NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of NIR178 and PDR001 in people with certain types of cancer

Thank you!

Thank you to the participants who took part in the clinical trial for certain types of cancer. Every participant helped the researchers learn more about the trial drugs **NIR178**, also called taminadenant, 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: CNIR178X2201

Novartis drugs studied: NIR178, also known as taminadenant, and PDR001, also known as 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 only shows the results of a single clinical trial. Other clinical trials may have different results.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of **NIR178** and **PDR001** in participants with certain types of advanced or metastatic 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.

The types of cancer were:

- **Solid tumors**, which are cancers in organs and tissues and not in body liquids such as blood. The solid tumors in the trial were:
  - Triple negative breast cancer (TNBC)
  - Kidney cancer (renal cell carcinoma)
  - Pancreatic cancer
  - Bladder cancer (urothelial)
  - Prostate cancer (metastatic castration-resistant prostate cancer or mCRPC)
  - Head and neck cancer
  - Skin cancer (melanoma)
  - Non-small cell lung cancer (NSCLC)
  - Colon cancer (microsatellite stable colon cancer or MSS), including different types of mutations (changes) in cancer cells
- **Diffuse large B-cell lymphoma (DLBCL),** which is a type of blood cancer that is the most common and fast-growing type of non-Hodgkin lymphoma

NIR178, also called taminadenant, is a new type of trial drug that researchers designed to help the immune system kill cancer cells. By blocking the protein, it is designed to help the immune system kill cancer cells.

PDR001, also called spartalizumab, is a trial immunotherapy drug. It is designed to block a specific protein that prevents the immune system from killing cancer cells. By blocking the protein, it is designed to help the immune system kill cancer cells.

Trial drug
NIR178 also called taminadenant
Pronounced as
tam-in-uh-den-ant

Trial drug
PDR001 also called spartalizumab
Pronounced as
spar-ta-liz-ue-mab

This trial looked at different doses and combinations of **NIR178** and **PDR001** in groups of participants with different types of cancer. It also had a group of Japanese participants, which Japan's health authority requires.

The trial purpose was to answer these main questions:

- How many participants had their tumors shrink or disappear?
- What adverse events did the participants have?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial began in August 2017 and ended in February 2023. Participants were in this trial for up to about 5 years.

In November 2021, the sponsor decided to stop enrollment earlier than planned due to business reasons. The decision was not due to safety concerns. Participants who already started treatment continued treatment in the trial.

Who was in this trial?

315 participants with certain types of advanced or metastatic cancer received treatment in this trial – 196 men and 119 women. Participants' ages ranged from 22 to 85 years. Their average age was 60 years. The number of participants by race is shown below.

Race

1 American Indian or Alaska Native	78 Asian	10 Black or African American
5 Other	200 White	21 Unknown

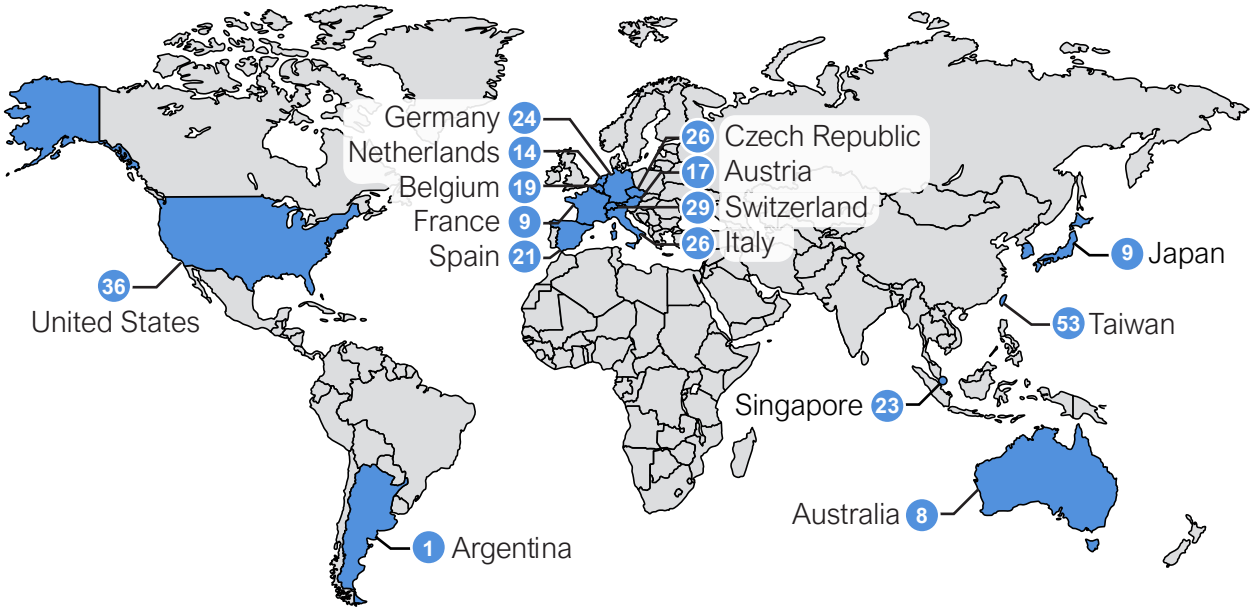
This trial had 3 parts that looked at different doses and combinations of **NIR178** and **PDR001** in groups of participants with certain types of cancer. The parts and groups in the trial were:

- **Part 1:** Solid tumors or diffuse large B-cell lymphoma (DLBCL)
- **Part 2:** Non-small cell lung cancer (NSCLC)
- **Part 3:** A certain type of triple negative breast cancer (TNBC)
- **The Japanese Group as required by Japan's health authority:** Solid tumors or DLBCL

The participants could take part in this trial if they:

- Had their cancer get worse or come back after receiving standard treatment for their type of cancer
- Were not receiving certain medicines for cancer or other conditions
- Had not had certain other diseases in the last 2 years, such as other types of cancer

315 participants from 15 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:

NIR178 taken by mouth as capsules or tablets twice a day. This trial looked at 3 doses of NIR178:

- **80 milligrams (mg)**
- **160 mg**
- **240 mg**

PDR001 400 mg, given through a needle into a vein as an intravenous (IV) infusion every 4 weeks

Each participant received their treatment until their cancer got worse, the researchers thought they were not benefiting from the treatment, or they had certain side effects.

Researchers assigned participants to the treatment dose and schedule based on the part of the trial they were in. The next page shows the doses and schedules.

In this trial, the participants and clinical trial team knew what treatment each participant received. All participants received **NIR178** and **PDR001**.

What happened during this trial?

Before treatment — Up to 3 weeks

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

During treatment — Up to about 4 and a half years


315 participants received **NIR178** and **PDR001** in one of these parts:

Part 1

238 participants with solid tumors or DLBCL

Everyone received:

- **160 mg** or **240 mg** of NIR178 as capsules twice a day continuously (every day)
- **PDR001** once every 4 weeks

Part 2

62 participants with NSCLC

Participants were randomly assigned to 1 of 3 dosing schedules:

- **Schedule 1: 160 mg** of NIR178 twice a day continuously and **PDR001** once every 4 weeks
- **Schedule 2: 160 mg** dose of NIR178 twice a day for 2 weeks then a pause for 2 weeks before taking again and **PDR001** once every 4 weeks
- **Schedule 3: 160 mg** dose of NIR178 twice a day for 1 week then a pause for 1 week before taking again and **PDR001** once every 4 weeks

Part 3

6 participants with a certain type of TNBC

Everyone received:

- **160 mg** of NIR178 twice a day continuously as tablets
- **PDR001** once every 4 weeks

Japanese group

9 participants with solid tumors or DLBCL

Everyone received **80 mg**, **160 mg**, or **240 mg** of NIR178 twice a day continuously. They also received PDR001 once every 4 weeks:

- Right away, if receiving **240 mg** of NIR178
- After receiving NIR178 for 4 weeks, if receiving **80** or **160 mg** of NIR178

After treatment — Up to 5 months after treatment or until cancer got worse


Participants in every part had:

- 3 follow-up visits at the trial site or by phone call to check their health until 5 months after their last dose of **PDR001** or 1 month after their last dose of **NIR178**, whichever happened later
- Follow-up visits to check their cancer every 2 or 3 months until their cancer got worse

In Parts 1, 2, and 3, trial staff contacted participants to check their survival until at least 2 years after their first dose of trial treatment.

What were the main results of this trial?

How many participants had their tumors shrink or disappear?

Less than 30% of participants in each group in Parts 1, 2, and 3 had their tumors shrink or disappear after treatment. Because of the low numbers, the researchers concluded that none of the trial treatments were likely to have enough of an effect on the types of cancer in this trial.

To learn this, researchers looked at the participants' physical exams and imaging tests to measure the change in the size of participants' tumors.

The tables on the next page show the percent of participants in each Part who had their tumors shrink or disappear. Based on this trial's plan or changes to the plan, researchers did not look at:

- Certain groups in Part 1 with colon or head and neck cancers
- The Japanese group

Some participants in this trial had previously received an immunotherapy to treat cancer, also known as **immuno-oncology (IO)**. These participants were considered to have been **IO pretreated**.

Part 1: Participants who had their tumors shrink or disappear

Cancer type	Dose of NIR178 (given with 400 mg PDR001)	How many participants had their tumors shrink or disappear
Kidney	**160 mg**	**3 of 11** 27%
Kidney	**240 mg**	**3 of 12** 25%
IO pretreated kidney	**240 mg**	**0 of 11** 0%
Pancreas	**160 mg**	**0 of 14** 0%
Bladder	**160 mg**	**1 of 14** 7%
Head and neck	**160 mg**	**2 of 15** 13%
IO pretreated head and neck	**160 mg**	**0 of 11** 0%
Colon	**160 mg**	**0 of 27** 0%
Colon with a mutation	**160 mg**	**1 of 29** 3%
TNBC	**160 mg**	**3 of 30** 10%
IO pretreated skin	**160 mg**	**0 of 13** 0%
Prostate	**240 mg**	**0 of 15** 0%
DLBCL	**160 mg**	**2 of 13** 15%

Part 2: Participants who had their tumors shrink or disappear

Cancer type	Dose of NIR178 (given with 400 mg PDR001)	How many participants had their tumors shrink or disappear
NSCLC	**160 mg** (Schedule 1)	**2 of 22** 9%
NSCLC	**160 mg** (Schedule 2)	**0 of 20** 0%
NSCLC	**160 mg** (Schedule 3)	**2 of 20** 10%

Part 3: Participants who had their tumors shrink or disappear

Cancer type	Dose of NIR178 (given with 400 mg PDR001)	How many participants had their tumors shrink or disappear
Certain type of TNBC	**160 mg**	**1 of 6** 17% 

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 from the first dose of trial treatment to 5 months (150 days) after the last dose.

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.

Almost all the participants (304 of 315) had adverse events. 139 participants had adverse events that were considered serious. 112 participants died. The most common cause of death was cancer. 17 participants left the trial due to an adverse event. The researchers concluded there were no safety concerns for **NIR178** and **PDR001** in this trial.

How many participants had adverse events?

Part 1

Cancer type	Dose of NIR178 (given with 400 mg PDR001)	Number of participants who: Had at least 1 serious adverse event	Had at least 1 other adverse event	Died during the trial
Kidney	160 mg	3 of 11	10 of 11	4 of 11
Kidney, including pretreated	240 mg	7 of 23	22 of 23	6 of 23
Pancreas	160 mg	9 of 14	14 of 14	10 of 14
Bladder	160 mg	7 of 14	14 of 14	6 of 14
Head and neck, including IO pretreated	160 mg	16 of 26	25 of 26	8 of 26
IO pretreated head and neck	240 mg	5 of 12	12 of 12	4 of 12
Colon, all types	160 mg	28 of 58	52 of 58	22 of 58
TNBC	160 mg	14 of 30	29 of 30	9 of 30
Skin, including IO pretreated	160 mg	4 of 16	14 of 16	7 of 16
DLBCL	160 mg	7 of 13	13 of 13	9 of 13
DLBCL	240 mg	0 of 6	5 of 6	2 of 6
Prostate	240 mg	5 of 15	14 of 15	2 of 15

Part 2

Cancer type	Dose of NIR178 (given with 400 mg PDR001)	Number of participants who: Had at least 1 serious adverse event	Had at least 1 other adverse event	Died during the trial
NSCLC	160 mg (Schedule 1)	11 of 22	22 of 22	6 of 22
NSCLC	160 mg (Schedule 2)	9 of 20	16 of 20	4 of 20
NSCLC	160 mg (Schedule 3)	7 of 20	17 of 20	6 of 20

Part 3

Cancer type	Dose of NIR178 (given with 400 mg PDR001)	Number of participants who Had at least 1 serious adverse event	Had at least 1 other adverse event	Died during the trial
Certain type of TNBC	160 mg	3 of 6	6 of 6	4 of 6

Japanese group

Cancer type	Dose of NIR178 (given with 400 mg PDR001)	Number of participants who Had at least 1 serious adverse event	Had at least 1 other adverse event	Died during the trial
All cancer types	80 mg	2 of 3	3 of 3	2 of 3
All cancer types	160 mg	1 of 3	2 of 3	0 of 3
All cancer types	240 mg	1 of 3	3 of 3	1 of 3

What serious adverse events did the participants have?

139 participants had serious adverse events. 112 participants died. The most common cause of death was cancer.

The most common serious adverse events that happened in **10 or more** participants were:

- **Physical condition got worse** (General physical health deterioration)
- **Trouble breathing** (Dyspnea)

What other adverse events did the participants have?

293 participants had other adverse events.

The most common other adverse events that happened in **67 or more** participants were:

- **Feeling tired or having low energy** (Fatigue)
- **Feeling sick to the stomach** (Nausea)
- **Feeling less hungry than usual** (Decreased appetite)

What was learned from this trial?

Researchers learned about the effects of **NIR178** and **PDR001** in people with certain types of advanced or metastatic cancer. The sponsor stopped enrolling participants earlier than planned due to business reasons.

The researchers concluded that:

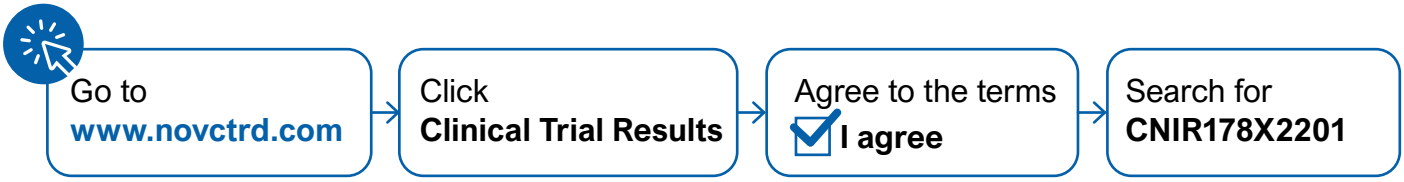
- None of the trial treatments were likely to have enough of an effect on any of the types of advanced or metastatic cancer in this trial
- The safety results in this trial were similar to other trials for **NIR178** and **PDR001**

When this summary was written, there were no plans for future trials of **NIR178** with **PDR001** in people with certain types of advanced or metastatic cancer.

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 these websites:

- clinicaltrials.gov – search using the number **NCT03207867**
- clinicaltrialsregister.eu/ctr-search/search – search using the number **2017-000241-49**

Other trials of **NIR178** and **PDR001** may also appear on the public websites above. When there, search for **NIR178** or **PDR001.**

Full clinical trial title: A Phase 2, multi-center, open label study of NIR178 in combination with PDR001 in patients with selected advanced solid tumors and non-Hodgkin lymphoma

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