NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of NIS793 with or without PDR001 in people with a certain type of pancreatic cancer

Thank you!

Thank you to the participants who took part in the clinical trial for **metastatic pancreatic ductal adenocarcinoma (mPDAC)**. Every participant helped the researchers learn more about the trial drug **NIS793** with or without **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: CNIS793B12201

Novartis drugs studied: **NIS793** and **PDR001**, also called 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 **NIS793 and standard treatment**, with or without **PDR001**, compared to **standard treatment alone** for people with metastatic pancreatic ductal adenocarcinoma (mPDAC).

Metastatic pancreatic ductal adenocarcinoma (mPDAC) is cancer that started in the tubes (ducts) of the pancreas that carry digestive juices to the small intestine. Metastatic means the cancer spread from where it started to other parts of the body.

mPDAC can be surrounded by tissues called the **tumor microenvironment** that may stop cancer treatments from working to kill cancer cells. The tumor microenvironment includes the cells, proteins, and blood vessels that surround and feed a tumor, which can help it grow and spread.

NIS793 is a trial drug developed to block a protein called transforming growth factor beta (TGFβ). Researchers think that blocking this protein may slow down or stop tumor microenvironment tissues from growing around mPDAC tumors. By blocking tissues in the tumor microenvironment, **NIS793** may stop mPDAC from growing and allow other cancer treatments, such as chemotherapy and immunotherapy, to kill cancer cells.

In this trial, researchers used a **recommended dose** based on previous trials of **NIS793** in people with mPDAC and other types of cancer. The recommended dose is the dose found to have effects on a disease while minimizing the risk (chance) of medical problems to the participants.

A **standard treatment** for mPDAC is gemcitabine and nab-paclitaxel, which are types of **chemotherapy**. Although **standard treatment** may shrink the tumors, it may stop working and the cancer may get worse over time.

PDR001, also called spartalizumab, is a trial drug. It is an **immunotherapy** that blocks a protein called programmed cell death protein 1 (PD-1). PD-1 prevents a cell in the immune system, called a T cell, from killing cancer cells. By blocking PD-1, **PDR001** may help T cells become more active to kill cancer cells.

What is immunotherapy and chemotherapy?

- **Immunotherapy** is a type of treatment that helps the immune system to kill cancer cells
- **Chemotherapy** is a type of treatment that kills cancer cells or stops them from growing

Trial drug

PDR001 also called spartalizumab

Pronounced as

spar-ta-liz-ue-mab

The trial's purpose was to answer these main questions:

- Was the recommended dose of NIS793 and standard treatment with PDR001 confirmed for participants with mPDAC?
- Did participants who received NIS793 and standard treatment, with or without PDR001, live longer than those who received standard treatment alone?
- 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 October 2020 and ended in May 2024. The participants could continue in this trial for as long as they were benefiting. On average, each participant was in the trial for about 5 months.

This trial was designed to have 2 parts:

- **Part 1:** A small group of participants received a recommended dose of **NIS793 and standard treatment with PDR001**, so researchers could confirm the dose to use in Part 2.
- **Part 2:** Researchers planned to compare the effects of **NIS793 and standard treatment**, with and without **PDR001**, to **standard treatment alone** in more participants with mPDAC. However, this part was not completed as planned.

In July 2023, the sponsor decided to stop giving **NIS793** to participants after reviewing available results from another trial of **NIS793** in participants with mPDAC. The decision was because adding **NIS793** to **standard treatment** for people with mPDAC was not beneficial.

Participants could continue receiving **standard treatment alone** until March 2024 when the trial was ended.

Who was in this trial?

164 participants with mPDAC were in this trial – 97 men and 67 women. Participants' ages ranged from 27 to 82 years. Their average age was 64 years.

The number of participants by race is shown below.

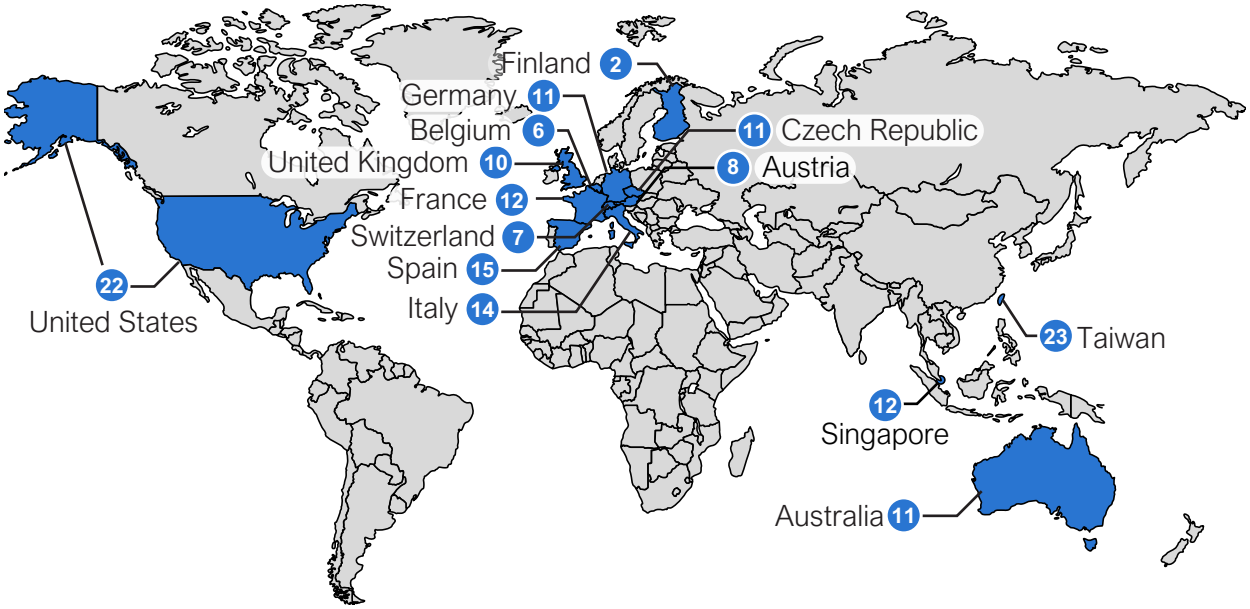
Race

41 Asian	5 Black or African American
116 White	2 Unknown

The participants could take part in this trial if they:

- Had mPDAC that had not yet been treated
- Could not have surgery to remove the cancer
- Did not have certain heart conditions

164 participants from 14 countries were in this trial. 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 given in 4-week cycles. A **cycle** is a treatment period that is repeated. The treatments in this trial were:

NIS793 – 2100 milligrams (mg) given through a needle in a vein called an intravenous (IV) infusion. **NIS793** was given on Days 1 and 15 of each 4-week cycle.

Standard treatment – given as an IV infusion on Days 1, 8, and 15 of each 4-week cycle. The doses for **standard treatment** were:

- Gemcitabine – 1000 milligrams per square meter (mg/m^2) of body surface area
- Nab-paclitaxel – 125 mg/m^2 of body surface area

PDR001 – 400 mg given as an IV infusion on Day 1 of each 4-week cycle.

What is body surface area?

Body surface area is a measure of the amount of skin that covers a person's body, based on their height and weight. Doctors use this to make sure a person gets the correct dose of treatment for their body size.

The participants could continue trial treatment as long as they were benefiting from it.

In **Part 1**, all participants received **NIS793 and standard treatment with PDR001**.

In **Part 2**, researchers used a computer to randomly assign participants to one of these treatments:

- **NIS793 and standard treatment with PDR001**
- **NIS793 and standard treatment**
- **Standard treatment alone**

In **both parts**, participants, researchers and trial staff knew what treatment each participant received.

What happened during this trial?

Before treatment — 3 weeks

The trial staff checked to make sure the participants could be in this trial. 13 participants left the trial before receiving treatment.

During treatment — Up to 21 months

In Part 1, 11 participants received **NIS793 and standard treatment with PDR001**.

In Part 2, 153 participants were assigned to one of these treatments:

- **NIS793 and standard treatment with PDR001** – 50 participants, 46 of whom received treatment
- **NIS793 and standard treatment** – 51 participants, 49 of whom received treatment
- **Standard treatment alone** – 52 participants, 45 of whom received treatment

After treatment — Until the trial ended

Trial staff checked participants for any medical problems up to:

- 1 month after the last dose of **standard treatment**
- 3 months after the last dose of **NIS793**
- 5 months after the last dose of **PDR001**

They also checked how long the participants lived until the end of the trial.

Trial staff checked the participants' general health throughout the trial.

What were the main results of this trial?

Was the recommended dose of NIS793 and standard treatment with PDR001 confirmed for participants with mPDAC?

The recommended dose of 2100 mg **NIS793** every 2 weeks **and standard treatment with PDR001** was confirmed for participants in Part 1 and was chosen as the dose to use in Part 2.

To learn this, researchers kept track of how many participants had:

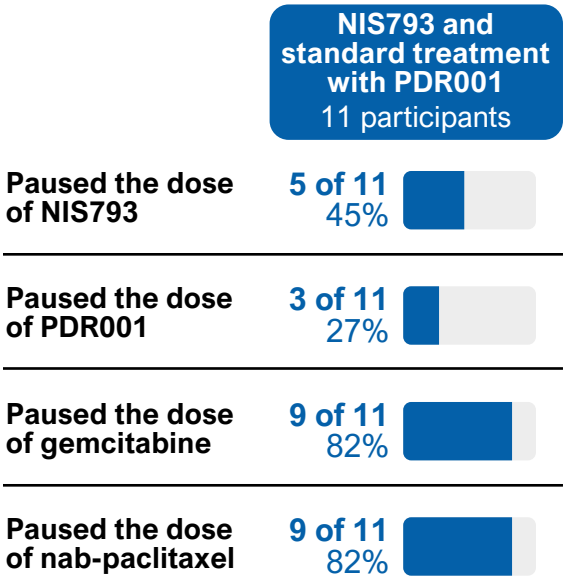
- **Dose limiting toxicities (DLTs) during the first treatment cycle of Part 1**. DLTs are medical problems that:
  - The trial doctors think could be related to the trial treatment
  - Lead to a pause in, or lowering of the dose of treatment
- **To pause a trial treatment during Part 1**, which means stopping a treatment for a period of time before receiving it again. This is called a dose interruption.
- **To lower the dose of a trial treatment during Part 1**, which means receiving a smaller amount or receiving it less often. This is called a dose reduction.

Number of participants who had DLTs in Part 1

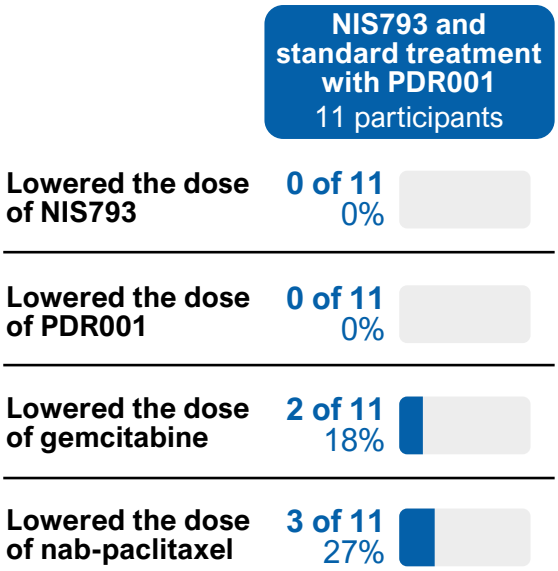
1 participant in Part 1 had a DLT, which was a **type of inflammation in intestines** (colitis).

Researchers only included participants who completed the first treatment cycle who had available results in the DLT results below. Out of the 11 participants who received treatment in Part 1, DLT results are available for 6 participants.

Number of participants who paused a trial treatment in Part 1



Number of participants who had to lower the dose of a trial treatment in Part 1



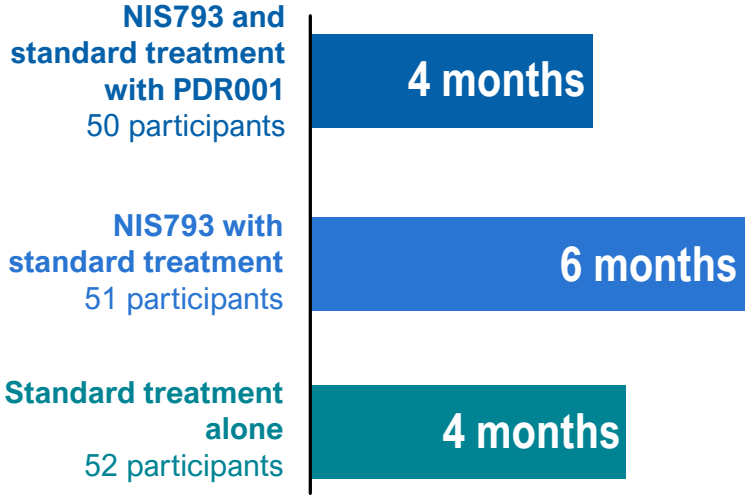
Did participants who received NIS793 and standard treatment with or without PDR001 live longer than those who received standard treatment alone?

In Part 2, participants who received **NIS793 and standard treatment** with or without **PDR001** lived about as long as those who received **standard treatment alone**. The researchers concluded the differences between the groups were not meaningful.

To learn this, researchers kept track of the length of time from when participants in Part 2 started the trial until new tumors appeared on imaging test results. This is called **progression-free survival**, or **PFS**. They calculated the median PFS for participants assigned to each trial treatment. **Median** is the middle number in an ordered list from lowest to highest.

Length of time participants lived without their cancer getting worse in Part 2

The graphic below shows the median progression-free survival (PFS) of participants assigned to treatment in Part 2 who had cancer imaging test results available.



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 until:

- 1 month after the last dose of **standard treatment**
- 3 months after the last dose of **NIS793**
- 5 months 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.

148 of 151 participants had adverse events, including serious and other adverse events:

- 96 participants had adverse events that were considered serious
- 25 participants left the trial due to an adverse event
- 46 participants died due to any cause, including due to mPDAC

How many participants had adverse events?

Participants who:	Part 1	Part 2		
	NIS793 and standard treatment with PDR001 11 participants	**NIS793 and standard treatment with PDR001** 46 participants	**NIS793 and standard treatment** 49 participants	**Standard treatment alone** 45 participants
Had adverse events, **including serious and other**	11 of 11	45 of 46	49 of 49	43 of 45
Had at least 1 **serious adverse event**	8 of 11	34 of 46	28 of 49	26 of 45
Left the trial due to an adverse event	4 of 11	11 of 50	5 of 51	5 of 52
Died	5 of 11	18 of 50	19 of 51	4 of 52

What serious adverse events did the participants have?

96 participants had serious adverse events. 46 participants died.

The table below shows the most common serious adverse events. Additional serious adverse events happened in fewer participants.

	Part 1	Part 2		
	NIS793 and standard treatment with PDR001 11 participants	**NIS793 and standard treatment with PDR001** 46 participants	**NIS793 and standard treatment** 49 participants	**Standard treatment alone** 45 participants
Fever Pyrexia	**2 of 11** 18%	**5 of 46** 11%	**3 of 49** 6%	**5 of 45** 11%
Serious complication of an infection Sepsis	**0 of 11** 0%	**4 of 46** 9%	**3 of 49** 6%	**3 of 45** 7%
Low number of red blood cells Anemia	**0 of 11** 0%	**2 of 46** 4%	**6 of 49** 12%	**2 of 45** 4%
Belly pain Abdominal pain	**1 of 11** 9%	**2 of 46** 4%	**0 of 49** 0%	**3 of 45** 7%
Type of inflammation in intestines Colitis	**1 of 11** 9%	**2 of 46** 4%	**1 of 49** 2%	**1 of 45** 2%
Frequent, loose, or watery stool Diarrhea	**0 of 11** 0%	**5 of 46** 11%	**0 of 49** 0%	**0 of 45** 0%
Lung infection Pneumonia	**1 of 11** 9%	**4 of 46** 9%	**0 of 49** 0%	**0 of 45** 0%

What other (not including serious) adverse events did the participants have?

The table below shows the most common other adverse events. Additional adverse events happened in fewer participants.

	Part 1	Part 2		
	NIS793 and standard treatment with PDR001 11 participants	NIS793 and standard treatment with PDR001 46 participants	NIS793 and standard treatment 49 participants	Standard treatment alone 45 participants
Low number of red blood cells Anemia	5 of 11 45%	29 of 46 63%	33 of 49 67%	20 of 45 44%
Feeling sick to the stomach Nausea	7 of 11 64%	20 of 46 43%	27 of 49 55%	20 of 45 44%
Frequent, loose, or watery stool Diarrhea	5 of 11 45%	26 of 46 57%	19 of 49 39%	18 of 45 40%
Feeling weak and tired Fatigue	7 of 11 64%	23 of 46 50%	18 of 49 37%	14 of 45 31%
Fever Pyrexia	7 of 11 64%	19 of 46 41%	11 of 49 22%	14 of 45 31%

What was learned from this trial?

Researchers learned about the effects of **NIS793 and standard treatment**, with or without **PDR001**, compared to **standard treatment alone** for people with metastatic pancreatic ductal adenocarcinoma (mPDAC).

The researchers concluded that:

- The recommended dose of 2100 mg **NIS793** every 2 weeks **and standard treatment with PDR001** was confirmed for participants in Part 1
- Participants who received **NIS793 and standard treatment** with or without **PDR001** lived about as long as those who received **standard treatment alone** in Part 2

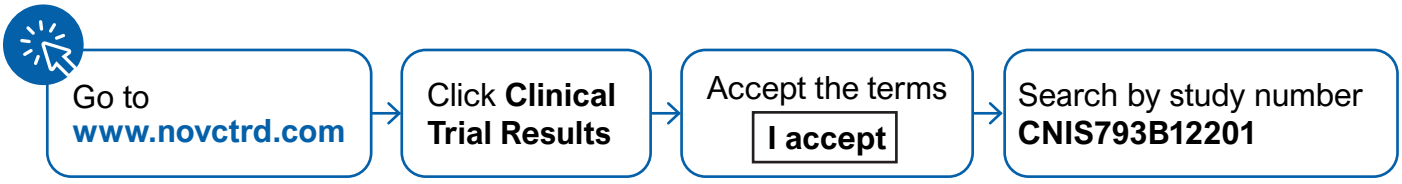
The sponsor decided to stop giving **NIS793** to participants after reviewing available results from another trial of **NIS793** in participants with mPDAC. The decision was made because adding **NIS793** to **standard treatment** for people with mPDAC was not beneficial.

When this summary was written, the sponsor had no plans for future trials of **NIS793** in people with mPDAC.

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 **NCT04390763**
- **clinicaltrialsregister.eu** – search using the number **2020-000349-14**

Other trials of **NIS793** and **PDR001** may appear on the public websites above. When there, search for **NIS793**, **PDR001**, or spartalizumab.

Full clinical trial title: A phase II, open label, randomized, parallel arm study of NIS793 (with and without spartalizumab) in combination with SOC chemotherapy gemcitabine/nab-paclitaxel, and gemcitabine/nab-paclitaxel alone in first-line metastatic pancreatic ductal adenocarcinoma (mPDAC)

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