NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of INC280 given in combination with pembrolizumab in people with non-small cell lung cancer (NSCLC)

Thank you!

Thank you to the participants who took part in the clinical trial for NSCLC. Every participant helped the researchers learn more about **INC280**, also known as capmatinib.

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

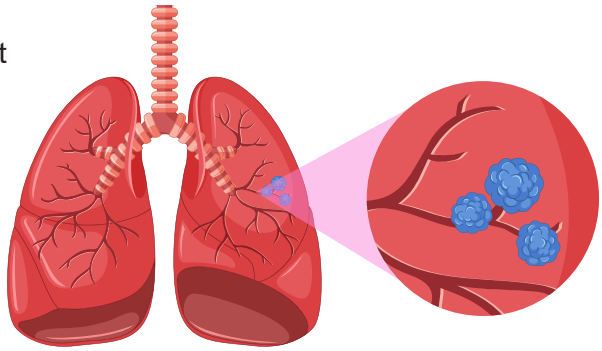
Trial number: CINC280I12201
Drug studied: INC280, also known as capmatinib
Sponsor: Novartis

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 findings.

What was the main purpose of this trial?

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. It begins when the healthy cells in the lungs grow out of control. These abnormal cells grow rapidly and affect the normal functioning of the lungs. Cancer is usually described in stages. In advanced NSCLC, or stages III and IV, cancer spreads to other parts of the body.



Common symptoms of **NSCLC** are:

- Continuous cough that worsens
- Coughing up blood or phlegm
- Chest pain or discomfort
- Shortness of breath
- Weight loss
- Weakness and loss of appetite

One of the causes of NSCLC is **gene mutations**. A mutation is a change in the gene's structure that affects its normal function. Some people with advanced NSCLC have mutations in the **Mesenchymal Epithelial Transition** or **MET** gene. The normal MET gene provides instructions to form MET proteins that help in normal cell growth and division. Mutations in the MET gene alter the MET proteins which may cause abnormal cells to grow and spread in the body.

Chemotherapy is the most common treatment used for cancer. It uses medicines to kill fast-growing cancer cells. **Immunotherapy** is a different kind of treatment that helps the immune system recognize the cancer cells and stop them. Cancer treatments do not always work or may stop working after some time. As a result, there is a constant need to find new treatments.

The trial drug, **INC280**, also known as capmatinib, blocks abnormal MET proteins and also allows the immune system to destroy the cancer cells. This may help keep the cancer from spreading. It is an approved drug in some countries for the treatment of advanced NSCLC with changes in the MET gene.

Certain proteins called **PD-L1** stop the immune system from attacking cancer cells. **Pembrolizumab**, an approved drug for NSCLC, is an immunotherapy that blocks PD-L1 protein and helps the immune system to attack the cancer cells and slow down cancer growth**.**

In this trial, researchers wanted to see how well **INC280** worked when given in combination with pembrolizumab as compared to pembrolizumab given alone in people with NSCLC having higher amounts of PD-L1 proteins.

The main questions that researchers wanted to answer were:

- How long did the participants live without their cancer getting worse or dying from any cause?
- What adverse events did participants have during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial began in January 2020 and ended in February 2023. Participants were allowed to continue with the trial treatment as long as they benefited from it.

The trial ended earlier than planned due to safety concerns seen in the **INC280 + Pembrolizumab** group. All participants in this combination group stopped taking INC280 but were allowed to continue treatment with **pembrolizumab**.

When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Who was in this trial?

76 participants from **16 countries** with NSCLC received treatment in this trial.

Participants' ages ranged from 49 to 84 years. Their average age was 65 years.

The number of participants by gender and race are shown below.

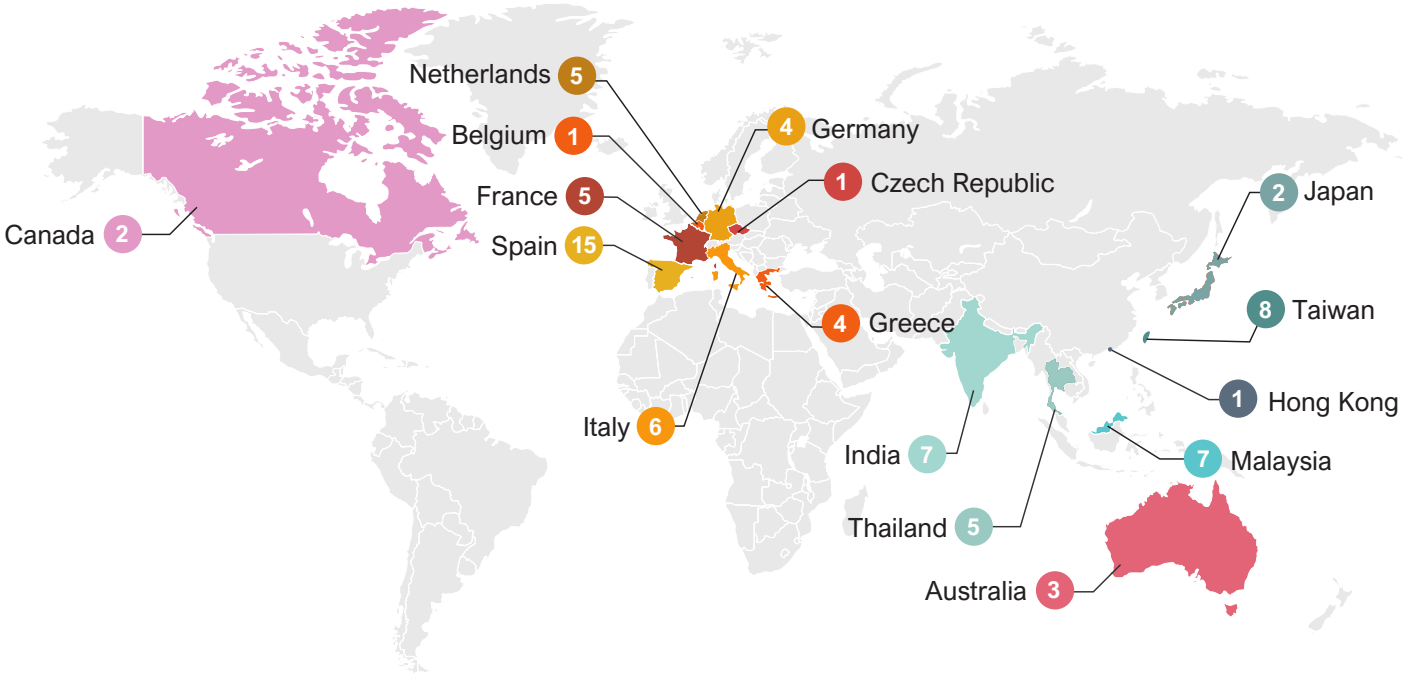
Gender

51 Men	25 Women

Race

41 White	30 Asian	5 Unknown

The map below shows the number of participants who took part in each country.



Participants **could take part** in this trial if they:

- Were at least 18 years old
- Had confirmed advanced stage III or IV of NSCLC with high PD-L1 protein
- Had at least 1 tumor that could be measured
- Were able to at least move around and perform daily self-care activities
- Did not receive prior MET blocker treatment, or immunotherapy

What treatments did the participants receive?

Researchers studied the following treatments:

INC280: 400 milligrams (mg), provided as tablets, taken by mouth twice a day.

Pembrolizumab: 200 mg, given as a slow injection into a vein, every 3 weeks.

The participants, trial doctors, and trial staff all knew which treatments the participants received.

What happened during this trial?

Before treatment

Up to 28 days

Trial doctors checked the participants' health and NSCLC to make sure they could be in this clinical trial.

During treatment

Up to 25 months

Participants received the treatment in **cycles.**

In this trial, a cycle is a 21-day treatment period, that can be repeated as needed, and during which **INC280** treatment was given daily and **pembrolizumab** was given on Day 1.

Participants were randomly assigned to 1 of 2 treatment groups by a computer. The treatment groups were:

Group 1
51 participants

INC280 + Pembrolizumab

INC280
400 mg,
2 times a day

+

Pembrolizumab
200 mg, once per 21-day cycle

Group 2
25 participants

Pembrolizumab alone

Pembrolizumab
200 mg, once per 21-day cycle

Participants were required to visit the trial center every 21 days. At each visit, the trial doctor conducted medical exams and checked for any adverse events. Blood tests and CT scans were done regularly to monitor participants' cancer and overall health.

Due to safety concerns, all participants in the **INC280 + Pembrolizumab** group stopped taking INC280 and were allowed to continue to receive pembrolizumab. Participants received pembrolizumab for up to 35 cycles, until their cancer worsened, or they had unexpected adverse events.

After treatment

Up to end of the trial

Participants were:

- Checked for adverse events by telephone call or follow-up visit 30 days after the last dose of **pembrolizumab**.
- Followed up until their cancer worsened or they started taking other cancer treatments or they died or up to the end of the trial.

What were the main results of this trial?

How long did the participants live without their cancer getting worse or dying from any cause?

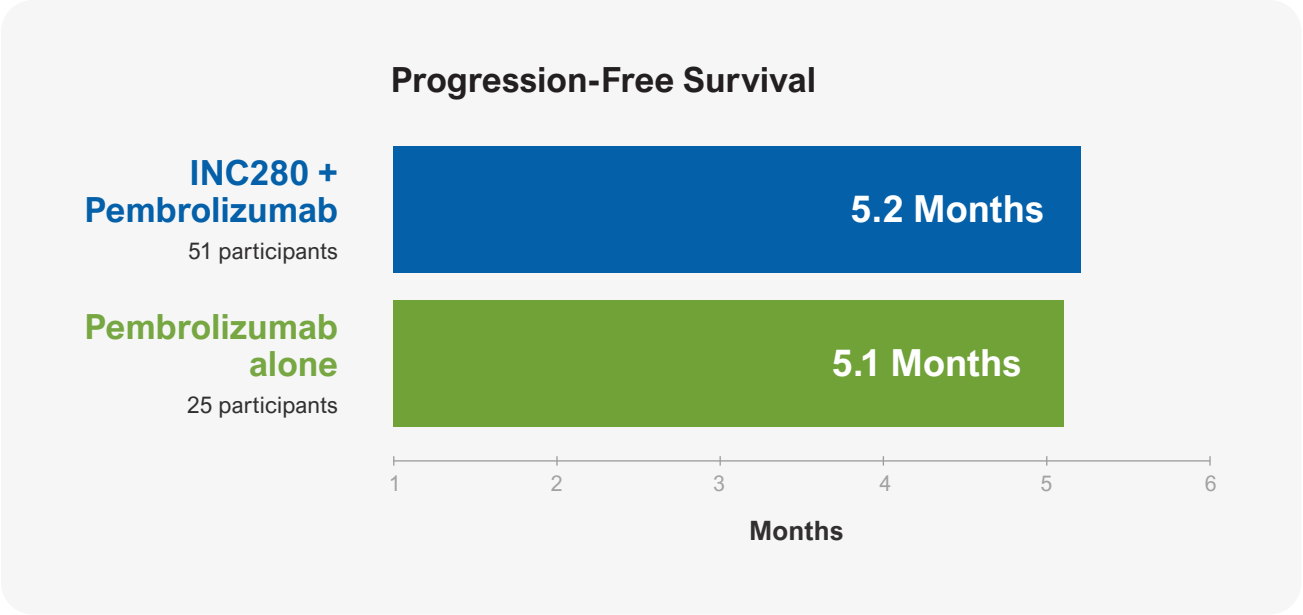
The progression-free survival for participants in both the **INC280 + Pembrolizumab** group and the **Pembrolizumab alone** group was about 5 months.

To find out how long participants lived without their cancer worsening, researchers closely monitored the participants and checked them for **progression-free survival.**

Progression-free survival is how much time it takes from the beginning of treatment until the participants' cancer gets worse or they die.

Due to safety concerns with the combination of INC280 and pembrolizumab, participants stopped receiving INC280 during the treatment period.

The figure below shows the progression-free survival for all 76 participants who received at least 1 dose of trial drug.



What adverse events did the participants have?

Trial doctors keep track of all **adverse events** that happen in trials, 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 during the treatment period, and up to 30 days after the last dose of the trial drug.

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.

Although there were 76 participants in the trial, the 51 participants who first took INC280 and then stopped were counted again in a separate group. As a result, the safety results consider a total number of 127 participants.

94 participants had adverse events.

- **48 participants** had adverse events that were considered serious.
- **13 participants** died due to any cause, including participants who died from their disease.
- **12 participants** stopped the treatment due to an adverse event.

How many participants had adverse events?

After participants in the combination group stopped taking INC280, their adverse events were reported separately in the **Pembrolizumab after stopping INC280** group.

The table below shows how many participants had adverse events during the treatment and follow-up periods.

Summary of adverse events

Participants who:	These groups include the same **51 participants** **INC280 + Pembrolizumab** 51 participants	**Pembrolizumab after stopping INC280** 51 participants	**Pembrolizumab alone** 25 participants
Had at least 1 serious adverse event	26 of 51 **(51%)**	9 of 51 **(18%)**	13 of 25 **(52%)**
Had at least 1 other adverse event	41 of 51 **(80%)**	29 of 51 **(57%)**	24 of 25 **(96%)**
Died during the trial	8 of 51 **(16%)**	2 of 51 **(4%)**	3 of 25 **(12%)**

What serious adverse events did the participants have?

The table below shows the most common serious adverse events that happened in at least 2 participants in any group.

Serious adverse events

	These groups include the same **51 participants**		
	INC280 + Pembrolizumab 51 participants	**Pembrolizumab after stopping INC280** 51 participants	**Pembrolizumab alone** 25 participants
Lung infection Pneumonia	2 of 51 **(4%)**	1 of 51 **(2%)**	2 of 25 **(8%)**
Fever Pyrexia	3 of 51 **(6%)**	1 of 51 **(2%)**	0 of 25 **(0%)**
Inflammation of the airways in the lungs Bronchitis	2 of 51 **(4%)**	0 of 51 **(0%)**	1 of 25 **(4%)**
Difficulty breathing Dyspnoea	0 of 51 **(0%)**	1 of 51 **(2%)**	2 of 25 **(8%)**
Fluid buildup in the space around the heart Pericardial effusion	1 of 51 **(2%)**	2 of 51 **(4%)**	0 of 25 **(0%)**
Extreme immune response to an infection Sepsis	2 of 51 **(4%)**	1 of 51 **(2%)**	0 of 25 **(0%)**
Sudden kidney injury Acute kidney injury	2 of 51 **(4%)**	0 of 51 **(0%)**	0 of 25 **(0%)**
Chronic lung disease Chronic obstructive pulmonary disease (COPD)	0 of 51 **(0%)**	0 of 51 **(0%)**	2 of 25 **(8%)**

What other adverse events did the participants have?

The table below shows the other adverse events that happened in at least 25% of participants in any group.

Other adverse events

	These groups include the same **51 participants**		
	INC280 + Pembrolizumab 51 participants	**Pembrolizumab after stopping INC280** 51 participants	**Pembrolizumab alone** 25 participants
Swelling of the ankles and feet Oedema peripheral	14 of 51 **(27%)**	6 of 51 **(12%)**	1 of 25 **(4%)**
Itching Pruritus	**5 of 51 (10%)**	7 of 51 **(14%)**	8 of 25 **(32%)**
Vomiting	14 of 51 **(27%)**	1 of 51 **(2%)**	2 of 25 **(8%)**
Nausea	13 of 51 **(25%)**	1 of 51 **(2%)**	2 of 25 **(8%)**

What was learned from this trial?

This trial helped researchers learn about the effects of INC280 when given along with pembrolizumab in people with NSCLC.

The researchers concluded that:

- The progression-free survival in both treatment groups was similar, about 5 months.
- The desired effect with **INC280** was not achieved.

Researchers found that participants in the **INC280 + Pembrolizumab** group had a higher number of **adverse events that were considered related to the treatment** than those in the **Pembrolizumab alone** group.

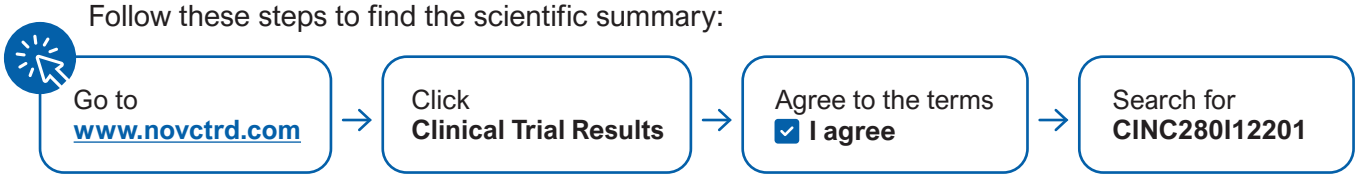
As a result, the trial ended eariler than planned due to these safety concerns seen in the **INC280 + Pembrolizumab** group.

Currently, there are no further studies with INC280 planned.

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:



For more information about this trial go to any of the following websites:

- **clinicaltrials.gov** – search using the number **NCT04139317**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2019-002660-27**

Other trials of INC280 may appear on the public websites above. When there, search for INC280 or capmatinib.

Full clinical trial title: A Randomized, Open Label, Multicenter Phase II Study Evaluating the Efficacy and Safety of Capmatinib (INC280) Plus Pembrolizumab Versus Pembrolizumab Alone as First Line Treatment for Locally Advanced or Metastatic Non-small Cell Lung Cancer With PD-L1≥ 50%

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