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Clinical Trial Results Summary

A clinical trial to learn about the safety of several immunotherapy combinations in people with triple negative breast cancer

Thank you!

Thank you to the participants who took part in the clinical trial for breast cancer. Every participant helped the researchers learn more about the trial drugs **PDR001** (spartalizumab), **LAG525**, **NIR178**, **INC280** (capmatinib), **MCS110**, and **ACZ885** (canakinumab).

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 information

Trial number: CADPT01A12101C

Drugs studied: PDR001 (spartalizumab), **LAG525**, **NIR178**, **INC280** (capmatinib), **MCS110**, and **ACZ885** (canakinumab)

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 more about the safety and effects of several immunotherapy combinations of **PDR001** (spartalizumab) and **LAG525** with **NIR178**, **INC280** (capmatinib), **MCS110**, or **ACZ885** (canakinumab) in people with advanced **triple negative breast cancer (TNBC)**. This trial was designed so that if some of the combination treatments did not work, they could be stopped, and new treatments could be added during the trial.

Breast cancer happens when cells in the breast start growing uncontrollably and form a lump, called a tumor. There are different types of breast cancer. Participants in this trial had the following type of breast cancer:

Immunotherapy (pronounced as immun-o-ther-apy) is a type of treatment that helps the immune system (the body's natural defense system) recognize the cancer cells and stop them from growing.

- **Advanced**: Breast cancer that has spread from the breast to areas around it and/or to other parts of the body. This is also called **metastatic breast cancer**.
- **Hormone receptor-negative (HR-negative)**: This is a type of breast cancer where the cancer cells do not have estrogen or progesterone receptors (proteins). This means that the cancer does not respond to treatment with estrogen or progesterone hormone therapy.
- **Human epidermal growth factor receptor 2-negative or HER2-negative**: Breast cancer cells that have a normal number of **HER2** receptor (proteins). HER2 receptors help cancer grow faster. Treatments that target the **HER2** receptors do not work to treat this type of breast cancer.

The **HR-negative** and **HER2-negative** cancer is collectively called **TNBC**. **TNBC** does not respond to hormonal therapy or therapies that target HER2 receptors.

PDR001 and **LAG525** have already been tested for their effect in increasing the immune response against cancer cells in people with advanced **TNBC**. In this trial, researchers wanted to know if adding a third treatment to **PDR001** and **LAG525** combination helps further reduce the size of the tumor in people with **TNBC**.

PDR001 and **LAG525** work by increasing the body's immune response against cancer cells.

Trial drug
PDR001 (spartalizumab)
Pronounced as
spar-tuh-**LIZ**-oo-mab
INC280 (capmatinib)
Pronounced as
cap-ma-tinib
ACZ885 (canakinumab)
Pronounced as
Kana-KI-nu-mab

Other immunotherapies that were added as a third treatment in this trial were **NIR178**, **INC280**, **MCS110**, and **ACZ885**. These therapies aim at strengthening the body's immune response against cancer cells.

The trial purpose was to answer these main questions:

- What was the highest dose of the combination of **PDR001** and **LAG525** with **NIR178**, **INC280**, **MCS110**, or **ACZ885**, that was safe for participants to receive during the first treatment cycle?
- How many participants had to stop or reduce their dose of the combination of **PDR001** and **LAG525** with **NIR178**, **INC280**, **MCS110**, or **ACZ885** during the trial?
- How many participants had adverse events during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial that may or may not be caused by the trial treatments.

How long was this trial?

The trial began in January 2019 and ended in February 2023. It was planned for participants to be in this trial for about 4 years.

This trial was planned to have **2 parts**:

During **Part 1**, participants received fixed doses of **PDR001** and **LAG525** with increasing doses of **NIR178**, **INC280**, **MCS110**, or **ACZ885**. The purpose of **Part 1** in the trial was to find the highest dose of **NIR178**, **INC280**, **MCS110**, and **ACZ885** that participants could safely take in combination with **PDR001** and **LAG525**.

Part 2 was planned to study further the safe dose and combination of drugs, which was determined in **Part 1**. However, the trial ended early, and **Part 2** was not conducted because the combination of **PDR001** and **LAG525** with **INC280** showed limited benefit to the participants. Also, the researchers decided to stop the development of **MCS110**. This decision was not based on any safety concerns.

Who was in this trial?

64 women with **TNBC** received treatment in this trial. Participants' ages ranged from **29** to **82** years. Their average age was **52** years.

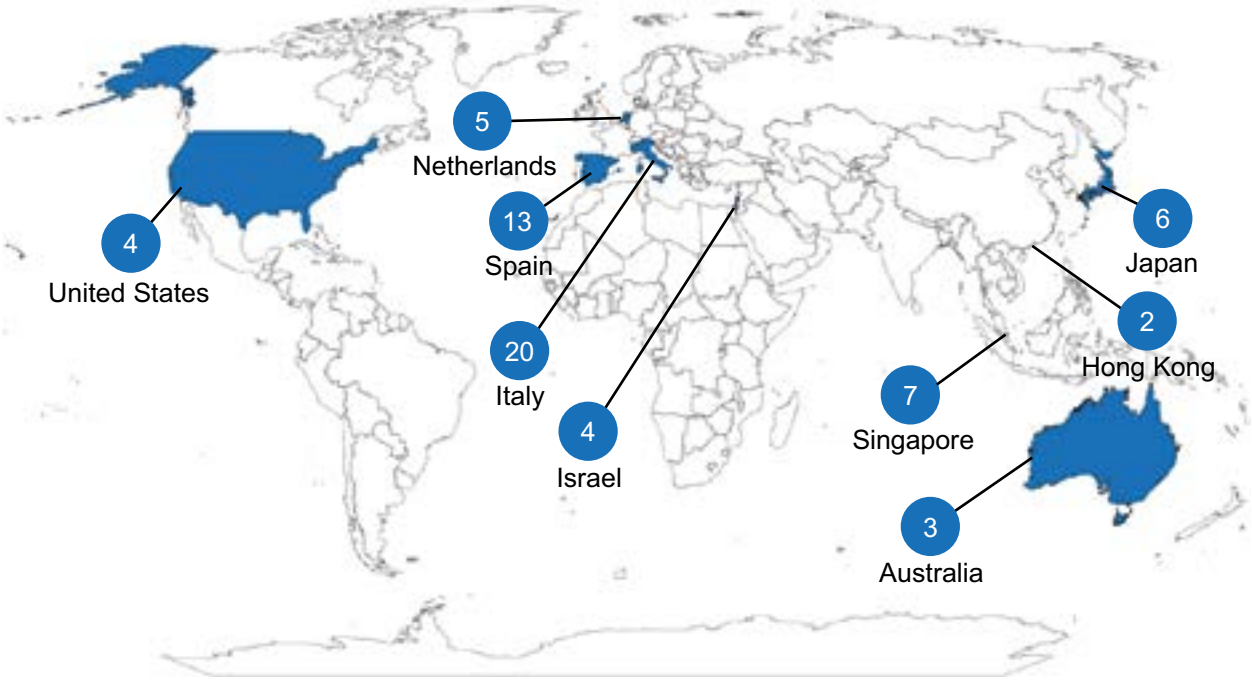
The number of participants by race is shown below:

Race	
17 **Asian**	47 **White**

The participants could take part in this trial if they:

- were 18 years of age or older
- had advanced **TNBC** that worsened even after receiving chemotherapy
- were able to walk and do light work

64 participants from 9 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 given in **cycles**.

In this trial, a **cycle** was a 28-day treatment period during which participants received trial treatments. A cycle could be repeated until the time the cancer did not grow or spread further or the study doctor approved of the participant's continuation in the trial.

PDR001: participants received 400 milligrams (mg) of **PDR001** as an infusion into a vein once on Day 1 of each cycle.

LAG525: participants received 600 mg of **LAG525** as an infusion into a vein once on Day 1 of each cycle.

NIR178: participants received 80, 160, or 240 mg of **NIR178** capsules by mouth two times each day during each cycle.

INC280: participants received 200 or 300 mg of **INC280** tablets by mouth two times each day during each cycle.

MCS110: participants received 5 mg per kilogram of the participant's body weight (mg/kg) of **MCS110** as an infusion into a vein once on Day 1 of each cycle.

ACZ885: participants received 600 mg of **ACZ885** as an injection under the skin once during every other cycle.

Each participant, the trial doctors, and the trial staff knew which treatments and doses the participants were receiving.

What happened during the trial?

Before treatment — Up to 1 month

Trial doctors checked participants' overall health to ensure they could be in this trial.

During treatment — Up to 1 year

This trial had 2 parts:

Part 1: In this part of the trial, trial doctors wanted to find out the highest dose that was safe to receive. They tested different doses and combinations of drugs. For each of the groups below, increasing doses of the third drug were tested. These doses were increased until researchers found the highest dose that was safe for the participants to receive.

PDR001 + LAG525 + NIR178 24 participants	• **PDR001 400 mg** + **LAG525 600 mg** + **NIR178 80 mg** (7 participants) • **PDR001 400 mg** + **LAG525 600 mg** + **NIR178 160 mg** (12 participants) • **PDR001 400 mg** + **LAG525 600 mg** + **NIR178 240 mg** (5 participants)
PDR001 + LAG525 + INC280 13 participants	• **PDR001 400 mg** + **LAG525 600 mg** + **INC280 200 mg** (8 participants) • **PDR001 400 mg** + **LAG525 600 mg** + **INC280 300 mg** (5 participants)
PDR001 + LAG525 + MCS110 10 participants	• **PDR001 400 mg** + **LAG525 600 mg** + **MCS110 5 mg/kg** (10 participants)
PDR001 + LAG525 + ACZ885 17 participants	• **PDR001 400 mg** + **LAG525 600 mg** + **ACZ885 600 mg** (17 participants)

Part 2: This part was not conducted as the trial ended early because the combination of **PDR001** and **LAG525** with **INC280** showed limited benefit to the participants. Also, the researchers decided to stop the development of **MCS110**.

Participants could continue treatment as long as they benefitted from the treatment and did not have any adverse events.

After treatment — Up to 5 months

Participants either visited the study clinic or were contacted on the phone, **1**, **3**, and **5** months after they received the last dose of trial treatment.

What were the main results of this trial?

What was the highest dose of the combination of PDR001 and LAG525 with NIR178, INC280, MCS110, or ACZ885, that was safe for participants to receive during the first treatment cycle?

Researchers found that **NIR178 160 mg** was the highest dose that was safely given in combination with **PDR001 400 mg** and **LAG525 600 mg**.

To answer this, researchers closely monitored participants for **dose-limiting toxicities (DLTs)** during the first treatment cycle. A **DLT** is an adverse event that occurs at the start of the treatment and is serious enough to prevent increasing the dose of that treatment.

As it was important to confirm the highest dose that was safe for participants to receive, researchers also checked how many participants had to stop or reduce their dose of the combination of **PDR001** and **LAG525** with **NIR178**, **INC280**, **MCS110**, or **ACZ885** during the trial.

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 of the participants did not complete the first treatment cycle and were not included in the **DLT** results. Therefore, the total number of participants with **DLTs** and those who stopped or reduced taking the trial drugs could be different.

Group 1: PDR001 + LAG525 + NIR178

Participants who:	combination of PDR001 + LAG525 with		
	NIR178 80 mg 7 participants	NIR178 160 mg 12 participants	NIR178 240 mg 5 participants
Had DLTs	0	2 of 10 20%	2 of 3 67%
Stopped taking or reduced their dose of PDR001	3 of 7 43%	2 of 12 17%	1 of 5 20%
Stopped taking or reduced their dose of LAG525	2 of 7 29%	2 of 12 17%	1 of 5 20%
Stopped taking or reduced their dose of NIR178	4 of 7 57%	3 of 12 25%	1 of 5 20%

Group 2: PDR001 + LAG525 + INC280

Participants who:	combination of PDR001 + LAG525 with INC280 200 mg 8 participants	combination of PDR001 + LAG525 with INC280 300 mg 5 participants
Had DLTs	2 of 7 29%	2 of 3 67%
Stopped taking or reduced their dose of PDR001	0	0
Stopped taking or reduced their dose of LAG525	0	0
Stopped taking or reduced their dose of INC280	1 of 8 13%	3 of 5 60%

Group 3: PDR001 + LAG525 + MCS110

Participants who:	combination of PDR001 + LAG525 with MCS110 5 mg/kg 10 participants
Had DLTs	0 of 9
Stopped taking or reduced their dose of PDR001	2 of 10 20%
Stopped taking or reduced their dose of LAG525	2 of 10 20%
Stopped taking or reduced their dose of INC280	2 of 10 20%

Group 4: PDR001 + LAG525 + ACZ885

Participants who:	combination of PDR001 + LAG525 with ACZ885 600 mg 17 participants
Had DLTs	0 of 15
Stopped taking or reduced their dose of PDR001	6 of 17 35%
Stopped taking or reduced their dose of LAG525	6 of 17 35%
Stopped taking or reduced their dose of INC280	4 of 17 24%

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 start of the trial treatment up to **5 months** after the last dose of the 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.

All participants had adverse events. 32 out of 64 participants had events that were considered serious. 2 participants died during the trial due to adverse events. 15 participants left the trial due to an adverse event.

How many participants had adverse events?

Number (percentage) of participants who had adverse events

Participants who:	combination of PDR001 + LAG525 with						
	NIR178 80 mg 7 participants	NIR178 160 mg 12 participants	NIR178 240 mg 5 participants	INC280 200 mg 8 participants	INC280 300 mg 5 participants	MCS110 5 mg/kg 10 participants	ACZ885 600 mg 17 participants
Had at least 1 serious adverse event	2 of 7 29%	6 of 12 50%	2 of 5 40%	4 of 8 50%	4 of 5 80%	4 of 10 40%	10 of 17 59%
Had at least 1 other adverse event	7 of 7 100%	12 of 12 100%	4 of 5 80%	8 of 8 100%	5 of 5 100%	10 of 10 100%	16 of 17 94%
Left the trial due to an adverse event	3 of 7 43%	3 of 12 25%	2 of 5 40%	2 of 8 25%	1 of 5 20%	1 of 10 10%	3 of 17 18%
Died due to adverse events	0	0	0	0	1 of 5 20%	0	1 of 17 6%

What serious adverse events did the participants have?

32 out of **64** participants had serious adverse events. The table below shows the most common serious adverse events that happened in **15% or more** participants in any group.

Number (percentage) of participants who had serious adverse events

	combination of PDR001 + LAG525 with						
	NIR178 80 mg 7 participants	**NIR178 160 mg** 12 participants	**NIR178 240 mg** 5 participants	**INC280 200 mg** 8 participants	**INC280 300 mg** 5 participants	**MCS110 5 mg/kg** 10 participants	**ACZ885 600 mg** 17 participants
Inflammation of pancreas Pancreatitis	0	0	1 (20%)	0	0	0	0
Sudden inflammation of the pancreas causing severe pain in the belly and back Pancreatitis acute	0	0	0	0	1 (20%)	0	0
Inflammation of the inside lining of the body such as mouth or gut Mucosal inflammation	0	0	0	0	1 (20%)	0	0
Fever Pyrexia	1 (14%)	0	0	0	2 (40%)	0	1 (6%)
COVID-19 infection	0	0	0	0	1 (20%)	0	0
Lung infection Pneumonia	0	0	0	0	1 (20%)	0	0
Long-lasting burning pain in the nerve Neuralgia	0	0	0	0	1 (20%)	0	0
Being short of breath Dyspnea	0	0	1 (20%)	0	0	0	2 (12%)
Unable to breathe Respiratory failure	0	0	0	0	1 (20%)	0	0
Itchy rash Urticaria	0	0	0	0	1 (20%)	0	0

What other adverse events did the participants have?

All participants had at least one other adverse event. The table below shows the other adverse events that happened in **45% or more** participants in any group.

Number (percentage) of participants who had other adverse events

	combination of PDR001 + LAG525 with						
	NIR178 80 mg 7 participants	**NIR178 160 mg** 12 participants	**NIR178 240 mg** 5 participants	**INC280 200 mg** 8 participants	**INC280 300 mg** 5 participants	**MCS110 5 mg/kg** 10 participants	**ACZ885 600 mg** 17 participants
Low number of red blood cells Anemia	1 (14%)	3 (25%)	1 (20%)	4 (50%)	0	1 (10%)	1 (6%)
Constipation	1 (14%)	6 (50%)	0	1 (13%)	0	0	3 (18%)
Feeling sick Nausea	3 (43%)	2 (17%)	2 (40%)	4 (50%)	0	2 (20%)	6 (35%)
Vomiting	1 (14%)	2 (17%)	1 (20%)	4 (50%)	2 (40%)	1 (10%)	2 (12%)
Weakness Asthenia	2 (29%)	2 (17%)	0	1 (13%)	0	6 (60%)	1 (6%)
Increased level of enzyme called aspartate aminotransferase in the blood, a sign of liver damage Aspartate aminotransferase increased	3 (43%)	3 (25%)	1 (20%)	3 (38%)	1 (20%)	6 (60%)	3 (18%)
Increased level of an enzyme called creatine phosphokinase in the blood, a sign of muscle tissue damage Blood creatine phosphokinase increased	2 (29%)	0	1 (20%)	0	1 (20%)	6 (60%)	2 (12%)

What was learned from this trial?

This trial helped researchers learn about the safety of several immunotherapy combinations in people with triple negative breast cancer. However, the trial ended early as the combination of **PDR001** and **LAG525** with **INC280** showed limited benefit to the participants. Also, the researchers decided to stop the development of **MCS110**.

Additionally, the researchers could not determine the highest and recommended dose of **MCS110** and **INC280**, that participants could safely take in combination with **PDR001** and **LAG525** in Part 2 of the trial.

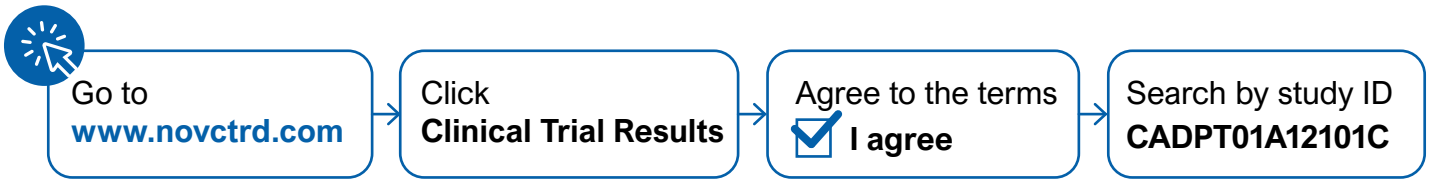
Researchers did not find any new safety concerns with the use of a combination of **PDR001** and **LAG525** with **NIR178**, **INC280**, **MCS110**, or **ACZ885**.

Some participants who benefitted from the combination of **PDR001** and **LAG525** with **NIR178**, **INC280**, **MCS110**, or **ACZ885** continued receiving the trial treatments in another trial (CPDR001X2X01B).

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**.

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



- **www.clinicaltrials.gov** - search using the number **NCT03742349**
- **clinicaltrialsregister.eu/ctr-search/search** - search using the number **2018-002244-82**

If more trials are planned, they will appear on the public websites above. When there, search for **PDR001**, **LAG525**, **NIR178**, **INC280**, **MCS110**, **ACZ885**.

Full clinical trial title: A Phase Ib, multicenter, open-label dose escalation and expansion platform study of select immunotherapy combinations in adult patients with triple negative breast cancer

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