NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the safety of INC280, also called capmatinib, given with osimertinib in people with a type of non-small cell lung cancer (NSCLC)

Thank you!

Thank you to the participants who took part in the clinical trial for a type of **advanced or metastatic non-small cell lung cancer (NSCLC).** Every participant helped the researchers learn more about the trial drug **INC280**, also known as **capmatinib**, given with osimertinib.

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: CINC280L12301

Novartis drug studied: INC280 (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?

The purpose of this trial was to learn about the safety of INC280 given with osimertinib in people with advanced or metastatic non-small cell lung cancer with both EGFR mutations and MET amplification. The trial was also designed to learn about the effects on NSCLC, including whether tumors shrank and how long people lived. However, this part of the trial did not start.

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. **Advanced or metastatic** means that cancer has spread from where it started to other parts of the body, or cannot be removed with surgery.

EGFR mutations and **MET amplification** are types of changes in cancer cells that cause cancer to grow and spread. There are treatments that target cancer cells with certain changes.

EGFR and MET are proteins on cells that help them grow.

- **EGFR** stands for epidermal growth factor receptor
- **MET** stands for mesenchymal-to-epithelial transition factor

INC280, also known as **capmatinib**, is a drug designed to block MET. It is approved in certain countries for people with NSCLC with a different MET change called MET exon 14 skipping mutation (also called METex14 deletion mutation). However it is not approved for people with NSCLC and MET amplification.

Osimertinib is a drug designed to block EGFR. It is approved in certain countries for people with NSCLC with EGFR mutations.

Trial drug
INC280 also called capmatinib
Pronounced as
kap-**ma**-ti-nib

Trial drug
Osimertinib
Pronounced as
oh-sih-**mer**-tih-nib

The trial purpose was to answer these main questions:

- Was INC280 400 milligrams, or mg, twice a day given with osimertinib 80 mg once a day safe for participants?
- What adverse events did the 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 started in September 2021 and ended in December 2022.

This trial was designed to have 2 parts:

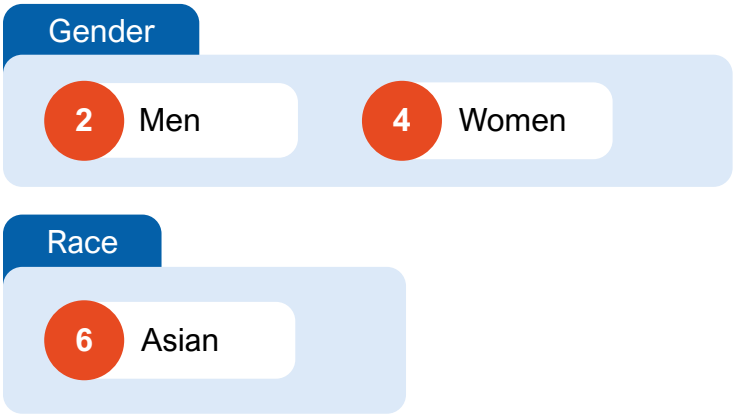
- **Part 1** learned if INC280 400 mg twice a day given with osimertinib 80 mg once a day was safe for a small number of participants. Researchers planned to use INC280 given with the safe dose of osimertinib in Part 2.
- **Part 2** did not start, but was planned to learn about the effects of INC280 given with osimertinib on NSCLC compared to chemotherapy in more participants

The researchers did not complete this trial as planned. The sponsor **ended this trial early because of difficulty finding participants to join** due to other treatments for this type of NSCLC becoming available. The decision to stop the trial early was not due to safety concerns.

Who was in this trial?

6 participants with NSCLC were in Part 1 of this trial. Participants' ages ranged from 52 to 74 years. Their average age was 62 years.

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



The participants could take part in this trial if they had **advanced or metastatic NSCLC** that:

- Had both EGFR mutations and MET amplification
- Got worse after previous treatment that blocks EGFR
- Had not been treated with a treatment that blocks MET

6 participants from 3 countries received treatment:

- Japan | 2 participants
- Republic of Korea | 2 participants
- Singapore | 2 participants

What treatments did the participants receive?

All participants took both of these treatments:

INC280, also known as capmatinib: 400 mg twice a day by mouth as a tablet

Osimertinib: 80 mg once a day by mouth as tablets. If needed, trial doctors could lower the dose to 40 mg once a day.

In this trial, the participants and clinical trial team knew what treatment each participant took. All participants took INC280 with osimertinib.

What happened during this trial?

The graphic below shows what happened during Part 1.

Before treatment **Up to 1 month**

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

During treatment: Part 1 **Up to 9 months**

6 participants took these treatments together:

- **INC280** 400 milligrams (mg) twice a day by mouth as tablets
- **Osimertinib** 80 mg once a day by mouth as tablets

All 6 participants started at the same dose of INC280 with osimertinib. Researchers checked the participants' NSCLC and general health throughout the trial. If needed, researchers could lower a participant's dose.

After treatment **About 1 month**

Trial staff called each participant about 1 month after receiving their last dose of treatment to check for safety concerns.

If a participant's cancer had not gotten worse during treatment, trial staff continued to check on their tumors until they got worse or the trial ended.

What were the main results of this trial?

Was INC280 400 mg twice a day given with osimertinib 80 mg once a day safe for participants?

Because the trial ended early and due to the small number of participants, the researchers could not confirm if the dose of INC280 400 mg twice a day given with the suggested dose of osimertinib 80 mg once a day was safe for participants.

Researchers looked at the participants' physical exams and blood tests and kept track of participants who had a **dose limiting toxicity (DLT)** during the first 3 weeks after starting trial treatment.

Researchers could not measure DLTs in 1 of the 6 participants because they did not complete 3 weeks of treatment. Out of 5 remaining participants, none had DLTs during the first 3 weeks of treatment.

A **dose limiting toxicity (DLT)** is a medical problem with risk of serious harm if the dose went up. DLTs are not related to cancer and the researchers think they could possibly be related to the trial treatment.

Researchers could not conclude if the dose of INC280 with osimertinib was safe because the number of participants was too small due to the trial ending early.

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 treatment and up to 30 days after the last dose of trial treatment.

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.

2 participants had serious adverse events. 5 participants had other adverse events. The researchers concluded there were no safety concerns for the participants in this trial.

How many participants had adverse events?

Participants who:	INC280 and osimertinib 6 participants
Had at least 1 **serious adverse event**	**2 of 6** 33%
Had at least 1 **other adverse event**	**5 of 6** 83%
Stopped treatment due to an adverse event	**0 of 6** 0%
Died during the trial	**1 of 6** 17%

What serious adverse events did the participants have?

2 participants had serious adverse events. 1 participant died due to a lung infection (pneumonia).

The table below shows **all** the serious adverse events that happened in participants.

	INC280 and osimertinib 6 participants
COVID-19	**1 of 6** 17%
Feeling less hungry than usual Decreased appetite	**1 of 6** 17%
Feeling sick to the stomach Nausea	**1 of 6** 17%
A buildup of fluid around the heart Pericardial effusion	**1 of 6** 17%
A lung infection Pneumonia	**1 of 6** 17%

What other adverse events did the participants have?

5 participants had other adverse events. The table below shows the other adverse events that happened in **2 or more** participants (33% or more).

	INC280 and osimertinib 6 participants
Swelling in the lower legs or hands Oedema peripheral	**4 of 6** 67%
Low levels of a protein in the blood Hypoalbuminemia	**3 of 6** 50%
Rash	**3 of 6** 50%
Feeling sick to the stomach Nausea	**2 of 6** 33%

What was learned from this trial?

None of the 5 participants who completed the first 3 weeks of treatment had a dose limiting toxicity (DLT).

Because the trial ended early and due to the small number of participants, researchers could not confirm if INC280 400 mg twice a day given with osimertinib 80 mg once a day was safe for participants.

There are no plans for future trials of INC280 given with osimertinib 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:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Agree to the terms ☑ **I agree** → Search for **CINC280L12301**

For more information about this trial, go to any of these websites:

- **clinicaltrials.gov** – search using the number **NCT04816214**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2020-003677-21**

Full clinical trial title: A phase III randomized, controlled, open-label, multicenter, global study of capmatinib in combination with osimertinib versus platinum - pemetrexed based doublet chemotherapy in patients with locally advanced or metastatic NSCLC harboring EGFR activating mutations who have progressed on prior generation EGFR-TKI therapy and whose tumors are T790M mutation negative and harbor MET amplification (GEOMETRY-E)

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

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