NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of the treatment combination of INC280 and PDR001 in people with non small cell lung cancer

Thank you!

Thank you to the participants who took part in the clinical trial for non-small cell lung cancer. Every participant helped the researchers learn more about the trial drugs **INC280**, also called capmatinib, and **PDR001**, also called spartalizumab.

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: CINC280J12201

Drugs studied: INC280 / capmatinib and PDR001 / spartalizumab

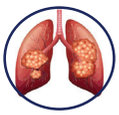
Sponsor: Novartis

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

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of the treatment combination of INC280 and PDR001 in people with advanced or metastatic non small cell lung cancer, where the tumor contains a gene mutation called 'MET exon 14 skipping'.



Non small cell lung cancer (NSCLC) is the most common type of lung cancer. It happens when an abnormal growth of large cells in the lungs occurs and forms a tumor. Symptoms of continuous cough, coughing with blood, shortness of breath, chest pain, weakness, and weight loss are not visible until the cancer becomes **advanced** or **metastatic**.

In **advanced NSCLC**, the cancer spreads beyond the lungs to nearby tissues or glands.

In **metastatic NSCLC**, the cancer spreads to distant parts of the body, such as the liver, bones, or brain.

Most types of NSCLC occur due to **mutations** in genes. Some people with advanced or metastatic NSCLC have a type of mutation in a gene known as 'MET' gene and the mutation is called the '**MET exon 14 skipping**' mutation. Mutations in the MET gene result in changes in the MET protein which may cause abnormal cells to grow and spread in the body.

Mutation is a change in the gene

INC280, is also known as capmatinib. It works by blocking the MET protein. The MET protein is essential in normal organ development and wound healing as it can control how the cells grow and divide.

It is an approved drug in some countries used for the treatment of people with advanced or metastatic NSCLC with changes in the MET gene.

PDR001, is also known as spartalizumab. It helps the immune system fight cancer by blocking the activity of a protein called PD-1. PD-1 can prevent the immune system from killing cancer cells.

In this trial, researchers tried the combination of **INC280** and **PDR001** in people with advanced or metastatic NSCLC.

This trial was designed to have 2 parts:

- **Part 1 -** In Part 1, researchers wanted to find out if the treatment combination of **INC280** and **PDR001** is effective and if it is safe.
- **Part 2 -** In Part 2, researchers wanted to compare the effects of the treatment combination of **INC280** and **PDR001** to **INC280** alone. Part 2 did not take place due to the results of Part 1.

The main questions the researchers wanted to answer in Part 1 of this trial were:

- Did the participants' tumors completely disappear or become at least 30% smaller after treatment with **INC280** and **PDR001**?
- What adverse events did the participants have during Part 1 of this trial?

How long was this trial?

The trial began in August 2020 and ended in January 2023.

Researchers decided to stop the trial early due to safety concerns with the use of the combination of **INC280** and **PDR001** during Part 1 of the trial. The results for Part 1 suggested that the treatment combination of **INC280** and **PDR001** resulted in a higher number of **adverse events*** (AEs) that were considered serious and higher number of AEs that required treatment to be stopped permanently compared with results from previous studies with **INC280** alone. Therefore, researchers decided to stop Part 1 early and did not conduct Part 2 of the trial.

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

Who was in this trial?

31 participants with NSCLC received treatment in this trial. Participants' ages ranged from 52 to 89 years. The average age was 72 years.

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

Gender

15 **Men**	16 **Women**

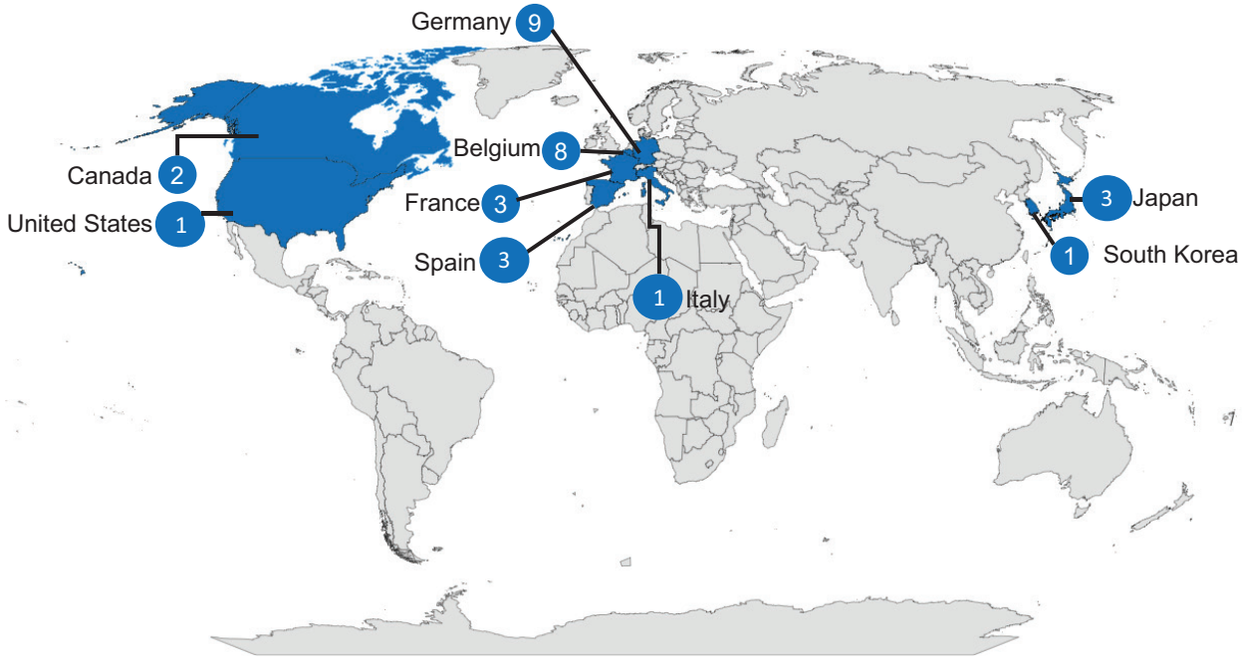
Race

23 **White**	6 **Asian**	1 **Black** or **African American**
1 **Not reported**		

The participants could take part in this trial if they:

- were at least 18 years of age
- had NSCLC with 'MET exon 14 skipping' mutation
- had not received any systemic treatment (treatment that affects the entire body) for advanced or metastatic NSCLC
- had at least one measurable area of tumor
- were able to at least move around and were able to perform self care in daily life

31 participants from 9 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:

INC280, 400 milligram (mg) taken by mouth as tablets.

PDR001, 400 mg given as an infusion into a vein.

During Part 1 of this trial, the participants, trial doctors, and trial staff knew what treatment each participant received.

What happened during Part 1 of this trial?

Before treatment

28 days

Trial doctors checked the participants' health to ensure they could take part in this clinical trial.

During treatment

Repeated 28-day cycles for as long as the participants benefitted from the treatment.

A cycle is a 28-day treatment period, that can be repeated as needed, and during which INC280 treatment is given daily and PDR001 is given as an infusion into a vein on Day 1.

Participants received the following treatments:

INC280: Participants took 400 mg of **INC280** as tablets by mouth, twice daily

PDR001: Participants received 400 mg of **PDR001** as an infusion into the vein once in each 28-day **cycle**

Because of safety concerns with the treatment combination of **INC280** and **PDR001**, this trial stopped enrolling participants after completing enrollment in Part 1. After stopping the enrollment, participants who were already in the trial stopped receiving **PDR001** and continued with only **INC280** and those who had not started treatment yet began treatment with **INC280** alone.

After treatment

30 days after the last dose of INC280, or 150 days after the last dose of PDR001

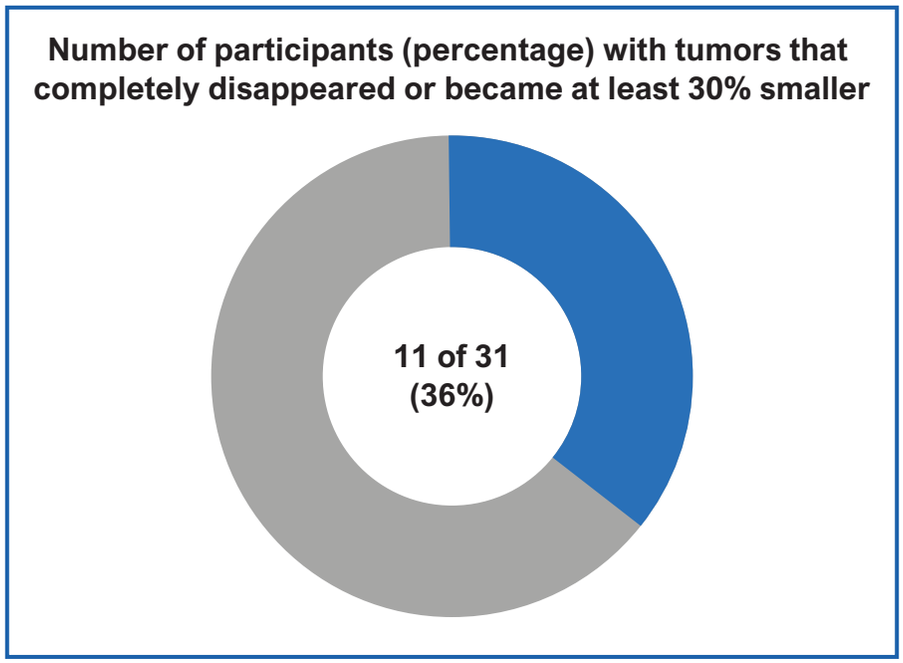
Researchers monitored the participants' health during this time.

What was the main result of this trial?

Did the participants' tumor completely disappear or become at least 30% smaller after treatment with INC280 and PDR001?

Eleven out of 31 (36%) participants had tumors that completely disappeared or became at least 30% smaller after treatment.

To answer this question, researchers used different imaging tests which could include CT scan, MRI, and PET scan.



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 up to 30 days after the last dose of **INC280**, or 150 days after the last dose of **PDR001**.

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.

Information on adverse events is available for participants who were on **INC280** + **PDR001** before and after discontinuing **PDR001** and participants who were on **INC280** alone.

Most participants had adverse events. The researchers found safety concerns for the combination of **INC280** and **PDR001** in this trial.

How many participants had adverse events?

Participants who:	INC280 + PDR001 (Before discontinuing PDR001) (28 participants)	INC280 + PDR001 (After discontinuing PDR001) (28 participants)	INC280 alone (3 participants)
Had at least 1 adverse event	25 of 28	18 of 28	3 of 3
Had at least 1 serious adverse event	11 of 28	8 of 28	1 of 3
Died during the trial	4 of 28	0	0

What serious adverse events did the participants have?

The following serious adverse events were experienced by 1 participant each in the respective treatment groups:

List of serious adverse events that occurred in each treatment group.

INC280 + PDR01 (Before discontinuing PDR001)	INC280 + PDR001 (After discontinuing PDR001)	INC280 alone
• **Abnormal liver function** (hepatic function abnormal) • **Bone infection** (osteomyelitis) • **Brain damage** (encephalopathy) • **Brain swelling** (brain edema) • **Build-up of excess fluid in the lungs** (pleural effusion) • **Chest infection** (respiratory tract infection) • **Health deterioration** (general physical health deterioration) • **Increase in the liver test value of alanine aminotransferase enzyme** (alanine aminotransferase increased) • **Increase in the liver test value of aspartate aminotransferase enzyme** (aspartate aminotransferase increased) • **Inflammation of the digestive tract caused by a virus** (gastroenteritis rotavirus) • **Inflammation of the thin layers of tissue that separate the lungs from chest wall** (pleurisy) • **Kidney injury** (acute kidney injury) • **Liver damage caused by medicines** (drug-induced liver injury) • **Lung infection** (pneumonia) • **Skin rash** (rash maculo-papular)	• **Bleeding at medical device site** (medical device site haemorrhage) • **Increase in the liver test value of alanine aminotransferase enzyme** (alanine aminotransferase increased) • **Infection of the colon caused by a bacteria** (clostridium colitis) • **Inflammation of the pancreas** (pancreatitis) • **Joint injury** (joint dislocation) • **Liver damage** (hepatotoxicity) • **Liver infection** (hepatitis) • **Low blood sodium levels** (hyponatraemia) • **Narrowing of the vein that carries blood from the lower body to the heart** (inferior vena cava syndrome) • **Reaction due to infusion** (infusion related reaction) • **Severe breathing problems due to insufficient oxygen in the blood** (acute respiratory failure) • **Swelling** (edema)	• **Health deterioration** (general physical health deterioration) • **Bacterial infection** (streptococcal infection) • **Chest infection** (respiratory tract infection) • **Fever** (pyrexia) • **Lung infection** (pneumonia) • **Swelling in the arms and legs** (oedema peripheral)

What other adverse events did the participants have?

The table below shows the other adverse events that happened in **40% or more** participants.

	INC280 + PDR001 (Before discontinuing PDR001) (28 participants)	INC280 + PDR001 (After discontinuing PDR001) (28 participants)	INC280 alone (3 participants)
Constipation	8 of 28 29%	1 of 28 4%	2 of 3 67%
COVID-19 infection	0 of 28 0%	0 of 28 0%	2 of 3 67%
Swelling in the arms and legs (Oedema peripheral)	11 of 28 39%	15 of 28 54%	3 of 3 100%
Infection of the nose and throat (Upper respiratory tract infection)	0 of 28 0%	0 of 28 0%	2 of 3 67%
Increased levels of creatinine in the blood (Blood creatinine increased)	10 of 28 36%	11 of 28 39%	2 of 3 67%
Shortness of breath (Dyspnoea)	1 of 28 4%	4 of 28 14%	2 of 3 67%
Low levels of albumin in the blood (Hypoalbuminemia)	1 of 28 4%	5 of 28 18%	2 of 3 67%

What was learned from this trial?

Researchers learned about the effects of the combination of INC280 and PDR001 in people with advanced or metastatic NSCLC, where the tumor contains a gene **mutation** called 'MET exon 14 skipping'.

The researchers found that:

- Eleven out of 31 (36%) participants had tumors that completely disappeared or became at least 30% smaller after treatment with the combination of **INC280** and **PDR001**.
- the treatment combination of **INC280** and **PDR001** also resulted in a higher number of AEs that were considered serious and a higher number of AEs that required the treatment to be stopped permanently compared with results from previous studies with **INC280** alone.

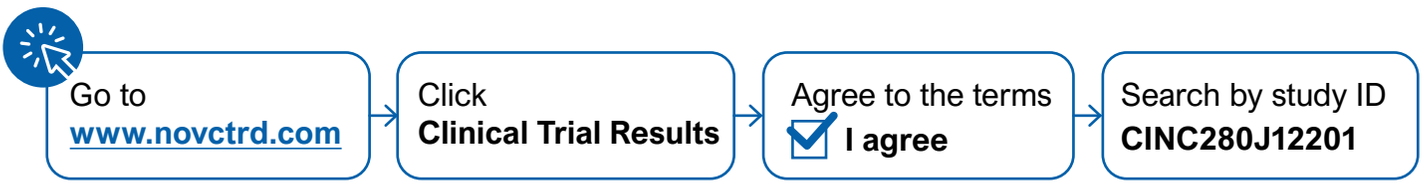
The researchers decided to stop the trial early due to safety concerns with the use of the combination of **INC280** and **PDR001** during Part 1 of the trial. Part 2 of the study was not done.

When this summary was written, there were no plans for future trials with the combination of **INC280** and **PDR001** in people 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**

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 NCT04323436
- clinicaltrialsregister.eu/ctr-search/search search using the number 201900309711

If more trials are planned, they will appear on the public websites above. When there, search for INC280, capmatinib, PDR001, spartalizumab, or NSCLC.

Full clinical trial title: A double-blind, placebo controlled, randomized, phase II study evaluating the efficacy and safety of capmatinib (INC280) and spartalizumab (PDR001) combination therapy versus capmatinib and placebo as first line treatment for locally advanced or metastatic non small cell lung cancer patients with MET exon 14 skipping mutations

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

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