NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the best dose of NIZ985 given alone and in combination with PDR001 in people with advanced solid cancer and lymphoma

Thank you!

Thank you to the participants who took part in the clinical trial for **advanced solid cancer and lymphoma**. Every participant helped the researchers learn more about **NIZ985**.

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: CNIZ985B12101
Drug studied: NIZ985
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?

Cancer is a disease where abnormal cells grow rapidly and affect the normal functioning of the body. **Advanced cancer** means the cancer has spread from its original site to other parts of the body. At this stage, cancer can be controlled but is unlikely to be cured.

Solid cancers are lumps of abnormal cells that are formed in different parts of the body, such as the breast, lungs, or skin.

Lymphoma is a type of cancer that starts in the body's lymphatic system and disturbs the immune system. It occurs when lymphocytes, a type of white blood cell, begin to grow out of control.

The advanced cancers studied in this trial include:

- Non-small Cell Lung Cancer (NSCLC)
- Melanoma (Skin Cancer)

Often, one medicine is not enough to treat cancer. Available treatments do not always work or may stop working after some time. When cancer comes back after treatment, it is called a **relapse**. One way of finding new treatments is to study a combination of cancer treatments.

The trial drug, **NIZ985**, is an immunotherapy that helps activate immune cells to attack the cancer cells and slow down cancer growth.

Researchers wanted to test increasing doses and treatment combinations in different groups of participants. The goal was to find the best dose of **NIZ985** to use with 2 other drugs:

- **PDR001**, also known as spartalizumab
- **VDT482**, also known as tislelizumab

The researchers also needed to carefully check all the medical problems that happened during the trial and identify any problems that could cause changes in dosing. This is what researchers call a **dose escalation trial**.

PDR001 and **VDT482** help the immune system fight cancer by blocking a protein called PD-1. PD-1 can prevent the immune system from killing cancer cells. These drugs are called checkpoint inhibitors (CPI).

VDT482 has been approved in China for **NSCLC**, liver cancer, bladder cancer and lymphoma.

In this trial, researchers wanted to test **NIZ985** in people with **advanced cancer** who had previously responded to CPI but had relapsed.

The main questions that researchers wanted to answer were:

- What was the best dose of NIZ985 that was safe for participants to receive alone or in combination with PDR001 or VDT482?
- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

How long was this trial?

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

The trial ended earlier than planned due to a decision by the sponsor. This decision was not due to any safety concerns with **NIZ985** or the other drugs.

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

Who was in this trial?

60 participants with advanced solid cancer and lymphoma received treatment in this trial. Participants' ages ranged from 25 to 79 years. Their average age was 57 years.

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

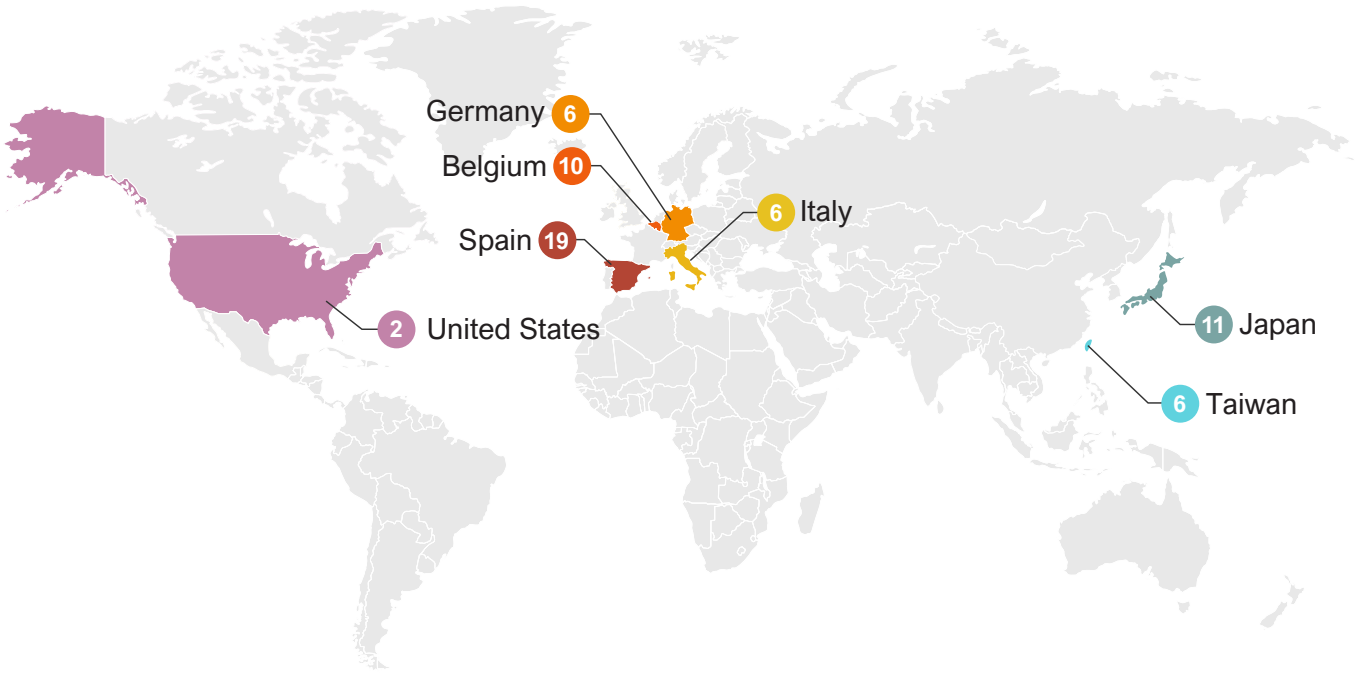
Gender

- 33 Men
- 27 Women

Race

- 42 White or Caucasian
- 18 Asian

60 participants from **7 countries** took part in the trial. 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 solid cancer** or **lymphoma** that did not respond to checkpoint inhibitor (CPI) treatments or surgery
- Did not take other drugs that worked similarly to **NIZ985**
- Did not have uncontrolled central nervous system cancer

What treatments did the participants receive?

Participants received treatment in 28-day (4-week) cycles. A cycle is a treatment period that is repeated.

The treatments in this trial were:

NIZ985: Researchers started with a low dose of **2 micrograms per kilogram of body weight (mcg/kg)** given as an injection under the skin, once a week for 3 weeks and one week off treatment. The dose was slowly increased in the next group of participants depending on how well it could be tolerated.

The doses of **NIZ985** that could be given to participants were **2, 4, 8, 12** or **16 mcg/kg**.

NIZ905 was also given with **PDR001** or **VDT482**.

PDR001: **400 milligrams (mg)**, given as an intravenous (IV) infusion, which is a slow drip through a tube directly into a vein, once every 4 weeks.

VDT482: **300 mg**, given as an IV infusion, once every 4 weeks.

In this trial, the participants, trial doctors, and trial staff knew which treatments and doses the participants received.

What happened during this trial?

Before treatment — Up to 28 days

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

During treatment — Up to 2 years and 10 months

The trial had **2 parts:**

Dose Escalation

In this part, trial doctors wanted to find out the best dose that was safe for participants to receive. They tested different doses and combinations of drugs for each of the 2 groups below.

Participants in Group 1a and Group 1b were started on the lowest dose of **NIZ985**. If there were no safety concerns after participants completed 4 weeks of treatment, a higher dose of **NIZ985** was tested in the next group of participants. The doses were increased until researchers found the best dose of **NIZ985** that was safe and well tolerated by participants.

Group 1a
NIZ985 alone

27 participants

- **NIZ985 2 mcg/kg - 3 participants**
- **NIZ985 4 mcg/kg - 4 participants**
- **NIZ985 8 mcg/kg - 6 participants**
- **NIZ985 12 mcg/kg - 7 participants**
- **NIZ985 16 mcg/kg - 7 participants**

Group 1b
NIZ985 + PDR001

29 participants

- **NIZ985 2 mcg/kg + PDR001 400 mg - 6 participants**
- **NIZ985 4 mcg/kg + PDR001 400 mg - 4 participants**
- **NIZ985 8 mcg/kg + PDR001 400 mg - 6 participants**
- **NIZ985 12 mcg/kg + PDR001 400 mg - 6 participants**
- **NIZ985 16 mcg/kg + PDR001 400 mg - 7 participants**

Participants received treatment in 28-day cycles. Based on all the available data, researchers chose the recommended dose of **NIZ985** to be given in the next part of the trial.

However, due to a business decision by the sponsor, researchers used **VDT482** instead of **PDR001** in combination with **NIZ985** in the dose expansion part. Since **VDT482** and **PDR001** work similarly, this change was not expected to have any impact on the participants' safety.

Participants from Group 1a were able to add **PDR001** to their treatment after they had their safety and cancer checked.

Dose Expansion

The dose expansion started only after the dose escalation ended. Based on all available data, researchers only conducted the dose expansion in participants with advanced NSCLC.

Group 2
NIZ985 12 mcg/kg **+** **VDT482** 300 mg

4 participants

After treatment — Up to the end of the trial

Participants were checked:

- For adverse events, for up to 5 months after the last dose.
- For their cancer status, until their cancer got worse or they started other cancer treatments, up to the end of the trial.

What were the main results of this trial?

What was the best dose of NIZ985 that was safe for participants to receive alone or in combination with PDR001 or VDT482?

Researchers concluded that **NIZ985 12 mcg/kg** was the best dose that was safe when given alone or in combination with **PDR001 400 mg**.
No conclusion could be drawn regarding the combination of **NIZ985** with **VDT482**.

To find the best dose that was safe, researchers closely monitored participants for **dose-limiting toxicities (DLTs)** during the 1st treatment cycle of Dose Escalation.

DLTs are medical problems that:

- The trial doctors think could be related to the trial treatment.
- Lead to a pause or lowering of the dose of treatment.

Researchers also checked how many participants had to pause their doses of **NIZ985**, **PDR001**, or **VDT482** during the treatment period. For **NIZ985**, doses could have also been reduced, while doses of **PDR001** or **VDT482** were kept the same.

The tables below show how many participants had **DLTs** and how many had to pause or reduce their dose of trial drugs during the treatment period. Only participants who received at least 2 doses of **NIZ985** during Cycle 1 were included in the DLT results.

Group 1a - NIZ985 alone

The table below shows how many participants had DLTs during Cycle 1.

Group 1a - NIZ985 alone					
NIZ985	**2 mcg/kg**	**4 mcg/kg**	**8 mcg/kg**	**12 mcg/kg**	**16 mcg/kg**
Participants who:	3 participants	4 participants	6 participants	7 participants	7 participants
Had DLTs	0 of 3 **(0%)**	0 of 4 **(0%)**	0 of 6 **(0%)**	1 of 7 **(14%)**	0 of 6 **(0%)**

The DLT observed in one participant from the **NIZ985 12 mcg/kg group** was tiredness (fatigue).

The table below shows how many participants had to pause or reduce their dose of trial drugs during the study. Some participants from Group 1a could receive **PDR001** after the 1st cycle of **NIZ985** treatment and after their cancer was checked.

Group 1a - NIZ985 alone					
NIZ985	**2 mcg/kg**	**4 mcg/kg**	**8 mcg/kg**	**12 mcg/kg**	**16 mcg/kg**
PDR001	**400 mg**	**400 mg**	**400 mg**	**400 mg**	**400 mg**
Participants who:	3 participants	4 participants	6 participants	7 participants	7 participants
Paused or reduced their dose of NIZ985	0 of 3 **(0%)**	2 of 4 **(50%)**	2 of 6 **(33%)**	4 of 7 **(57%)**	5 of 7 **(71%)**
Paused their dose of PDR001	--	0 of 4 **(0%)**	2 of 3 **(67%)**	0 of 2 **(0%)**	1 of 4 **(25%)**

Group 1b - NIZ985 + PDR001

The table below shows how many participants had DLTs during Cycle 1.

Group 1b - NIZ985 + PDR001					
NIZ985	**2 mcg/kg**	**4 mcg/kg**	**8 mcg/kg**	**12 mcg/kg**	**16 mcg/kg**
PDR001	**400 mg**	**400 mg**	**400 mg**	**400 mg**	**400 mg**
Participants who:	4 participants	4 participants	6 participants	6 participants	6 participants
Had DLTs	0 of 4 **(0%)**	0 of 4 **(0%)**	0 of 6 **(0%)**	1 of 6 **(17%)**	1 of 6 **(17%)**

The DLTs observed in Group 1b are as follows:

- One participant from the **NIZ985 12 mcg/kg** + **PDR001** group had injection site reactions and inflammation of the skin with blisters (dermatitis bullous).
- One participant from the **NIZ985 16 mcg/kg** + **PDR001** group had injection site reactions.

Injection site reactions involve redness, swelling, or pain and usually go away after a short time.

The table below shows how many participants had to pause or reduce their dose of trial drugs during the study.

Group 1b - NIZ985 + PDR001					
NIZ985	**2 mcg/kg**	**4 mcg/kg**	**8 mcg/kg**	**12 mcg/kg**	**16 mcg/kg**
PDR001	**400 mg**	**400 mg**	**400 mg**	**400 mg**	**400 mg**
Participants who:	6 participants	4 participants	6 participants	6 participants	7 participants
Paused or reduced their dose of NIZ985	2 of 6 **(33%)**	0 of 4 **(0%)**	3 of 6 **(50%)**	2 of 6 **(33%)**	5 of 7 **(71%)**
Paused or reduced* their dose of PDR001	2 of 6 **(33%)**	0 of 4 **(0%)**	2 of 6 **(33%)**	1 of 6 **(17%)**	1 of 7 **(14%)**

While **PDR001 doses were not supposed to be reduced, 1 participant had their dose reduced by mistake.*

Researchers decided that a dose of **16 mcg/kg NIZ985** was not tolerated well enough. They chose **12 mcg/kg NIZ985** to be used in the Dose Expansion part of the trial.

Due to a business decision by the sponsor, researchers used **VDT482** instead of **PDR001** in combination with **NIZ985** in the dose expansion part.

Group 2 - NIZ985 + VDT482

The table below shows how many participants had to pause or reduce their dose of trial drugs during the study.

Group 2 - NIZ985 + VDT482	
NIZ985	**12 mcg/kg**
VDT482	**300 mg**
Participants who:	4 participants
Paused or reduced their dose of NIZ985	3 of 4 **(75%)**
Paused their dose of VDT482	3 of 4 **(75%)**

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events 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 start of treatment up to 5 months after the last 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.

All 60 participants had adverse events.

- **21 participants** had adverse events that were considered serious.
- **6 participants** left the trial due to an adverse event.
- **18 participants** died due to any cause, including participants who died from their disease.

How many participants had adverse events?

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

Summary of adverse events

	NIZ985 2 mcg/kg	NIZ985 4 mcg/kg	NIZ985 8 mcg/kg	NIZ985 12 mcg/kg	NIZ985 16 mcg/kg	NIZ985 2 mcg/kg + PDR001 400 mg	NIZ985 4 mcg/kg + PDR001 400 mg	NIZ985 8 mcg/kg + PDR001 400 mg	NIZ985 12 mcg/kg + PDR001 400 mg	NIZ985 16 mcg/kg + PDR001 400 mg	NIZ985 12 mcg/kg + VDT482 300 mg
Participants who:	3 participants	4 participants	6 participants	7 participants	7 participants	6 participants	4 participants	6 participants	6 participants	7 participants	4 participants
Had at least 1 serious adverse event	1 of 3 (33%)	1 of 4 (25%)	1 of 6 (17%)	3 of 7 (43%)	1 of 7 (14%)	2 of 6 (33%)	1 of 4 (25%)	2 of 6 (33%)	2 of 6 (33%)	3 of 7 (43%)	4 of 4 (100%)
Had at least 1 other non serious adverse event	3 of 3 (100%)	4 of 4 (100%)	6 of 6 (100%)	7 of 7 (100%)	7 of 7 (100%)	6 of 6 (100%)	4 of 4 (100%)	6 of 6 (100%)	6 of 6 (100%)	7 of 7 (100%)	4 of 4 (100%)
Left the trial due to an adverse event	0 of 3 (0%)	0 of 4 (0%)	1 of 6 (17%)	0 of 7 (0%)	0 of 7 (0%)	2 of 6 (33%)	0 of 4 (0%)	0 of 6 (0%)	0 of 6 (0%)	3 of 7 (43%)	0 of 4 (0%)
Died	1 of 3 (33%)	3 of 4 (75%)	2 of 6 (33%)	2 of 7 (29%)	0 of 7 (0%)	2 of 6 (33%)	2 of 4 (50%)	1 of 6 (17%)	1 of 6 (17%)	3 of 7 (43%)	1 of 4 (25%)

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.

Serious adverse events	NIZ985 2 mcg/kg	NIZ985 4 mcg/kg	NIZ985 8 mcg/kg	NIZ985 12 mcg/kg	NIZ985 16 mcg/kg	NIZ985 2 mcg/kg + PDR001 400 mg	NIZ985 4 mcg/kg + PDR001 400 mg	NIZ985 8 mcg/kg + PDR001 400 mg	NIZ985 12 mcg/kg + PDR001 400 mg	NIZ985 16 mcg/kg + PDR001 400 mg	NIZ985 12 mcg/kg + VDT482 300 mg
Participants who:	3 participants	4 participants	6 participants	7 participants	7 participants	6 participants	4 participants	6 participants	6 participants	7 participants	4 participants
Injection site reaction	0 of 3 (0%)	0 of 4 (0%)	0 of 6 (0%)	0 of 7 (0%)	0 of 7 (0%)	0 of 6 (0%)	0 of 4 (0%)	0 of 6 (0%)	1 of 6 (17%)	1 of 7 (14%)	1 of 4 (25%)
A condition causing fever, vomiting, shortness of breath, headache and low blood pressure Cytokine release syndrome	0 of 3 (0%)	0 of 4 (0%)	0 of 6 (0%)	0 of 7 (0%)	0 of 7 (0%)	0 of 6 (0%)	0 of 4 (0%)	0 of 6 (0%)	1 of 6 (17%)	1 of 7 (14%)	0 of 4 (0%)
Lung infection Pneumonia	0 of 3 (0%)	0 of 4 (0%)	0 of 6 (0%)	0 of 7 (0%)	0 of 7 (0%)	1 of 6 (17%)	0 of 4 (0%)	0 of 6 (0%)	0 of 6 (0%)	1 of 7 (14%)	0 of 4 (0%)
Breathing difficulty Dyspnoea	0 of 3 (0%)	0 of 4 (0%)	0 of 6 (0%)	0 of 7 (0%)	0 of 7 (0%)	0 of 6 (0%)	0 of 4 (0%)	0 of 6 (0%)	1 of 6 (17%)	0 of 7 (0%)	1 of 4 (25%)
Lack of oxygen in body tissues Hypoxia	0 of 3 (0%)	0 of 4 (0%)	0 of 6 (0%)	1 of 7 (14%)	0 of 7 (0%)	0 of 6 (0%)	0 of 4 (0%)	0 of 6 (0%)	1 of 6 (17%)	0 of 7 (0%)	0 of 4 (0%)

What other non serious adverse events did the participants have?

The table below shows the other non serious adverse events that happened in at least a total of 15 participants.

Other non serious adverse events

	NIZ985 2 mcg/kg	NIZ985 4 mcg/kg	NIZ985 8 mcg/kg	NIZ985 12 mcg/kg	NIZ985 16 mcg/kg	NIZ985 2 mcg/kg + PDR001 400 mg	NIZ985 4 mcg/kg + PDR001 400 mg	NIZ985 8 mcg/kg + PDR001 400 mg	NIZ985 12 mcg/kg + PDR001 400 mg	NIZ985 16 mcg/kg + PDR001 400 mg	NIZ985 12 mcg/kg + VDT482 300 mg
Participants who:	3 participants	4 participants	6 participants	7 participants	7 participants	6 participants	4 participants	6 participants	6 participants	7 participants	4 participants
Injection site reaction	3 of 3 (100%)	1 of 4 (25%)	4 of 6 (67%)	6 of 7 (86%)	6 of 7 (86%)	5 of 6 (83%)	2 of 4 (50%)	6 of 6 (100%)	6 of 6 (100%)	4 of 7 (57%)	3 of 4 (75%)
Fever Pyrexia	1 of 3 (33%)	2 of 4 (50%)	5 of 6 (83%)	6 of 7 (86%)	6 of 7 (86%)	3 of 6 (50%)	2 of 4 (50%)	5 of 6 (83%)	4 of 6 (67%)	4 of 7 (57%)	2 of 4 (50%)
Increased liver protein Alanine aminotransferase increased	1 of 3 (33%)	0 of 4 (0%)	0 of 6 (0%)	3 of 7 (43%)	3 of 7 (43%)	0 of 6 (0%)	1 of 4 (25%)	2 of 6 (33%)	2 of 6 (33%)	3 of 7 (43%)	2 of 4 (50%)
Increased liver protein Aspartate aminotransferase increased	1 of 3 (33%)	0 of 4 (0%)	0 of 6 (0%)	2 of 7 (29%)	3 of 7 (43%)	0 of 6 (0%)	0 of 4 (0%)	2 of 6 (33%)	3 of 6 (50%)	3 of 7 (43%)	2 of 4 (50%)
Tiredness Fatigue	0 of 3 (0%)	2 of 4 (50%)	3 of 6 (50%)	1 of 7 (14%)	0 of 7 (0%)	3 of 6 (50%)	1 of 4 (25%)	3 of 6 (50%)	0 of 6 (0%)	1 of 7 (14%)	1 of 4 (25%)

What was learned from this trial?

This trial helped researchers learn about the safety of **NIZ985** in people with advanced solid cancer and lymphoma.

The researchers concluded that:

- **NIZ985 12 mcg/kg** was the recommended dose for further testing, both alone or in combination with **PDR001 400 mg**. Since **PDR001** and **VDT482** work similarly, **VDT482** was used in the Dose Expansion phase of the trial.
- There were no unexpected safety concerns with **NIZ985** given alone or in combination with **PDR001** or **VDT482**.
- Since the trial ended earlier than planned, no conclusion could be drawn regarding the combination of **NIZ985** with **VDT482**.

At the time this summary was written, there were no further studies with **NIZ985** 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:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Agree to the terms **I agree** → Search for **CNIZ985B12101**

For more information about this trial, go to the website below:

- **clinicaltrials.gov** – search using the number **NCT04261439**

Other studies with NIZ985 appear on the public website above. When there, search for NIZ985.

Full clinical trial title: A Phase I/Ib Study of Subcutaneous Recombinant Human NIZ985 ((hetIL-15)(IL-15/sIL-15Rα)) in Combination With Spartalizumab in Patients With Check Point Inhibitor (CPI) Relapsed Advanced Solid Tumors and Lymphoma

NOVARTIS

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.novartis.com/clinicaltrials