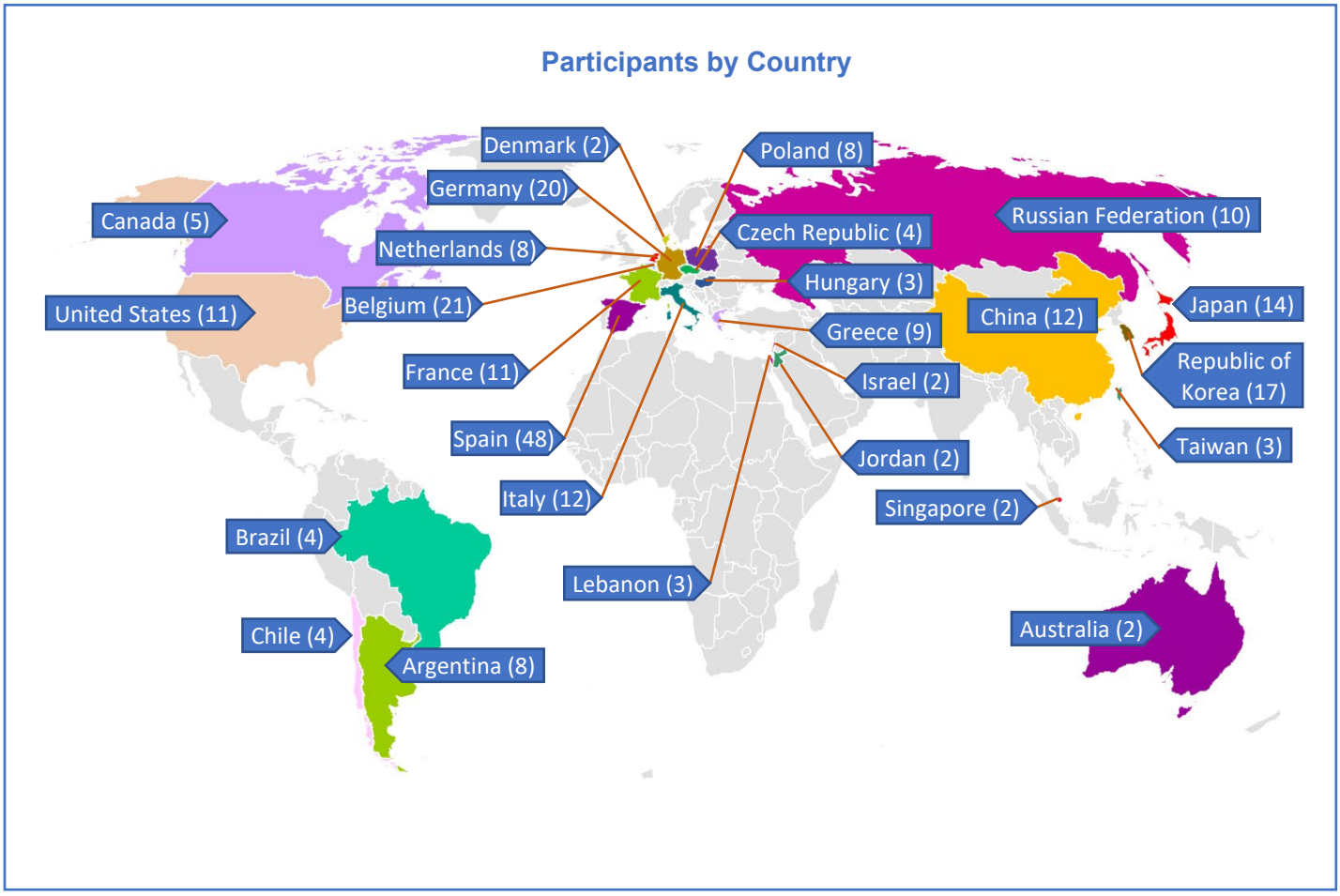
Part 1 was done first to confirm the dose and the safety of canakinumab + docetaxel in 8 participants.

Once the dose and safety were confirmed, Part 2 was started.

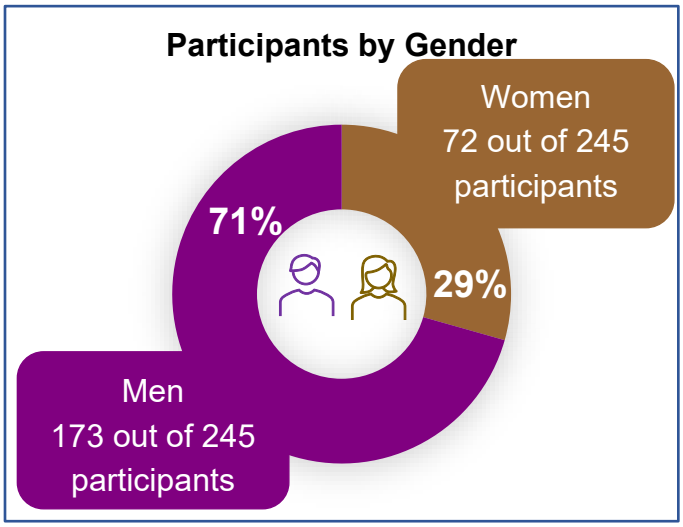
Part 2 included 237 participants randomly assigned to one of the following treatment groups using a computer system, in a process called randomization. This meant that each participant could be assigned to either group, so it helped to make sure the groups were distributed fairly.

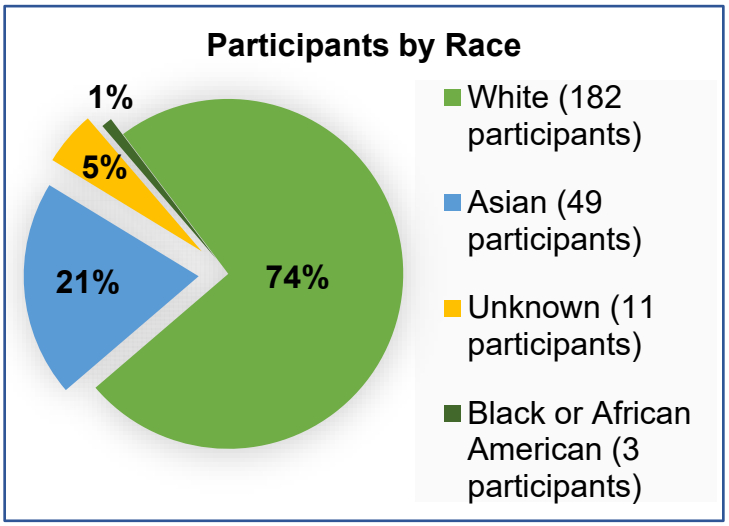
- **Group A**: 120 participants were assigned to receive canakinumab (every 3 weeks or every 6 weeks) + docetaxel (every 3 weeks) or
- **Group B**: 117 participants were assigned to receive placebo (every 3 weeks or every 6 weeks) + docetaxel (every 3 weeks).

Of the 237 who were randomized, 234 actually received study treatment.

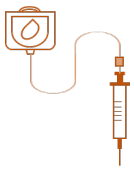
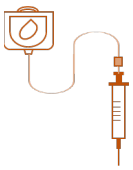


Participants' age ranged from 22 to 82 years. The average age of participants was 63 years.





What treatments did the participants take?

Treatment		Comparator	
	**Canakinumab**, 200 milligram (mg) injection was given under the skin every 3 weeks or every 6 weeks. + **Docetaxel**, 75mg/m^2, given as an infusion into the vein on Day 1 of each 21 day cycle.		**Placebo**, which 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. + **Docetaxel**, 75mg/m^2, given as an infusion into the vein on Day 1 of each 21 day cycle.
			

ⓘ Docetaxel 75mg/m^2 means 75 mg of docetaxel infusion for each square meter (area) of the body.

What happened during this trial?

Before treatment

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

Up to 2 weeks

During treatment

- Safety run-in part (Part 1): researchers treated some participants with the full dose of canakinumab and docetaxel to confirm the dose to be used in part 2.
- Treatment part (Part 2): researchers randomly assigned the participants to one of the following treatment groups:
  - **Group A**: canakinumab + docetaxel
  - **Group B**:: placebo + docetaxel
- None of the participants, trial doctors, or trial staff knew what treatment the participants were receiving.
- Researchers evaluated each participant to assess the effect of the treatment.
- Each participant continued with the treatment until any reason for stopping was met, for example, pregnancy or disease worsened.

Participants continued until their disease worsened

After treatment

- Researchers contacted all the participants to confirm their wellbeing for up to 130 days after the end of the treatment.
- After participants stopped the study treatment, the trial doctor contacted them via phone every 3 months to follow up on their status and asked if they have started different cancer treatment. Until they withdrew consent, lost contact during follow-up, or passed away.

Follow-up for safety (19 weeks after the last dose) and survival

What was the main result of this trial?

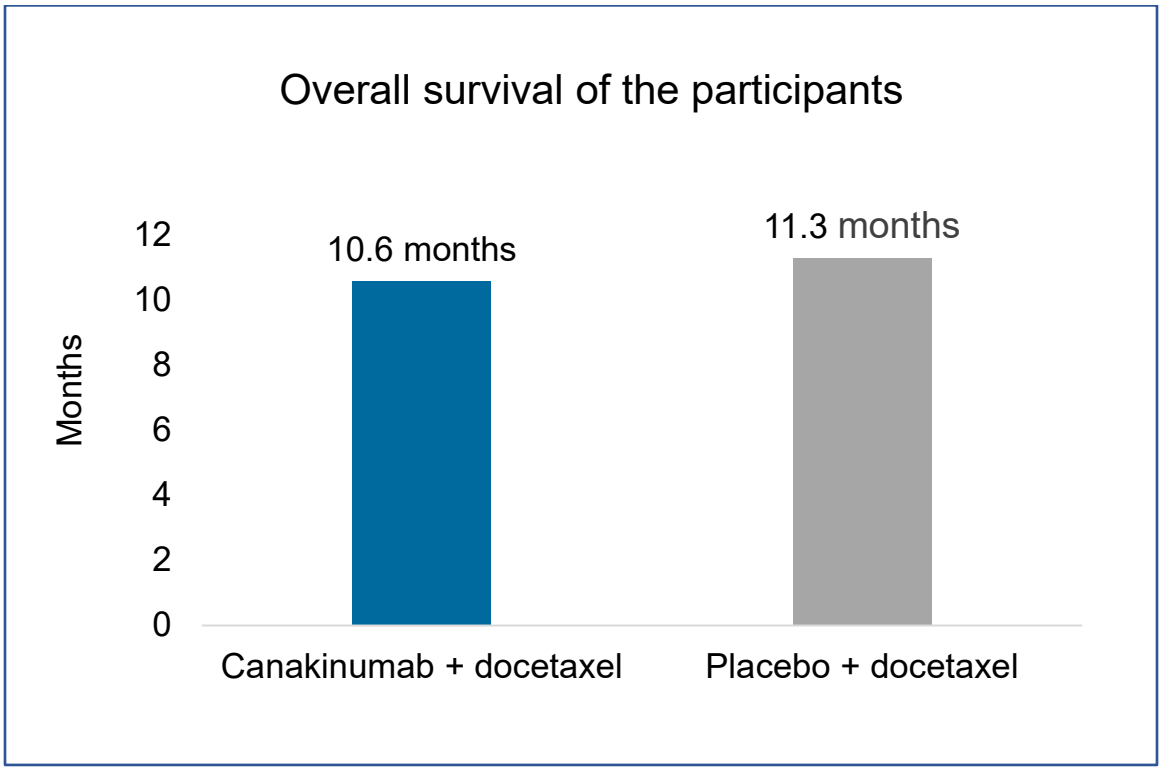
The objective of Part 1 was to confirm the dose to be used in Part 2, by checking safety with a small number of participants. 1 out of 7 (14%) experienced a severe side effect. The planned dose was found to be acceptable for use in Part 2.

The main question asked in Part 2 of the study was:

Was there any difference in the overall survival of the participants on canakinumab plus docetaxel compared with those on placebo plus docetaxel?

ⓘ Overall survival is the average length of time participants are alive after the start of treatment.

Researchers did not find any notable difference between the overall survival of the participants on canakinumab plus docetaxel compared with those on placebo plus docetaxel.



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?

Although 237 participants were randomized, 234 received the treatment. Of these 120 participants received canakinumab plus docetaxel and 114 participants received placebo plus docetaxel.

Number of Participants (%) With Adverse Events

	Part 1 Safety Run-In Canakinumab + docetaxel (Out of **8** participants)	**Group A Canakinumab + docetaxel** (Out of **120** participants)	**Group B Placebo + docetaxel** (Out of **114** participants)
At least 1 adverse event	7 (88%)	111 (93%)	109 (96%)
At least 1 serious adverse event	6 (75%)	55 (46%)	50 (44%)
Stopped drug due to adverse event	—	28 (23%)	33 (29%)
Death	6 (75%)	45 (38%)	37 (32%)

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 shown in the table below:

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

	Part 1 Safety Run-In Canakinumab + docetaxel (Out of **8** participants)	**Group A Canakinumab + docetaxel** (Out of **120** participants)	**Group B Placebo + docetaxel** (Out of **114** participants)
Abnormally low number of neutrophils accompanied with fever (Febrile neutropenia)	0	6 (5%)	8 (7%)
Abnormally low number of neutrophils (Neutropenia)	1 (13%)	4 (3%)	5 (4%)
Blockage of lung's blood vessel (Pulmonary embolism)	1 (13%)	0	3 (3%)
Break in the thighbone (Femur fracture)	1 (13%)	0	0
Coughing of blood (Haemoptysis)	1 (13%)	3 (3%)	1 (1%)
Fever (Pyrexia)	0	6 (5%)	2 (2%)
Lung infection (Pneumonia)	2 (25%)	13 (11%)	8 (7%)
Infection caused by bacteria (Bacterial infection)	1 (13%)	0	0
Flu (Influenza)	1 (13%)	0	0

	Part 1 Safety Run-In Canakinumab + docetaxel (Out of **8** participants)	Group A Canakinumab + docetaxel (Out of **120** participants)	Group B Placebo + docetaxel (Out of **114** participants)
Lung infection caused by pneumococci bacteria (Pneumonia pneumococcal)	1 (13%)	0	0

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 20% (20 out of 100) of participants in any group are presented below.

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

	Part 1 Safety Run-In Canakinumab + docetaxel (Out of **8** participants)	Group A Canakinumab + docetaxel (Out of **120** participants)	Group B Placebo + docetaxel (Out of **114** participants)
Constipation	0	22 (18%)	24 (21%)
Cough	2 (25%)	16 (13%)	19 (17%)
Decrease in appetite (Decreased appetite)	0	32 (27%)	31 (27%)
Decreased red blood cell count (Anemia)	1 (13%)	32 (27%)	33 (29%)
Decreased white blood cell count (White blood cell count Decreased)	2 (25%)	12 (10%)	8 (7%)
Decreased neutrophil count (Neutropenia)	2 (25%)	22 (18%)	25 (22%)

	Part 1 Safety Run-In Canakinumab + docetaxel (Out of **8** participants)	**Group A Canakinumab + docetaxel** (Out of **120** participants)	**Group B Placebo + docetaxel** (Out of **114** participants)
Diarrhea	3 (38%)	41 (34%)	31 (27%)
Difficulty in breathing (Dyspnoea)	2 (25%)	27 (23%)	26 (23%)
Feeling sick to the stomach (Nausea)	1 (13%)	28 (23%)	29 (25%)
Feeling tired (Fatigue)	1 (13%)	33 (28%)	19 (17%)
Hair loss (Alopecia)	1 (13%)	31 (26%)	44 (39%)
Increase in liver enzyme (Gamma-glutamyltransferase increased)	2 (25%)	5 (4%)	6 (5%)
Swelling in the lower leg or hands (Edema peripheral)	3 (38%)	22 (18%)	25 (22%)
Vomiting	2 (25%)	15 (13%)	14 (12%)
Weakness (Asthenia)	2 (25%)	28 (23%)	37 (32%)

How many participants stopped treatment due to adverse events?

16 out of 120 participants (13%) stopped canakinumab due to adverse events. 3 out of 120 participants (3%) stopped canakinumab due to a low number of red blood cells (anemia), and lung infection (pneumonia), and 2 out of 120 participants (2%) stopped canakinumab due to an extreme response of the body to an infection (septic shock), and fever (pyrexia).

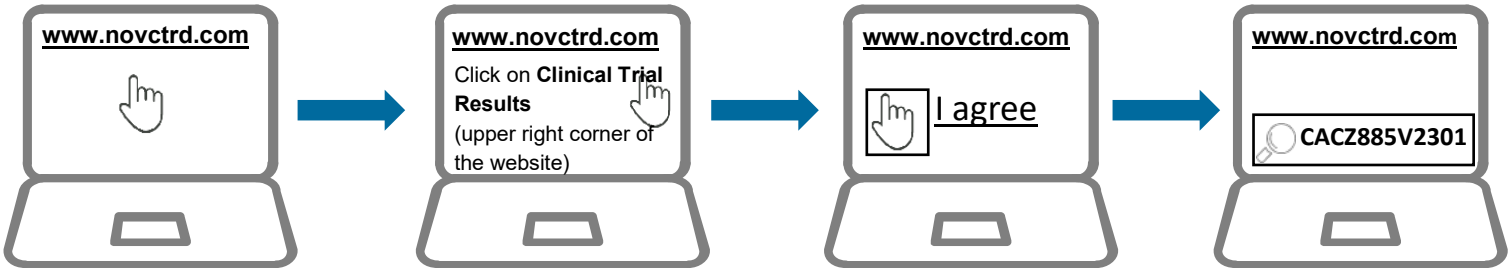
How was this trial useful?

This trial helped researchers to learn that Group A treatment with canakinumab + docetaxel did not increase the overall survival as compared to the Group B treatment with placebo and docetaxel. The overall safety results of the canakinumab plus docetaxel group were either similar to or in favor of the placebo plus docetaxel group in participants with advanced NSCLC. Tolerability observed in this study was consistent with the known safety profile of canakinumab or docetaxel.

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 below steps:



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

- www.clinicaltrials.gov Use the NCT identifier NCT03626545 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search/search Use the EudraCT identifier 2018-002480-26 in the search field.

Full clinical trial title: A randomized, double-blind, placebo-controlled, phase III study evaluating the efficacy and safety of canakinumab in combination with docetaxel versus placebo in combination with docetaxel in subjects with non-small cell lung cancer (NSCLC) previously treated with PD-(L)1 inhibitors and platinum-based chemotherapy (CANOPY-2)

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

NOVARTIS