NOVARTIS

# Clinical Trial Results Summary

## A clinical trial to learn about the safety of NZV930 given alone and in combination with PDR001 and/or NIR178 in people with advanced cancer

## Thank you!

Thank you to the participants who took part in the clinical trial for advanced cancer. Every participant helped the researchers learn more about **NZV930**.

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:** CNZV930X2101
**Drug studied:** NZV930
**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 that cancer has spread from its original site and cannot be controlled or cured by standard treatments. Advanced cancer is also called end-stage or terminal cancer.

The advanced cancers studied in this trial include:

- Non-small Cell Lung Cancer (NSCLC)
- Triple Negative Breast Cancer (TNBC)
- Pancreatic Ductal Adenocarcinoma (PDAC)
- Colorectal Cancer Microsatellite Stable (MSS)
- Ovarian Cancer
- Renal Cell Carcinoma (RCC)
- Metastatic Castration Resistant Prostate Cancer (mCRPC)

**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. Often, one medicine is not enough to treat cancer and treatments do not always work or may stop working after some time. As a result, there is a constant need to find new treatments. One way of finding new treatments is to study a combination of cancer treatments.

The trial drug, **NZV930**, is an immunotherapy that helps the immune system to attack the cancer cells and slow down cancer growth.

Because cancer treatment often requires more than one drug, researchers also wanted to test the safety of different combinations of treatment. They studied 2 other immunotherapies – **PDR001 and NIR178 – in combination with NZV930.** None of the 3 drugs tested in this trial are currently approved for the treatment of advanced cancer.

**The main questions that researchers wanted to answer were:**

- What was the highest dose of NZV930 that was safe for participants to receive alone or in different combinations with PDR001 and/or NIR178?
- How many participants had to stop or reduce their dose of NZV930, PDR001, or NIR178 during the treatment period?
- 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 July 2018 and ended in October 2022. It was planned for the participants to be in the trial as long as they continued to receive benefit from the trial treatment.

The trial ended earlier than planned because the results showed there was a low chance of reaching the desired effect in people with the studied diseases. The decision was not due to any safety concerns with NZV930 or the other trial 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?

**127 participants** with advanced cancer received treatment in this trial.
Participants' ages ranged from 31 to 80 years. Their average age was 57 years.

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

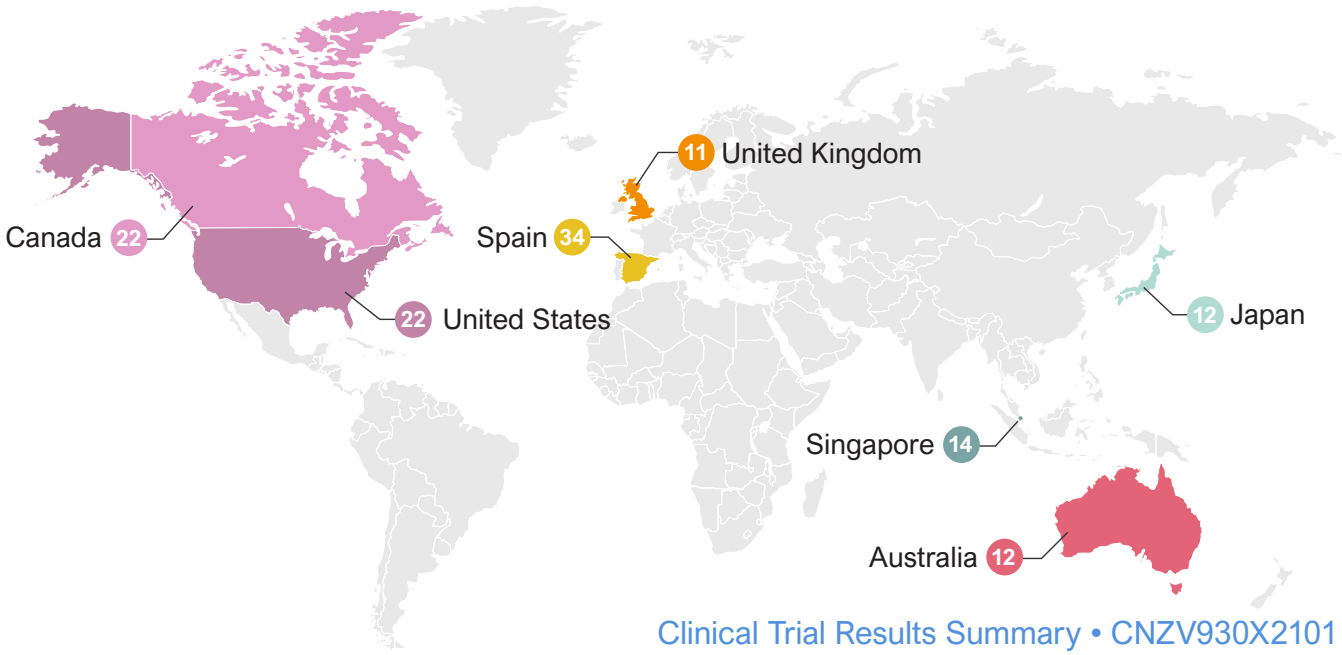
**Gender**

| | |
|---|---|
| 49 Men | 78 Women |

**Race**

| | | |
|---|---|---|
| 90 White | 32 Asian | 3 Black or African American |
| 1 Multiple | 1 Missing | |

127 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 cancer that did not respond to multiple treatments.

Participants **could not take part** in this trial if they:

- Had uncontrolled cancer that spread to the brain and required ongoing treatment.

# What treatments did the participants receive?

Researchers studied the following immunotherapy treatments, which were given in 28-day cycles:

**NZV930:** 60, 200, 400, 600, or 1000 milligrams (mg), given alone as a slow injection into a vein, every 2 weeks.
NZV930 was also given with PDR001 and/or NIR178.

**PDR001:** 400 mg, given as a slow injection into a vein, every 4 weeks.

**NIR178:** 80, 160, or 240 mg, provided as capsules, taken by mouth twice a day.

Participants received the treatments in a 28-day cycle that can be repeated as needed.

A **cycle** is a pre-defined treatment period, that can be repeated as needed, and during which the treatment is given in a pre-determined frequency.

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 21 days

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

## During treatment

Up to 90 weeks

The trial had **2 parts:**

### Dose Escalation

In this part of the trial, trial doctors wanted to find out the highest dose that was safe for participants to receive. They tested different doses and combination of drugs. For each of the groups below, increasing doses were tested. These doses were increased until researchers found the highest dose that was safe for participants to receive.

**NZV930 alone** — 24 participants

- NZV930 60 mg
- NZV930 200 mg
- NZV930 400 mg
- NZV930 600 mg
- NZV930 1000 mg

**NVZ930 + PDR001** — 18 participants

- NZV930 200 mg + PDR001 400 mg
- NZV930 400 mg + PDR001 400 mg
- NZV930 600 mg + PDR001 400 mg

**NVZ930 + NIR178** — 28 participants

- NZV930 200 mg + NIR178 80 mg
- NZV930 200 mg + NIR178 160 mg
- NZV930 400 mg + NIR178 160 mg
- NZV930 600 mg + NIR178 160 mg
- NZV930 600 mg + NIR178 240 mg

**NVZ930 + PDR001 + NIR178** — 35 participants

- NZV930 200 mg + PDR001 400 mg + NIR178 80 mg
- NZV930 200 mg + PDR001 400 mg + NIR178 160 mg
- NZV930 400 mg + PDR001 400 mg + NIR178 160 mg
- NZV930 600 mg + PDR001 400 mg + NIR178 160 mg
- NZV930 600 mg + PDR001 400 mg + NIR178 240 mg
- NZV930 600 mg (step-up) + PDR001 400 mg + NIR178 240 mg

Participants received treatment in 28-day cycles. Based on all the available data, researchers chose the ideal dose combination of **NVZ930,** PDR001, and **NIR178** to use for the next part of the trial.

### Dose Expansion

In this part of the trial, trial doctors tested one of the safe dose and combination of drugs, which was determined in the dose escalation part. Based on all available data from this and other trials, researchers only conducted the dose expansion in participants with pancreatic ductal adenocarcinoma (PDAC) and ovarian cancer with the triple combination.

**NVZ930, 600 mg + PDR001, 400 mg + NIR178, 240 mg** — 22 participants

## After treatment

Up to 150 days after last dose

Participants were:

- Checked for adverse events by telephone call or follow-up visit up to 150 days after the last treatment dose.
- Followed up until their cancer worsened or they started taking other cancer treatments or they died.

# What were the main results of this trial?

## What was the highest dose of NZV930 that was safe for participants to receive alone or in different combinations with PDR001 and/or NIR178?

Researchers concluded that **NZV930 600 mg** was the highest dose that was safe when given alone or in combination with **PDR001 400 mg** and **NIR178 240 mg.**

To find the highest dose that was safe, researchers closely monitored participants for **dose-limiting toxicities (DLTs)** during the 1st treatment cycle of Dose Escalation. A **DLT** is an adverse event that occurs at the start of the treatment and is serious enough to prevent an increase in the dose of that treatment.

Researchers also checked how many participants had to stop or reduce their dose of NZV930, PDR001, or NIR178 during the treatment period.

The tables below show how many participants had **DLTs** and how many had to stop or reduce their dose of trial drugs during the treatment period. Some participants did not complete the 1st treatment cycle and were not included in the **DLT** results.

**Group 1 - NVZ930 alone**

| **NZV930** | **60 mg** | **200 mg** | **400 mg** | **600 mg** | **1000 mg** |
|---|---|---|---|---|---|
| **Participants who:** | 3 participants | 4 participants | 6 participants | 9 participants | 2 participants |
| Had DLTs | 0 of 3 **(0%)** | 0 of 4 **(0%)** | 0 of 6 **(0%)** | 0 of 8 **(0%)** | 1 of 2 **(50%)** |
| Stopped taking or reduced their dose of NZV930 | 0 of 3 **(0%)** | 0 of 4 **(0%)** | 0 of 6 **(0%)** | 0 of 9 **(0%)** | 0 of 2 **(0%)** |

**Group 2a - NVZ930 + PDR001**

| **NZV930** | **200 mg** | **400 mg** | **600 mg** |
|---|---|---|---|
| **PDR001** | **400 mg** | **400 mg** | **400 mg** |
| **Participants who:** | 6 participants | 6 participants | 6 participants |
| Had DLTs | 0 of 5 **(0%)** | 1 of 6 **(17%)** | 1 of 6 **(17%)** |
| Stopped taking or reduced their dose of NZV930 | 0 of 6 **(0%)** | 0 of 6 **(0%)** | 0 of 6 **(0%)** |
| Stopped taking or reduced their dose of PDR001 | 0 of 6 **(0%)** | 0 of 6 **(0%)** | 1 of 6 **(17%)** |

| Group 2b - NVZ930 + NIR178 | | | | | |
|---|---|---|---|---|---|
| **NZV930** | **200 mg** | **200 mg** | **400 mg** | **600 mg** | **600 mg** |
| **NIR178** | **80 mg** | **160 mg** | **160 mg** | **160 mg** | **240 mg** |
| **Participants who:** | 5 participants | 6 participants | 5 participants | 6 participants | 6 participants |
| Had DLTs | 0 of 4 **(0%)** | 0 of 6 **(0%)** | 0 of 4 **(0%)** | 0 of 5 **(0%)** | 0 of 5 **(0%)** |
| Stopped taking or reduced their dose of NZV930 | 0 of 5 **(0%)** | 0 of 6 **(0%)** | 0 of 5 **(0%)** | 0 of 6 **(0%)** | 1 of 6 **(17%)** |
| Stopped taking or reduced their dose of NIR178 | 0 of 5 **(0%)** | 2 of 6 **(33%)** | 1 of 5 **(20%)** | 3 of 6 **(50%)** | 2 of 6 **(33%)** |

| Group 3 - NVZ930 + PDR001 + NIR178 | | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Dose Escalation** | | | | | | **Dose Expansion** |
| **NZV930** | **200 mg** | **200 mg** | **400 mg** | **600 mg** | **600 mg** | **600 mg (Step-up)*** | **600 mg** |
| **PDR001** | **400 mg** | **400 mg** | **400 mg** | **400 mg** | **400 mg** | **400 mg** | **400 mg** |
| **NIR178** | **80 mg** | **160 mg** | **160 mg** | **160 mg** | **240 mg** | **240 mg** | **240 mg** |
| **Participants who:** | 7 participants | 5 participants | 6 participant | 6 participants | 6 participants | 5 participants | 22 participants |
| Had DLTs | 1 of 5 **(20%)** | 1 of 5 **(20%)** | 1 of 6 **(17%)** | 0 of 6 **(0%)** | 1 of 6 **(17%)** | 0 of 5 **(0%)** | - |
| Stopped taking or reduced their dose of NZV930 | 0 of 7 **(0%)** | 1 of 5 **(20%)** | 1 of 6 **(17%)** | 1 of 6 **(17%)** | 0 of 6 **(0%)** | 1 of 5 **(20%)** | 3 of 22 **(14%)** |
| Stopped taking or reduced their dose of PDR001 | 0 of 7 **(0%)** | 1 of 5 **(20%)** | 1 of 6 **(17%)** | 1 of 6 **(17%)** | 0 of 6 **(0%)** | 1 of 5 **(20%)** | 2 of 22 **(9%)** |
| Stopped taking or reduced their dose of NIR178 | 1 of 7 **(14%)** | 2 of 5 **(40%)** | 3 of 6 **(50%)** | 3 of 6 **(50%)** | 1 of 6 **(17%)** | 0 of 5 **(0%)** | 6 of 22 **(27%)** |

***NZV930 600 mg (Step-up)**
For this group, participants received increasing doses of NZV930, starting from 200 mg until 600 mg.

# 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 150 days after the last dose of 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.

All 127 participants had adverse events.

- 56 participants had adverse events that were considered serious.
- 58 participants died due to any cause, including participants who died from their disease.
- 13 participants left the trial due to an adverse event.

## How many participants had adverse events?

Researchers tested different doses and combinations of drugs during **Dose Escalation** and based on all the available data, an ideal dose combination of NZV930, PDR001, and NIR178 was used in the **Dose Expansion.**

There were 5 participants from the Dose Escalation, who received the same doses of NVZ930, PDR001 and NIR178 as given in the Dose Expansion. For these results, they were reported in the Dose Expansion group. The table below shows how many participants had adverse events during the treatment and the follow-up period.

| | Dose Escalation | | | | Dose Expansion |
|---|---|---|---|---|---|
| **Participants who:** | **NVZ930 alone** 24 participants | **NVZ930 + PDR001** 18 participants | **NVZ930 + NIR178** 28 participants | **NVZ930 + PDR001 + NIR178** 30 participants | **NVZ930 + PDR001 + NIR178** 27 participants |
| Had at least 1 adverse event | 24 of 24 **(100%)** | 18 of 18 **(100%)** | 28 of 28 (100%) | 30 of 30 (100%) | 27 of 27 (100%) |
| Had at least 1 serious adverse event | 10 of 24 **(42%)** | 9 of 18 **(50%)** | 12 of 28 (43%) | 13 of 30 (43%) | 12 of 27 (44%) |
| Left the trial due to an adverse event | 2 of 24 **(8%)** | 2 of 18 **(11%)** | 1 of 28 (4%) | 3 of 30 (10%) | 5 of 27 (19%) |
| Died during the trial | 9 of 24 **(38%)** | 10 of 18 **(56%)** | 16 of 28 (57%) | 14 of 30 (47%) | 9 of 27 (33%) |

Many participants died due to their cancer during the follow-up period.

# What serious adverse events did the participants have?

A total of 56 participants who received at least 1 dose of trial drug had serious adverse events. The table below shows the most common serious adverse events that happened in at least 3 participants.

| | Dose Escalation | | | | Dose Expansion |
|---|---|---|---|---|---|
| | **NVZ930 alone** 24 participants | **NVZ930 + PDR001** 18 participants | **NVZ930 + NIR178** 28 participants | **NVZ930 + PDR001 + NIR178** 30 participants | **NVZ930 + PDR001 + NIR178** 27 participants |
| **Headache** | 3 of 24 **(13%)** | 2 of 18 **(11%)** | 2 of 28 **(7%)** | 0 of 30 **(0%)** | 1 of 27 **(4%)** |
| **Lung infection** Pneumonia | 1 of 24 **(4%)** | 1 of 18 **(6%)** | 3 of 28 **(11%)** | 2 of 30 **(7%)** | 1 of 27 **(4%)** |
| **Fever** Pyrexia | 2 of 24 **(8%)** | 2 of 18 **(11%)** | 1 of 28 **(4%)** | 0 of 30 **(0%)** | 2 of 27 **(7%)** |
| **Nausea** | 1 of 24 **(4%)** | 1 of 18 **(6%)** | 1 of 28 **(4%)** | 0 of 30 **(0%)** | 1 of 27 **(4%)** |
| **Fluid around the lungs** Pleural effusion | 0 of 24 **(0%)** | 1 of 18 **(6%)** | 1 of 28 **(4%)** | 0 of 30 **(0%)** | 1 of 27 **(4%)** |
| **Worsening of cancer** Disease progression | 0 of 24 **(0%)** | 0 of 18 **(0%)** | 2 of 28 **(7%)** | 1 of 30 **(3%)** | 0 of 27 **(0%)** |
| **Vomiting** | 2 of 24 **(8%)** | 1 of 18 **(6%)** | 0 of 28 **(0%)** | 0 of 30 **(0%)** | 0 of 27 **(0%)** |
| **Stomach pain** Abdominal pain | 1 of 24 **(4%)** | 1 of 18 **(6%)** | 0 of 28 **(0%)** | 1 of 30 **(3%)** | 0 of 27 **(0%)** |

# What other adverse events did the participants have?

All the 127 participants who received at least 1 dose of trial drug had other adverse events. The table below shows the other adverse events that happened in at least 20 participants.

| | Dose Escalation | | | | Dose Expansion |
|---|---|---|---|---|---|
| | **NVZ930 alone** 24 participants | **NVZ930 + PDR001** 18 participants | **NVZ930 + NIR178** 28 participants | **NVZ930 + PDR001 + NIR178** 30 participants | **NVZ930 + PDR001 + NIR178** 27 participants |
| **Headache** | 16 of 24 **(67%)** | 11 of 18 **(61%)** | 16 of 28 **(64%)** | 21 of 30 (70%) | 21 of 27 (78%) |
| **Nausea** | 11 of 24 **(46%)** | 5 of 18 **(28%)** | 16 of 28 **(61%)** | 12 of 30 (40%) | 17 of 27 (63%) |
| **Vomiting** | 13 of 24 **(54%)** | 4 of 18 **(22%)** | 16 of 28 **(46%)** | 13 of 30 (43%) | 9 of 27 (33%) |
| **Fever** Pyrexia | 9 of 24 **(38%)** | 7 of 18 **(39%)** | 16 of 28 **(36%)** | 8 of 30 (27%) | 13 of 27 (48%) |
| **Fatigue** | 7 of 24 **(29%)** | 5 of 18 **(28%)** | 16 of 28 **(21%)** | 11 of 30 (37%) | 7 of 27 (26%) |
| **Decreased appetite** | 7 of 24 **(29%)** | 4 of 18 **(22%)** | 16 of 28 **(32%)** | 5 of 30 (17%) | 6 of 27 (22%) |
| **Constipation** | 5 of 24 **(21%)** | 5 of 18 **(28%)** | 16 of 28 **(18%)** | 5 of 30 (17%) | 8 of 27 (30%) |
| **Increased liver protein (abnormal liver test)** Aspartate aminotransferase increased | 4 of 24 **(17%)** | 4 of 18 **(22%)** | 16 of 28 **(11%)** | 7 of 30 (23%) | 6 of 27 (22%) |
| **Weakness** Asthenia | 2 of 24 **(8%)** | 1 of 18 **(6%)** | 16 of 28 **(32%)** | 4 of 30 (13%) | 7 of 27 (26%) |
| **Stomach pain** Abdominal pain | 4 of 24 **(17%)** | 2 of 18 **(11%)** | 16 of 28 **(11%)** | 7 of 30 (23%) | 7 of 27 (26%) |
| **Diarrhea** | 2 of 24 **(8%)** | 3 of 18 **(17%)** | 16 of 28 **(14%)** | 4 of 30 (13%) | 7 of 27 (26%) |

# What was learned from this trial?

This trial helped researchers learn about the safety and effects of NZV930 given alone and in combination with other immunotherapies, PDR001 and/or NIR178 in people with advanced cancer.

The researchers concluded that:

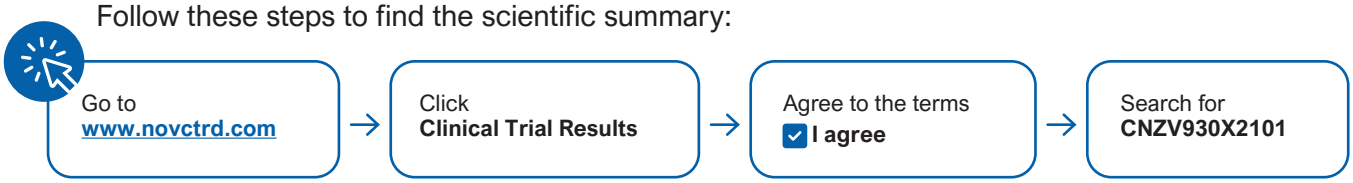
- NVZ930 had an acceptable safety when given in increasing doses along with other medications to manage headaches, fever, nausea, and vomiting.
- NZV930 600 mg was the recommended dose for further testing, both alone or in combination with PDR001 400 mg and NIR178 240 mg.

There are further studies with NZV930 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 **NCT03549000**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2018-000153-51**

Other studies with NZV930 appear on the public websites above. When there, search for NZV930.

**Full clinical trial title:** A Phase I/Ib, Open-Label, Multi-center Study of NZV930 as a Single Agent and in Combination with PDR001 and/or NIR178 in Patients with Advanced Malignancies.

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